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Leprosy Review is published by the British Leprosy Relief Association (LEPRA) with the main objective of contributing towards the better understanding of leprosy and its control. Original papers on all aspects of leprosy, including research, are welcomed. In addition, *Leprosy Review* seeks to publish information of educational value which is of direct benefit to the control of leprosy under field conditions, and hence to the individual patient. The Journal aims to interpret what is being done in other disciplines, particularly for field workers.

From time to time the Editorial Board invites special articles or editorials from experts in various parts of the world, and gives consideration to the production of a supplement or special number devoted to a particular subject or theme of major importance.

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Editorial

THE USE OF HISTOPATHOLOGY IN LEPROSY DIAGNOSIS AND RESEARCH

Introduction

The way we think and talk about leprosy, using the terms 'tuberculoid' and 'lepromatous', is histopathologically orientated. In the most widely used system of leprosy classification—the Ridley–Jopling classification—histology plays the major role.[1] In clinical practice, there is no doubt that the histological assessment by an experienced pathologist of a representative skin (and/or nerve) biopsy and enumeration of bacilli provides information as significant as that derived from the clinical examination of a patient.

Only a small proportion of the estimated 10+ million patients with leprosy have been biopsied. The current uses of tissue biopsy fall into two broad categories: diagnosis of leprosy and leprosy reactions; and research into inflammatory processes. Some aspects, particularly those with practical applications, are discussed here.

Diagnosis of leprosy—early disease

Early diagnosis of leprosy is a prerequisite for control as well as for effective therapy. Epidemiologically, the total number of cases of leprosy needs to be established for a region, and much underestimation may ensue from the poor detection of early cases. There is no independent 'gold standard' for the diagnosis of leprosy. Neither serological nor skin tests have sensitivity and specificity high enough to be useful in confirming or eliminating all suspect cases of leprosy. How useful is histopathology? The two cardinal histological features of leprosy are appropriate patterns of inflammation involving certain sites in skin (e.g. nerves), and the demonstration of acid-fast bacilli (AFB) in appropriate sites. The degree of confidence that individual pathologists place in a diagnosis of early leprosy is variable.

The importance of accurate histological assessment is emphasized by the widespread poor performance of slit-skin smear bacteriology: low densities of AFB in skin are underestimated or missed entirely, so that cases are missed as well as being misclassified.[2]

Only one systematic study has been published on the performance of pathologists on leprosy. Three experienced histopathologists examined the same 143 skin biopsies from leprosy suspects in Malaŵi, where 95% of leprosy is paucibacillary.[3] The results appear disturbing. The proportions of biopsies classed as showing strong or definite evidence of leprosy ranged from 39% to 58%. The proportions of biopsies thought to be 'possibly leprosy' ranged from 11·5% to 38·5%, reflecting an unexpectedly large variation in degree of uncertainty. Nonetheless, considering only the 82 cases that were clinically thought certain to be leprosy, the histopathologists did agree in 63% to 83% of cases.[4] Much of the discrepancy in diagnostic certainty derived from differences in the interpretation of nerve involvement by granulomatous or nongranulomatous inflammation. AFB were uncommonly detected in the biopsies from this population.

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The category 'indeterminate' was used by one pathologist in 1·5% of cases, yet in 21·5% of cases by another. Evidently there is much dissent on what is meant by 'indeterminate'.[1] It has to be said that the material used in this study, being derived from intensive population surveys for leprosy, is much 'earlier' than is generally seen in biopsies from patients who self-present; the great majority of these biopsies had granuloma fractions of $< 10\%$ (see below).

If pathologists cannot consistently diagnose early, indeterminate leprosy, are there alternative methodologies? Specifically, since the histological evaluation of inflammatory patterns cannot be automated, could tissues be better analysed for the presence of *Mycobacterium leprae* and thus support a diagnosis of leprosy?

Immunocytochemistry using polyclonal rabbit anti-BCG antibodies is certainly effective in demonstrating *M. leprae* antigen in multibacillary tissues, even when the bacilli are reduced to debris or are invisible on acid-fast stains.[5] However, convincing demonstration of antigen where AFB density is effectively zero has not been shown. Monoclonal antibodies against phenolic glycolipid-1 (PGL-1) and various defined antigens of *M. leprae* have been used. With fluorescent labelling, anti PGL-1 antibodies detected positive staining in 7/19 cases of indeterminate leprosy, only one of which was positive by acid-fast staining.[6] Immunoperoxidase staining with a panel of monoclonals showed occasional deposits of the 36 kd antigen in macrophages of tuberculoid leprosy skin biopsies where AFB were not ordinarily visible.[7] Immunogold staining in tissues processed for electron microscopy demonstrates PGL-1 well in bacillary capsular material, but it has not been tried on paucibacillary cases.[8]

Whilst techniques of *in situ* DNA hybridization have great sensitivity in detecting the DNA of viruses in tissues, it has not been applied to the detection of mycobacterial DNA. Theoretically, it is unlikely to be useful since it can only label and bring out the quantity of bacillary DNA that is already present.

However, the recent technique of polymerase chain reaction (PCR) amplifies DNA nucleotide sequences in tissues to bring out minute quantities: the results are not read on tissue sections but as bands on Southern blot gels. The sensitivity that can be achieved is impressive. With a suspension of *M. leprae* used as the substrate, the detection limit appears to be 1–10 bacilli. Using homogenates of armadillo livers as substrate, 10^7 bacilli per gram were detectable.[9] How the technique of PCR will work using sections from fixed human tissues is under investigation.

Of these alternative techniques for detecting small numbers of AFB in tissues, the immunocytochemical methods are, in our opinion, difficult to interpret and are not reliable in early diagnosis; often there is much background staining. The PCR may be a breakthrough in sensitivity (it must be remembered that acid-fast stains can theoretically detect positive bacilli at a concentration of about 500 per cc of tissue), but it is technically demanding, and like the other techniques, will be difficult to perform adequately in those developing countries where leprosy is endemic. Finally, histologically, the presence of an acid-fast bacillus in sections is convincing when it is located in an appropriate site and when the associated inflammation, however slight, is consistent with our experience of leprosy. It remains to be seen whether the apparent identification of *M. leprae* DNA in tissue by PCR is *per se* convincing evidence of leprosy in a suspect case, or whether effort might not be more profitably put into the examination of more sections stained by classical techniques.

Diagnosis of leprosy—more advanced disease

Histologically, multibacillary leprosy presents little problem once it has been considered. Foamy macrophages containing bacillary debris may be considered xanthomas, but immunocytochemistry and Grocott methods will demonstrate the mycobacterial nature of the inflammation.[5]

However, granulomatous dermatitis without apparent AFB has a large differential diagnosis: sarcoidosis, granuloma annulare, granuloma multiforme, syphilis, leishmaniasis and other mycobacterioses are the main problems. The new techniques of bringing out AFB or their DNA are

discussed above. The detection of nerve involvement is important, and the staining combination of periodic acid-ethanol gelatine and methenamine silver can show both bacterial cell walls and myelin in the same section, given that AFB are present.[10] Apart from these, the only new technique is the immunocytochemical demonstration of dermal nerves using antibodies to S100 protein. This can show single Schwann cells and may confirm endoneurial nerve involvement or destruction by granulomas, so confirming leprosy.[11] Like most aspects of leprosy histology, this has not undergone a formal trial of sensitivity and applicability. Whilst the nonhistological methods of diagnosis of lesions confusable with leprosy constantly improve, it seems unlikely that systematic alternatives to good histological sections and experience of leprosy pathology will develop in the forseeable future.

In the comparability study quoted earlier,[4] there was reasonably good concordance between the pathologists on classification of determined leprosy lesions (only early leprosy was problematic). Further studies of pathologists' performance are now continuing, with intraobserver as well as interobserver variation being investigated. The degree to which different types of leprosy prevail in different parts of the world may have, uncomfortably, much to do with the variation between observers as well as that between the patients.

When patients present themselves, the problem of histopathological diagnosis of leprosy is considerably less. Personal observations (SBL) of biopsies from 508 near-consecutive patients suspected of having leprosy seen in the Marie Adelaide Leprosy Centre, Karachi, indicate that 89% were readily diagnosable as leprosy. Of those, 2·2% were indeterminate (nongranulomatous) with positive AFB, and the rest were determined paucibacillary or multibacillary leprosy. Only 6% were possibly but not certainly indeterminate leprosy (i.e. had no AFB in sections), and 5% were diagnosed as disease other than leprosy. In summary, the histopathological difficulties in establishing leprosy increase markedly when active surveying for early lesions is undertaken.[3]

Neuritis

It has become evident that the bacillary indices in skin and peripheral nerve biopsies taken from patients at the same time are discrepant in many cases (possibly 50%).[12–14] The nerves may contain a bacterial density up to one thousand (log 3) times that of skin. At least two implications follow. The classification of a patient as paucibacillary or multibacillary is according to skin bacterial index; but it would appear that if nerves are assessed routinely by biopsy, more patients would be classed as multibacillary. The regimes of multidrug therapy (MDT) may need to be considered accordingly. Secondly, the higher neural bacillation supports the impression that many relapses of leprosy commence in nerves.[12] Long-term post-MDT studies with particular attention to nerve pathology are needed.

Immunocytochemical staining for neuropeptides in skin biopsies has demonstrated the fine terminal nerves that permeate the upper dermis and epidermis. In leprosy there is progressive reduction in their number through indeterminate, lepromatous and tuberculoid lesions, indicating that in even very early lesions, dermal nerves are being damaged.[15] Future studies with these markers may provide evidence that a common location of AFB in early lesions, the apparently acellular subepidermal zone, may actually represent location within fine unmyelinated nerves. The patterns of regrowth of these dermal nerves after chemotherapy is of great interest.

Cellular characterization of leprosy lesions

Immunocytochemical staining techniques for inflammatory cell phenotypes are now a routine research procedure in leprosy. The earlier established patterns of T-cell subsets are confirmed, namely: T-helper (CD4+):suppressor/cytotoxic (CD8+) ratios are greater in tuberculoid lesions than in lepromatous; CD4+ lymphocytes are distributed throughout tuberculoid granulomas;

CD8+ lymphocytes are restricted to the outer mantle of tuberculoid granulomas but are randomly distributed through lepromatous lesions.[16,17] More subtle (but still controversial) differential patterns of helper/inducer cells, suppressor/inducer cells and cytotoxic versus suppressor CD8+ cells are also described.[16] Such T-cell subset patterns in leprosy have stimulated similar examination of tuberculosis,[18] leishmaniasis[19] and sarcoidosis[18] lesions: the differences that emerge in cell reactions between leprosy and these other granulomatous diseases will provide information on their pathogenetic mechanisms.

Immunocytochemical studies in leprosy are helping to unravel the nature of the immune defect in lepromatous leprosy, as well as the causes of leprosy reactions. The local production of inflammatory mediators such as the monokine interleukin-1 (IL-1), and the lymphokines interleukin-2 (IL-2) and interferon-gamma (IFN-γ) can be estimated. The lack of these two lymphokines in lepromatous lesions [17,20] may underlie the inability of macrophages to kill and clear *M. leprae* bacilli (IFN-γ is an activator of macrophages).

In situ hybridization probes for mediators such as IFN-γ mRNA is providing deeper insights into the pathogenesis of leprosy reactions, by allowing the enumeration of IFN-γ-producing cells. For example, whilst in both reversal reactions and erythema nodosum leprosum (ENL) reactions the number of CD4+ T-cells in lesions increases, increased IFN-γ production occurs in the former but not the latter reaction:[17] hence the lack of effective clearance of bacteria and antigen in ENL. Administering intradermal IFN-γ induces delayed hypersensitivity phenomena in lepromatous lesions so that the lesions locally upgrade. The local bacterial index is rapidly reduced by an average of log 1.[21,22] (Effective chemotherapy reduces bacterial load by only log 1 per annum.) Intradermal injection of IL-2 into lepromatous lesions has an even more powerful effect on bacillary load: the range of reduction is 5-1000, with a mean of 100 (log 2).[23] These *in vivo* experiments support the current views on the immune defects in lepromatous leprosy. Moreover, there are possible therapeutic implications if IL-2 injection, into the skin or parenterally, is safe. Recurrent ENL is associated with large, persistent deposits of *M. leprae* antigen. IL-2 therapy may be able to reduce this load systemically and so ameliorate the condition of these unfortunate patients.

In situ studies of further inflammatory mediators will follow, using both direct estimates of concentration by immunocytochemistry and estimates of potential production using probes for mRNA. Of great interest will be the analysis of tumour necrosis factor (TNF), a macrophage product whose release is stimulated by IFN-γ. It is already implicated in the necrosis of tuberculosis lesions as well as some of that disease's systemic effects.[24] TNF may also be responsible for the necrosis seen in severe reversal reactions in leprosy.

Global aspects of leprosy histopathology

The provision of general histopathology services for many developing countries is poor or nonexistent and much biopsy material is sent to developed countries for assessment.[25,26] For leprosy histopathology, even less reporting is done on site, with wholesale despatch of tissues from leprosy hospitals to a few centres in Europe and the USA. Lack of laboratory facilities and finance, the difficulty of maintaining technical standards, and lack of pathologists are the major reasons. Inevitably this means that local pathologists are less familiar with the nuances of leprosy than they could and should be. If histopathology is important in overall leprosy management, then this situation is to be deprecated.

Conclusion

The difficulty and lack of agreement in diagnosing early (paucibacillary) leprosy by histopathology is frustrating. There is no reason why the essentially subjective nature of histological observation

and diagnosis should change in the future. Whether the newer techniques of detecting *M. leprae* DNA or antigens will facilitate early diagnosis is not yet known; if they can help in a research centre, will they be useful in more peripheral laboratories? The study of cell types and mediators operating in leprosy lesions tells us about pathogenetic immune mechanisms, and may have therapeutic spin-offs. The global provision of histopathology is woefully inadequate. For leprosy, its present vertical arrangement is unlikely to change in the near future, and many endemic countries will continue to be dependent on the pathological expertise of developed countries.

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Primary dapsone resistance in China

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Summary Ninety-seven strains of *Mycobacterium leprae* recovered from patients with previously untreated multibacillary leprosy were tested for dapsone susceptibility. The specimens originated from Shanghai Municipality, Jiang-su Province and Fu-jian Province. Approximately 28% of the strains either did not infect the mice or the results of susceptibility were inconclusive due to the low proportion of viable organisms in the bacterial populations. Among the 70 strains in which dapsone susceptibility could be tested in mice, 31 (44%) strains were found with primary dapsone resistance. Although the majority of the primary dapsone resistant strains were shown to be of a low- or intermediate-degree, one-sixth of them were of high-degree resistance.

Introduction

In order to assess the severity of the problem of dapsone resistant leprosy in China, where dapsone monotherapy has been widely used for the treatment of leprosy since the beginning of the 1950s, surveys of secondary and primary dapsone resistance in China were undertaken according to the THELEP Protocol for Surveys of Dapsone Resistance.[1] The results of the survey of secondary dapsone resistance in Shanghai Municipality have already been published.[2] The survey on primary dapsone resistance was conducted between 1982 and 1986 and its preliminary results have been presented in a review article.[3] The complete information from the survey is now available.

Materials and methods

For the study of primary dapsone resistance, only previously untreated multibacillary (MB) leprosy patients with bacterial index (BI) ≥ 3 in at least one lesion should be included. Since the incidence rate of leprosy has become very low in most parts of China, in order to accumulate more convincing data, we also obtained random specimens from nearby provinces including Jiang-su, Fujian and An-hui in addition to virtually all the newly detected MB cases from Shanghai Municipality. During the study period, 97 skin biopsies from previously untreated MB patients were collected: 16 from Shanghai Municipality, 44 from Jiang-su Province, 34 from Fu-jing Province and 3 from An-hui

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Province. Of the 97 cases, 78 were male and 19 female; 47 were LL, 6 LL/BL, 37 BL, 5 BB and 2 BB/BT: ages ranged from 12 to 74 with a median of 31.

The dapsone-susceptibility tests were carried out following the standard technique.[4] In brief, as soon as the specimens arrived at our Leprosy Research Laboratory, they were homogenized, and the *M. leprae* were recovered, counted, diluted so as to provide an inoculum of 10^4 organisms per footpad, and inoculated into both hind footpads of 40–60 outbreed Swiss albino mice per specimen. One group of 10–20 mice were administered a drug-free diet, and three additional groups were fed diets into which dapsone had been incorporated in concentrations of 0·0001, 0·001 or 0·01 g respectively per 100 g diet. Six months after inoculation, *M. leprae* was harvested from the inoculated footpads of two to four untreated mice and pools of both hind footpads from each mouse counted. This was repeated at intervals of about two months, until the average number of organisms per footpad was found to be at least 5×10^5. At this time, harvests of *M. leprae* were performed on the inoculated footpads of the remaining control mice and all treated mice. If after 12 months the organisms were found to have multiplied in the control mice, but to an average of fewer than 5×10^5 organisms per footpad, harvests were also performed on both the control and the treated mice. Multiplication of *M. leprae* was judged to have taken place when they had increased to $\geq 10^5$ per footpad. Using this criterion, the results of the susceptibility test were interpreted as follows: (a) non-infective in mice—no multiplication was observed in a single control mouse; (b) inconclusive—although no multiplication was observed in the treated mice, multiplication occurred in so few of the control mice that one could not distinguish the number of control mice demonstrating multiplication from zero; (c) susceptible—multiplication of *M. leprae* was observed only in untreated mice but not in treated mice; (d) resistant—the organisms were observed to have multiplied in at least one drug-treated mouse. The degree of resistance was determined by the diet containing the largest concentration of dapsone that permitted multiplication of *M. leprae*, and was then defined as low, intermediate or high, depending on the ability of the organisms to multiply in mice which had been administered dapsone in concentrations of, respectively, 0·0001, 0·001 or 0·01 g per 100 g diet.

Results

The results of the study are presented in Table 1. Out of 97 specimens, the organisms from 14 of them did not infect mice; and the results from 11 specimens were inconclusive because multiplication of *M. leprae* was observed in only a very few control mice. Obviously, the proportion of viable organisms in the bacterial populations of these specimens was too small. In addition, the results of another two specimens were also considered to be inconclusive because the mice administered the 0·0001 g% dapsone diet were lost before harvest, whereas no multiplication was

Table 1. Results of dapsone-susceptibility test among 97 untreated multibacillary leprosy patients in China

Non-infective in mice	14
Inconclusive due to low-infectivity	11
Inconclusive due to loss of mice administered dapsone in smallest concentration	2
Susceptible	39
Resistant	31
0·0001 g%	16
0·001% g%	10
0·01 g%	5

Table 2. Comparison of the results of dapsone-susceptibility test among untreated multibacillary leprosy patients in three different areas in China

Results	Shanghai	Jiang-su	Fu-jian
Susceptible	6 (50%)	15 (43%)	18 (78%)
Resistant	6 (50%)	20 (57%)	5 (22%)

observed in treated mice which had been administered higher concentrations of dapsone in their diet. Therefore, it was possible to assess the susceptibility to dapsone of the *M. leprae* recovered from 70 specimens.

Of the 70 specimens, *M. leprae* recovered from 39 of them were judged to be dapsone susceptible and the remaining 31 strains were dapsone resistant. Therefore, the prevalence of primary dapsone resistance was found to be 44%. Regarding the degree of dapsone resistance among the 31 resistant strains, 16 (52%) were low-degree, 10 (32%) were intermediate-degree and 5 (16%) were high-degree. Although the first two categories were in the majority, it should be noted that close to one-sixth of the primary resistant strains were of high-degree dapsone resistance.

Table 2 compares the results of dapsone-susceptibility tests among untreated MB leprosy patients from three different areas in China. It appears that the prevalence of primary dapsone resistant leprosy in Fujian Province (22%) was significantly lower ($P < 0{\cdot}05$) than that in Jiang-su Province (57%). However, the differences between Shanghai and either Jiang-su Province or Fu-jian province were not statistically significant ($P > 0{\cdot}05$).

Discussion

Prior to 1977, dapsone susceptibility of 73 strains of *M. leprae* recovered from patients with previously untreated lepromatous leprosy had been tested in six laboratories including our laboratory, but none of the strains was resistant to dapsone.[5] However, since primary dapsone-resistant leprosy was first reported from Ethiopia in 1977,[6] the prevalence of primary dapsone-resistant leprosy has reached an alarming level. Prior to the current study, there have been only two other reports of extensive investigations of primary dapsone resistance. In the study carried out with specimens obtained from Bamako and Chingleput in India, 37% of the 131 patients harboured strains with primary resistance to dapsone;[7] in the other study, in which biopsies were received from Guadeloupe, Martinique, New Caledonia, Senegal and Paris, 39% of the 133 patients were infected with primary dapsone resistant *M. leprae*.[8] Not only were both studies conducted at almost the same period of time as ours, but the prevalence of primary dapsone resistance from both studies was also very similar to those in the current report. Thus, there is no doubt that primary dapsone resistant leprosy had become a worldwide phenomenon by the early 1980s.

In contrast to secondary dapsone resistant leprosy,[2,3] the majority of primary resistant strains of *M. leprae* were resistant to low or intermediate levels of dapsone. The explanation for this difference may lie in the long incubation period of MB leprosy. It is possible that most patients recognized today as having primary resistance were infected 10 or more years ago, at which time the degree of dapsone-resistance among most secondary resistant strains may have been much lower than that of today. If this is the case, one may anticipate that future primary dapsone-resistant strains will manifest higher degrees of resistance than those encountered at present. In fact, high-degree dapsone resistance did occur in some previously untreated patients as is shown in the current report and also in the literature.[8]

Since secondary and primary dapsone-resistant strains of *M. leprae* have been found wherever they were sought, there is clearly an urgent need for all leprosy control programmes to implement the multidrug regimens recommended for paucibacillary and multibacillary leprosy by the WHO Study Group.[9]

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Increased incidence in leprosy of hypersensitivity reactions to dapsone after introduction of multidrug therapy

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Summary In order to address the question whether hypersensitivity reactions to dapsone are becoming more frequent, the clinical data of 7300 leprosy patients treated between 1949 and September 1988 at the McKean Rehabilitation Centre in Thailand were reviewed.

Information from the period 1949 to 1969 was too incomplete to allow conclusions. The incidence of hypersensitivity reactions to dapsone between 1970 and 1982 was 0·3%. From 1982 (with the introduction of multidrug therapy) to September 1988, the incidence was 3·6%; a tenfold increase compared with the previous period. Of the 19 cases seen since 1982, 12 were diagnosed as Dapsone syndrome. Of a total of 13 patients seen since 1980 with Dapsone syndrome, 3 ended fatally, indicating the severity of the complication.

The question is raised whether an unexplained drug interaction with rifampicin is responsible for the increase of hypersensitivity reactions to dapsone in patients treated for leprosy.

Introduction

Diaminodiphenylsulphone (dapsone or DDS) has been used for over 40 years in the treatment of a variety of conditions including leprosy, dermatitis herpetiformis and a number of less common dermatological diseases. Although dapsone is considered a very safe drug, side-effects are many and varied. Apart from a number of adverse reactions and toxic effects associated with dapsone,[1–3] a distinct hypersensitivity reaction to dapsone has been described.[4–7]

This reaction or 'Dapsone syndrome', was originally described as characterized by the sudden onset of a papular or exfoliative rash, accompanied by fever, malaise and weakness and followed by enlargement and tenderness of the liver, jaundice, lymphadenopathy and mononucleosis after 5 or 6 weeks of dapsone therapy. Not all symptoms were necessarily present.[5]

Cutaneous manifestations in hypersensitivity reactions to dapsone show wide variations, including erythroderma, papuloerythematous eruptions, erythema multiforme, toxic epidermal necrolysis and the Stevens–Johnson syndrome.[8]

Hypersensitivity reactions were reported in a very limited number of leprosy patients up to the late 1970s. Since then there has been an increasing number of case reports from different continents. These reports have recently been reviewed.[9] The question was raised whether hypersensitivity reactions to dapsone are becoming more frequent. In an attempt to answer this question on a more

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regional level, we reviewed the histories of leprosy patients treated with dapsone at the McKean Rehabilitation Centre in Chiang Mai, northern Thailand during the past 40 years.

Methods

The McKean Rehabilitation Centre in Chiang Mai, northern Thailand, has been a (church-related) treatment institute for leprosy patients since 1908. It serves patients from the whole of the northern Thailand area (population approximately 10 million). Sulphones were introduced at the Centre in 1949. In the late 1950s, 1960s and 1970s, dapsone monotherapy was the mainstay of therapy, alternating because of intolerance (which usually meant erythema nodosum leprosum (ENL)) with antibacterial drugs such as thiacetazone, thiambutosine, streptomycin, isoniazid and clofazimine. Multidrug therapy (MDT) according to the recommendations of the WHO,[10] was introduced by the end of 1982. A minor variation on the WHO regimen was made in that rifampicin 600 mg was given on 2 consecutive days per month instead of once monthly.

The available clinical data of patients treated with dapsone between 1949 and September 1988 were reviewed for the occurrence of adverse reactions attributed to dapsone. Case histories had to meet a number of criteria before the diagnosis of a true dapsone hypersensitivity reaction was made:

1, the symptoms appeared within 8 weeks after commencement of dapsone and disappeared after discontinuation of the drug; 2, the symptoms could not be ascribed to any other drug given simultaneously with dapsone; if any other drugs were taken at the same time, these could be resumed after stopping dapsone without inducing similar reactions; 3, symptoms were not attributable to lepra reactions; and 4, no other diseases liable to cause similar symptoms were diagnosed.

Final proof by trial administration of dapsone after the original reaction had subsided (as was performed in a number of cases), was not considered necessary as an absolute criterion due to the risks involved in some patients.

A hypersensitivity reaction was classified as 'Dapsone syndrome' when, apart from the above stated criteria: 1, symptoms started between 2 and 8 weeks after commencement of dapsone, and 2, at least two of the following signs or symptoms were present: fever, skin eruption, lymphadenopathy and liver pathology (in the form of hepatomegaly, jaundice and/or abnormal liver function tests).

Results

In reviewing the clinical data accumulated at the Centre, three distinct periods could be distinguished: 1, the period from the introduction of dapsone in 1949 to 1969; 2, 1970 to November 1982; and 3, November 1982 to September 1988. The first period was characterized by incomplete data. Since 1970 records have been kept more consistently, the caseload decreased gradually and more time was spent on the individual patients. At the end of 1982 the new era of MDT was commenced. A total of 7300 charts were examined. Table 1 reviews the treatment regimen policies during these periods.

Hypersensitivity reactions attributed to dapsone could be divided into four categories (Table 2). In a number of cases sufficient information was not available. These are listed separately. In 13 cases the reaction was positively proven to be caused by dapsone by giving a trial administration of the drug after the original symptoms had subsided.

Table 3 gives general data of the 13 patients diagnosed as having a 'Dapsone syndrome' and Table 4 shows the main clinical signs and symptoms associated with the reaction. Finally, in Table 5, attack rates of hypersensitivity reactions in the period 1982 to 1988 are analysed according to age group and sex. There is no significant age or sex association.

Table 1. Analysis of treatment regimen policies at the McKean Rehabilitation Centre, 1949–88.

Period	Years	Dominant therapy policy	Alternatives
I	1949–50	Chaulmoogra oil	Diasone drug trials
	1951–56	Dapsone: low dose start, reaching 300 mg 2/week after 6 months	Sulphetrone Avlosulfon injections
	1957–69	Dapsone, low dose, irregular, intermittent. Policy of stopping whenever ENL occurred	Rimifon (INAH) Thiacetazone (TB1) Thiambutosine (CIBA 1906) Streptomycin
II	1970–74	Dapsone, starting 10 mg 2/week, reaching 100 mg 3/week after 8 months	Thiambutosine Clofazimine (B663)
	1975–76	Dapsone, starting 50 mg 2/week, reaching 100 mg 3/week after 4 months	Clofazimine Thiacetazone
	1977–80	Dapsone, starting 50 mg daily in combination with clofazimine 100 mg 3/week (MB)	Rifampicin (for relapsed cases only) Thiacetazone
		Dapsone 50 mg daily (PB)	
	1981–82	Dapsone 100 mg daily with clofazimine 100 mg 3/week (MB)	Rifampicin (for relapsed cases only)
		Dapsone 100 mg daily (PB)	
III	1982–88	Dapsone 100 mg daily plus clofazimine 100 mg 3/week plus rifampicin 1200 mg per month (MB)	Ethionamide (if intolerant to MDT)
		Dapsone 100 mg daily plus rifampicin 1200 mg per month (PB)	

PB, paucibacillary; MB, multibacillary.

A summary of five significant case histories follows:

Case No. 1 concerns a 22-year-old Thai male, was admitted on 16/5/1980 for elective surgical correction of a dropped foot, which had existed for 6 years. The diagnosis of tuberculoid leprosy (TT) was made and he was started on dapsone monotherapy (100 mg daily). Surgery was performed on 4/6/1980. Recovery was uneventful and there were no postoperative complications or infections. On 16/6/1980 an erythematous rash developed on both arms, which spread over the whole body during the following few days. On 21/6/1980 it was described as a general maculopapular rash with an itchy and burning sensation and diagnosed as Stevens–Johnson syndrome. Fever existed. Dapsone was now stopped and antihistamines were given, followed by corticosteroids. The skin lesions progressed into a vesiculopustular rash with purpuric background. On 25/6/1980 a facial oedema and throat discomfort developed. The same afternoon the patient died suddenly. Blood examination showed thrombocytopenia and agranulocytosis.

Case No. 6 is a 28-year-old male of Hilltribe origin. He was admitted on 8/11/1984 with

Table 2. Number and nature of hypersensitivity reactions to dapsone at the McKean Rehabilitation Centre, 1949–88

Category of reaction	Number per time period		
	1949–69	1970–82	1982–88
Reported dapsone 'allergy', but not enough data to substantiate claim.	9	6	0
Early (within 2 weeks) reaction after start of dapsone, characterized by a skin eruption only.	7 (6)*	6 (2)	3 (2)
Delayed (2–8 weeks) reaction after start of dapsone, characterized by a skin eruption only.	0	1	4 (1)
Hepatitis only	1 (1)	0	0
Dapsone syndrome	0	1	12 (1)
Total	17	14	19

* Number of cases (in brackets) in which the reaction was proven by trial administration of dapsone.

lepromatous leprosy (LL). The skin smear was 3·7 +. He was started on MDT–MB. Spiking fevers were first noticed on 14/12/1984. There was no ENL and no other cause of the fever was found. On 19/12/1984 scleral icterus was seen, followed by generalized adenopathy. The liver was enlarged. On 20/12/1984 a non-itchy rash appeared on the limbs (peripheral distribution) which became more generalized in the following 2 days. Differential diagnosis included typhus, typhoid, malaria, glandular fever, dengue, hepatitis and ENL. Liver function tests showed slightly elevated SGOT, SGPT, alkaline phosphatase and bilirubin values. Malaria smears were negative. Thalidomide,

Table 3. General data of 13 patients with Dapsone syndrome at the McKean Rehabilitation Centre

No.	Sex	Age in years	Leprosy class	Date of start	Dose of dapsone	Other antileprosy medication	
						MDT–MB	MDT–PB
1	M	22	TT	05/1980	100 mg	–	–
2	M	24	TT	02/1983	100 mg	–	+
3	F	18	BL	02/1983	100 mg	+	–
4	M	22	BT	11/1983	100 mg	–	+
5	M	18	BT	01/1984	100 mg	–	+
6	M	28	LL	11/1984	100 mg	+	–
7	M	35	LL	02/1986	100 mg	+	–
8	F	46	BL	01/1987	100 mg	+	–
9	M	76	BL	04/1987	100 mg	+	–
10	M	31	LL	05/1987	100 mg	+	–
11	M	10	TT	09/1987	50 mg	–	+
12	M	27	BL	10/1987	100 mg	+	–
13	F	22	BL	03/1988	100 mg	+	–

Table 4. Medical data of 13 patients with Dapsone syndrome at the McKean Rehabilitation Centre

No.	Time of onset (days)	Skin eruptions			Fever	Lymphadenopathy	Hepatic involvement	Outcome
		itch	erythema	exfoliation				
1	31	+	+	+	+	−	−	died
2	35	+	+	−	+	−	−	recovered
3	36	+	+	+	+	−	−	recovered
4	46	+	+	+	+	−	+	recovered
5	28	−	+	+	+	+	+	recovered
6	36	−	+	−	+	+	+	died
7	25	−	+	+	+	+	+	recovered
8	18	+	+	+	+	−	−	recovered
9	28	−	+	−	+	+	+	died
10	28	−	+	+	+	?	+	recovered
11	39	−	+	+	+	?	+	recovered
12	42	+	+	+	+	+	+	recovered
13	14	+	+	+	+	+	−	recovered

chloramphenicol and penicillin were started but had no effect. The condition of the patient deteriorated and on 25/12/1984 he was transferred to the University Hospital of Chiang Mai under the diagnosis of possible Dapsone syndrome. The patient died on 2/1/1985 due to hepatic failure and toxic shock.

Case No. 9 is a 76-year-old Chinese man who was admitted on 28/4/1987 after borderline lepromatous leprosy (BL) was diagnosed (skin smear 3·7+). He was started on MDT–MB. Low grade fevers developed n 20/5/1987, but no signs of ENL or other causes for the fever were found. Penicillin was started orally on 26/5/1987, but this had no effect and was stopped on 28/5/1987. Before other examinations could be initiated, his condition deteriorated rapidly. He developed sores in the mouth, a diffuse erythematous rash appeared and he became jaundiced. On 31/5/1987 dapsone was stopped and he was transferred to the University Hospital of Chiang Mai where he died on 7/6/1987 because of hepatic failure.

Table 5. Incidence of hypersensitivity reactions to dapsone in previously untreated leprosy patients started on MDT in the period 1982 to 1988 at the McKean Rehabilitation Centre, divided into age group and sex

Age group (years)	Male			Female		
	n	Dapsone reaction	%	*n*	Dapsone reaction	%
0–4	1	0	0	1	0	0
5–9	16	0	0	3	0	0
10–14	21	1	4·8	8	0	0
15–19	29	1	3·4	10	1	10
20–24	39	2	5·1	13	2	15·4
25–34	85	3	3·5	28	0	0
35–44	56	1	1·8	22	1	4·5
45–54	68	2	2·9	23	1	4·3
55–64	46	2	4·3	14	1	7·1
>65	27	1	3·7	14	0	0
Total	388	13	3·4	136	6	4·4

Case No. 10 concerns a 31-year-old male of Hilltribe origin. He was diagnosed with lepromatous leprosy (LL; skin smear 2·8+). MDT-MB was started and he returned home on the same day (18/5/1987). On 18/6/1987 he presented himself at the University Hospital of Chiang Mai with high grade fever and a generalized maculopapular rash. Dapsone syndrome was suspected, dapsone and rifampicin were discontinued, a course of prednisolone was started and he was referred back to the Centre. On 3/7/1987 jaundice was noticed and liver function tests showed slight elevations of SGOT, SGPT and alkaline phosphatase. Serological tests for Hepatitis A and B were negative. The patient recovered well and continued treatment on clofazimine. Rifampicin has not yet been resumed.

On 21/9/1987 Patient No. 10 brought in his 10-year-old son (Case No. 11). The boy had hypopigmentated patches on his face; the (R) great auricular nerve and (R) ulnar nerve were enlarged. Skin smears showed no acid-fast bacteria. He was diagnosed as having tuberculoid leprosy (TT) and started on MDT–PB (child dose: half strength). On 2/11/1987 he returned with fever and abdominal pain and swelling, accompanied by nausea and vomiting. There was a marked erythematous papular rash with exfoliation. Symptoms had started 4 days previously. The liver was enlarged and ascitis existed. All therapy was stopped and the patient was sent to the University Hospital and treated for Dapsone syndrome with prednisolone. This had to be continued for 2 months, but eventually there was a good recovery and the boy continued with rifampicin and clofazimine afterwards without further problems.

Discussion

Dapsone syndrome is basically a clinical diagnosis and often made and treated under 'field conditions'. Thorough analysis of haematological, immunological and biochemical features of hypersensitivity reactions to dapsone was beyond the scope of this retrospective study.

The information gathered between 1949 and 1969 is too incomplete for valid analysis. In the period between 1970 and 1982, 2350 new, previously untreated patients were started on dapsone. Hypersensitivity was observed in 8 patients, of which 6 had an early onset with skin eruptions only (incidence 0·3%). If we include the other 6 cases of dubious diagnosis, the incidence is 0·6%. After implementation of MDT in 1982, 19 cases of dapsone hypersensitivity have been diagnosed: 12 were labelled as Dapsone syndrome, 3 as early onset and 4 as delayed onset with skin eruptions only. In this period, 524 new, previously untreated, patients were started on MDT. The incidence of dapsone hypersensitivity reaction is thus 3·6%, a tenfold rise compared with the 1970–1982 period.

A number of important factors can be mentioned as possibly contributing to the observed rise:

1 *Increased awareness*. Although experience with side -effects from dapsone have always existed in the Centre, it can be argued that awareness amongst medical staff was enhanced by the sudden tragic death of a young patient in 1980 (No. 1, Tables 3 and 4). The increase in the number of reports in literature since 1980 may also have contributed to greater awareness. Besides this, the implementation of MDT has intensified monitoring of patients starting treatment.

2 *Low dose regimens of dapsone before 1976*. Table 1 shows that it was common practice before 1976 to start treatment with low amounts of dapsone and gradually increase the dosage. One wonders if this policy desensitized patients to the drug. Successful desensitization to dapsone in a comparable way was described by Browne in 1963.[11]

3 *Quality of dapsone*. Changes in manufacturing since 1949 and even storage time might explain chemical changes leading to hypersensitivity. This needs to be clarified.

4 *Combination with other antileprosy drugs*. The combination of high dose dapsone with rifampicin seems to be the common factor when comparing the various drug regimens to explain the increased incidence of hypersensitivity reactions. Dapsone 50 or 100 mg daily combined with clofazimine 100 mg three times per week was used between 1976 and 1982 without a noticeable increase of reactions.

Since the introduction of MDT, hypersensitivity reactions have been seen in both patients on MDT-MB (with clofazimine) and MDT–PB (without clofazimine).

The question is whether rifampicin sensitizes certain susceptible people to dapsone, especially in the combination of dosages used in MDT.

Our study shows an apparent increase in hypersensitivity reactions to dapsone after the introduction of MDT. We believe, certainly within the context of the Centre, that this observation reflects a true rise in incidence. The possibility of rifampicin as a contributing factor to the increase of dapsone reactions is suggestive and should be seriously considered and investigated. In our experience, no patients who were previously on dapsone monotherapy, developed a hypersensitivity reaction after beginning MDT. It could be advised that MDT treatment schedules are adapted in such a way that dapsone is given at least 8 weeks before starting rifampicin.

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Dapsone-induced erythroderma with Beau's lines

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Summary A 35-year-old female with borderline lepromatous (BL) leprosy who suffered from dapsone-induced erythroderma is reported. Sudden onset of erythroderma gave rise to a temporary arrest of the function of nail matrix with the resultant Beau's lines. She rapidly recovered with omission of dapsone and therapy with systemic corticosteroids and a topical emollient. In view of the potentially fatal hypersensitivity reaction, we suggest that any patient on multidrug therapy for leprosy needs an urgent referral to a dermatologist if the patient developes a skin rash during the first two months of treatment.

Introduction

Diaminodiphenylsulphone (dapsone), the most widely used antileprosy drug, is remarkably nontoxic. In addition to its prolonged and extensive use in the treatment of leprosy, it also has been widely used in some other dermatological conditions like dermatitis herpetiformis, bullous pemphigoid, subcorneal pustular dermatosis, acne conglobata, erythema elevatum diutinum and vesiculobullous lesions of lupus erythematosus.[1,2] The hypersensitivity reaction to dapsone is usually confined to the first 6 weeks of treatment and may manifest with fever, eosinophilia, mononucleosis, hepatitis, lymphadenopathy and a skin rash.[3] In the early years of its use, it was termed 'Dapsone syndrome' and was frequent when high doses of dapsone were used. However, it rapidly became infrequent between the mid 1950s and the late 1970s when low doses of the drug were in vogue.[4] There are sufficient reasons to believe that the hypersensitivity reactions to dapsone are becoming more frequent.[4,5]

We are reporting one case in which erythroderma of sudden onset was the only feature of dapsone hypersensitivity.

Case report

A 35-year-old female presented to an urban health clinic on 13 September 1988 with erythematous skin lesions on face, back, hands and knees. She had not received any treatment. On examination, she was found to have erythematous infiltrated plaques on face, back, dorsa of hands and knees.

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Both the ulnar, lateral popliteal and posterior tibial nerves were thickened and tender. Her bacteriological index was found to be 2+ on the Ridley scale. The attending physician diagnosed her as a case of multibacillary leprosy (BL) and put her on multidrug therapy as recommended by the WHO, dapsone (100 mg/day), rifampicin (600 mg/month, supervised) and clofazimine (300 mg once a month, supervised and 50 mg/day). The first month was uneventful and she was asked to continue the therapy. On 15 October, she noticed scaly, erythematous lesions on face, trunk and extremities. These were present on the skin not previously affected by the leprosy lesions. Thinking that she might be having a 'lepra reaction', she continued to take the prescribed drugs. The rash rapidly generalized with a stinging and burning sensation all over the body. On 1 November she was referred by the attending physician to our hospital as a 'lepra reaction' case.

On admission, she was found to have exfoliative dermatitis. The previous skin lesions of BL leprosy could not be identified due to the diffuse erythema and scaling all over the body (Figure 1). Both the ulnar, lateral popliteal and posterior tibial nerves were thickened and tender. She was afebrile and there was no evidence of icterus, generalized lymphadenopathy or hepatomegaly. Systemic examination revealed no abnormality. Examination of fingernails revealed transverse lines on all the fingernails about 3 mm anterior to the proximal nail fold (Figure 2). The laboratory investigations revealed the following: haemoglobin 120 g/l; total leukocyte count $8{\cdot}6 \times 10$ g/l; polymorphs 65%; lymphocytes 31%; monocytes 2%; and eosinophils 2%. Urine examination did not reveal any abnormality. Bacteriological index was 2+ (Ridley scale) and morphological index 5%. Serum bilirubin was 11 μmol/l, SGPT 7 units/l and serum alkaline phosphatase was 46 μ/l.

She was diagnosed as a case of exfoliative dermatitis most probably induced by dapsone.

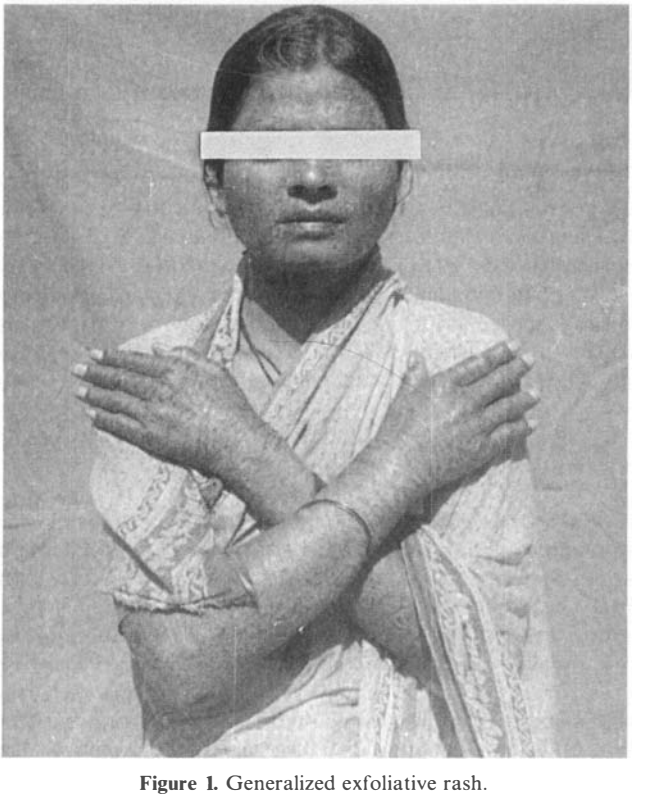

Figure 1. Generalized exfoliative rash.

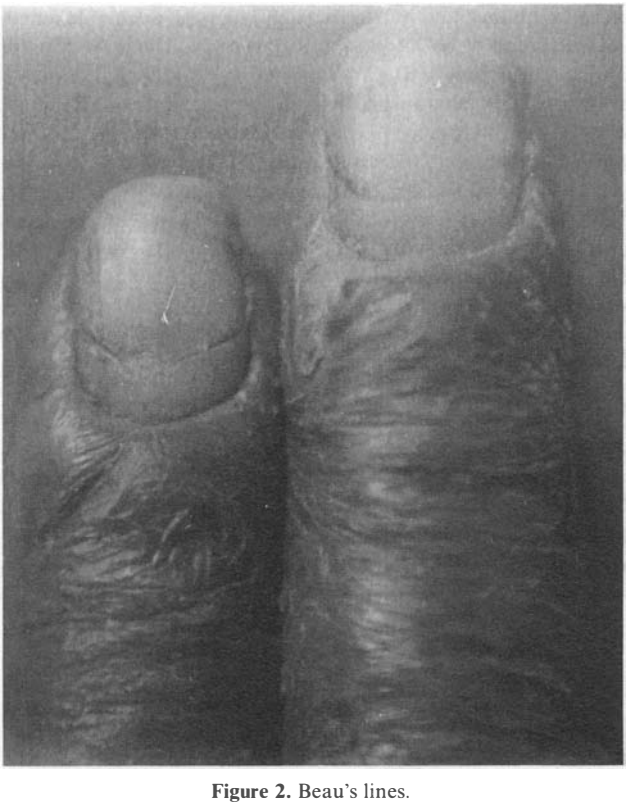

Figure 2. Beau's lines.

Dapsone was omitted and she was put on oral prednisolone 30 mg/day in three divided doses and topical application of petrolatum jelly. Clofazamine and pulsed dose of rifampicin were continued. At the end of one week a marked improvement was seen and the scaling and erythema had reduced. The dose of prednisolone was reduced to 15 mg/day in divided doses. At the end of the second week, the erythema and scaling had completely disappeared and the original leprosy lesions were not visible. Prednisolone was omitted at the end of the second week and she was discharged from the hospital with the advice not to take dapsone again. Isoniazid 300 mg/day was substituted in place of dapsone and she was asked to continue clofazimine and rifampicin.

Comments

Dapsone hypersensitivity was recognized in 1950[6] and was termed 'Dapsone syndrome' by Allday & Barnes.[7] It is characterized by dermatitis, hepatitis, generalized lymphadenopathy and mononucleosis. Of these various features, dermatitis is always present.[7] Our case was peculiar in that exfoliative dermatitis was the only feature of dapsone hypersensitivity.

Beau's lines are due to a temporary alteration of nail growth rate and occur as a result of measles, mumps, pneumonia, myocardial infarction, pulmonary embolism, zinc deficiency etc.[8] They are said to be frequent in exfoliative dermatitis.[9] Although nail matrix arrest occurs in all the erythrodermas, it is of a shorter duration in drug-induced erythrodermas if the offending drug is quickly omitted. This results in resumption of normal nail plate formation. The changes are less dramatic in toe nails because of their slower growth rate and thickness. The depth and width of

Beau's lines will depend on the severity and duration of the illness. Recently, a sign termed 'shoreline nails' has been described[10] in patients with recurrent drug induced erythroderma leading to waves of interrupted nail plate formation preceded by a white leukonychial band. The cessation of nail matrix function due to stressful condition is similar to telogen effluvium where the hair follicles in anagen phase are converted to telogen phase.

We attribute the Beau's lines to localized thinning of the nail plate due to the acute onset of erythroderma causing defective nail plate formation. It has been shown that the linear nail growth is not affected during the episode of formation of Beau's lines.[11] The observation that the lines were 3-mm distal to the proximal nail fold even though the onset of erythroderma was only 15 days ago could be explained by the fact that the nails grow faster in cases of skin disorders with increased epidermal turnover. Examples of these disorders in which increased growth rate of the nails have been reported include psoriasis,[12] pityriasis rubra pilaris,[13] and bullous ichthyosiform erythroderma.[14] In cases of exfoliative dermatitis like the one observed by us, the epidermal turnover is faster[15] and this may have been responsible for the faster distal movement of the Beau's lines after their formation.

In view of the increasing incidence of dapsone hypersensitivity and potential fatality of the condition, we suggest that any leprosy patient who develops a rash during the first two months of treatment needs an urgent referral to a dermatologist.

Dapsone hypersensitivity has to be differentiated from both Type 1 and Type 2 reactions which may occur in the course of chemotherapy of leprosy. It is differentiated by the rash which causes pruritus and burning and is more or less generalized. In contrast, the lesions of Type 1 reaction consist of erythema and swelling of pre-existing lesions and the appearance of new lesions because inapparent lesions may become clinically apparent. Type 2 reaction gives rise to erythematous, tender and discrete nodules especially on face, arms and thighs.

Dapsone has to be avoided in a patient who develops hypersensitivity. We do not advocate desensitization as suggested by Browne[16] because of the availability of other antileprosy drugs. Because of the high prevalence of leprosy in India—a total of 4·5 million cases—dapsone is used extensively. Cases of dapsone hypersensitivity are reported in which the syndrome displays several features simultaneously including erythroderma. In the case under report, an incomplete form showing only erythroderma was presented—this being a rare and unique feature. It is also relevant that though the patient continued with dapsone for a period of 15 days after developing erythroderma, no additional signs of dapsone hypersensitivity syndrome appeared.

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Do we need trials of agents alleged to improve healing of plantar ulcers?

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Summary The assumptions underlying trials of agents claiming to heal plantar ulcers 'faster' and 'better' are shown to be fallacious and it is pointed out that in most cases these ulcers fail to heal for lack of attention and not for want of a specific topical agent. Clinical trials in this area are difficult and are not worth the trouble as they do not add to our knowledge about these ulcers or their management in the clinic or in the field.

Introduction

Physicians working in leprosy are approached now and again with a request to carry out a trial of an agent, a chemical, biological or a synthetic preparation, to assess its value (to certify its usefulness would be more correct) in healing plantar ulcers in leprosy patients. As a consequence, we see periodic publications reporting the usefulness of some agent or the other in obtaining or accelerating healing of plantar ulcers, some even claiming that the test agent prevented or reduced recurrence of those ulcers. A variety of 'healing agents' have been advocated in this manner, leaving leprosy workers, doctors and others, rather confused and making them feel that they should also be using the 'latest' such 'healing agent' for successfully tackling the ulcer problem in their area. In this context it was felt necessary to examine the rationale of the claims made on behalf of these 'healing agents' before accepting them. Further, it was also necessary to examine whether these trials, conducted as they have been, contribute in any way to the corpus of our knowledge about plantar ulcers, or, help us to take better care of them.

Claims and fallacies

The claims made on behalf of these 'healing' agents are: (i) they 'get' plantar ulcers healed; (ii) they clean up the ulcer better and thus help in healing; (iii) they make ulcers heal faster; or (iv) that the healing obtained with the agent is sounder and so fewer of the 'treated' ulcers will recur. Let us examine the soundness of these claims.

(i) *Claim regarding 'getting' ulcers healed:* It would appear that plantar ulcers are normally incapable of healing and the assistance of the 'healing agent' is necessary to induce or restore the power of healing. The fact is, as we all know from our experience, *plantar ulcers nearly always heal*

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provided they are attended to and healing is not interfered with. As far as we know, there is no gross defect in the healing process in leprosy patients either because of leprosy or because of denervation and so there is no real reason why these ulcers should not heal. It is only occasionally that one finds it impossible to get the ulcer healed and in such cases the reasons can usually be found, such as deep infection, poor ulcer bed, or, onset of pseudoepitheliomatous or malignant change. To state that an agent 'gets' the ulcer healed is therefore tantamount to saying that the agent does not interfere with healing and nothing more.

(ii) *Claim that the agent cleans up the ulcer better and helps healing:* This claim is usually advanced on behalf of antibiotic/antiseptic preparations, others which 'draw the fluid off' the ulcer by osmosis or other such physical forces (e.g. Magsulph, micronized plastic granules) and proteolytic enzyme preparations. The point is that *in most cases the ulcer is clean to start with and should not be allowed to become dirty but kept clean by simple barrier dressings.* As for dirty ulcers, there are simple and cheap ways of effectively cleaning them—thorough and frequent washing, irrigation, or soaking—and it is only rarely that a special agent will be required for this purpose. For ulcers with lots of dead tissue, freshly prepared EUSOL (12·5 g of boric acid crystals and 12·5 g of bleaching powder per litre of water) or even just bleaching powder in water may be used for it is one of the few preparations active even in the presence of necrotic tissue, and it will be far cheaper to use than any other cleanser.

As for antibiotics, as a general rule it is not advisable to use a systemic antibiotic locally, to avoid the possibility of the patient developing hypersensitivity and the infecting organisms developing resistance. Further, dirty ulcers often carry 'street infection'—a mixed bag of organisms, many of which are not susceptible to commonly used and cheaper antibiotics. Indiscriminate and routine use of antibiotics in the treatment of ulcers is to be strongly condemned because by such use they are often rendered ineffective or even dangerous just when the patient may be urgently in need of them. Antibiotics must be kept in reserve for such occasions and should be used only when there are systemic signs of infection, like fever and acute regional adenitis, indicating a failure of localization of infection. As for local antibiotics and antiseptics, their use is not essential as the ulcers can generally be cleansed by irrigation and drainage. Their routine use makes people feel 'safe' and they become lax in the other necessary measures of keeping the ulcer clean. Unfortunately, faith in the magic of medicine is still very strong among the public including many doctors and medical auxillaries and the use of drugs as magic remedies tends to make them ignore other essential precautions.

(iii) *Claim that healing agent obtains 'better and quicker' healing:* This slogan is an advertising trick which has unfortunately crept into medicine. 'Better and quicker than what?' should be our automatic response to such a claim. But having become used to slogans like 'Detergent Blank washes whiter!' and 'Toothpaste Blank Blank cleans your teeth better!!', we tend to accept this claim equally uncritically.

The following points need to be noted in respect of this claim. (i) We already have a method of healing an ulcer by the shortest time, in two weeks or less, in skin grafting, if that is what is wanted. I am not aware of any 'healing agent' which equals this efficacy. In addition, skin grafting provides epithelial covering from the time the graft is applied, that is, from day zero, which no healing agent does. The technique is not very difficult and the procedure can be carried out in any primary health centre having facilities for clean surgery. (ii) In my experience, an uncomplicated, reasonably clean ulcer of average size takes about five weeks to heal under conditions of limited walking, when kept covered with saline dressings or Vaseline gauze only, without a plaster cast or bed rest (unpublished data). Marginal shortening of healing time is of no practical significance even when the difference is statistically significant. To be of practical significance, the healing time should be consistently and substantially reduced, say, by about 50% or more. To the best of my knowledge none of the 'healing agents' has been shown to be that effective. (iii) Healing can become defective and healing time can get prolonged in conditions like gross nutritional deficiencies (e.g. vitamin, protein or trace metal deficiencies), diabetes, uraemia, and malignancy. But, these are not common and the two most

common causes for delayed healing of plantar ulcers in leprosy patients are (a) continued injury to the ulcer by unlimited and unprotected walking, and (b) deep or persistent infection. If these are taken care of, the ulcer will heal normally. 'Early' healing of plantar ulcers thus requires removal or mitigation of factors that interfere with healing.

(iv) *Claim that healing is sounder and recurrences are reduced:* This claim is usually only implicitly made, as a bonus benefit from using the 'healing agent', by stating there were fewer instances of recurrent ulceration during the period of observation, or, just mentioning that the scar was 'more supple', hinting at a lesser possibility of recurrence. The facts are (a) that not all plantar ulcers recur, and (b) that any plantar ulcer can recur so long as the original factors that led to ulceration (anaesthesia, plantar intrinsic paralysis and unrestricted or unprotected walking) continue to be operative. Unlike in cancer, reliable estimates of recurrence rates for various kinds of plantar ulcers in leprosy patients are not available and so we are not in a position to predict the probability of recurrent ulceration for different periods of time after obtaining healing. Many persons show interest in the problem of plantar ulcers only for the duration of the trial and are, therefore, not in a position to make proper estimates of probable recurrence based on experience. In view of all this, statements on prevention of recurrence do not carry conviction.

We must remember that plantar ulcers recur because (i) original conditions that led to ulceration in the first instance continue to operate, (ii) the scar is unable to withstand normal stresses of walking, (iii) excessive stresses fall on the scar, and (iv) because of flare up of latent infection. It follows that prevention of recurrent plantar ulceration requires a variety of actions such as (i) using protective foot-wear and limiting walking to within safe limits, (ii) minimizing scar formation and improving its quality, (iii) reducing the stresses on the scar, and (iv) eradicating infection. The quality of scars is improved by limiting tissue loss to the minimum, healing the ulcer early, local physiotherapy (gentle massage etc.,) and, where needed, by surgical revision. Reducing the stress on the scar will require (i) modifications in foot-wear, (ii) limiting walking to within safe limits, and (iii) surgical measures to correct evident and not so evident anatomical abnormalities and deformities which throw excessive stress on the scar.

It should be clear from the above that getting the ulcer healed and preventing its recurrence are quite different propositions and that the latter is a far more complex task than the former. In such a situation, to depend on a 'healing agent' for preventing recurrence is like relying on better management of injuries from automobile accidents for preventing such accidents.

The trials—a critique

The trials themselves pose a number of problems which are briefly touched upon below.

(i) *Trials are laborious and expensive:* Properly planning and carrying out a trial of a 'healing agent' requires much time and labour. It needs to be a well thought out and properly controlled double-blind study. Matching controls have to be carefully selected taking a number of parameters into account, such as age, sex, body-weight, pressure at ulcer site, distances walked by the subjects, past ulcer behaviour, local condition of the ulcer, integrity of blood flow and many other compounding factors. This is a laborious task as anybody experienced in these procedures will aver. Accurate records have to be maintained, patients may have to be hospitalized, additional investigations carried out and these further increase work all round.

(ii) *Reliability of data:* All this trouble may be worthwhile if the information collected is reasonably reliable and correct. Since plantar ulcers are a chronic problem with numerous remissions and exacerbations, information collected about them is often quite inaccurate. Investigators, when they become aware of these deficiencies, tend to become cursory in data collection adding to the unreliability of the data collected.

(iii) *Eliminating bias:* This is a major problem. Double-blind trials are necessary but are not usually possible as the person who attends to the ulcers (and the patients as well) will know whether

the 'healing agent' is being used or not, and many investigators do not seem to realize that that is sufficient to introduce bias. The subtle ways in which such bias works is incredible but true. Perusal of the literature shows that anybody who has tested any remedy or agent seems to have always found the test remedy/agent superior to the control agent/remedy in some way or other, using tables, graphs, photographs and *p* values to support their claim! It is very much like the situation regarding non-steroid anti-inflammatory drugs and gastric irritation. Each new drug is heralded with the fanfare 'this has proved to be far more kind to the stomach than all the previous ones', citing well-conducted trial reports to support the claim. If all these claims were really true, by now the latest such drug should be causing hardly any gastric irritation, which is of course not the case. Evidently some bias has crept in somewhere, somehow.

The fact seems to be that when one tests a 'healing agent', bias is inevitably introduced, whether one is aware of it or not and better results are obtained with the trial agent. This is best exemplified by the Canadian experiment[1] in which exposure to a non-functioning gadget (placebo device) healed bed-sores better because it was believed by the attendants to emit an invisible healing ray! (I will be happy to supply a copy of this report to any one who is interested). It is evident that extraordinary care has to be taken in conducting these trials, with each step meticulously planned and executed to eliminate bias. Results of trials conducted without such care and attention to details (unfortunately many reported trials fall into this category) help only to misinform the reader.

(iv) *Relevance of results:* Assuming a careful study did show that an agent healed plantar ulcers a little earlier than the control remedy, it is difficult to see how this information becomes relevant. As pointed out earlier, if a 'healing agent' is advocated for plantar ulcers, the results become relevant only, (i) if the healing time is substantially shortened (by 50% or more) and not otherwise, and (ii) if it is shown that the use of that agent would make ulcer care in institutions or in the field operationally easier and cheaper. To show merely that the 'healing agent' helped to heal plantar ulcers does not mean anything, for, as pointed out earlier, it is extremely rare to find that one cannot get a plantar ulcer healed. However, some leprosy patients do have recalcitrant extra-plantar ulcers (like stasis ulcers in the leg) and there may be a case for trying 'healing agents' on them.

Concluding remarks

From the time Ambroise Pare (16th Century) substituted egg white for boiling oil for treating war wounds, the quest for wound healing agents has been going on and will probably continue as long as people keep getting wounds and burns. The literature in leprosy is strewn with reports of agents that have helped healing plantar ulcers 'quicker and better'. They include acriflavin, amino acids, amniotic membrane, bacitracin, cod-liver oil, coffee powder, collagen sheet, dapsone, Debrisan, Furacin, gentian violet, hydnocarpus oil, hydrogen peroxide, hyperbaric oxygen, Livoderm, Madecassol, mercurochrome, Neomycin, Novolep, phenytoin, placental extract, polymyxin, sulphonamides, uracil, Vasodilators, vitamins, zinc salts and zinc tape. The list is not exhaustive and there are probably a lot more. The variety of 'healing agents' shown to be effective only demonstrates that plantar ulcers heal provided they are attended to, and not the effectiveness or superiority of any of these remedies.

Barring the few permanently settled in institutions, all leprosy patients live in their homes and a proportion of them have plantar ulcers. Leprosy clinics can at the most get the ulcer cleaned and dressed once or twice a month. It is evident that plantar ulcers will have to be attended to and cared for in the homes of patients, by the patients themselves or by some members of their families. Therefore the primary need is for leprosy patients with plantar ulcers to know how to manage their ulcers properly in their own homes. For this they require to know why they got their ulcers, how they can keep them clean, covered and protected so that they will heal and how they should conduct themselves to prevent recurrence. They also need to be helped to put this knowledge into practice, as well as when they have failed in their own efforts to get the ulcer healed. The offering of supposed

'healing agents', whether they are the latest technological wonders or traditional remedies, only helps to perpetuate the myth of magic remedies encouraging the patients and the others to rely on the agent and not on their own health practices which are the basic requirements to get plantar ulcers healed and prevent their recurrence.

It is evident that trials of 'healing agents' for plantar ulcers may, at best, provide information of dubious value but not knowledge. Promoters of these agents may be interested in getting a certificate from an authority that 'agent X heals plantar ulcers better and faster', but that is no reason why people in authority should waste their efforts and oblige them.

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Sensory recovery in the plantar aspect of the foot after surgical decompression of posterior tibial nerve. Possible role of steroids along with decompression

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Summary In leprosy, involvement of the posterior tibial nerve leads to sensory loss in the plantar aspect of the foot. As a result plantar ulcers are common and lead to deformity and disability. Restoration of plantar sensation can prevent ulcer formation.

Posterior tibial decompression was done for the recovery of sensation in the plantar aspect of the foot. Seventy-two patients under went decompression on 84 feet, 25 received steroids pre- and post-operatively. The recovery of sensation was better if surgery was done before 6 months of onset of anaesthesia. Decompression along with steroids gave better results than decompression alone in patients with active neuritis especially in BT cases whereas in BB, BL and LL cases there was no significant improvement of sensation. The results are discussed.

Introduction

Involvement of the posterior tibial nerve is common in leprosy and leads to loss of sensation in the plantar aspect and paralysis of the small muscles of the foot. Plantar ulcers are an unfortunate problem due to anaesthesia of the feet. If sensory function is restored to the foot it is possible to prevent ulcers and late complications.

Various studies[1,2,4,6] have reported recovery of sensation and motor function after decompression of the ulnar nerve. An analysis of the recovery of sensation after PT decompression was done at CLT & RI, Chengalpattu. Initially PT decompression was done for painful neuritis and patients were on steroid therapy as well. Because there was a good recovery of sensation after surgery, patients with plantar anaesthesia but without neuritis were also considered for surgery although they were not given steroids. The results were analysed for recovery of plantar sensation after PT decompression with and without steroids. Steroids help in suppressing the immunological response in the nerve and relieve the tension by decreasing the oedema and inflammation. Surgical decompression relieves external and internal compression of the nerve.

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Materials and methods

The study was done at the Central Leprosy Teaching and Research Institute, Chengalpattu to find the effect of posterior tibial decompression on recovery of sensation. The study was carried out from November 1982 to December 1986. The type of disease according to the Ridley–Jopling scale, treatment, bacteriological status and duration of anaesthesia were recorded. Due importance was given to the cases with anaesthesia of short duration and some patients who had painful neuritis were given steroids as well as surgery. The dosage of steroids varied from 60 to 20 mg and was given for 3–4 months.

Touch, pain, pressure and vibration were tested over the plantar aspect of the foot. Touch was tested with No. 5 Nylon, pain with a pinprick, pressure with the blunt end of a pin and vibration with a tuning-fork. Thermal and two-point discrimination were not tested as there was difficulty in testing them in the plantar area. The foot was divided into six areas, namely; big toes, lateral and medial aspect of forefoot, instep and outerside of midfoot, and heel. Each area was tested for sensation, touch, pain and pressure. Vibration sensation was tested over the head of the 1st MTH, 5th MTH and heel for both high and low frequency. Motor deficit was not considered as it was difficult to assess the same without EMG.

Assessment was done by giving a score. For presence of each type of modality of sensation in one area one mark was given. A total of six areas were tested for 4 modalities the maximum total score being 24. If touch, pain, pressure and vibration were absent in 3 areas, the score would be 12 (24 minus 12). Post-operatively if there were recovery of all sensation in 2 areas the score would be 20. The percentage of recovery was 50% compared to the loss, i.e. 6 points out of 12.

The results were grouped into five categories:

Excellent, recovery of 76%,
Good, recovery of 51–75%,
Fair, recovery of 26–50%,
Poor, no recovery or less than 25% recovery,
Loss, deterioration of intact sensation in partial anaesthesia.

According to the area of recovery, it was grouped into four. Recovery in heel, midfoot, forefoot and toes. PT decompression with steroids and without steroids were analysed. Duration of loss of sensation was another important factor in assessing the results.

Posterior tibial decompression was done using standard incision. The nerve and its branches, namely calcaneal, medial and lateral plantar were identified and traced to the plantar aspect. Epifascicular epineurotomy was done. Intrafascicular decompression was not done. The posterior tibial vessels were identified and traced upwards and downwards. A part of the flexor retinaculum was excised. Those who had steroids pre-operatively continued to have steroids post-operatively.

Post-operative assessment was done 4 weeks after surgery and repeated every 3 months in the 1st year and every 6 months in the next year and later yearly assessment was carried out. The patients were advised about their feet and MCR footwear was given to all patients.

Observation and analysis

During the period from November 1982 to December 1986, 94 posterior tibial decompressions were done for sensory loss in the plantar aspect of the foot. Twelve patients underwent bilateral decompression. There were 68 males and 4 females. The age of the patients varied from 14 to 57 years with an average of 28·6 years. In 42 cases decompression was done on the right side, 30 on the left side and bilaterally on 12 cases. There was thickening of the posterior tibial nerve in all patients, tenderness over the nerve in 34 cases and a history of recurrent neuritis in 21 cases. The posterior tibial pulsations were well felt in 77 limbs and were feeble in seven. The duration of anaesthesia in

Table 1. Duration of anaesthesia before surgery

Period	No. of cases in steroid group	No. of cases in no steroid group	Total
<6 months	12	23	35
6–12 months	7	9	16
1–2 years	4	7	11
>–2 years	2	20	22
Total	25	59	84

the plantar aspect of the foot varied from 1 month to 15 years. In 25 cases steroids were given along with decompression of the nerve and in 59 cases only decompression was done. The type of leprosy was classified according to Ridley–Jopling T-1, BT-35, BB-14, BL-07, LL-15. All the patients were on chemotherapy before surgery. Thirteen patients received MDT and 59 received monotherapy (DDS). The period of treatment varied from 6 months to 20 years. Most of the patients had developed anaesthesia in their feet during treatment, most probably due to reactions. Twenty-two patients were bacteriologically positive and 50 were negative. The follow-up period varied from 1·5 years to 5·5 years.

Loss of sensation varied from complete anaesthesia to loss of one modality in a few areas. Post-operatively sensation was tested in the ward. Patients reported some subjective improvement but no recovery was found. Fourth week post-operative assessment showed recovery of sensation which continued to improve for up to 6 months after which not much recovery was found. Recovery of sensation stayed constant without deterioration in cases where there was improvement.

The results were graded into 5 groups as discussed in Materials and methods. The results are given in Tables 2 and 3, depending upon whether they received steroids or not.

The recovery of sensation in different areas of the foot was as follows:

Toes, 53·03% (35/66)
Forefoot, 70·14% (47/67)
Midfoot, 68·91% (51/74)
Heel, 54·68% (35/64)

Complete recovery of sensation was found in 15 out of 84 cases (17·85%).

Table 2. Recovery/duration of anaesthesia with PT decompression alone

Result	Duration of anaesthesia				Total %
	<6 m	6–12 m	1–2 yr	>2 yr	
Excellent	9	5	1	3	18 (30·5)
Good	5	2	3	3	13 (22·03)
Fair	5	1	0	1	7 (11·86)
Poor	2	1	3	9	15 (25·02)
Loss	2	0	0	4	6 (10·16)
Total	23	9	7	20	59 —

Table 3. Recovery/duration of anaesthesia after decompression along with steroids

Result	Duration of anaesthesia				
	<6 m	6–12 m	1–2 yr	>2 yr	Total (%)
Excellent	10	0	2	1	13 (52)
Good	0	4	1	0	5 (20)
Fair	2	2	1	1	6 (24)
Poor	0	0	0	0	0 (0)
Loss	0	1	0	0	1 (4)
Total	12	7	4	2	25 —

Table 4. Type of leprosy and recovery of sensation

Type of leprosy	Patients without steroids (No. of feet)						Patients with steroids (No. of feet)					
	Exce.	Good	Fair	Poor	Loss	Total	Exce.	Good	Fair	Poor	Loss	Total
T	—	1	—	—	—	1	—	—	—	—	—	0
BT	11	2	1	8	4	26	9	2	2	—	—	13
BB	2	5	3	2	—	12	2	1	3	—	—	6
BL	1	3	1	2	2	9	—	—	—	—	—	0
LL	4	2	2	3	—	11	2	2	1	0	1	6
Total	18	13	7	15	6	59	13	5	6	0	1	25

Type of leprosy and recovery of sensation is given in Table 4.

Although it is not possible to compare the type of leprosy and recovery of sensation, it is found that in cases of BT leprosy decompression with steroids gave better results than decompression alone. In other types of leprosy the recovery of sensation was not very significant whether patients received steroids or not.

Discussion

Restoration of sensation in the plantar aspect of the foot plays a major role in prevention of the most troublesome problem in leprosy, namely plantar ulcers, which lead to mutilation, absorption, and amputation, so that the rehabilitative measures which are difficult are avoided.

Eighty-four feet underwent decompression of the posterior tibial nerve, in which there was complete recovery of sensation in 15 (17·8%). The results were satisfactory which include excellent, and good results in 49 (58%). There was minimal or no recovery in 15 (17·8%) and deterioration of sensation in partial anaesthetic feet was found in 7 (8·3%).

Recovery of sensation was better in cases where decompression was done within 6 months of onset of anaesthesia. Satisfactory results (excellent and good) were found in 24 out of 35 (68%) who had anaesthesia of less than 6 months duration.

Comparing the results of PT decompression with and without steroids, it was found that

steroids with PT decompression gave better results ($P < 0{\cdot}05$). Satisfactory (excellent and good) results were found in 31 out of 59 where steroids were not given (52·4%) whereas with steroids satisfactory results were found in 18 out of 25 (72%). The results of steroid and non-steroid groups were quite significant in BT cases. Thirteen out of 26 cases in the non-steroid group had satisfactory whereas in the steroid group, 11 out of 13 cases had satisfactory results.

Even in the patients where steroids were used, the results were better if the duration of anaesthesia was less than 6 months ($P < 0{\cdot}01$). The recovery was satisfactory (excellent and good) in 10 out of 12 cases (83·33%) with steroids, whereas in patients not given steroids satisfactory result were found in 14 out of 23 (60%). Regarding the type of leprosy and recovery of sensation, it was found that in the 'BT' type of leprosy, decompression with steroids gave better results than decompression alone. The pattern of recovery was similar in BB, BL and LL cases whether they received steroids or not. Out of 32 cases who had decompression alone there was satisfactory recovery in 17 cases and satisfactory results were found in 7 cases out of 12 who received steroids along with decompression. Therefore there was no significant improvement of sensation with the addition of steroids.

Deterioration of anaesthesia after surgery was found in cases where the anaesthesia was of a longer duration and without steroids.

In anaesthesia of a shorter duration in the plantar aspect of the foot, decompression of the posterior tibial nerve along with steroids gives a better chance for the recovery of sensation. Decompression is both external and internal. External decompression as the tough flexor retinaculum was incised and later, as a part of it was excised. Internal decompression was done by epineurotomy. It is not possible to say how much internal decompression is done by epineurotomy. Internal neurolysis was not done as it may damage the nerve rather than help recovery.

Corticosteroids have a definite role in helping recovery by suppressing the immunological response within the nerve. Internal compression is also relieved to a great extent as the inflammatory oedema subsides with steroids. Addition of steroids together with decompression makes a significant contribution to the recovery of sensation in BT cases. To evaluate the significant role of steroids in recovery of sensation a controlled study is essential, keeping all the parameters constant.

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A second report on multidrug therapy for leprosy in Trinidad and Tobago

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Summary Multidrug therapy consisting of rifampicin, clofazimine and dapsone, was introduced to Trinidad and Tobago in January 1982. This was with slight modification of the WHO regimens. Since then 717 patients have completed multidrug therapy up to the end of December 1987. Of these, 272 patients have completed surveillance and have been discharged from clinic attendance. Thirty-four patients died before completing surveillance and three are known to have migrated. Of the remaining 408 cases still under surveillance, the majority are multibacillary.

This paper reviews the outcome of multidrug therapy in Trinidad and Tobago between January 1982 and December 1987—a period of 6 years, and presents some of the statistics related to the newly diagnosed patients within the same period.

Introduction

Trinidad and Tobago is a twin-island republic situated in the Caribbean Sea, to the north of the South American continent. The country has a population of over one million (1,059,825) by 1980 population census. Trinidad and Tobago launched its programme of multidrug therapy (MDT) in January 1982, using the short course regimens recommended by the World Health Organization (WHO),[1] with slight modification.

A preliminary report was published in 1984[2] and described the history of antileprosy treatment in Trinidad and Tobago. This report also outlined the approach to the implementation of MDT.

Since there are no facilities for reliably determining drug resistance and because of a concern for compliance at the start, all patients whether paucibacillary (PB) or multibacillary (MB) receive triple therapy. Patients are considered paucibacillary if they are diagnosed clinically or histologically as indeterminate, tuberculoid or borderline tuberculoid on the Ridley–Jopling scale with a bacterial index (BI) of less than 2. Any patients who are diagnosed mid-borderline, borderline lepromatous, or lepromatous on the Ridley–Jopling scale or with a BI of more than 2, are classified as multibacillary.

Paucibacillary patients receive at least 6 monthly doses of 600 mg rifampicin monthly supervised, 300 mg clofazimine monthly supervised and 100 mg daily unsupervised (50 mg capsules were unavailable) and 100 mg dapsone daily unsupervised. This regimen is to be completed in 9 months. Newly diagnosed multibacillary patients receive the same drugs for at least 24 monthly

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Table 1. Duration of MDT according to period of bacteriological negativity—MB Patients

Period of bacteriological negativity	Duration of MDT (months)
4 years or more	6
2–4 years	12
2 years or less	24 minimum
New patients	24 minimum

doses and until smear negativity. However, old multibacillary patients were treated according to the period of negativity on the smear examination, as shown in Table 1. Monthly injection of acedapsone (Hansolar) was abandoned in 1984.

At this time there are six outpatient clinics operating. The Hansen's Disease Control Unit was integrated with the Dermatology Unit of the Port of Spain General Hospital in January 1986. This is a 1000-bed hospital with a general admission. Three medical officers of the Dermatology Unit assumed responsibility for the clinics, which became joint Skin–Leprosy Clinics. There is also a medical officer attached to the Control Unit full time. Staff of the Control Unit continue in their specialized roles as district health visitors–nurses (3), medical lab technician (1), follow-up workers (5), medical social worker (1), physiotherapist (1) and shoemaker (1). Their functions have not been integrated into the rest of the primary health care system. Treatment is administered on an outpatient basis.

Paucibacillary patients are placed under surveillance on completing treatment and examined every 6 months for 3 years. Multibacillary patients are examined with slit smear testing at 6-month intervals for 5 years after completing treatment.

Results

POST-TREATMENT SURVEILLANCE

Seven hundred and seventeen patients have completed the modified multidrug therapy during the 6-year period from January 1982 to December 1987. Three hundred and seventeen were paucibacillary and 400 multibacillary. One hundred and seventy-six patients (80 PB, 96 MB) who were under surveillance up to the end of 1987 have not been seen and therefore are retained on the register. Some of these have been seen on at least one occasion during the surveillance period. Others have never been examined since completing MDT and have not been found or refuse to attend. Many patients seem to believe that completion of treatment implies discharge from clinic.

Two hundred and seventy-two patients have been seen and discharged from surveillance (187 PB, 85 MB). Fifty-seven patients who entered the surveillance register are known to have died. Of these, 34 died before completing the period of surveillance. Causes of death include complications of diabetes, hypertension, congestive cardiac failure, cerebrovascular accidents and carcinomas. No deaths have been recorded as related to leprosy or chemotherapy.

At least three patients are known to have migrated during the period of surveillance. We suspect however, that many more may have migrated, thereby accounting for failure of attendance. Four hundred and eight cases remain under surveillance, the majority of them are MB cases.

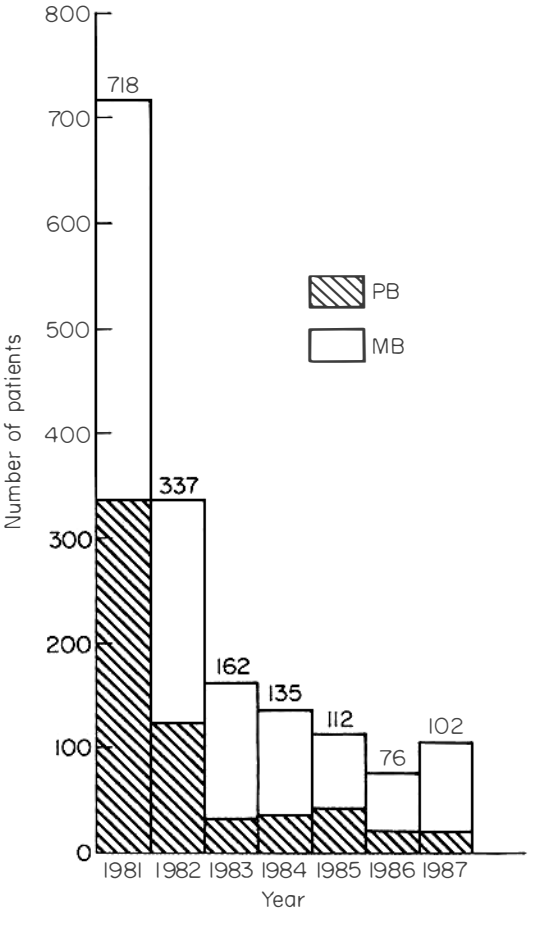

Figure 1. Patients on treatment register at year end.

PATIENTS ON REGISTER

Since MDT was introduced there has been a significant fall in the number of patients on the treatment register. This is shown in Figure 1. The number was practically halved from 1981 to 1982 and then from 1982 to 1983. There has been only a slight fall in the prevalence rate between 1983 and 1987 (Figure 2).

The marked fall in prevalence between 1981 and 1983 was due to a large number of patients completing the short-term MDT during 1982 and 1983.

The majority of patients registered continue to be over age 15 years. The number of children age 0–14 years registered was significantly reduced from 1981 to 1982. This is shown in Table 2. The lowest proportion was registered in 1983 (1·2%). In 1985 and 1987 the increase was due to the occurrence of new cases in the child contacts of mainly MB patients. The figures are represented in Figure 3.

In the pre-MDT era, there were as many as 21% of children 0–14 years old at the end of 1975 (total patients, 803).

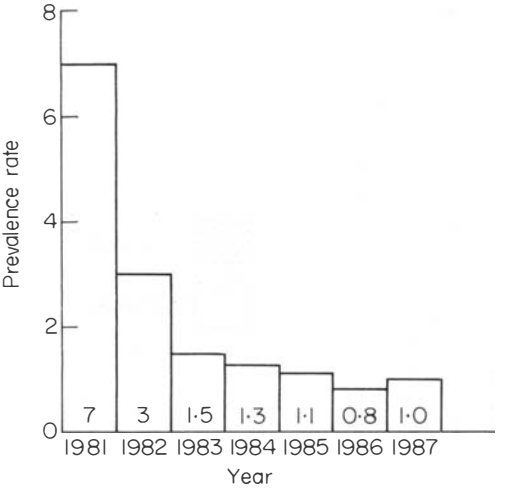

Figure 2. Prevalence rate per 10,000 population.

Table 2. Patients on register by age

	YEAR						
Age	1981	1982	1983	1984	1985	1986	1987
0–14 years	55	15	2	3	11	6	11
15+ Years	663	322	160	132	101	70	91
Total	718	337	162	135	112	76	102
0–14 years (%)	8	4	1·2	2	10	8	11

TREATMENT OF MB PATIENTS

Two hundred and fifty MB patients received at least 6 months treatment, 69 received at least 12 doses of MDT and 36 received at least 24 monthly doses. The remaining 45 multibacillary patients (newly diagnosed as well as old patients) had more than 24 months treatment.

ACCEPTABILITY OF TREATMENT

Regularity of treatment was determined by the proportion of patients taking 75% of their recommended doses of MDT during the year. A large number of patients completed 6 months of MDT in 1982, many of these being multibacillary patients who were bacteriologically inactive at the time of starting. Regularity is represented in Table 3, and the year immediately prior to MDT is shown for comparison.

There was a fall in regularity in 1983 and 1984 to a level closer to that observed in 1981. However, overall regularity increased in 1985 and has been consistent since then.

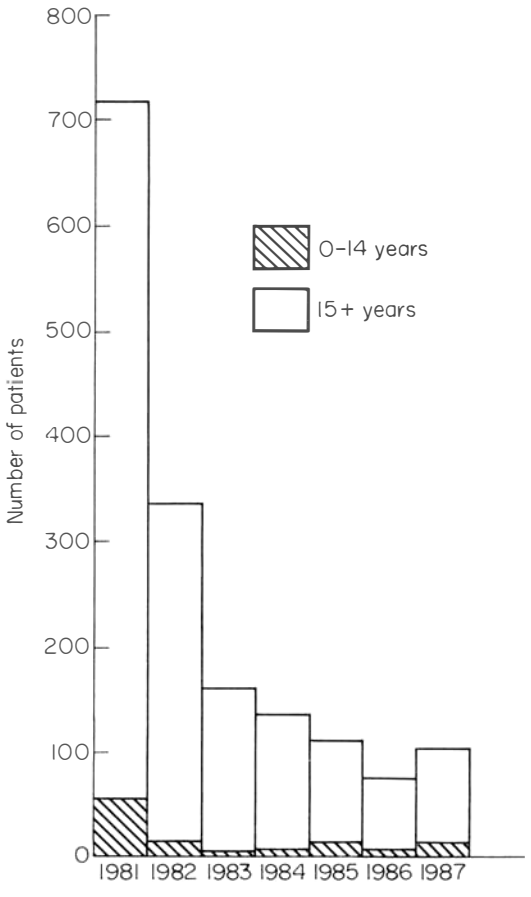

Figure 3. Number of patients on register by age.

Thirty-two patients refused entirely to accept MDT and were removed from the register. In most instances, the reasons for refusal were not recorded, but some patients believed that the new regimen was experimental and were afraid of possible side-effects. Others believed that they had been cured and did not require further treatment.

Three newly diagnosed MB patients who entered the register during the 6-year period developed sensitivity to dapsone and the drug was discontinued. Two of these had jaundice, erythematous skin

Table 3. Regularity of treatment

Year	Regularity (Overall) (%)
1981	36
1982	75
1983	41
1984	40
1985	63
1986	63
1987	68

Table 4. Bacteriologically positive patients, 1982–1987

Year	Number of bacteriologically positive patients	Total patients (%)
1982	35	10%
1983	42	26%
1984	30	22%
1985	20	18%
1986	34	45%
1987	34	33%

rash and fever; one had abdominal pain and vomiting. One has since completed treatment (in 1988) after 36 monthly doses of rifampicin and clofazimine. One TT case with dapsone sensitivity subsequently complained of generalized erythema and swelling within hours of her monthly dose of rifampicin and clofazimine. She completed treatment with clofazimine only and has shown no relapse after 24 months (up to the time of writing).

Of the 102 patients registered at the end of 1987, four took no treatment in 1986 but two of these resumed in 1987 although irregularly. These patients have refused drugs on the grounds of religious beliefs and also because they consider that their disease is no longer active.

Eleven of the patients on register at the end of 1987 have had more than 24 months of regular MDT and three of them were still bacteriologically positive at the end of 1987.

BACTERIOLOGICALLY POSITIVE PATIENTS

The number of bacteriologically positive patients on register at year end has not changed significantly (see Table 4).

The increase in proportion in 1986 was partly due to a proportionally larger number of MB patients (16/29 = 55%) diagnosed in 1986 as compared with 1985 (14/37 = 38%). In addition, more PB (and bacteriologically negative) patients completed treatment during 1986. Many of these were BT patients who had received more than 6 monthly doses because it was felt that 6 months treatment was inadequate and that lesions were still changing. A decision was made to terminate treatment since this did not truly comply with WHO's regimen and did not seem to be justified.

RELAPSES IN PATIENTS COMPLETING TREATMENT

Nineteen patients who have completed the modified MDT between 1982 and 1987 appeared to have relapsed. The details are recorded in Table 5.

CASE HISTORIES

Case No. 12. This male patient was diagnosed BB in 1979. He had at the time slit-skin smears showing 3+ of AFB. He received rifampicin for 3 months and daily lamprene and dapsone when the diagnosis was made. He received 24 months of regular MDT and became smear negative. Seventeen months after completing he presented with clinical reactivation of the old lesions. A skin biopsy showed 'focal inflammation around appendages and nerves. ZN Negative.' Slit-skin smears were negative. MDT was restarted. He has been repeatedly smear negative and the skin lesions have responded to the repeat course of MDT.

Table 5. 'Relapses' after modified MDT

Case number	Initial type	Type on relapse	Therapy prior to MDT	No. of MDT doses	Time to relapse (Months)	Smear result	Biopsy confirmed
1	BT	BT	No	9	10	Neg	Yes
2	BT	BT	No	6	9	Neg	ND
3	Neural	Neural	No	6	8	Neg	ND
4	BT	BT	No	6	14	Refused	Refused
5	BT	BT	No	6	23	Neg	Yes
6	BT	BT	Dapsone	Irregular 6	20	Neg	Refused
7	BT	BT	Rifampicin × 3/12, dapsone and lamprene	6	42	Neg	ND
8	BT	BT	No	6	5	Neg	ND
9	BT	BT	Dapsone	6	7	Neg	ND
10	BT	BT	Dapsone and lamprene	6	19	Neg	ND
11	TT	TT	No	10	28	Neg	Yes
12	BB	BB	Rifampicin × 3/12, dapsone and lamprene streptomycin and isoniazid	24	17	Neg	Suggestive
13	LL	LL	Streptomycin isoniazid, dapsone and PAS	6	23	1+	Refused
14	LL	LL	Dapsone and lamprene	6	4	2+	ND
15	LL	LL	Dapsone and lamprene	13	19	Neg	ND
16	BT	BT-BL	No	18	12	2+	Yes
17	LL	LL	Dapsone and lamprene	6	58	Refused	Yes
18	TT	TT	Dapsone and lamprene	6 Irregular	32	Neg	Yes
19	Neural TT	Neural TT	Dapsone	14	12	Neg	No

ND, Not done.

Case No. 13. This female LL patient was diagnosed in 1938. She had received treatment with dapsone monotherapy but also had streptomycin and isoniazid in the early years. At the time of starting MDT she had been smear negative for 4 years and was on dapsone only. She received 6 regular monthly doses and 23 months later on routine follow up was found to be AFB 1+ without visible skin lesions. The smears were repeated 3 months later and were still 1+. She has since completed 24 regular MDT doses and achieved smear negativity. No skin biopsy was performed since she refused the procedure.

Case No. 14. This male LL patient was diagnosed in 1970. He had had past treatment with dapsone, streptomycin, isoniazid and PAS, he was receiving treatment with dapsone daily and lamprene three times weekly when MDT was started in 1982. He was bacteriologically inactive for 8 years when 6 doses of MDT were started. Four months after completing this treatment, he returned with skin lesions and slit-skin smears positive at 2+. No skin biopsy was performed. He died after

Table 6. Relapse rates from 1982 to 1987

Year	PB patients (%)	MB patients (%)
1982	—	1·1
1983	3·4	—
1984*	16	—
1985	—	—
1986	—	2·6
1987	—	—

* Three (3) out of nineteen paucibacillary cases completing in 1984 relapsed.

his 23rd dose of MDT and was still clinically active at the time of death. Death was reported to be due to complications of bronchial asthma.

Case No. 15. This man was diagnosed LL in 1955. He had received dapsone and lamprene in the past and had missed 3 months treatment when MDT was started. He had been smear negative for 2 years and received 13 regular doses of MDT. Nineteen months after completing treatment his skin lesions were noted to have become raised. Slit-skin smears were negative and no biopsy was performed. His treatment was resumed.

Case No. 16. This man was diagnosed BT in 1984. He had a single hypoaesthetic lesion on the right shoulder, multiple enlarged nerves, associated with anaesthesia. A slit-skin smear was negative. During his 6 months of MDT he developed right ulnar neuritis and a left drop foot. Prednisolone was started and MDT continued to a total of 18 monthly doses. Twelve months later he presented with nasal stuffiness and infiltrated facial lesions. There were also hypoaesthestic plaques on the upper arms. A skin biopsy from the arm showed foamy histiocytes and lymphocytes, ZN negative. Slit-skin smears however were 2+ from both ear lobes.

We believe that this man is a BT relapse with downgrading to BL.

Case No. 17. This male patient was diagnosed LL in 1936. He had prior treatment with dapsone but was on lamprene only since 1972. When MDT was started there had been an 8-month hiatus in

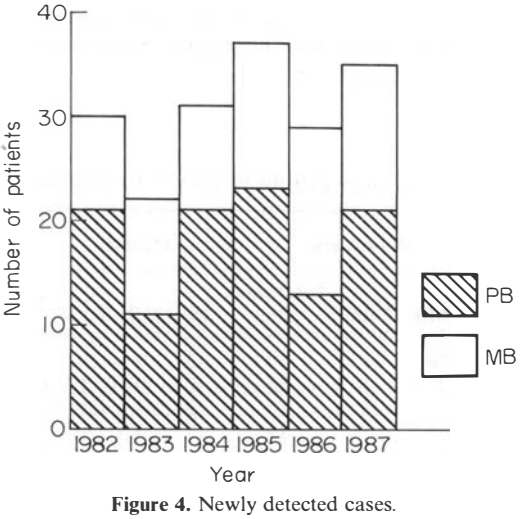

Figure 4. Newly detected cases.

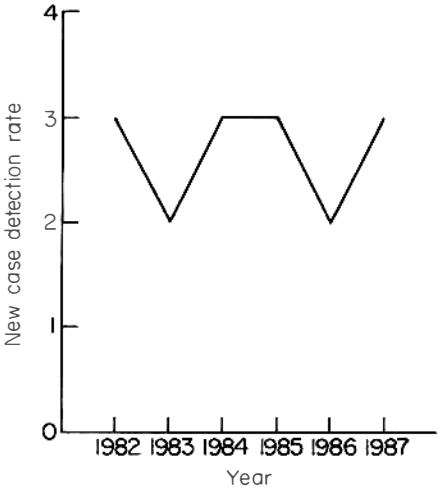

Figure 5. New case detection rate (per 100,000 population).

his treatment. He had been smear negative for 4 years and so he received 6 months of MDT. He presented 2 months before his 5-year surveillance was to end, with skin nodules present for several months. He refused to have slit-skin smears but a skin biopsy showed lepromatous leprosy with numerous acid-fast bacilli. MDT has been resumed.

It is possible that several of the cases were late reactions rather than relapses, e.g. Case Nos 12 and 15. Nine of the paucibacillary cases were not biopsied and therefore suspected relapses were not laboratory confirmed and were treated on the basis of clinical presentation. Eleven out of 14 PB cases (79%) were BT and the remaining 21% TT. We wonder whether this indicates that 6 months of MDT may not be adequate for these patients. Eight out of 14 PB cases (57%) were new and had no prior chemotherapy.

The true paucibacillary relapses are probably represented by Case Nos 1, 5, 11 and 18, while Case Nos 14, 16, 17 are true multibacillary relapses. The overall relapse rate for the 6-year period was therefore 1·7% for paucibacillary patients and 1% for multibacillary patients. Relapse rates (up to the time of writing) for the years 1982–1987 and based on the year of completion of therapy of the relapsed patients are shown in Table 6. The figures have been calculated separately for paucibacillary and multibacillary groups.

Table 7. Newly detected patients by age and type of disease

	0–14 years				15 years			
Year	PB	MB	Total	Total cases (%)	PB	MB	Total	Total cases (%)
1982	9	0	9	30	12	9	21	70
1983	4	1	5	23	12	10	22	77
1984	5	0	5	16	12	14	26	84
1985	6	1	7	19	17	13	30	81
1986	4	1	5	17	9	15	24	83
1987	9	1	10	28	12	12	25	72

Table 8. Male to female ratio in new patients

Year	M : F ratio
1982	1·7
1983	2·1
1984	1·4
1985	4·3
1986	3·1
1987	1·1

Only one of the relapsed BT cases had completed the 3-year surveillance before presenting with apparent relapse. All except two of the others presented within 24 months of stopping treatment (WHO recommends at least 2-year surveillance). The period ranged from five months to 42 months with a mean of 17 months.

Only one of the multibacillary relapses (Case No. 16) had 24 months of MDT. The others were clinically and bacteriologically inactive when MDT was started and received only 6 months of MDT. So far the number of relapses in that group of old patients (i.e. diagnosed before MDT and receiving less than 24 monthly doses) has been low. The regimen administered was contrary to that recommended by WHO and may indicate that 6 months of treatment was inadequate.

NEW PATIENTS

The number of newly detected cases has remained relatively consistent during the 6-year period. It is difficult to determine a trend for MB *vs* PB cases but the proportion of MB cases has risen from 30% in 1982 to 40% in 1987. The larger proportion of newly detected cases is paucibacillary ranging from 45% (1986) to 70% (1982). This is shown in Figure 4.

The new case detection rate had already begun to fall before MDT was introduced from 70 cases and a rate of 6 per 100,000 in 1975 to 25 cases and a rate of 2 per 100,000 in 1981. The rate changed only slightly between 1982 and 1987. This is shown in Figure 5.

The age groups of the newly detected patients according to type of disease are shown in Table 7. The majority of the children (0–14 years) were PB cases however, in the adult group, PB and MB cases were almost equally represented.

Although male patients predominate, the male to female ratio has varied from year to year as is shown in Table 8.

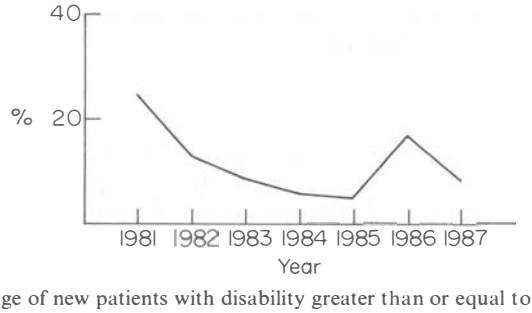

Figure 6. Percentage of new patients with disability greater than or equal to Grade 2 (WHO).

Table 9. Mode of detection of new patients

Mode of detection*	1982	1983	1984	1985	1986	1987
Notification	20	19	23	23	27	20
Voluntary	3	0	1	4	0	1
Contact survey	3	3	7	10	2	12
Group survey (School)	4	0	0	0	0	2
Total	30	22	31	37	29	35

* No general survey was performed.

DISABILITIES IN NEW PATIENTS

Disabilities greater than or equal to WHO Grade 2 according to WHO Disability Grading Scale[3] are infrequent and have been at a low level even before MDT. In 1981 a high of 28% (seven out of 25 newly detected patients) was recorded. The figure dropped to 5% in 1985 but rose again in 1986 to 17%. Figure 6 shows the trend in the disability figures.

All of these patients were over 15 years old at the time of presentation. The mean age for this group was 55 years (range 17–90 years). The youngest patient with any disability was 13 years old at presentation (Grade 1). The minimum time from onset of disability to diagnosis was 6 weeks in one BL patient with an ulnar nerve palsy. The maximum was 10 years.

Of the five patients with Grade 2 and 3 disabilities diagnosed in 1986, four out of five had histories of 1–3 years of illness before diagnosis. This, to us, underlines the importance of failure of early diagnosis in the development of disabilities.

REACTIONS

Overall, it appears that the incidence of reactions is less now, than before MDT was introduced. No figures are available for comparison. There are four MB patients at this time experiencing chronic ENL and receiving treatment with prednisolone and increased dosage of clofazimine.

MODE OF DETECTION OF NEW PATIENTS

The majority of cases are diagnosed within the Skin–Leprosy Clinics with a few referrals from other physicians. School surveys have been relatively unproductive as a source of new cases and are usually carried out when new cases attending school have been discovered. Table 9 shows the mode of detection. The relatively high figures for contacts in 1985 and 1987 were due to presence of disease in child contacts (0–14 years) of index cases.

Conclusion

We are of the opinion that multidrug therapy, although slightly modified in our situation, has proved successful so far. The drugs are acceptable to the majority of patients. We hear few complaints about clofazimine-induced pigmentation and patients prefer to be receiving effective medication at the expense of a temporary colour change.

At this time, while the number of new cases remains relatively consistent, we plan to continue our vigilance and will persist in our efforts to educate medical personnel and the general public.

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'Flu' syndrome on once monthly rifampicin: a case report

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Summary 'Flu' syndrome as a complication of intermittent weekly administration of rifampicin is well documented. The rare occurence of 'flu' syndrome on once monthly rifampicin is reported in this paper.

Case report

A 54-year-old male patient completed 11 monthly doses of rifampicin as part of the WHO multibacillary multidrug regimen uneventfully. Following administration of the twelfth dose the patient reported that about 2 hr later he had developed malaise, fever and body aches lasting for approximately 12 hr. The patient reported this to the clinical team a month later at the time of the thirteenth pulsed MDT clinic. A presumptive diagnosis of 'flu' syndrome was made, the patient admitted for investigation, and with his consent, given a provocative dose of rifampicin.

At the time of admission, the patient was asymptomatic. Clinical examination as well as routine blood and urine tests and chest X-rays were done to rule out any underlying cause for the symptoms. All tests were normal.

A dose of rifampicin 600 mg was administered 5 days after the last therapeutic dose in hospital on an empty stomach. Two hours later the patient complained of malaise followed by chills, body ache and headache. Six hours after the administration of rifampicin the patient developed fever and 2 hr later the oral temperature reached 101·8°F. At this stage, with the diagnosis of 'flu' syndrome due to rifampicin established, the patient was given an injection of Paracetamol following which the symptoms and temperature subsided.

Two days after the challenging dose of rifampicin, a second dose of rifampicin 600 mg was given to the patient along with tablets of Paracetamol 500 mg 6 hourly for 24 hr. Six hr after the rifampicin administration the patient experienced some malaise, which lasted for 1 hr, but was otherwise asymptomatic. There was no rise in temperature.

At the time rifampicin was administered in the hospital a decision was taken to continue the standard WHO multibacillary multidrug regimen along with oral antipyretics. The patient has completed 18 doses to date without further problems and has shown a satisfactory response to treatment.

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Discussion

Several syndromes resulting from intermittent rifampicin therapy have been described, cutaneous, abdominal, flu, respiratory and purpura. These may occur singly or in combination, the severity being greater when they occur in combination.[1]

'Flu' syndrome is unlikely to complicate once-a-month rifampicin administration[2] and reports of its occurence as a result of antileprosy therapy are few.[3] Its low incidence in leprosy is attributable not only to the interval of administration, but also to the dose employed (600 mg for adults, WHO regimen) the highest incidence of the syndrome being recorded in intermittent regimens for tuberculosis employing doses of between 20 and 30 mg/kg bodyweight.[4] 'Flu' syndrome is also less common when intermittent rifampicin administration is preceded by a period of daily administration[5] and is therefore even less likely to be seen in India where, as per the Government of India guidelines, intermittent monthly rifampicin is preceded by a period of daily intensive therapy for multibacillary cases in which rifampicin is administered 600 mg daily along with other drugs (DDS and clofazimine).[6]

The syndrome as classically described begins 1–2 hr after administration of the drug and lasts for 8 hr, the symptoms coinciding with the period of maximum rifampicin plasma concentration. It is now known that the syndrome has an immunological basis, and that it is caused by the formation of rifampicin-antibody complexes.[5] Antibodies to rifampicin have been detected from 4 months after starting therapy but have also been detected for the first time as late as the 16th month. While patients with rifampicin-dependent antibodies have a significantly higher incidence of side-effects, those who have no detectable antibodies are also known to develop adverse reaction.[7] On the other hand, patients with rifampicin dependent antibodies may remain asymptomatic.[8]

It has been proposed that the drug acts as a hapten, which in the presence of plasma macromolecules induces the formation of antibodies against it. It has been suggested that symptoms of the 'flu' syndrome might be due to a minor degree of haemolysis, a haemolytic anaemia appearing with higher titres of rifampicin dependent antibodies.[5] Other studies have, however, shown no direct correlation between antibody titres and the presence or absence of symptoms.[7]

While potentially dangerous reactions to rifampicin such as purpura, shock and renal failure are clear indications to stop the drug,[2] management of 'flu' syndrome is ill defined. Episodes of the syndrome are known to stop spontaneously, after temporary interruption of treatment, after reduction of the dose, or following institution of daily therapy. In this patient daily therapy was not considered because of the cost involved and the inability to supervise intake. Reduction of dose is particularly appropriate to high dose tuberculosis regimens where the reduction in the dose does not markedly effect therapeutic efficacy. As this patient's symptoms were well controlled with symptomatic treatment a decision was taken to continue treatment. This is in accordance with advocated procedures.[1]

Acknowledgment

We sincerely acknowledge Dr V Ekambaram, Consultant for Multidrug Therapy, Chittoor District, AP for his valuable suggestions and for reviewing this paper.

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Penile and scrotal lesions in leprosy: case reports

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Summary Six leprosy patients in the Ridley–Jopling spectrum of BT–BL showing lesions on penis and scrotum are presented, as we believe that this common enough clinical feature is not well documented in the literature.

Introduction

Groin, perineum along with scalp, axilla and the narrow band of lumbosacral area are considered to be 'immune zones' in leprosy. To the best of our knowledge, clinical involvement of genitals in leprosy has not been well documented in the literature. We report six cases of leprosy, showing involvement of male external genitalia. Lesions on the external genitalia may be encountered in leprosy of all types in the entire Ridley–Jopling spectrum. It is however not known whether lesions due to indeterminate leprosy, representing the earliest clinical manifestation of the disease, can occur in these organs.

Case reports

We report six cases with leprosy lesions ranging from BT to BL types with clinical photographs (Figures 1 and 2) showing involvement of the penis and the scrotum.

All six patients had borderline leprosy of more than 6 months duration. Three patients had lesions on glans penis. Two cases were in Type 1 lepra reaction. The slit-smear examination was positive in four cases.

Observations and conclusions

It is known that *Mycobacterium leprae* has a distinct predilection for the cooler areas of the body. Anish[1] demonstrated higher temperature of the axilla and scalp as compared to that of the forearm.

Sahni *et al.*[2] studied 20 untreated BL and LL cases. They observed groin involvement clinically in five cases, skin-smear positivity in three, while all showed histological changes. Bedi *et al.*[3] observed histological involvement of groin in 10 out of 20 LL patients under monotherapy. Pandya

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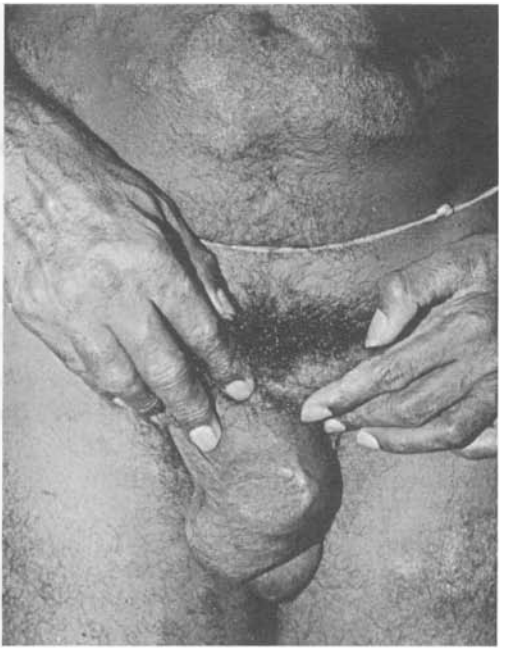

Figure 1. Case No. 2. Erythematous annular lesion on the scrotum.

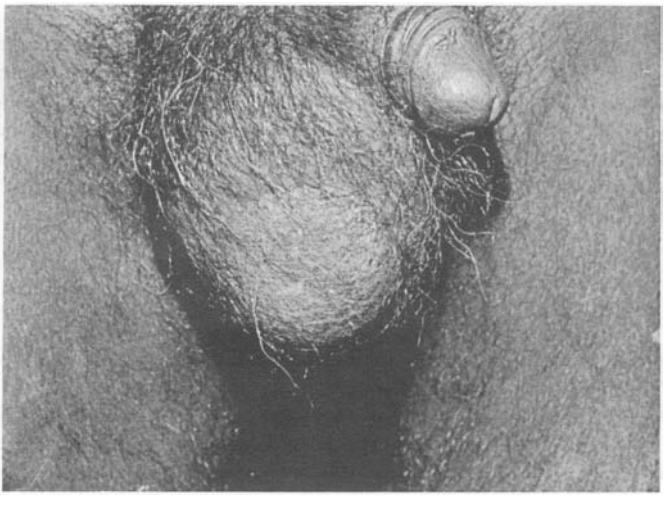

Figure 2. Case No. 6. Hypopigmented dry scaly patch on the scrotum with partial loss of sensation.

& Antia[4] studied scrotal skin and underlying dartos biopsies from 45 patients suffering from various types of leprosy (12 TT, 22 borderline & 11 LL) most of them treated. In almost all the cases histology showed involvement of the neurovascular bundles. According to them, scrotal skin involvement is due to a liberal supply of larger nerves as compared to cutaneous nerves elsewhere.

If the clinical examination of any male leprosy patient is to be considered exhaustive, it must include examination of external genitalia.

Table 1

Case No.	Age	Type of leprosy	Skin-smear report for AFB	Site of genital involvement
1	15	BT–BB	+	Erythematous, odematous plaque on prepuce and shaft of penis. Lesions are also seen on buttock and thigh.
2	48	BL	+	Erythematous annular lesion on the scrotum. Leprosy lesions are also present on abdomen, thigh and hands.
3	25	BL	+	Hypopigmented, hypoaesthetic patch on scrotum extending up to shaft of the penis. Infiltrated lesions are seen on thigh.
4	12	BL	+	Erythematous, oedematous, plaques on scrotum and prepuce.
5	25	BT–BB	– ve	Small patch on the glans along with erythematous plaque on the left thigh.
6	28	BT	– ve	Hypopigmented dry scaly patch on the scrotum with partial loss of sensation.

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SPECIAL ARTICLE

Leprosy control: the rationale of integration

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Summary After considering the situation and the perspectives of integration and the drawbacks that a vertical approach can represent for leprosy control, the author proposes the framework of control programmes as a systemic model for comprehensive health care. The structure that health services in developing countries are adopting in order to implement PHC allows for an horizontal integration of specific activities; conversely, activities which have already proved their value for leprosy control can easily enlarge their scope and include other prevalent conditions. Integration leads to an improvement in patients' and health workers' attitudes; provided that the necessary supervision is guaranteed, integration is feasible and warrants more effective patients' care and a better exploitation of resources in order to reduce the specific risk in the community.

Introduction

This paper is based on experience gathered in a developing country, of a leprosy control programme whose strategical guidelines were subsequently adopted for the management of the national health system.[1] Its objective is to stimulate discussion on the various ways in which the contents and functions of leprosy control can be effectively incorporated in the 'horizontal' framework of the general health services. This may possibly necessitate confining the specific component to technical advice and supervision and central referral facilities.

The meaning and implications of integration—general considerations

'Integration' of leprosy control has been a matter of debate for a long time. The term is generally taken to mean, either the horizontal implementation of activities previously carried out by a vertical programme—that is an integration of resources[2]—or a combination of various objectives under a single vertical programme—as in leprosy–TB control.[3] Another concept is 'Integration' between different leprosy control programmes, such as between government and voluntary agencies or between neighbouring countries, implying standardization of criteria to improve performance, results and evaluation.

The application of MDT has opened up new perspectives for leprosy control which have fostered the specific, vertical approach with the aim of eradicating the disease, so that today, most, if

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not all, control programmes continue to be run on vertical lines. It is by no means certain, however, that this strategy will succeed. Leprosy disappeared from several countries before the introduction of any chemotherapy and declined markedly in other countries during the era of dapsone monotherapy, concomitant with, and probably largely due to, socio-economic development.[4] Further, experience in tuberculosis control, shows that highly effective multiple drug regimens can be applied for many years without any great impact on the incidence of the disease in poorer countries.[5] Accordingly, the integrated approach still merits serious consideration.

Countries with a high prevalence of leprosy generally face complex health problems and have to optimize the use of the resources available. Their populations are exposed simultaneously to many risk factors—each of which may be specific for a certain condition, but which together constitute a serious threat to health or life—in the face of which any action which is too specific is inevitably of limited effectiveness.

It is of note that, in general, public opinion considers that 'integration' already exists; people do not distinguish between a vertical programme and the general health services, and patient compliance, being dependent on trust in the effectiveness of treatment, may be influenced as much by the failure, for example, of treatment for epilepsy in a family member as by the advertized merits of antileprosy treatment.[6]

An overall improvement in general health services is a step towards a more effective leprosy control and, conversely, leprosy control can contribute to such an improvement. Indeed, it constitutes a good model, organized as it is in a comprehensive programme, even within the limits of its specific objectives, catering for a wide range of patients' needs and reaching out into the community. Specific tasks are defined at each level and effectively integrated in terms of planning and implementation. Due attention is given to standards of treatment, adequate technologies and health education, while the need for permanent supervision and training of staff is fully recognized. Its management is increasingly geared to information systems and provides for local decision-making within the national strategy, especially on account of variations of incidence and prevalence from area to area. All these features are inherent in primary health care (PHC), and any experience gathered in their application in a specific field ought to be relevant to the management of a general health system.

Leprosy control has always emphasized the importance of health education and community involvement which is the core of PHC. The role played by voluntary agencies and charitable institutions is of particular note, both in relation to the community—which often shows a preference for them because they offer more comprehensive care and often have more highly motivated staff—and in relation to the wider political debate about development, international aid and health.

A public health approach

The majority of publications on leprosy concern it's microbiology, immunology, pharmacology and clinical aspect, while those on its control in the community are written from the standpoint of epidemiology, anthropology or sociology. Some authors[7] have discussed leprosy control in the perspective of PHC, but in the main these papers have been limited to the grounding of vertical programmes in the community (it should, however, be emphasized that village health workers can reasonably be expected to undertake leprosy control[8] only if the superior levels of the system can provide integrated care for all the problems likely to arise in a community-based programme). There are very few papers—or even editorials—dealing with operational aspects of integration (with the exception of some from integrated leprosy–TB projects) and this is possibly due to lack of experience. The greatest need at the present time, however, is to improve the operational efficiency of leprosy control programmes and this can best be achieved by application of the principle of public health administration as enunciated by Leavell & Clark in their classical model of the natural

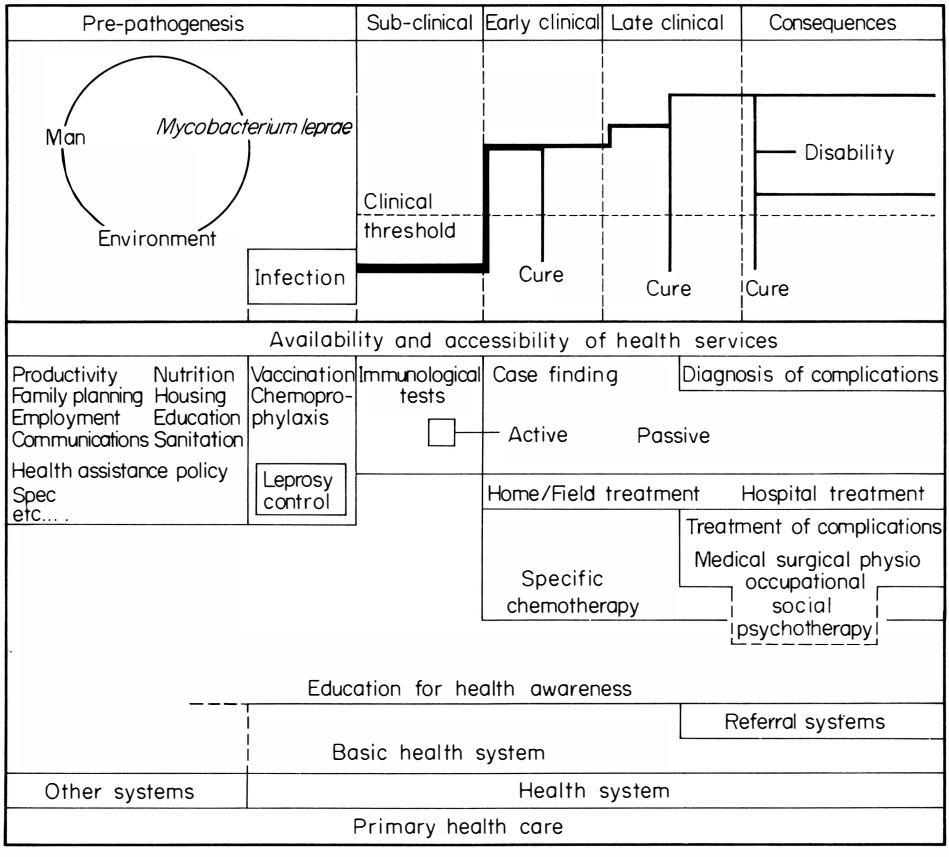

Figure 1. Leprosy control: activities, levels and resources (Loretti 1983 after Leavell & Clark).

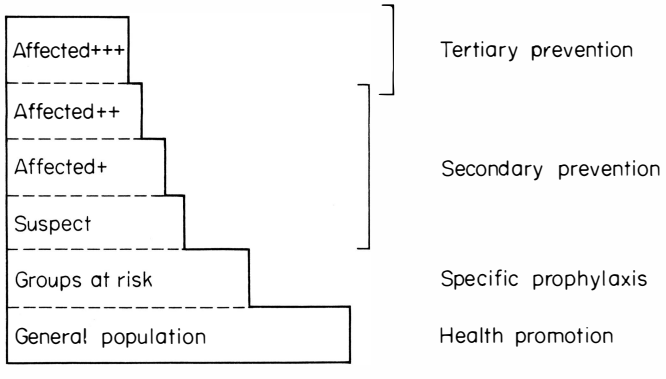

Figure 2. Public health programmes and population (Loretti 1986).

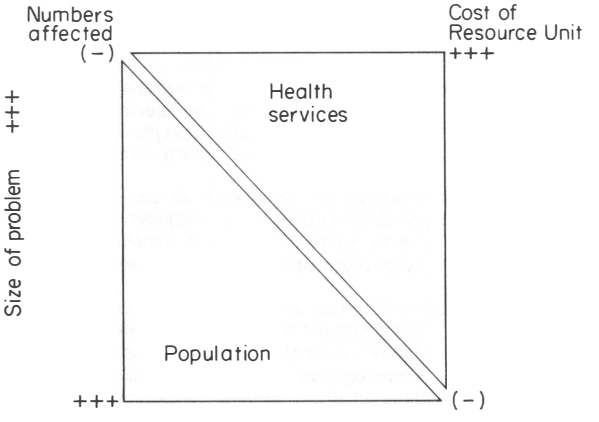

Figure 3. Health problems in a population and costs of health resources (Loretti 1986).

history of disease.[9] Figure 1 illustrates how the general features of leprosy and its control fit into the model; the feasibility of integration can then be assessed by analysis of the model along two different lines.

The population—services analysis

The first analysis relates the health system to the population, in order to ensure that its structure is adequate to undertake leprosy control activities.

Figure 2 illustrates how the general population are the object of health promotion, groups at risk need specific prophylaxis, while suspects and individuals increasily affected need actions directed at secondary and tertiary prevention.

Figure 3 shows that in the population, the highest number of individuals can be cared for at the primary level of the health system at minimum cost; as the extent of the problem increases, the

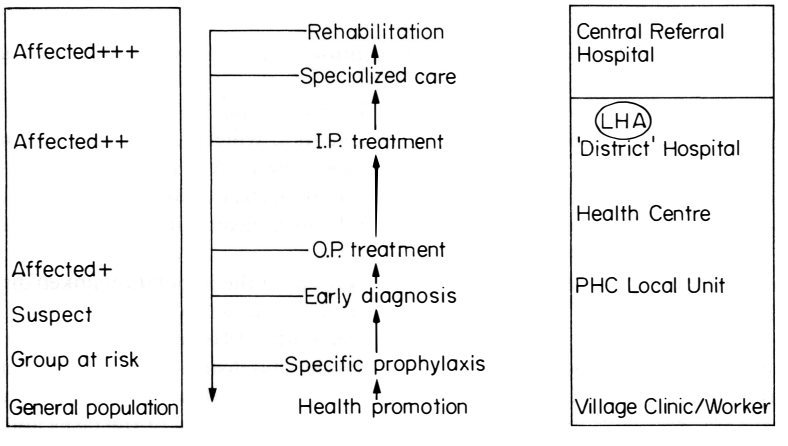

Figure 4. Health care delivery: relation between the population served, the services and their activities. LHA, Local Health Authority (Loretti 1986).

	M.C. health care	Leprosy control	TB control	
Affected +++	Diagnosis, treatment Special care: Paediatrics and obstetrics	Diagnosis, treatment by specialist; orthesis Reconstructive surgery Long-term admissions	Diagnosis, treatment by specialist; Specific surgery Long-term admissions	Central Referral Hospital
Affected++	I.P. treatment, Paed. and obstetrics Hospital delivery Premature care	Diagnosis and treatment of complications Septic surgery Short-term admissions	Lab. confirmation Diagnosis and treatment of complications Short-term admissions	(LHA) 'District' Hospital
Affected+	O.P. Treatment, Paed and obstetrics Assisted delivery FP counselling IUD insertion Umbilical Care PCM diagnosis and follow-up	Clinical-Lab diagnosis OP treatment and Follow-up, Spotting of complications Physiotherapy, sandals suspect screening	Clinical-Lab diagnosis OP treatment and follow-up, spotting of complications Suspect screening	Health Centre
Suspect	Family observation Special follow-up Referral	Skin screening, Family observation, Special follow-up, Referral	Cough screening, Sputum collection, Referral, Family observation,	PHC local unit
Group at risk	Breastfeeding promotion, immunizations, F.P., U-5 and ante-natal clinics Home delivery	Treatment control absentee tracing Ulcer care Education for disabled Contact control	Special follow-up treatment control, absentee tracing, BCG, Contact control	
General population	Promotion of traditional midwives Pregnancy register Birth register Health awareness Promotion	Leprosy awareness Promotion Treatment delivery Contact register Suspect register	TB awareness promotion Treatment delivery Contact register Suspect register	Village Clinic/Worker

Figure 5. Mother and child health care, leprosy control and tuberculosis control integrated in a horizontal setting. LHA, Local Health Authority. (Loretti & Carvalho 1986).

numbers affected decrease, but the cost of intervention at the intermediate and superior levels progressively increases.

Figure 4 is a development of Figure 2 showing the operational levels of the health services and the activities of primary, secondary and tertiary prevention which constitute a continuous flow, from the basic comprehensive services to the most specialized. At each point there is an outlet, which returns the patient/user to the general population. In the health structures column, the area of management and supervision normally entrusted to the local health authority (LHA) is shown as being from the district hospital downwards.

In Figure 5, the activities are listed and the target groups of the population linked directly to the operational structure. In this example, leprosy control is shown together with MCH and TB control, but the model could well be enlarged to include other PHC programmes. It is necessarily merely a summary, aiming to systematize levels of activity and distribution of tasks. Possible ways of integration will be suggested by reading transversely; practical details have to be added as local conditions dictate. The various activities have to be analysed in terms of the tasks and techniques involved, compared with the competences and resources available at each level and then planned according to local conditions of demography and morbidity. In addition, provision must be made

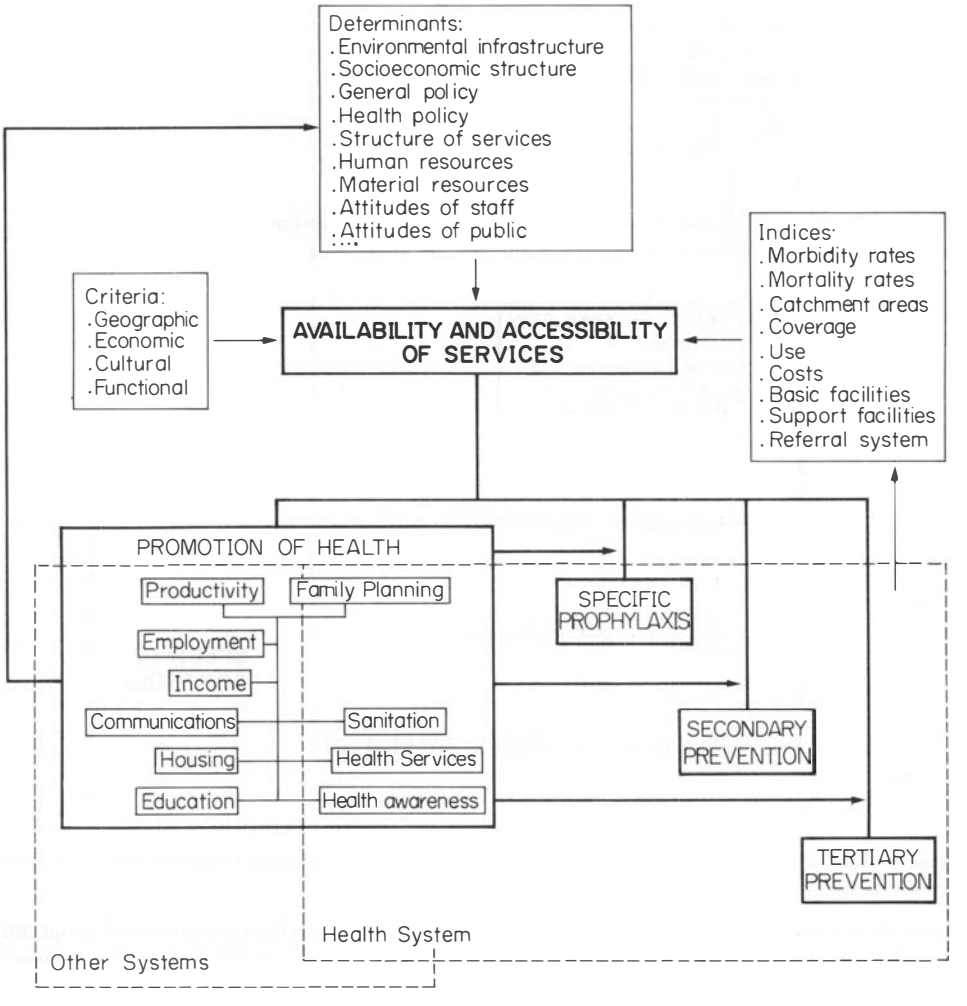

Figure 6. Availability and accessibility of services, promotion of health and prevention of disease (Loretti 1987).

for management and logistics, normally carried out at higher levels, and the integration of vertical programmes may well entail strengthening the administrative resources of the general health service.

The activities analysis

The second analysis concerns the extent to which leprosy control activities can be adapted to other objectives.

Figure 6 relates the promotion of health, prophylaxis, secondary and tertiary prevention, to the availability and accessibility of services, as conditioned by a number of determinants, defined by certain criteria and measured by several indices coming from data collected by the health system.

Figure 7 shows that promotion of health must take into account various socio-economic components, some of which are the responsibility of the health system: family planning, sanitation,

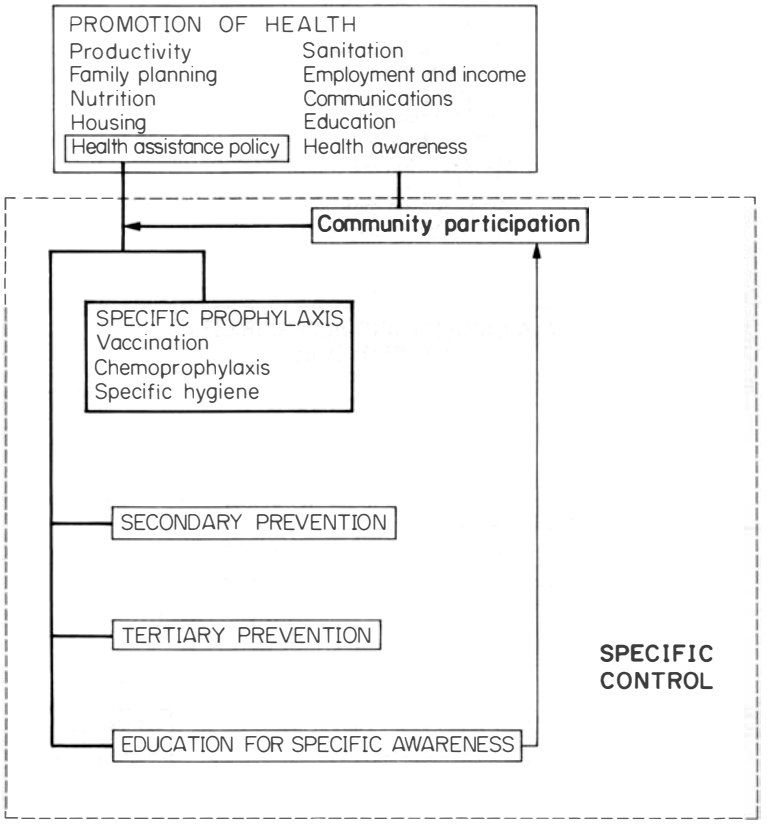

Figure 7. Promotion of health, prophylaxis, disease prevention, community participation and disease control (Loretti 1987).

health awareness and overall health policy. Health policy defines the specific control programme, but unless all the components of the promotion of health are being fulfilled, it will not enjoy full community participation, which in any case has to be fostered by education for public awareness to the problem.

Figure 8 shows that the health education of the population is essential for any programme and that it receives feedback from the outcome of the activities implemented. In leprosy control, reliance is still at present on secondary prevention, with two provisos: firstly, that tertiary prevention—rehabilitation—contributes to health education by limiting disabilities; secondly, that specific prophylaxis, that is the reduction of specific risk in the community, is limited to the control of regularity of treatment and absentee tracing, which are both tasks of the basic worker and should be given due merit accordingly.

Figure 9 analyses secondary prevention by early detection and effective treatment in greater detail and systematizes their principal components. It makes it possible to identify items needing emphasis in some circumstances, e.g. the definition of the population being surveyed, the importance of an early diagnosis of complications, the role of a workable registration system, and the distribution of different therapeutic measures at various levels. For both early detection and effective treatment there are listed resources, criteria for quality control, basic requirements and a number of indices for the purpose of evaluation.

Figure 10 is a composite table showing how leprosy and other conditions can be considered together in an integrated approach. It includes:

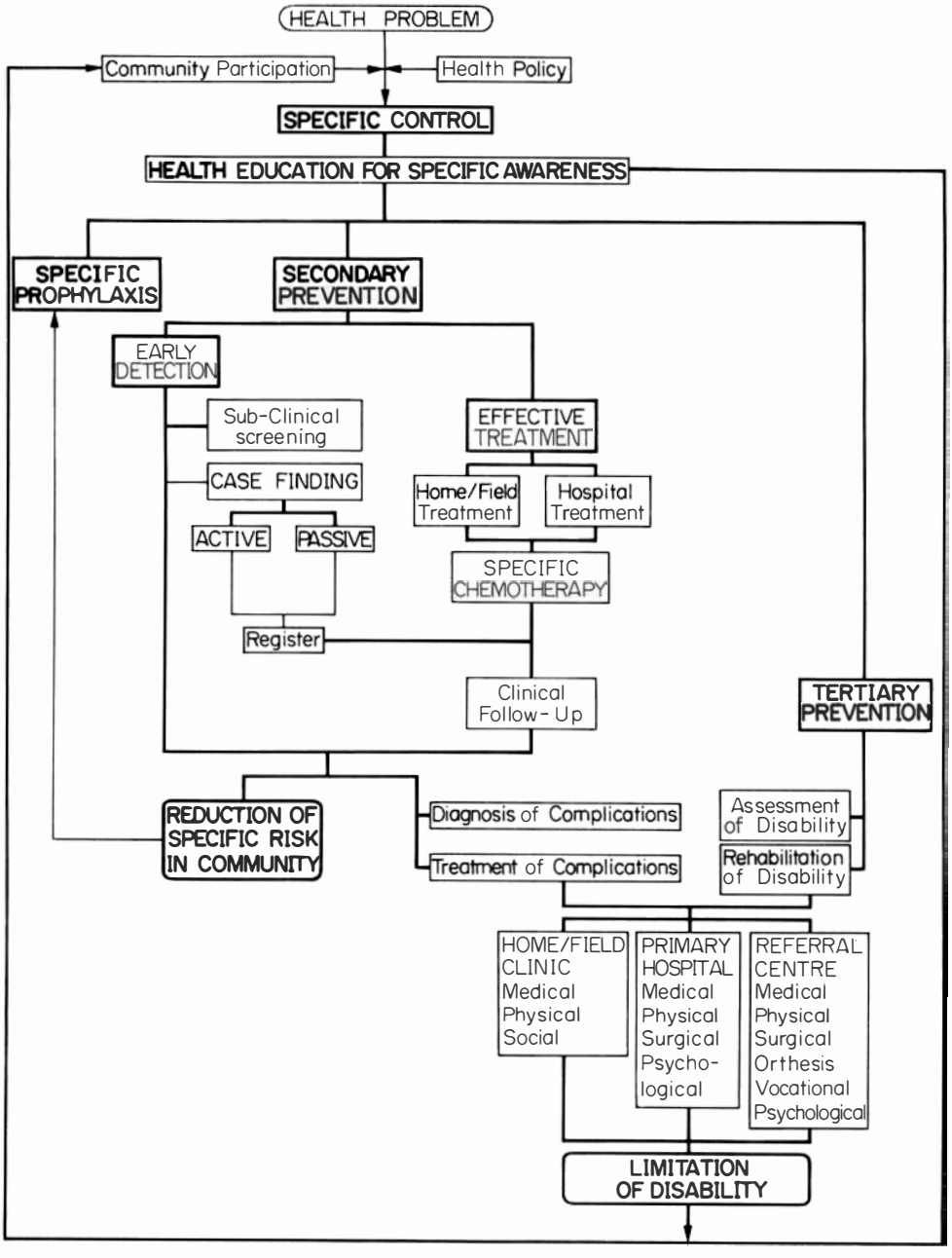

Figure 8. Model for control of infectious diseases based on secondary prevention.

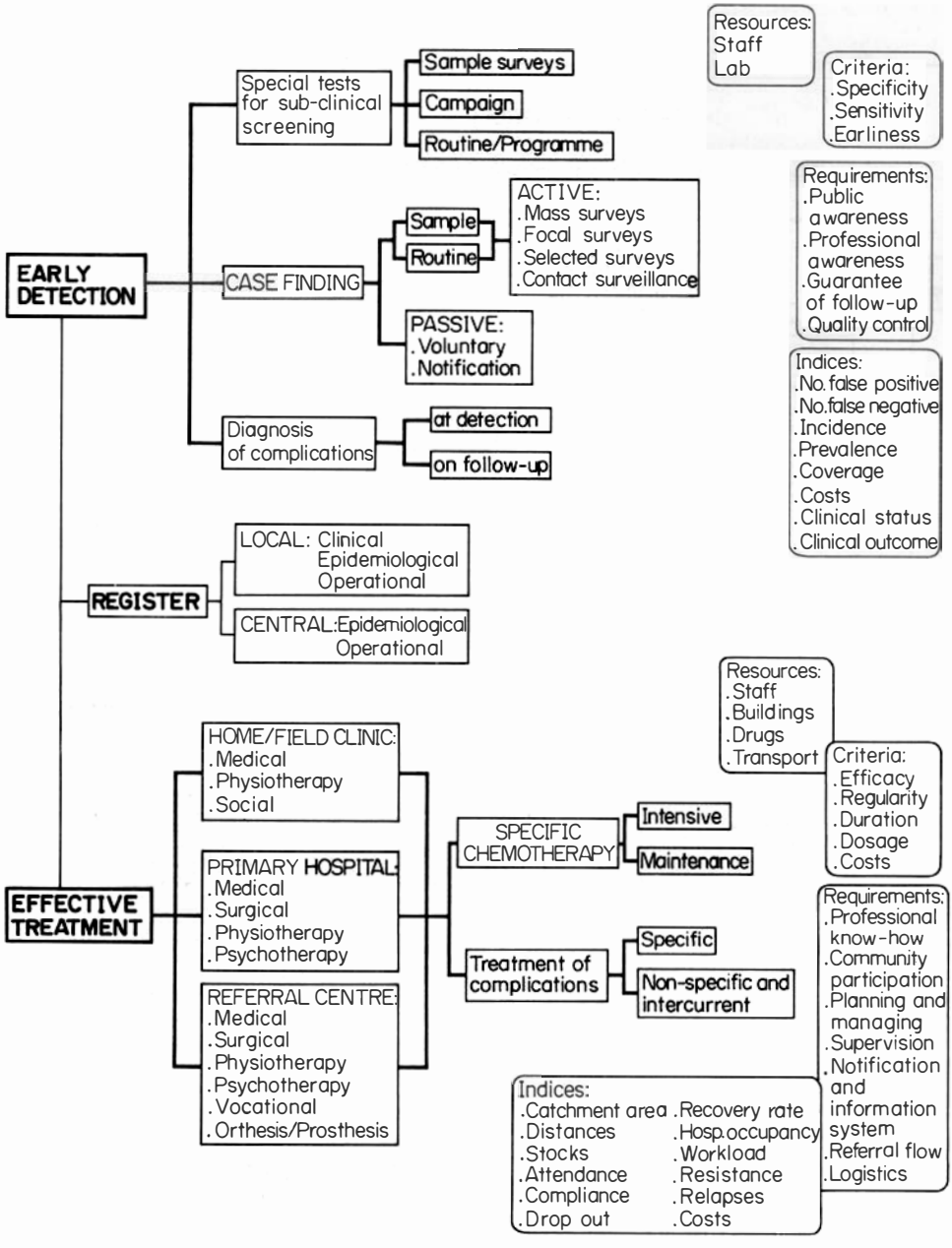

Figure 9. Secondary prevention: activities, resources, requirements, criteria and indices for evaluation.

ISSUE	MOST FEASIBLE INTEGRATION	RATIONALE
ACCESS TO SERVICES: . effective coverage of population . human and material resources . technical know-how . attitudes of staff . attitudes of population	Leprosy and Tuberculosis — Mental disorders Epilepsy — Sex. transm. dis's. Asthma — Diabetes	.Same need for community involvement .Similar problems with patients' attendance and compliance .Same/similar social stigma and demotivation of staff .Same need for lengthy treatment .Same need for updating the curricula
PROMOTION OF HEALTH: . Production — Family planning . Employment — Income . Communications — Housing . Sanitation — Health policy . Health awareness — Education	Leprosy and all 'poverty diseases'	By historically evident relationship
SPECIFIC PROPHYLAXIS: Specific vaccination	Polio, pertussis, tuberculosis, tetanus, diptheria, measles and leprosy	.Same overall strategy .Same target group .Same logistic needs .Similar evaluation problems
Immunological tests	Leprosy and tuberculosis AIDS B-hepatitis	.Same strategic problems .Similar logistic problems .Similar interpretation problems
CASE FINDING: .ACTIVE Mass surveys Focal surveys Selected surveys Contact surveillance	Leprosy and Tuberculosis — Nutritional disorders Epilepsy — Mental diseases Asthma — Hypertension Diabetes — Parasitosis	.Use of multipurpose screenings .Use of basic level screening subject to qualified confirmation .Same interest for community involvement in the case .Same need for immediate family check Laboratory essential for Leprosy and TB
.PASSIVE Regular clinic	Leprosy and skin conditions	.Same clinical branch: diff. diagnosis
TREATMENT and FOLLOW-UP: .HOME/FIELD CLINIC by PH Workers with supervision	Leprosy and Tuberculosis — Diarrhoeal diseases Epilepsy — Hypertension Asthma — Mental disorders Diabetes — Nutritional disorders	.Administration of standard treatment by primary level staff .Same need for compliance control .Same need for family participation .Same need for supervision of treatment .Same need for early diagnosis of complications
.HOSPITAL in general hospital or specialized referral centre	Leprosy and Skin conditions — Trauma sequelae Polio sequelae — Trophic disorders Neurological sequelae	.Need for long-term admission .Many common needs: physiotherapy, surgery, orthesis, vocational therapy, psychotherapy, social rehabilitation health education
EDUCATION FOR HEALTH: .TO GENERAL PUBLIC prophylaxis, early signs; treatment and cure	Leprosy and Tuberculosis — Mental disorders Epilepsy — Sex. transm. Dis's.	.Similar social stigma against disease .Similar social stigma against patients .Similar need for community involvement .Same concern for early diagnosis
.TO THE PATIENT "regular treatment, self esteem, complications"	Lerosy and Tuberculosis — Polio sequelae Trauma sequelae — Neurological disorders	.Similar patterns of treatment .Similar risks of complication .Similar kind of self-care needed
INFORMATION SYSTEM: .EPIDEMIOLOGICAL DATA Local and Central Register	Leprosy and Tuberculosis, malnutrition, all other diseases subject to surveillance	.Same interest in permanent monitoring of Incidence and Prevalence
.OPERATIONAL DATA Activity register (Treatment, Surveys, etc.)	Leprosy control activities and TB control, M C Health Care, EPI	.Same interest in permanent monitoring of coverage, effectiveness, efficacy and efficiency

Figure 10. Leprosy control: how specific items are suitable to cover other conditions (Loretti 1987).

global strategies, when common causes are recognized for otherwise dissimilar problems; practical activities, which are more efficient when directed to more than one goal; and methods, where conditions affecting patients and community in similar ways call for a similar approach and attitude.

As might be expected, conditions appearing most frequently in Figure 10 are other chronic infectious diseases, those carrying loss of self-esteem and those associated with social stigma. The association of leprosy with tuberculosis is already well accepted but what may be new is the idea that any activity relevant to leprosy control can be applied to facilitate access to health care for a number of conditions, and vice versa.

Conclusion

Textbooks teach us that health is an integral entity and that there is no point in stating that 'disease X is like any other disease'—arising from the interaction of various biological, social and economic factors—if in practice we act as if only 'our' disease was real. Indeed, the average man recognizes this in his daily life, albeit unconsciously.

It is proper to give a problem, or even just one of its facets, priority when an effective remedy is available, but care has to be taken not to defeat objectives through the means. Vertical programmes are authoritarian in their definition and essence and have a negative impact upon health awareness, reducing patients to mass consumers of prepacked goods and worse, failing to meet all their felt needs. We all know the result: poor public participation in the programmes and poor patient compliance, both of which we try to improve by health education. Poor public participation contributes to demotivation and deterioration of standards and attitudes on the part of staff and this blatantly contradicts the message of our health education and counterbalances the advantage arising from concentration of effort. Accordingly, an integrated approach to our professional activities contributes more to the growth of awareness in the public than any specific health education programme.

Integration is feasible if supervision, which is a *sine qua non*, can be guaranteed. The current structure of health services in most leprosy endemic countries allows for a suitable distribution of specific activities at various operational levels, so that the features of leprosy control, from policy setting to the most basic tasks, can be exploited for other conditions.

All too often, there is a gap between the political statement of intent, e.g. 'Integration', and its practical implementation. To ensure the optimum utilization of human resources this gap has to be filled by a synthesis between policy and practice and for this, public health as a science, and systems analysis as a method, constitute the most effective tools.

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SPECIAL ARTICLE

Value of thermal sensibility testing in leprosy diagnosis in the field—field trial of a pocket device*

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Summary A handy thermal sensibility testing device has been developed and field tested in different centres in Africa and India. The device performed satisfactorily under field conditions and made testing for thermal sensibility in the field practicable and easy. Examination of the results of testing 260 persons, most of them having a few lesions of early leprosy, showed that the expected increase in the rate of diagnosis of sensory impairment in the skin lesions, and so in the diagnosis of leprosy, would be about 15–25% when thermal sensibility testing using this device was added to the other sensibility tests routinely used in the field. Regular use of this device in the field will help to bring more leprosy patients under treatment than at present.

Introduction

Eliciting impairment in sensibility in a suggestive skin lesion ('patch') is a vital part of clinical examination of a person suspected of having leprosy. In such cases, demonstration of impaired sensibility in the skin lesion clinches the diagnosis of leprosy. It is customary to test for perception of pain and/or touch for this purpose. Any method of sensibility testing will be all right in the later stages of the disease because by then all modalities of sensation will have been impaired. In the early stages, the patch may show dissociated loss of sensibility and in such cases perception of pain and warmth is impaired earlier than that of touch or other modalities.[1-4] However, testing for thermal sensibility impairment is not routinely carried out even in the clinic because the method described for testing, such as using test-tubes with hot and cold water, is cumbersome and time consuming.

The modalities of pain and thermal sensations are subserved through the same, unmyelinated and thinly myelinated (C and A) fibre systems.[5-7] Since infection of individual Schwann cells with *Mycobacterium leprae* is likely to be a random phenomenon, we may expect 'thermal fibres' to be affected first in some cases and 'pain fibres' first in others. By not being able to test for impaired thermal sensibility we will be missing those cases with initial impairment of only that modality. If we can test for impairment of thermal sensibility, particularly in the field where most leprosy work is being carried out, we should be able to identify those with isolated thermal sensibility impairment and bring them under treatment at that stage.

* Lepra wishes to thank the World Health Organization for permission to reproduce this article from the *WHO Bulletin.*

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In view of this, WHO has been helping to develop a thermal sensibility tester suitable for use in the field. Such a tester should be light, easy for field personnel to carry and operate, sturdy, small, not too expensive, capable of attaining a predetermined temperature in a short time and should not consume too much power. The first prototype of such a device was fabricated and field tested in a number of centres in Africa, Asia and South America. Based on that experience an improved second prototype was developed and limited field testing was carried out for assessing the suitability, acceptability and sturdiness of the device. Based on feedback information from the use of these two prototypes, a third and final prototype has been developed. Limited numbers of this device were distributed to some centres in Africa and Asia for testing in the field in order to assess the extent of improvement in diagnostic sensitivity by doing thermal sensibility testing, in addition to the sensibility tests customarily used in these centres. The results of this exercise are reported here.

The device

An earlier prototype device (prototype I) used the body of a pen torch on which a relatively sophisticated electronic head was mounted to control the warm end to a present temperature of 40°C. Field testing using prototype I had shown the potential value of using such a device for the diagnosis of early leprosy, but it was realized that the technical specification, particularly temperature control, and the robustness of the device had to be improved. To cope with these problems it was decided to produce prototype II which was completely different from prototype I. Prototype II had the warm tip temperature as a function of the ambient temperature. Experimenting with a new type of ceramic semiconductor material, it was found possible to develop a special heating element able to control its own temperature according to the desired specification. The advantages of this heating element were simpler and more reliable electronics, smaller power consumption, faster warm-up time, capacity to perform under a range of temperature conditions and lower cost. Prototype III evolved from the previous model after further improving the 'on-off' switching mechanism and the hot tip design. The variable hot tip temperature was chosen so that it was always greater than the skin temperature even for very low ambient temperatures (10°C) but not excessively high (to avoid burning) at very high ambient temperatures (45°C).

Details of the prototype III device are given in Table 1 and in Figures 1 to 4. The device is shown in Figure 5.

Results

The three prototypes were tested in the field as and when they were developed. Prototype III was field tested in Africa and India to find out the extent of improvement in diagnostic sensitivity using thermal sensibility testing and to satisfy ourselves that the device was not degraded by use.

Data covering 319 people participating in this field trial of prototype III were received from 6 centres (3 from Africa and 3 from India). The findings from one centre regarding 59 people were non-informative but the findings on the remaining 260 people from the other 5 centres are presented here.

The study included both sexes and practically all ages. The duration of patches in these 260 people was under one year for 172 people, one to two years for 31 and more than two years for 17. Information was not available for 40 people.

The clinical diagnosis of the skin lesion is given in Table 2. In over 80% of instances the clinical diagnosis was tuberculoid, indeterminate or 'suspicious' and of all the patients about one half had single lesions while the remainder had two or more. Sensibility testing was done on one lesion in 184 persons, on two lesions in 41 and on three lesions in 35.

Sensibility testing for touch was routinely used in all the centres and the pinprick test for pain perception was also in use in 4 of the 5 centres. Thus all three modalities of sensation were tested on

Table 1. Thermal sensibility tester technical specifications.

Battery types	Preferably rechargeable 1·2 V nickel–cadmium types OR 1·5 V good quality alkaline
Battery size	AA-R6-UM3-MIGNON
Power consumption (still air)	(approx.) 240 mA at ambient temp. 15°C 200 mA at ambient temp. 25°C 120 mA at ambient temp. 45°C
Typical hot tip temperature	45°C at ambient temp. 15°C 50°C at ambient temp. 25°C 60°C at ambient temp. 45°C
Recommended working temp. examinations	10°C to 45°C ambient temp.
Time before use after power on	15 sec. for amb. temp. > 15°C 30 sec. for amb. temp. < 15°C
Power ON–OFF	POWER IS ON: When button end is turned fully clockwise until end stop. POWER IS OFF: When button end is turned anticlockwise until dotted line is visible.
Recommended min. battery voltage before recharge or change or change	1 V each battery
Dimensions	Tip size 7 mm diameter. Body length 133 mm. Body diameter 22 mm. Area exposed to the skin 38·5 mm^2.
Weight	83 g without batteries

210 people only, although thermal sensibility testing using the tester device was carried out on all 260 people.

First, the findings are given taking the skin lesion as the unit of observation and then they are given taking the individual as the unit of observation.

Observations on skin lesions

Pain, touch and thermal sensibility had all been tested on 263 skin lesions of 210 people. Information regarding 8 lesions (on 6 people) was incomplete and therefore analysis of comparison of all three modalities of sensation is based on 255 lesions in 204 persons (Table 3).

The capacity of the different modalities of sensory loss and their combinations to identify early lesions is shown in Figure 6.

Observations regarding persons

The above observations relate to individual skin lesions. It will be evident that when more than one lesion is tested in a person, that person would be identified as having sensory impairment (and so as a case of leprosy) even if it were demonstrated in only one of the lesions. Therefore the data were re-examined keeping the person, and not the lesion, as a unit. As mentioned earlier, four of the five centres routinely used tests for pain and touch sensibility, whereas one centre used only touch

Figure 1

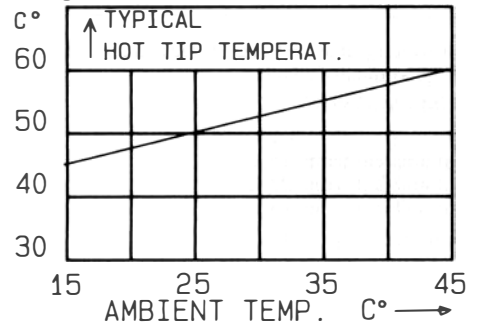


Figure 2

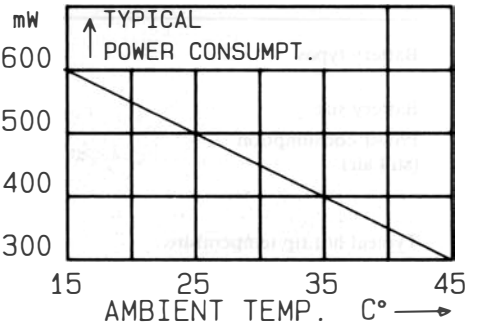


Figure 3

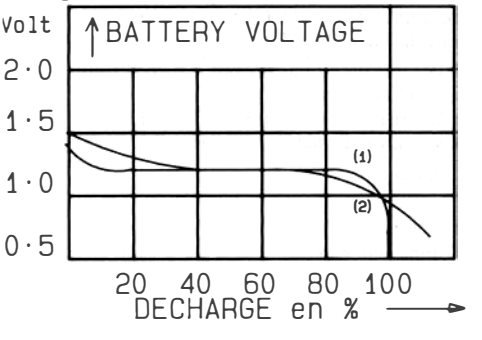
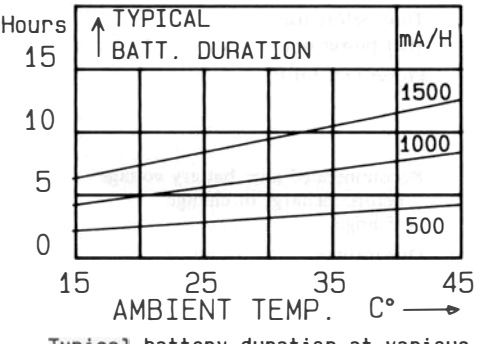


Figure 4



(1) Typical battery discharge characteristics for rechargeable "NICKEL-CADMIUM" batteries .

(2) non rechargeable "ALKALINE-MANGANESE" battery types .

The use of rechargeable batteries is recommended for following reasons :
- lower operational costs
- flatter decharge characteristic
- smaller waste disposal problems

Minimum battery voltage before change or recharge 1V . (Each battery) .

- Typical battery duration at various ambient temperatures and different capacity.
- A standard rechargeable battery has a capacity of 500 mA/Hours.
- A good quality ALKALINE battery can have a capacity of 1500 mA/Hours.

EXAMPLE :
* At 30 C° a rechargeable battery (500 mA/H) will last 3.1 hours.
* At 30 C° a standard Alkaline battery (1000 mA/H) will last 6.2 hours .
(Mean battery voltage 2, 5v)

Figures 1–4.

sensibility for recognizing sensory impairment. Table 4 shows the pooled findings from the four centres using routine pain and touch sensibility tests.

The capacity of the different modalities of sensory loss and their combinations to identify early cases of leprosy is shown in Figure 7.

Discussion

Successful leprosy control depends on effective treatment with multidrug therapy[8] and early

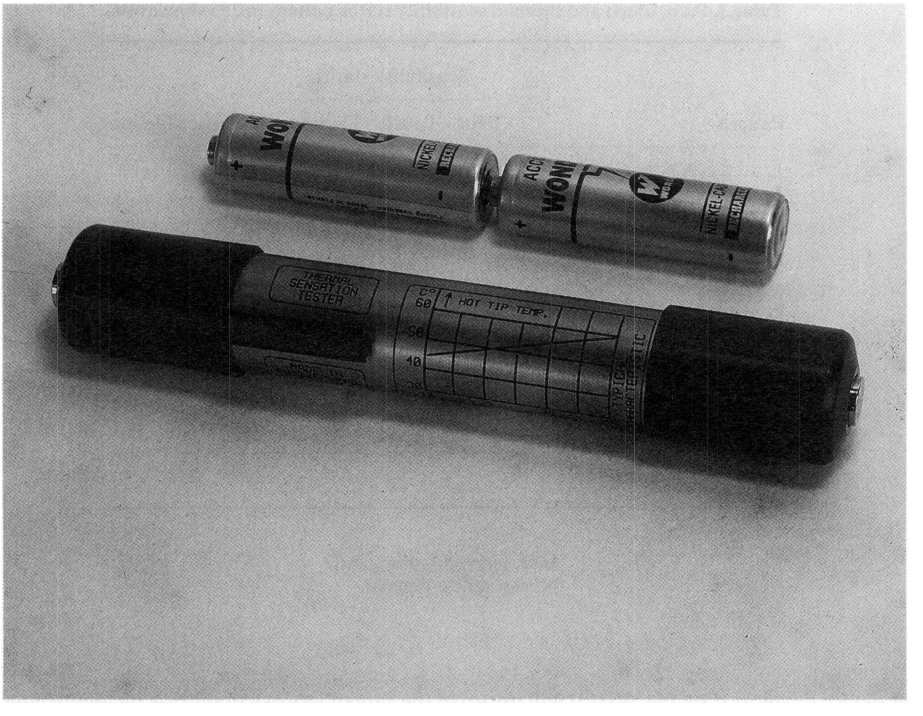


Figure 5. Thermal sensibility tester.

Table 2. Clinical diagnosis of skin lesions

Clinical diagnosis	Number of people
'Suspicious'	51
Indeterminate	22
Tuberculoid	64
Tuberculoid (borderline)	79
Borderline	5
Lepromatous (borderline)	9
Lepromatous	29
Not recorded	1
All diagnoses	260

diagnosis of all cases. The addition of thermal sensibility testing to the other sensibility testing procedures in routine use in the field may be expected to meet the need for improving the rate of leprosy diagnosis and for bringing additional numbers of patients under effective treatment. This has not been possible so far because the method of testing for thermal sensibility in the field was not practicable.

The present investigation was not an academic enquiry about the pattern of impairment of thermal or other sensibility. It was a pragmatic exercise with the operational aims of finding answers to two questions: (i) To what extent the addition of thermal sensibility testing in the field (using the

Table 3. Pain, touch and thermal sensibility status pattern in 255 skin lesions

	Sensibility status			
Pattern	Pain	Touch	Thermal	Number of lesions
1	Imp.	Imp.	Imp.	132
2	Imp.	Imp.	N	8
3	Imp.	N	Imp.	13
4	Imp.	N	N	7
5	N	Imp.	Imp.	6
6	N	Imp.	N	3
7	N	N	Imp.	27
Lesions with impairments	160	149	173	196
Lesions with no impairments: Pattern 8	N	N	N	59
Total lesions tested				255

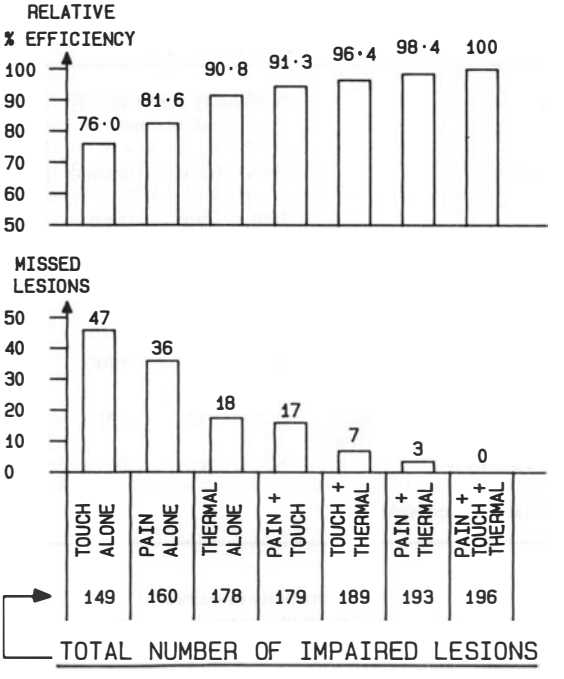
Imp, sensibility impaired.
N, sensibility normal.

tester device developed by the WHO) will improve the rate of leprosy diagnosis by identifying cases of isolated impairment of thermal sensibility in the skin lesions? (ii) Is it feasible to use this tester device in the field for this purpose?

In order to find answers to these questions, the device had to be tested by different people in different parts of the world, under a variety of field conditions. Therefore a multicentric trial was planned and the participants were requested to carry out thermal sensibility testing *in addition to the tests they were routinely using in the field.* It was gratifying to note that clear answers to both the questions have emerged from this study.

Performance of the device

All the investigators felt that the performance of the device was quite satisfactory. It was easy to carry and it made thermal sensibility testing simple and feasible in the field. The size of the warm end (7 mm diameter and 38·5 mm^2 area) was suitable for testing all but very small lesions. Power consumption was not excessive and ordinary leak-proof pen torch cells, which were used in most centres, needed to be changed after testing 50–70 people, dependent on the type of battery and ambient temperature. However, when the ambient temperature was very low, in the range of 10°–15°C or lower, it naturally took longer to warm up and the drain on the cells was heavy, making it difficult for some types of batteries to deliver the current needed during the warm-up period. This problem could be solved by using rechargeable batteries for which the unit cost per test is cheaper. When rechargeable batteries are used the additional investment cost is expected to be about US$25.00 which would include the cost of a battery charger, two sets of two rechargeable batteries and a battery checker. The cost of the thermal tester will be around US$35.00. A set of rechargeable batteries can be charged over 500 times which means that two sets can be used for over 50,000 examinations at the rate of 50 examinations per charge. The cost of electricity to charge for 1000 times ($2.00) together with the cost of the charger and battery checker is US$27.00 which enables



Relative efficiency of touch , pain and thermal methods when the total number of impaired lesions found by all three methods together (196) is set to be 100% .
A total of 255 lesions was examined

Figure 6.

the unit cost per examination to be limited to only \$0.00054. On the other hand, if non-rechargeable batteries are used, then at the rate of \$1.00 per set of 2 good quality batteries and at the rate of 70 examinations per set, the unit cost would be approximately \$0.014. Thus, the use of rechargeable batteries enables the cost to be reduced by a factor of about 26. In addition, the use of rechargeable batteries markedly reduces the problem of waste disposal.

The other problem in the tester occurred when the ambient temperature was above 40°C, then the temperature difference between the so-called 'cold' end and the 'warm' end was relatively less and it was not always easy to distinguish the 'cold' from the 'warm' end which was what the patient had to do in this test.

Advantage of including thermal sensibility testing

One may expect that inclusion of thermal sensibility testing would identify more people who had sensibility impairment, but so far there has been no way of knowing what this additional number is. In this study, the routine tests for light-touch and pin-prick pain identified 132 people as having

Table 4. Pain, touch and thermal sensibility status in 204 people taking the individual as a unit of observation

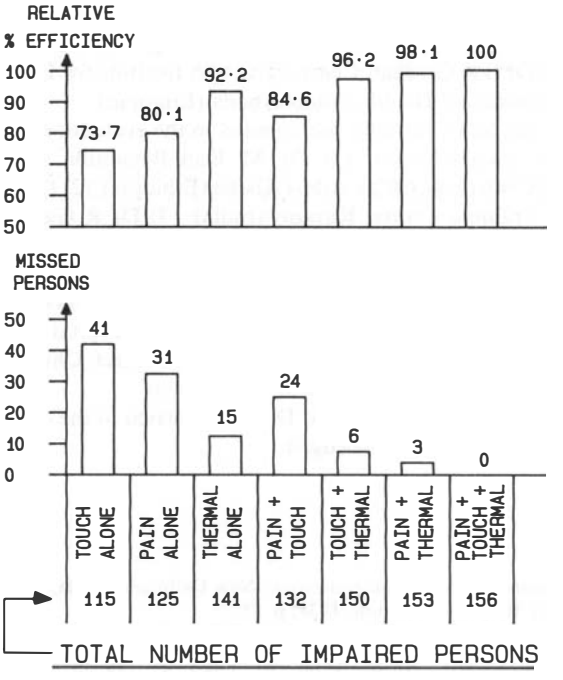
Pattern	Sensibility status in any or all lesions			No. of people
	Pain	Touch	Thermal	
1	Imp.	Imp.	Imp.	102
2	Imp.	Imp.	N	6
3	Imp.	N	Imp.	11
4	Imp.	N	N	6
5	N	Imp.	Imp.	4
6	N	Imp.	N	3
7	N	N	Imp.	24
People with impairment	125	115	141	156
People with no impairment: Pattern 8	N	N	N	48
Total people tested				204

Imp, sensibility impaired.
N, sensibility normal.

sensory impairment (Table 4, patterns 1–6) and 72 (Table 4, patterns 7 and 8) as not having sensory impairment. Thermal sensibility testing, using the tester device, revealed that 24 of these 72 people (33%) had in fact impaired (thermal) sensibility (pattern 7). The addition of thermal sensibility testing thus led to a substantial improvement in the rate of diagnosis, from 132 to 156, i.e. by about 15%. It appears that we can improve the rate of diagnosis by about 10–20% by adding thermal sensibility testing to the other tests routinely used in the field. It will therefore be worthwhile to do so.

Comparing the relative efficacy of touch and thermal sensibility testing, we find that of the 156 patients with one or other type of sensory loss only 115 (73·7%) were identified as having sensory deficit by testing for touch perception, whereas thermal sensibility testing identified 141 (90·4%) as having sensory deficit. The addition of thermal sensibility improved the rate of diagnosis substantially, from 115 to 141, i.e. by 18% (Table 4). It should also be noted that of the 150 people identified as having impaired sensibility for either light-touch or thermal (patterns 1 to 3 and 5 to 7), isolated loss of perception of light-touch was found in only 9 (pattern 2 and 6) while this modality was spared in as many as 35 persons (patterns 3 and 7). It is clear that testing for touch is the less sensitive of the two tests for assessing sensibility status in leprosy lesions.

Pinprick pain perception test is commonly used in the field for identifying sensory impairment in lesions suspected to be due to leprosy. Comparing the relative efficacy of pinprick and thermal sensibility tests, we find that of the 156 persons with one or other type of sensory loss, 125 (80·1%) had loss of pain, whereas testing for thermal sensibility identified 141 (90·4%) as having impaired sensibility. Again, taking only these two tests into account, it is seen from Table 4 that 12 people showed only loss of pinprick pain perception (patterns 2 and 4) and 28 showed only loss of thermal sensibility (patterns 5 and 7) in their lesions. Thermal sensibility testing alone would have missed the former 12 cases and pinprick test alone would have missed the latter 28 cases. Lesion-wise a substantial number of those that gave a negative result to pinprick testing, no loss of pain, had impaired thermal sensibility. Notwithstanding the above, the pinprick has the merit of being extremely cheap and simple. Hence we feel it should continue to be used.



Relative efficiency of touch , pain and thermal methods when the total number of impaired persons found by all three methods together (156) is set to be 100% .
A total of 204 persons was examined

Figure 7.

Conclusion

From this multicentric field trial we can therefore conclude that the addition of thermal sensibility testing increased the relative efficiency by up to 25%, depending on which combination of tests were used. The thermal sensibility tester developed and tested in this trial will therefore be a suitable instrument for use in the field for this purpose.

Acknowledgments

The development and field testing of the thermal tester were supported by the Leprosy Unit, Division of Communicable Diseases, WHO, Geneva.

The contributions of the following investigators who participated in the evaluation of the final version of the tester is gratefully acknowledged: (1) Dr M D Gupte, Central JALMA Institute for Leprosy Field Unit for Epidemiology of Leprosy, Madras (India); (2) Dr N N'Deli, Institute Raoul

Follereau D'Adzopé, Adzopé (Côte d'Ivoire); (3) Dr V K Pannikar, Schieffelin Leprosy Research and Training Centre, Karigiri (India); (4) Dr J M Ponnighaus, LEPRA Evaluation Project, Chilumba (Malawi); (5) Dr B K Girdhar, Central JALMA Institute for Leprosy, Agra (India); and (6) Mr Tadele Tedla, Ministry of Health, Addis Abada (Ethiopia).

The contribution of the following who participated in the evaluation of the earlier versions of the tester is gratefully acknowledged: (1) Dr M Becx-Bleumink, All Africa Leprosy and Rehabilitation Training Centre (ALERT), Addis Ababa (Ethiopia); (2) Dr M Christian, Schieffelin Leprosy Research and Training Centre, Karigiri (India); (3) Dr R Ganapati, Bombay Leprosy Project, Bombay (India); (4) Dr Lim Kuan Joo, National Leprosy Control Centre, Sungai Buluh (Malaysia); (5) Dr P N Neelan, Central Leprosy Teaching and Research Institute, Chingleput (India); (6) Dr J O Nyawalo, Alupe Leprosy Centre, Busia (Kenya); (7) Dr P Ochasanond, Ministry of Public Health, Bangkok (Thailand); (8) Dr D Opromolla, Hospital "Lauro de Souza Lima", Bauru (Brazil); (9) Dr J M Ponnighaus, LEPRA Evaluation Project, Chilumba (Malawi); and (10) Dr M Zuniga, Instituto de Biomedicina, Caracas (Venezuela).

The contributions of Mr M J O'Regan and Dr H Sansarricq in the development of the earlier versions of the tester is gratefully acknowledged.

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Obituary

BISHOP THOMAS McGETTRICK DD
1905–1988

After 50 years of dedicated service to the people of Ogoja, Nigeria, Bishop Thomas McGettrick died aged 83. He first came to Nigeria in 1930 and in 1939 was appointed to Ogoja. In Ogoja Province at that time there was an estimated 42,000 leprosy patients. As there was only one doctor the Government was unable to deal with the then large scale problem of leprosy. Bishop McGettrick's compassion for these leprosy patients and his desire to do something for them, prompted him to begin fund raising in Ireland, his native country. He ran a raffle for the 'Leprosy Scheme' and raised £12,000. He invited Dr Joe Barnes to initiate the care of the leprosy patients and the control of the disease in Ogoja. He invited the congregation of Medical Missionaries of Mary, Ireland, to provide the necessary medical and nursing care under Dr Barnes' direction and supervision. They came to Ogoja in 1946 and the Central Hospital, at Moniaya Ogoja, was opened with wards in which the very ill could be cared for. As segregation of leprosy patients was the order of the day, a village to provide homes for them was started at Moniaya. As a result of negotiations with the Clan Heads similar villages with treatment centres were set up in every clan area and local staff were trained to care for the patients. In 1947, the leprosy treatment centre and hospital were opened at Mile 4, Abakaliki. Since those days leprosy patients in the area have received constant treatment, and now we see the fruit of those labours in the effective control of leprosy in the area.

Bishop McGettrick held in high esteem the leprosy patients, the work and the workers, and throughout his administration made adequate financial provision for the continuous treatment and care of the patients. His care and concern for the sick and suffering did not end with the leprosy patients. He opened general hospitals and maternity hospitals supporting and providing for the establishment of clinics and maternity homes in the rural areas.

Although initially the maternity hospitals were opened to provide for the pregnant leprosy patients, more and more women availed themselves of the facilities both in the hospitals and the rural clinics—so began the long slow struggle for integration of leprosy control into the basic health services and the breakdown of the stigma attached to the disease.

After the trauma of the Civil War, 1966–71, he spear-headed the relief for the war victims and established throughout the Diocese feeding centres and clinics to provide for their needs.

Bishop McGettrick lived through the years of development of leprosy control from the days of Chaulmoogra oil injections to the present use of effective MDT therapy. Throughout, he gave encouragement and support.

May we be inspired by his great qualities of compassion, dedication and zeal to continue the work which he began.

C BOURDILLON

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Letters to Editor

EYE LESIONS IN LEPROSY—GLAUCOMA AND TENSION

Sir,

In the article by Soshamma and Suryawanshi, Eye lesions in leprosy, *Lepr Rev* 1989; **60:** 33–8, there are the following statements: 'Glaucoma has been reported to be rare in leprosy,' and 'Tension was assessed digitally.'

Firstly, there is the misconception in the literature on ocular leprosy that glaucoma is rare or uncommon in leprosy patients. At the GWL Hansen's Disease Center, Carville, LA, USA, 39 of the 190 inpatients are being followed as glaucoma or as glaucoma suspects. That is 20·5% of the hospital population, and that percentage is many times greater than the incidence in the general (non-leprosy) population.

Secondly, digital assessment of intraocular pressure through the eyelids is not an accurate method and should be discouraged. For example, I would challenge any examiner to determine with consistency the difference in ocular pressures of 20 and 26 mm Hg: 20 mm Hg is normal; 26 mm Hg is dangerously high.

VAN C JOFFRION

Department of Health & Human Services
Public Health Service
Gillis W Long Hansen's Disease Center
Carville, LA 70721
USA

WOUND HEALING AND TREATMENT OF ULCERS IN LEPROSY

Sir,

I am pleased to read of the good results obtained using sugar paste in the treatment of abscess cavities and pressure sores as related in L. A. Wiseman's letter, *Lepr Rev* **60:** 1989; 67–8.

This has encouraged me to share my experience of wound healing in leprosy ulcers using silver-sulphadiazine cream. A study conducted of 30 cases of such non-healing ulcers of predominantly leprosy origin, showed remarkably good results (83%) in a relatively short period—4 weeks. This is attributable to the beneficial antibacterial effect of zinc sulphadiazine which, although much cheaper, has an almost similar action to topical silver sulphadiazine. In addition, the role of zinc per se in the process of wound healing has been recognized since time immemorial.

I feel, that apart from other aspects of wound healing, clinical trials of such innovative measures do have a role in the management of such recalcitrant and chronic leprosy ulcers. Knowledge of such a vital but day-to-day common problem should be pooled in order to have a better striking potential because with the effectiveness of MDT., non-healing ulcers require better attention so as to rehabilitate the patient and enable them to return to work.

B M S BEDI

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New Delhi 110001
India

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Book Reviews

Manual for field treatment of leprosy reactions. **Second revised version**

As nerve damage is the most important cause of deformity and disability in leprosy, early and adequate treatment of nerve reactions is essential, and ALERT produced in April 1987 a standardized scheme for diagnosis and treatment in field clinics (where reactions are usually first seen), which was found 'feasible and fairly successful'. The Director of Leprosy Control states in the Preface that this manual, although applicable in Ethiopia, is not intended to be an authoritative document for general use, and he would welcome comments from leprosy workers in other countries.

The pages in this manual cover all the problems associated with leprosy reactions as observed in field clinics, and basing treatment on the use of prednisolone alone in reversal reaction (RR) and on prednisolone combined with clofazimine in ENL reaction. Every possible eventuality has been covered, and detailed advice is given to clinic supervisors and to health assistants on routine steps to take on recording their findings, on when to admit to hospital, on initiating and supervising treatment in field clinics, and on follow-up care. It is emphasized that all these aspects included in the manual are routinely taught in seminars.

Appendices include advice on the treatment of some common conditions not related to leprosy, on the diagnosis of tuberculosis, and on ophthalmic complications of leprosy.

W H Jopling

Published by ALERT, Addis Ababa, Ethiopia, 1989. 40 pp.

A history of leprosy in Tanzania. **Knud Balslev**

The author, a leprologist who worked in Tanzania from 1970 to 1986, has performed a valuable service in producing this account of the history of leprosy in that country. He covers four periods: pre-colonial times dating from 1888 when the first attempt at leprosy work was made by the French Holy Ghost Mission; the period when the country was German East Africa, 1891–1914; when it was Tanganyika Territory under British administration 1914–1961; and the post-independence period from 1961, when the name was finally changed to Tanzania.

The number of leprosy cases remained stable up to 1950, but there was an explosive increase in the 1950's from 4,468 in 1950 to 28,727 in 1958, and a further rapid increase from 28,289 in 1962 to 64,170 in 1968, after which the numbers dropped to 31,659 by 1977. The author clearly illustrates the co-operation between Government and missions in leprosy treatment and control, and highlights the important work of Dr James Ross Innes between 1947 and 1953, and of Dr Harold W. Wheate between 1956 and 1972. He describes the founding of the National Leprosy Advisory and Co-ordinating Committee (NLACC) in 1967, the East African Leprosy Association in 1970, and the National Tuberculosis and Leprosy Programme in 1977 which instituted treatment of both diseases at every medical unit in the country, notably the rural dispensaries.

An Appendix contains the names and locations of leprosy institutions and out-patient control schemes, together with a useful map.

W H Jopling

Published by African Medical and Research Foundation, P. O. Box 30125, Nairobi, Kenya, 1989. Available free from the publisher on request, 52 pp.

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Teaching Materials and Services

Leprosy: basic information management

The second revised edition of this booklet, intended as a source of basic information for non-medical readers including community leaders, social workers, teachers, students and journalists, was produced in English in 1989 and has already been widely circulated. A translation into French is currently in hand and approval recently obtained for Spanish; both should be completed before the end of 1989, with the possibility of publication in early 1990. Apply: Medical Department, Ciba-Geigy Ltd, CH-4002, Basle, Switzerland.

MEDUNSA: Medical University of Southern Africa

The following information is extracted from the University 'brochure' and the 1989 Teaching programme for medical students:

'From a white population in South Africa of 4·5 million, there are 21,000 qualified doctors, who serve people of all races throughout the country. From an African (black) population of 24 million, there are less than 1000 qualified medical practitioners.

There are 3500 qualified dentists in South Africa of whom only 18 are Africans. Of the approximately 1500 qualified veterinarians in the country, only two are Africans.

The Medical University of Southern Africa was established in 1976 to start to correct this imbalance and to fill the dire need for black health professionals.

The aim of the University is to train, each year, 200 doctors, 50 dentists, 50 veterinarians and 300 supplementary health-care personnel to the standard of any others trained in the country. Students have to comply with the requirements of the Medical and Dental Council, the Veterinary Council or the Nursing Council as appropriate and graduates are registered with those bodies on a par with their professional colleagues. This will call for a total enrolment of almost 5000 students per year against the 1988 student population of 1407.

Utilising existing facilities and personnel, the Faculty of Basic Sciences will begin functioning in 1989 thus contributing to the alleviation of the dire shortage of qualified science teachers in southern African schools.'

The basic philosophy of the MEDUNSA Medical School is described below:

'The Faculty of Medicine of the Medical University of Southern Africa states that a basic philosophy on undergraduate education is of prime importance in defining the task of the Faculty. The basic philosophy influencing undergraduate medical education at Medunsa is outlined below.

The Faculty should derive its objectives from health care, giving due emphasis on the needs of communities, families and individuals.

The Faculty must aim to raise the standards of the health care system of which it is part, making the most efficient use of the available human and physical resources. This should be done with due recognition of the needs of the students and Faculty itself.

The Faculty must exert influence on the educational and health care systems by contributing, in the form of research and experimentation, to the acquisition of the best possible structure for, and procedures in, the health care area. Research is necessary in relation to the supply and demand of

health care delivery and in connection with such matters as the definition and co-ordination of tasks; the education and training of doctors and other health care workers.

Based on these premises the Faculty further states that its philosophy on undergraduate education includes the following principles:

The end-product of undergraduate education and training must be a graduate who has acquired the knowledge, skills and attitudes, necessary to equip him for further vocational training in any direction open to the application of medical expertise.

Since the fundamental objective of graduate education and training is to produce a health professional who can think for himself and be able to make professional judgements, his education and training must be related to this primary objective. This means emphasising learning rather than teaching by promoting curiosity, awareness, precision of thought and expression. He must be made aware of the natural order of things and be taught how to collect and assess evidence. The manner of achieving these aims is to set clear objectives for students in some detail, and to plan a strategy to be used in the acquisition of these objectives.

The graduate must be able to participate effectively as a member of any health care team. He must have a balanced attitude to medicine which is a blend of the scientific and the humanitarian. For this reason the undergraduate training programme must equip him with certain communication skills and offer him a grounding in the human sciences.

The graduate should be motivated to remain a student all his life. The medical school should impart a core of concepts, knowledge and skills on which health professionals base their future self-education. This is best served by a broad education also in the biological sciences, clinical disciplines and skills, the psycho-social and socio-economic aspects of medicine, and in preventive medicine.

The ultimate objective must be to produce a health professional with empathy and concern for the whole person in his environment. The objective should meet academic requirements as well as the specific needs of the Southern African community. Respect and sensitivity for medical ethics and human life must also be fostered.

Assessment of progress must be part of the learning process and much of it must be planned self-assessment. Assessment should seek to promote learning.

The teachers should, in addition to maintaining a high standard of proficiency in their own field, continue to acquire knowledge, insight and skills which will prepare them for their role as effective teachers. They should be prepared (and given the opportunity) to attend relevant training.'

Contact: The Secretary, MEDUNSA Medical School, Near Pretoria, South Africa.

Graves Medical Audiovisual Library

This well known organization now supplies videocassettes, tape–slide programmes, slide sets, audiotapes and computer software booklets. The following information has recently been received:

'Graves Medical Audiovisual Library was started by Drs John and Valerie Graves in 1957. The library, formerly known as The Medical Recording Service Foundation, became the premier organization supplying audiovisual materials for the medical and paramedical professions.

Graves is a non-profit making educational charity whose aims are to make available all kinds of audiovisual materials for loan and sale and also to encourage new developments in medical and paramedical education.

In the past we were mainly associated with the distribution of tape–slide programmes, teaching slide sets and audiocassettes but we now have a rapidly expanding list of videos. Computer software and videodisc are examples of some of the newer media with which we are involved.

Our programmes come from several sources; many of them have been produced by ourselves, others have been made in medical schools and schools of nursing. We collaborate with professional bodies and organizations in producing and distributing programmes on their behalf. We are always pleased to hear of programmes that have been made for local needs which might be of value to others. We pay authors/producers royalties on all sale and hire income.

Single slides for teaching or publication are available from The National Medical Slide Bank, a new resource recently created by Graves. It is a collection of over 10,000 35 mm slides of all aspects of clinical medicine. Full details will be supplied on request.'

Apply: Graves Medical Audiovisual Library, Holly House, 220 New London Road, Chelmsford, Essex CM2 9BJ, England.

Leprosy control in South Africa

The Leprosy Mission (Southern Africa) recently organized a series of seminars in departments of health and hospitals in the homelands of Boputhatswana, Qwa Qwa, Ciskei, Transkei and Kwazulu in order to raise the level of awareness with regard to leprosy and to encourage further participation by members of the health services. The audiences included registered hospital and community nurses, doctors, physiotherapists, occupational therapists, laboratory technicians, medical students and administrators. Didactic teaching on the 'basics' of leprosy was reinforced by the distribution of appropriate booklets from TALMILEP (The Secretary, TALMILEP, German Leprosy Relief Association, P.O. Box 348, D-8700, Würzburg, West Germany) and the 9 panels on leprosy produced by the Wellcome Tropical Institute (200 Euston Road, London NW1 2BQ). The WHO *Weekly Epidemiological Record*, 1979 (No. 3) gives a total figure for registered cases of leprosy in South Africa of 16,000 in 1975, but there is currently a need to obtain up-to-date information on the number of active and inactive cases, together with disability and child rates, in the country generally, taking into account the presence of nearly half a million refugees from Mozambique, the progressive trend towards urbanization and the considerable population movement both within South Africa and from neighbouring countries. Since Westfort Leprosarium opened in 1897, over 20,000 cases of leprosy have been referred and treated there, 1600 of them in the past 10 years. Multiple drug therapy using dapsone, clofazimine and rifampicin is widely available for all cases on an outpatient basis, both at Westfort and elsewhere. Locally produced blister–calendar packs are in use (see 'Calendar–blister packs for multiple drug therapy in leprosy; an inexpensive, locally produced version', Letter to the Editor, L A Wiseman *Lepr Rev*, 1987; **58:** 85–9), and a local BATA factory has produced highly acceptable canvas shoes with space for a microcellular rubber insole. Further information: The Executive Director, The Leprosy Mission (Southern Africa), PO Box 890527, Lyndhurst, JHB 2106, South Africa.

OXFAM–LEPRA packs of teaching–learning materials, 1982–88

In early 1982, it was apparent that a very considerable range of teaching–learning material for leprosy was available and following discussion between representatives of OXFAM and LEPRA in Oxford, it was decided to assemble a 'package' of carefully selected items, mainly as basic information, but also to help nursing and paramedical tutors and other senior staff with responsibility for teaching. The pack consisted of books, booklets, WHO publications, transparency–text teaching sets and sample copies of leprosy journals, all in English. Twenty-five were made up in the first instance; a few were donated to key institutions, training centres and control programmes, but most were sold at £15·00 per pack, plus postage. Distribution was handled by the Health Unit in Oxfam, greatly aided by a retired pharmacist in Aylesbury, Mr Phillip Sadler, and a group of volunteers. It was almost immediately clear that there was a substantial and continuing demand for more packs and during 1982 and 1983, 200 were assembled and sold to individuals, training centres, medical and paramedical schools in virtually all leprosy-endemic areas. By late 1983/early 1984, new publications were available and it was decided to change to a smaller pack containing 10 items at a cost of £10·00. By the end of 1987, approximately 600 of these had been sold, again with world wide coverage, bringing the total of items distributed from the Oxfam Health Unit to well over 10,000 since 1982. Partly because demands were by this time dropping, but mostly because of the development of the TALMILEP system for the distribution of health learning materials for leprosy through the *International Federation of Anti-Leprosy Associations* (ILEP), it was decided to tail off and stop this service in early 1988. No systemic enquiry was ever attempted to

find out how the packs had in fact been used, but the impression is that they were particularly valuable to teachers as a source of basic information from reliable authors and agencies. In retrospect, the most remarkable and unexpected element in this project was the revelation, early on, that hundreds of people wanted to obtain a pack and were unhesitatingly prepared to pay for it.

Global surveillance and forecasting on AIDS

A summary of the 'Update' article in *Bulletin of the WHO*, 1989; **67:** 1–7 reads as follows:

'The short-term forecasting of future AIDS cases has been attempted by statistical extrapolations of the observed curve of reported AIDS cases. In areas where such reporting is very incomplete or has only recently started, extrapolation is not possible and an epidemiologically-based forecasting model has been developed to estimate the annual number of AIDS cases which may have occurred, and to project the annual number and distribution of AIDS cases for up to ten years. This model, which relies on the current understanding of the epidemiology and natural history of HIV infections, and on the available HIV serologic survey data, is used to provide estimates and short-term projections of AIDS cases for the USA, Europe, Africa and the world.

Because of the very long (mean of 8–9 years) incubation period between HIV infection and the development of AIDS, new cases over the next five years will be mostly derived from persons who became infected with HIV in or before 1987. WHO has estimated that 5–10 million persons worldwide were infected with HIV in 1987. Based on the lower estimate of 5 million, the cumulative number of AIDS cases which can be projected for the end of 1991 is over one million, and for the mid-to-late 1990s could reach 2 to 3 million.

HIV/AIDS will therefore be an increasing public health problem throughout the world. Health care systems everywhere will have to be strengthened to respond to this large toll of disease and death due to AIDS.

Technical guide for smear examination for leprosy

The first edition, in English only, was produced in 1983. A second, revised edition was published in 1987. Translations are available in French, Spanish, Turkish, Arabic, Thai and Bengali. Translations into Portuguese, Indonesian and Hausa (the latter for West Africa, mainly Nigeria) are in hand. English and Spanish versions may be obtained from TALMILEP, German Leprosy Relief Association, PO Box 348, D-8700, Würzburg, West Germany; French from Association Française Raoul Follereau, 31 rue de Danzig, Paris 15e, France; Turkish from Professor Saylan, I.U. Istanbul Tip Fakultesi, Dermatoloji Anabilim Dali, Baskanligi, Capa-Istanbul, Turkey; Arabic from the WHO Regional Office for the Eastern Mediterranean, PO Box 1517, Alexandra, Egypt; Thai from Mr Wolfgang Kampf, German Leprosy Relief Association, 257/3 Kaeonwarat Road, Main PO Box 215, Chiang Mai 50000, Thailand; Bengali from Dr D S Chaudhury, Greater Calcutta Leprosy Treatment and Health Education Scheme, 35/1/A Old Ballygunge 1st Lane, Calcutta 700 019, India.

This 32-pp guide covers all aspects of smear taking, staining and microscopy needed for routine clinical work and leprosy control programmes. (It is comparable to the *Technical guide for sputum examination for tuberculosis by direct microscopy*, 3rd edition revised 1986, produced by the International Union Against Tuberculosis and Lung Diseases.)

Single copies of the guide for leprosy are usually available without charge to individuals; a charge may be made however for larger orders and arrangements should be made with the agencies listed above.

Lepr Rev (1989) **60,** 334–339

News and Notes

Rifampicin pharmacology

The latest edition of the *British National Formulary* is a useful reminder of some of the interactions and pharmacological properties of rifampicin which may be of clinical importance:

Dapsone. It decreases plasma levels of dapsone, but in practice this is not significant in adults taking 100 mg daily.

2 Steroids (cortisone, dexamethasone, hydrocortisone, prednisolone and prednisone). Plasma levels are reduced in patients taking daily rifampicin this may mean that higher doses of steroid are needed, e.g. to control reactions.

3 Oral contraceptives. Here again plasma levels are reduced and some other, or additional, form of contraception may be indicated.

4 Phenytoin (an anti-epileptic). Plasma levels are reduced.

5 Chloramphenicol (a potent, potentially toxic, broad-spectrum antibiotic which should be reserved for the treatment of life-threatening infections such as those caused by *Haemophilus influenzae* and typhoid fever). Rifampicin reduces plasma levels.

6 Warfarin and nicoumalone (both anti-coagulants). Rifampicin inhibits their action.

7 Chlorporpamide, glymidine, tolbutamide and possibly other sulphonylureas (all anti-diabetic). Rifampicin reduces their effect.

8 Digitoxin (a cardia glycoside used for some forms of heart failure). Rifampicin inhibits its effect (but not, apparently, that of other glycosides).

9 Quinidine and mexiletine (both used for the treatment of cardiac arrhythimias). Rifampicin reduces plasma concentrations.

It may also be helpful to add that the absorption of rifampicin may be impaired by (a) taking the drug on a full stomach (it is better before meals) or (b) the regular use of antacids, i.e. for dyspepsia. Intake (and absorption) can be checked by simply collecting a specimen of urine between 2 and 10 hours after a supervised dose has been given to see if it has a characteristic orange/red colour. Rifampicin stands humidity and changes of temperature fairly well. Its 'shelf-life' (the period between the date of manufacture and the date of expiry, which any reliable manufacturer should mark on the container) is 3 years, which should be completely satisfactory in relation to the bulk order and turnover time of drugs in most leprosy control programmes.

Copies of the *British National Formulary* are obtainable from the British Medical Association, Tavistock Square, London WC1H 9JP.

Action Health 2000: Medical student electives in developing countries

We have received the following information from the Secretary, Action Health 2000, International Voluntary Health Association, The Bath House, Gwydir Street, Cambridge CB1 2LW, England. This is a voluntary charitable society concerned with health care issues in developing countries. The general purpose of Action Health 2000 is to work towards the World Health Organization's target of making health care accessible to all the world's peoples. The main work of the Society is summarized as follows:

Projects and volunteers. We provide personnel, technical and financial support for appropriate programmes.

2 Study and research issues related to health care in developing countries. We encourage technical collaborations on the planning, monitoring and evaluation of health care programmes.
3 'Awareness raising'. Action Health is committed to creating a greater awareness about the inequitable distribution of health care resources in the world, especially amongst health professionals in Britain. The Medical Students Electives Scheme is one part of this.
4 A forum for all. Through an international network we aim to provide a forum for the exchange of ideas, resources and expertise amongst health professionals and in so doing realise the vast potential for effective cooperation within developing countries.

Medical student electives in developing countries

All British medical schools allow an elective period in the clinical curriculum, to be used in an approved manner, but at the student's discretion. In recent years, an increasing number of medical students have ventured abroad for electives in developing countries. This has generally been a rewarding experience appreciated by the student visitors and their hosts.

Action Health 2000 organizes comprehensive Orientation Courses in conjunction with the Department of Infectious & Tropical Diseases, Addenbrooke's Hospital, Cambridge. The Course is usually over weekend (Friday to Sunday) and consists of an intensive programme of seminars, films and slide-shows. There is an opportunity to meet returned elective students and doctors/nurses who have worked in developing countries, as well as to get to know your own 'Project Supervisor'.

The topics covered in the Course include:

Organizational details:
Travel arrangements and insurance; immunizations; hints on fund raising for your elective.
Living in developing countries:
Country briefings: customs, culture, religion, politics, etc; personal health care; clothes and things to take with you; travel hints; food habits; other 'survival' hints; personal safety and security; what to do in an emergency; and communication skills.
Health and development:
Seminars on different aspects of primary health care; essentials of tropical medicine; development issues and related topics; comparative analysis of health care in developed and developing countries; and experiences of returned elective students.
Your elective:
Individual placement briefings; how to get the most out of it . . .; hints on photography; report writing and doing a project.

Further information from the address above.

Arthritis in leprosy

The *British Medical Journal*, Volume 298, 27 May 1989, carried an article on 'Clinical and laboratory studies of arthritis in leprosy' by Atkin *et al.* from the Departments of Radiology and Rheumatology, The Royal Victoria Infirmary, Newcastle upon Tyne, England and the Abou Zabel Leprosy Colony, Kaloubya, Egypt. The abstract reads as follows:

Arthritis associated with leprosy is underreported. In Egypt 66 patients from a leprosy colony were studied, 20 of whom had arthropathy. This was characterised by an inflammatory symmetrical peripheral polyarthritis. The wrist, metacarpal and proximal interphalangeal joints of the hands, the knees, and the metatarsophalangeal joints of the feet were affected with associated morning stiffness. The arthritis was erosive in 11 out of 20 patients, had no features of the arthritis associated with erythema nodosum leprosum reactions, but symptomatically responded to antileprosy treatment.

This arthritis would seem to be a previously unrecognised feature of leprosy.

The final paragraph of the discussion includes the statement:

Patients with rheumatoid arthritis have significantly raised titres of IgG and IgA binding to a 65 kilodalton mycobacterial heat shock protein. Binding to this mycobacterial antigen was reported to be greater than that seen in tuberculosis. Titres of agalactosyl IgG molecules are raised in rheumatoid arthritis and *M tuberculosis* infection but not in other diseases investigated. Both these factors may be relevant to the initiation and development of an arthritis by *M leprae*. This arthritis requires further study with a systematic survey of patients with leprosy and patients with rheumatoid arthritis, both within and between communities.

Handbook of leprosy, 4th edition

Stocks of the hardback of the *Handbook of leprosy*, 4th edition (Jopling and McDougall) are running low with an estimated few months supply left. Stocks of the International Edition are a little more plentiful and are obtainable from any reputable bookseller or direct from the publisher Heinemann Medical Books, Halley Court, Jordan Hill, Oxford OX2 8EJ, England. Price £8.50 plus £2.00 postage and packing.

The New Internationalist, Oxford, UK

The New Internationalist, a monthly journal published from Oxford, UK: 'exists to report on the issues of world poverty and inequality; to focus attention on the unjust relationship between the powerful and powerless in both poor rich and poor nations; to debate and campaign for the radical changes necessary within and between those nations if the basic material and spiritual needs are all to be met; to bring to life the ideas and the action in the fight for world development.' It was launched in 1973 as a joint venture between OXFAM and Christian Aid, but a few years later it became financially and in other ways independent. There are currently 65,000 subscribers.

The June issue includes a free copy of the Peters projection of the map of the world, showing countries in proportion to their relative sizes, based on Arno Peters' decimal grid which divides the surface of the earth into 100 longitudinal fields of equal width and 100 latitudinal fields of equal height.

Further enquiries: Wendy Slack, Subscription Services Dept, 120–126 Lavender Avenue, Mitcham, Surrey CR4 3HP, England. Editorial office: 42 Hythe Bridge Street, Oxford OX1 2EP, England.

Dapsone syndrome due to weekly 'Maloprim'

Since I have seen your announcement regarding maloprim (*Lepr Rev*, 1989; **59:** 278) I have started my research on the side-effects of this drug. The following is the result of my research.

In Kisangani there is only one pharmacy which sells this product. It is a relatively expensive product (about US$12.00). Generally it is not a popular drug and is used only by tourists and a few expatriates. None of my colleagues at the Kisangani University Clinic know of this drug. During the last few months I have found 15 people who have been using maloprim. They are from different age groups and are European or Asian in origin. Some have been introduced to this product by the local pharmacist while others have known of it already. None of the users have shown any allergic reactions. Twelve of the users were subjected to a simple complete blood count (CBC) test which yielded no special result. The usual weekly dose of maloprim is ineffective in malaria prevention for adults but it has proven effective for the prevention of malaria in children.

A Ansari

Rapid assessment of leprosy prevalence, WHO

A recent WHO 'Report of a meeting on methods for the rapid assessment of the leprosy situation', (unpublished document WHO/CDS/LEP.88.2) held in Geneva, 15–16 April 1988 has been summarized in the *Bulletin of the WHO* (1989) **67,** No.2 and the opening paragraph runs as follows:

'Leprosy still presents a serious health issue in many countries in Africa, Asia, and Latin

America. Globally the number of cases has been estimated to be 10–12 million and this level has been repeated for more than 20 years. However, the basis for this is weak and the only reasonably reliable number available is for registered cases, which has been around 5 million for the last few years. At the national level, data about the prevalence of the disease are directly proportional to the quantity and quality of the leprosy services available. Although some countries have undertaken sample surveys to define the extent of the problem posed by leprosy, these are expensive and have been few and far between; also the relatively low frequency and uneven distribution of the disease raise further difficulties. There is therefore a need, particularly at the national level, for a simple method of estimating the prevalence of leprosy, the more so since the introduction over the last few years of multidrug therapy for the treatment of the disease.'

The report deals with the pros and cons of assessment based on: (1) prevalences in children; (2) registered cases; (3) the number of cases of disability and deformity; (4) rapid village surveys. The unpublished document should be consulted in the original, where the importance of an assessment of the methods proposed is stressed. There are however some messages in this document which could be of immediate practical importance in leprosy control programmes. For instance, one of the expert contributors, referring to French-speaking West African countries, reported that a clinical and bacteriological examination of all registered patients usually revealed that only one third of them required treatment with multiple drug therapy, thus resulting in '. . . a dramatic drop in the leprosy prevalence, when the numerator is made of all cases eligible for treatment'.

Honey for leprosy

The *Journal of the Royal Society of Medicine*, Volume 82, 384–5, carries this interesting article 'Honey—a remedy rediscovered,' by A Zumla, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0RS, and A Lulat, Department of Medical Parasitology, London School of Hygiene and Tropical Medicine, London WC1E 7HT.

It reviews the use of honey as a traditional medicine throughout the centuries and its value as an antibacterial and antifungal agent; the treatment of infected surgical wounds; burns, decubitus ulcers; the promotion of healing in areas which would otherwise require skin grafting. The penultimate paragraph reads as follows:

'Although honey has been used for commercial and domestic uses for thousands of years, much of the literature is only descriptive. Further evaluation and application of the healing properties of honey in other clinical and laboratory situations is warranted. For example, use of it could be made in the field of leprosy. The foul smelling, chronic ulcers contribute to the social degradation and isolation of the patient. Could these be treated with this simple, acceptable and readily available remedy? Deoxyfructose serotonin, a substance derived from coffee-wax, has an anti-*Mycobacterium leprae* action and has been shown in preliminary studies to be of benefit in patients with active lepromatous leprosy. Honey obtained from beeswax contains fructose in its different forms and may possess an antileprosy effect. Effects of various components of honey on cell-mediated immunity needs evaluation'. Elsewhere attention is drawn to the fact that honey is extremely viscous, hygroscopic, contains enzymes such as catalase, and that together with its antibiotic properties, these may enable it to absorb water from surrounding oedematous tissue and clean the wound.'

Much of the information in this review article brings to mind a previous communication by L A Wiseman, Sugar as an aid to wound healing and the treatment of ulcers in leprosy, *Lepr Rev*, 1989; **60:** 67–8.

Leprosy in Haiti

Although previously mentioned in this Journal, we again draw attention to an excellent publication in French, entitled *La Maladie de Hansen de Haiti*, 1988 by Professor Claude Péan, dermatologist,

dermatopathologist and professor of the Faculty of Medicine, Port-au-Prince, Haiti. It is spiral bound with laminated pages. There are 78 high quality colour photographs in this publication of 48 pages. Many of the clinical pictures are of outstandingly high quality and those on differential diagnosis, including hypochromic lesions, tricophytosis, cutaneous tuberculosis, secondary syphilis, molluscum contagiosum, psoriasis, sarcoidosis, adenoma sebaceum, neurofibromatosis, Kaposi sarcoma, mycosis fungoides, are amongst the best available in books of this kind.

A section of particular interest is that on page 35: 'Prevalence and evolution of HIV infection in leprosy patients in Haiti'. This describes a preliminary study with Cornell University, New York and a group in Haiti called Gheskio (Groupe Haitien d'Etude du Sarome de Kaposi et des Infections Opportunistes, Port-au-Prince, Haiti). Early data are recorded and the concluding paragraph reads: 'Infact, the prevalence of HIV infections in leprosy patients is comparable to that found in the normal population. This prospective study continues. We shall know, in the fairly near future, if the natural history of HIV infection is influenced by leprosy or, if the evolution of leprosy is modified by HIV.' No price is given by the producers Institut Cardinal Leger contre la Lèpre (Fame Pereo), 130, avenue de l'Epee, Outremont, Québec H2V 3T2, Canada; and in Haiti: 160, rue Poupelard, Port-au-Prince, Haiti.

Ciba-Geigy Leprosy Fund, Fifth Meeting, Basle, June 1989

Under the chairmanship of Dr Klaus Leisinger, this meeting was held in Basle in June 1989 to review progress in projects already receiving financial support and to assess the value of new applications to the Fund. In Sri Lanka, in association with Emmaus Suisse, considerable progress has been made to extend and support the national leprosy control programme in close cooperation with Dr Dewapura at the Ministry of Health. An intensive programme of health education has been carried out using written and illustrated material produced locally, and in the near future an orientation and teaching programme will be started. This will be aimed at all grades of health staff, with emphasis on case detection, diagnosis, classification and the implementation of multiple drug therapy. All drugs are issued in blister–calendar packs. In the Maldives, in association with WHO and the Maldives' Ministry of Health, a combined programme of chemoprophylaxis (with rifampicin) and multiple drug therapy is making good progress, with the aim of total interruption of transmission and eventual eradication. In Sierra Leone in association with the German Leprosy Relief Association, work continues in the northern part of the country in the implementation of multidrug therapy and prevalence figures are beginning to decline. A mobile clinic has been provided for work in Nepal and is already in operation. In association with the Damien Foundation, a prevalence study is under way in Equatorial Guinea, and in Baroda, India, funds have been allocated for drug treatment, disability prevention and the production of grip aids. With regard to new applications, the most important concerns Indonesia, where it is planned to assist leprosy control programmes in West Java and West Kalimantan, subject to some improvements in operational support and the training of staff. The use of this Fund for projects implementing, or wishing to implement multidrug therapy, according to WHO recommendations, was judged by the Committee (K Leisinger, P Friedli, S J Yawalkar, E. Décosterd, P Grewal (Ciba-Geigy); H Sansarricq (France), N Chitimba (Malaŵi) and A C McDougall (UK)) to be increasingly satisfactory and no changes in the conditions for grants (already widely publicised) are to be made. The next meeting will be in mid-January 1990. Address: Ciba-Geigy, Leprosy Fund, PO Box K-24.2.09, 4002 Basle, Switzerland.

Women and tropical diseases; TDR Meeting, May 1989

The following is extracted from *TDR News*, published by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), No. 28, June 1989:

More questions were raised than answers could be given at a meeting on risk factors for infection and disease in women, held 1 May 1989 and organized by the Social and Economic Research component (SER) of TDR.

Questions like, 'Do women have different risks than men for infection and disease in the tropics?' And, 'At what periods of a woman's life are the risks greatest?' And 'How much do women know about their vulnerability to infection and disease?' And, 'What can women, and their local health services, do to reduce the risks?'

A number of the papers presented at the meeting, though, did give some answers. Pregnancy, for example, is clearly a risky time for a number of TDR target diseases.

Leprosy is a case in point. Scottish gynecologist Elizabeth Duncan, who has worked extensively with leprosy patients in Africa, particularly in Ethiopia, reminded meeting participants that increased estrogen levels during pregnancy lowers cell-mediated immunity. In teenage mothers, she said, 'the combined hormonal effect of puberty and the first pregnancy may be disastrous in terms of leprosy.'

With suppression of cell-mediated immunity, there is a gradual exacerbation of the disease as pregnancy progresses. Previously silent disease may become overt; women released from treatment may experience reactivation of disease, and those with mild-to-moderate leprosy may experience a worsening of the disease. 'There is a general downgrading along the leprosy spectrum,' Dr Duncan noted. This occurs in up to 45% of women.

With delivery of the baby, the woman's ordeal is not over. Restoration of cell-mediated immunity postpartum—and resumption of the battle between host immunity and leprosy bacilli—causes sometimes excruciatingly painful reactions (reversal or type I reactions) in up to 40% of women following delivery and during the early lactation period. Not to speak of the effect on the baby, 20% of whom suffer sometimes fatal fetal distress, and many of whom are of low birth weight from intrauterine growth retardation.

Dr Duncan, who is associate research gynecologist in the Department of Bacteriology, Edinburgh University Medical School, outlined the typical situation of a woman leprosy patient. 'To have two or three healthy children, she may have to have five or six pregnancies. With each pregnancy, her leprosy may deteriorate or become resistant to drug therapy and she may suffer sensory and motor nerve damage of the extremities. Ultimately, she may become debilitated to the point of being reduced to begging to earn money.'

Commenting, Dr. Shaik K. Noordeen, Chief of WHO's Leprosy Unit, said that the challenge for TDR is to find out how women with leprosy can be convinced to postpone pregnancy while they have active disease.

Contact: TDR Communications, WHO, 1211 Geneva 27, Switzerland.

Referees—acknowledgment

The Editor wishes to extend his grateful thanks to the following referees for their assistance in the review process of papers submitted to *Leprosy Review*: Drs G. Boerrigter, P. Brand, W. Brandsma, S. Brett, A.D.M. Bryceson, M. J. Colston, J. Curtis, P. Draper, G. Ellard, Mr T. ffytche, Drs R. Hastings, M. Jacob, J. Baohong, W. H. Jopling, Professor T. Lehner, Drs S. Lucas, A. C. McDougall, Miss J. Neville, Drs S. K. Noordeen, D. Palande, Professor P. Piper, Drs J. M. Ponnighaus, T. H. Rea, R. J. W. Rees, D. S. Ridley, P. Rose, T. Ryan, H. Srinivasan, J. L. Stanford, M. Waters and H. W. Wheate.

Submission of material

Papers submitted for publication in *Leprosy Review* should be sent to the Editor, Professor J. L. Turk, LEPRA, Fairfax House, Causton Road, Colchester CO1 1PU, England. Please see inside back cover for full requirements. For material that you would like mentioned in 'Teaching Materials and Services' or 'News and Notes' please send to Jennet Batten, Assistant Editor, 94 Church Road, Wheatley, Oxon OX9 1LZ, England.

Please note that the editorial office at the Slade Hospital, Oxford is now closed.

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Instructions to Authors

Papers submitted for publication in *Leprosy Review* should be sent to the Editor, Professor J. L. Turk, LEPRA, Fairfax House, Causton Road, Colchester CO1 1PU, England. The name(s) of the author(s) and the place where the work was done should be clearly indicated below the title of the paper. Degrees and diplomas are not to be included.

It is understood that the paper is offered to *Leprosy Review* alone, that it will be subject to editorial revision, and that its copyright becomes the property of the British Leprosy Relief Association. Manuscripts should be typewritten, in double spacing, on one side of A4 (297 × 210 mm) paper, with wide margins (4 cm all round). Contributors must send three complete copies of the text, tables and figures. On a separate sheet give the title, short title, name and postal address of the author, together with the name of the institution where the work was done. Abbreviations of titles of journals should follow the list of journals indexed in *Index Medicus*. References to books should include the editor(s), publisher and place of publication.

Units and Abbreviations. The Journal recognizes the adoption of the Système International d'Unitès (SI Units) proposed in *Units, Symbols and Abbreviations* (1972) published by the Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE. Abbreviations should only be used for unwieldy names, and only when they occur frequently.

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