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Leprosy Review

A journal contributing to the better understanding of leprosy and its control

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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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CONTENTS

Lepr Rev (1992) **63,** 97–100

Editorial

THE SERODIAGNOSIS OF LEPROSY

At the 44th World Health Assembly a statement was approved committing WHO to the elimination of leprosy as a public health problem by the year 2000. The main strategy to achieve this goal is likely to be through detection and effective treatment of cases of leprosy with multidrug therapy,[1] though BCG vaccination may also make an important contribution to the decline in leprosy incidence in some settings.[2] The first priority for national leprosy control programmes must be to ensure that currently identified cases are properly treated as this is likely to reduce rapidly their infectiousness to others.[3] Until this is achieved there is little to be gained by extending case-finding activities. In many countries it will be necessary to strengthen leprosy control activities substantially to ensure an adequate coverage of diagnostic and treatment facilities. In general, the earlier cases are diagnosed and treated the less chance they have to pass on the infection to others. Clinical examination by trained workers provides a reliable and efficient method of diagnosis for the majority of patients who present to medical facilities with suspect lesions. There is considerable uncertainty, however, in the clinical diagnosis of early lesions and improved diagnostic methods for such patients are required. Furthermore, in the right circumstances, it may be very useful to have a diagnostic method that identifies 'cases' before they have any symptoms of disease, as early treatment of this group would reduce the chance of deformities and lower the risk of disease in the community by eliminating them as a source of transmission. Research on serodiagnostic methods has sought to identify markers that may facilitate the diagnosis of cases with few or no clinical symptoms.

Of the potential serological tests which have been developed, the one that has raised most interest, that has been well standardized between laboratories, and has been best evaluated epidemiologically is that based on the detection of antibodies to phenolic glycolipid I (PGL-I). This is a highly specific antigen of *Mycobacterium leprae* characterized by Brennan *et al.* in the early 1980s.[4–6] Enzyme-linked immunosorbent assays (ELISA) have been developed to detect antibodies that react with the native antigen or with neoconjugates containing the carbohydrate component towards which the antibody response is directed.[7] Most of the epidemiological studies that have been reported have been cross-sectional, variously comparing antibody levels among multibacillary patients, paucibacillary patients, contacts of such patients and healthy individuals from leprosy endemic and nonendemic areas. The findings in a selection of these studies are summarized in Table 1. Various criteria have been used to define the cut-off criterion for a 'positive' test and this accounts for some of the variability in the results shown for different studies.

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Table 1. Cross-sectional studies of the prevalence of antibodies to PGL-I among leprosy patients, household contacts of leprosy patients and other groups

Authors (place)	Percent with antibodies to PGL-I (no. studied)			
	Multibacillary patients	Paucibacillary patients	Household contacts	Controls [sources]
Menzel *et al.*[17] (Ethiopia)	—	—	43 (54 MB)* 21 (39 PB)	33 (99) [non-hshd]
Gonzalez-Abreau *et al.*[18] (Cuba)	100 (23)	—	—	5 (185) [blood bank]
Burgess *et al.*[19] (Malawi)	100 (7)	75 (95)	—	20 (85) [Europeans]
Mwatha *et al.*[20] (India)	96 (26)	—	—	11 (18) [endemic]
Petchclai *et al.*[21] (Thailand)	84 (38)	17 (24)	17 (6 MB)	4 (54) [blood donors]
Agis *et al.*[22] (West Indies)	100 (14)	32 (40)	13 (109)	4 (51) [blood donors]
Dhandayuthapani *et al.*[23] (India)	100 (40)	63 (19)	—	0 (35) [endemic]
Desforges *et al.*[24] (Melanesia)	100 (13)	21 (14)	14 (309)	4 (104) [non-endemic]
Izumi *et al.*[8] (Japan)	72 (69)	1 (86)	7 (70)	5 (428) [non-contact]
Soebono *et al.*[25] (Indonesia)	98 (41)	57 (44)	—	8 (49) [blood donors]
Krishnamurthy *et al.*[9] (India)	40 (10)	13 (122)	15 (~400)	13 (~4000) [endemic]
Lefford *et al.*[16] (Ethiopia)	84 (51)	47 (38)	—	0? (57) [non-endemic]

* MB, contacts of multibacillary cases. PB, contacts of paucibacillary cases.

A reasonably consistent finding has been that a high proportion of patients with multibacillary disease have elevated antibody titres to PGL-I. Not all of the studies summarized in Table 1 have excluded treated patients and this is likely to be the reason for the lower levels of antibodies in some of them (e.g. Refs 8 and 9) as antibody levels have been found to correlate with bacillary load and decline with therapy.[10,11] In general, in excess of 90% of untreated multibacillary patients have positive serology. Among paucibacillary patients the findings are more variable between studies, but in all of them a substantial proportion of such patients, often in excess of 40–50%, have not been found to have elevated antibody levels. In some studies household contacts have been found to have higher antibody levels than controls, but in others marked differences have not been reported. The proportion of healthy individuals from leprosy-endemic areas with PGL-I antibodies varies from 0% in one study to 33% in another, but, in general, the proportion with antibodies is around 5–10%.

The results from the cross-sectional studies suggest that PGL-I antibodies provide a sensitive test for multibacillary leprosy, but the test is much less useful for the detection of paucibacillary cases. The findings offer little encouragement for the notion that screening sera from healthy individuals in leprosy-endemic areas to detect 'pre-clinical' cases is likely to be a very useful strategy in most leprosy control programmes. The annual incidence of leprosy in endemic areas may be 1/1000 or less. In such circumstances a test with very high specificity is required. Even with a test which had a specificity of 95%, if only 1/1000 of those screened really had leprosy, there would be 50 times as many false positives as true positives in detecting cases.

To assess more rigorously the usefulness of PGL-I antibody levels in predicting who will develop clinical disease it is necessary to conduct studies in which individuals are followed prospectively for signs of leprosy after sera have been collected from apparently healthy individuals. Because in most populations the incidence of leprosy is relatively low, such studies must be large and few have been conducted. Bagshawe *et al.*[12] measured

antibody levels to PGL-I in 877 persons in a village in Papua New Guinea in a highly endemic area and found no association between antibody levels and the risk of leprosy among the 16 cases that developed over a 2-year period. This study is difficult to interpret, however, as even patients with prevalent leprosy did not have elevated PGL-I antibody levels. Douglas *et al.*,[13] in a study of household contacts in the Philippines, found over a 2-year period that leprosy developed in 3 of 36 contacts with elevated PGL-I antibody levels but only in 1 of 285 of those without elevated levels. Chanteau *et al.*[14] followed 724 household contacts on Tahiti Island for 2 years after assaying antibodies to PGL-I—3 cases of paucibacillary leprosy developed among the 631 contacts with negative serology and 1 multibacillary case developed among the 93 contacts with positive serology.

The largest prospective study yet conducted has recently been reported by Ulrich *et al.*[15] Serum was collected from contacts of leprosy patients as they were entered into the leprosy vaccine trial that is being conducted in Venezuela and PGL-I antibody levels were assayed for about 13,000 contacts. In a subset of 9545 individuals, on whose sera the same antibody assay method was used, 20 cases of leprosy developed in the following 4 years. A strong association was found between the antibody level and the risk of leprosy. Those with high antibody levels were at over a 10-fold increased risk of leprosy compared to those in the lowest category and there was a gradient in risk with antibody level. However, a striking finding was that most of the 20 cases occurred in those who had not had elevated antibody levels. Although 2 cases of multibacillary leprosy were detected among the 10 contacts with the highest antibodies to PGL-I, it was necessary to screen over 9500 sera to identify these 10 persons. Thus it seems from this study that screening populations for elevated PGL-I antibody levels in leprosy control programmes would be unlikely to be a useful way of detecting persons at high risk of developing leprosy, even if the necessary infrastructure for performing the tests were available at an acceptable cost.

Serological testing for PGL-I antibodies may be of some limited value in diagnosis for those who present to a medical facility with symptoms or signs of leprosy.[16] In a proportion of such persons it may not be possible to make a firm clinical diagnosis of leprosy or not leprosy. In this group of 'suspect' cases serological testing may be of value. A positive serological test would increase the probability of leprosy being the correct diagnosis (especially if the level of antibodies was high), though the diagnostic value of a negative test would not be great as a high substantial proportion of paucibacillary cases do not have elevated PGL-I antibody levels.

Other serodiagnostic markers for leprosy have been less well studied than has PGL-I and it is to be hoped that tests which are more sensitive and specific will be developed. At the present time, however, it appears that the contribution that serodiagnostic methods can make over normal diagnostic procedures is rather limited.

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Lepr Rev (1992) **63,** 101–107

Competency of human-derived *Mycobacterium leprae* to use palmitic acid in the synthesis of phenolic glycolipid-I and phthiocerol dimycocerosate and to release CO_2 in axenic culture

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Summary Insufficient numbers of viable *Mycobacterium leprae* have hampered metabolic studies using human-derived *M. leprae*. In this study, sufficient numbers of *M. leprae* were obtained from an untreated lepromatous patient to titrate the effects of pH on the metabolism of ^{14}C-palmitic acid by *M. leprae*.

Catabolic metabolism (oxidation of ^{14}C-palmitic acid and release of $^{14}CO_2$) was maximal when *M. leprae* were incubated at 33°C and suspended in Middlebrook 7H9, ADC supplemented medium that had been buffered to maintain a pH of 4·8. Anabolic metabolism (synthesis of ^{14}C-phenolic glycolipid-I and its precursor, ^{14}C-phthiocerol dimycocerosate) was maximal when the pH was maintained at 6·8.

Introduction

Insufficient quantities of viable *Mycobacterium leprae* extracted from human tissues have severely hampered metabolic studies using human-derived *M. leprae*. Nevertheless, mycobacteria separated from human leprosy nodules have been shown to possess glutamic acid decarboxylase activity,[1] phenoloxidase activity,[2] and gamma glutamyl transpeptidase activity.[3]

In this study, we obtained *M. leprae* in sufficient numbers from an untreated human leproma to titrate the effects of low pH on the capacity of *M. leprae* to (a) oxidize ^{14}C-palmitic acid and release $^{14}CO_2$ and (b) assimilate ^{14}C-palmitic acid into ^{14}C-phenolic glycolipid-I (PGL-I) and its lipid precursor, phthiocerol dimycocerosate (PDIM).

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Materials and methods

SOURCE AND CHARACTERIZATION OF *M. LEPRAE*

A leproma weighing 52 mg was removed from the eyelid of an untreated, 18-year-old male Ethiopian. The patient has been histologically classified as BL/LL. The acid-fast bacteria (AFB) extracted from the leproma was not only able to synthesize PGL-I, but the DNA derived from the AFB was also reactive in an *M. leprae*-specific polymerase chain reaction assay.[4]

PREPARATION OF INOCULUM

The leproma was ground using a mortar in a pestle containing Middlebrook 7H9 medium (DIFCO, Detroit, MI, USA). The large tissue debris was allowed to settle for 10 min and the supernatant centrifuged at 10,000 $\times g$. The pellet was treated for 5 min with a 10% v/v solution of 0·25 N NaOH and washed with Middlebrook 7H9 medium. The processed leproma yielded $7{\cdot}8 \times 10^9$ AFB with a morphological index of 8%.

INCUBATION MEDIA AND CULTURE VESSELS

The pH of Middlebrook 7H9 medium was adjusted to 4·8, 5·8, 6·2, or 6·8 using citrate buffer.[5] We prepared suspensions containing 2×10^8 *M. leprae*/ml in citrate-buffered, Middlebrook 7H9 medium enriched with a 10% v/v solution containing albumin, dextrose and catalase (ADC, DIFCO) and supplemented with ampicillin (50 μg/ml), amphotericin B (2·5 μg/ml), and 1 (μCi/ml of universally labelled palmitic acid (NEC-534, palmitic acid [^{14}C(U)], 800 mCi/mmole; Dupont, Boston, MA, USA). In order to control for nonspecific, pH-influenced oxidation of ^{14}C-palmitic acid, the control cultures contained the 7H9 medium, ADC and antibiotic supplements and ^{14}C-palmitic acid. The above suspensions were placed in 10-ml glass serum vials (Wheaton Scientific, Vineland, NJ, USA). A plastic cup (Kontes, Scientific Glassware/Instruments, Vineland, NJ, USA) containing 400 μl of 4·0 N NaOH was suspended from a rubber stopper sealing the vials. These reaction vessels were incubated at 33°C for 7 days.

$^{14}CO_2$ ASSAY

The $^{14}CO_2$ that evolved from the oxidation of [U-^{14}C] palmitic acid was trapped in the solution of NaOH. After 7 days' incubation at 33°C, the cup containing the NaOH was removed and 100 μl was added to 6·0 ml of Aquasol-2 (NEN Research Products, Boston, MA, USA). After adding 1·0 ml of glacial acetic acid to clarify the scintillation fluid, the amount of $^{14}CO_2$ was assessed using a Model LS-5801 Beckman Liquid Scintillation Spectrophotometer.

LIPID EXTRACTION, ANALYSIS AND QUANTITATION OF PGL-I AND PDIM

The contents of the culture vessels were lyophilized and the lipids extracted overnight using 10 ml of chloroform:methanol, 2:1 v/v, in a 50°C water bath. The extract was filtered through cotton-plugged glass funnels and evaporated to dryness under a stream of nitrogen in a 50°C water bath. The dried extracts were redissolved in chlorofform:methanol, 2:1 v/v, and partitioned by adding 0·2 volumes of distilled water.[6] The lower organic

phase containing the lipid fraction was removed and dried using nitrogen. The dried material was dissolved in chloroform and applied to a florisil:silicic acid (2:1 w/w) column. The neutral lipid fraction containing PDIM was eluted with two volumes of chloroform and taken to dryness under nitrogen. The PGL-I fraction was eluted by first passing two volumes of 2% methanol in chloroform through the column, followed by two volumes of 5% methanol in chloroform. The 2% and 5% eluates were combined and dried using nitrogen.

The neutral lipid fraction containing PDIM and the glycolipid fraction containing PGL-I, along with authentic standards of PGL-I or PDIM which served as carrier lipids and Rf markers, were applied to thin-layer chromatographic plates (Silica Gel 60, E. Merck AG, Darmstadt, Germany). Migration of the samples was induced in the appropriate solvent (PDIM: hexane:ether, 95:5 v/v; PGL-I ether:acetone, 80:20 v/v). The plates were air-dried and sprayed with a solution of 0·1% orcinol in 40% sulfuric acid. The lipid fractions were located by heating the plate in an oven at 110°C for 3–5 min or until the spots became visible. An area approximately 1 cm × 1 cm corresponding to the spotted PDIM or PGL-I standards for migration was scraped from the plate. Additional samples approximately 1 cm × 1 cm above and below the standard regions were also removed from the plates. After transferring the samples to glass vials, 10 ml of scintillation fluid (Econofluor, New England Nuclear, Boston, MA, USA), was added to each vial and the radioactivity was measured.

Results

OXIDATION OF PALMITIC ACID

The maximum release of $^{14}CO_2$ from the oxidation of ^{14}C-palmitic acid by *M. leprae*

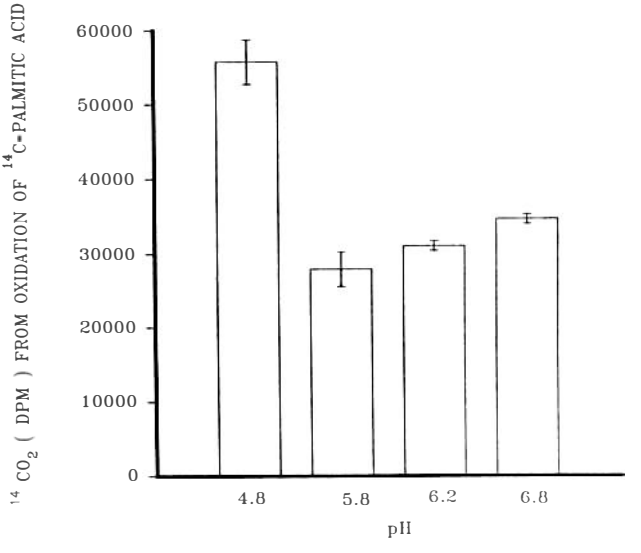

Figure 1. $^{14}CO_2$ trapped in NaOH from the oxidation of ^{14}C-palmitic acid by 2×10^8 human-derived *M. leprae*. ^{14}C activity in control cultures ranged from 140 to 97 disintegrations per minute (N = 8, two values per pH assayed).

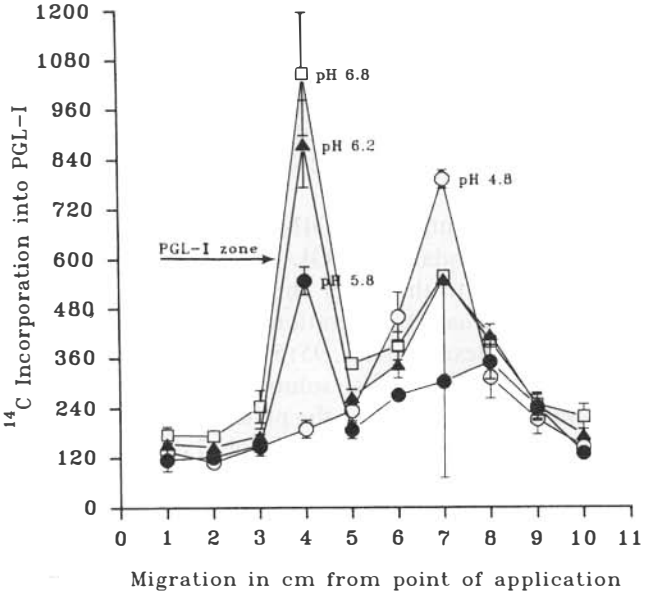

Figure 2. The effect of pH on the capacity of human-derived *M. leprae* to assimilate ^{14}C-palmitic acid into phenolic glycolipid-1 (PGL-I). Mean ± SD, N = 4.

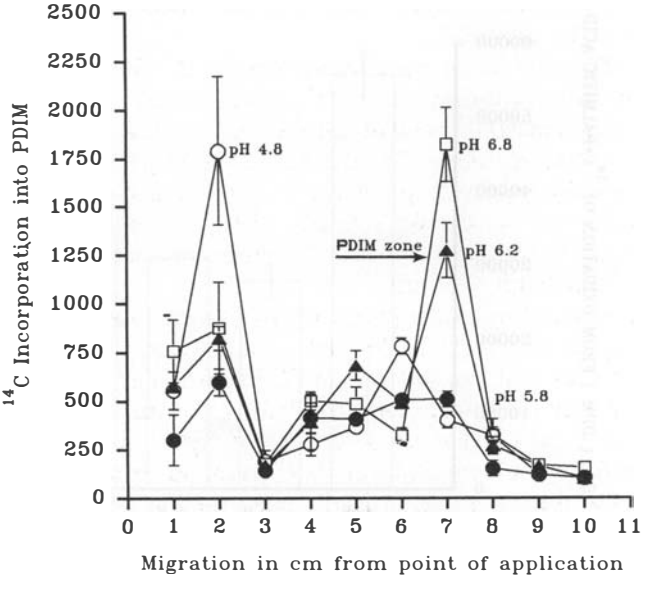

Figure 3. The effect of pH on the capacity of human-derived *M. leprae* to assimilate ^{14}C-palmitic acid into phthiocerol dimycocerosate (PDIM). Mean ± SD, N = 4.

occurred at a pH of 4·8. With an increase of 1 pH log unit to a pH of 5·8, the activity was reduced to approximately 50% (Figure 1).

SYNTHESIS OF PGL-I AND PDIM

The synthesis of PGL-I (Figure 2) and PDIM (Figure 3) increased progressively and significantly as the pH increased in the cultures. Maximum synthesis of ^{14}C-PGL-I and ^{14}C-PDIM occurred when the medium was buffered to maintain the highest pH (pH 6·8). A decrease by 1 pH log unit to a pH of 5·8 resulted in a reduction of greater than 50% in the synthesis of both ^{14}C-PGL-I and ^{14}C-PDIM. The synthesis of an unidentified lipid occurred at a pH of 4·8 (Figures 2 and 3).

Discussion

Utilization of radioactive palmitic acid as a substrate for metabolic activities of armadillo-or nude mouse-derived *M. leprae* has been demonstrated in axenic cultures[7–12] as well as a cell-culture system.[13] In the axenic culture systems, Franzblau[7] demonstrated the capacity of nude mouse-derived *M. leprae* to oxidize palmitic acid and release CO_2. The formation of ^{14}C-CO_2 from ^{14}C-palmitate has been described as the most easily detectable metabolic activity of *M. leprae*.[8] This activity is inhibited by the established antileprosy drugs and several other selected antimicrobial agents.[7,11] A limitation ascribed to the radiorespirometric procedure is the uncertainty about the enzymatic activity due to *M. leprae* rather than possible microbial contaminants or host tissues. This limitation has partially been overcome by the development of a radiometric procedure which measures the amount of ^{14}C-palmitate incorporated into the species-specific, phenolic glycolipid (PGL-I) unique to *M. leprae*.[8,9]

The ability of armadillo- or nude mouse-derived *M. leprae* to catabolize (^{14}C-CO_2 release) or to anabolize (assimilation of ^{14}C-palmitate into PGL-I) in axenic medium is routinely employed in metabolic and drug-sensitivity experiments conducted at the Gillis W Long Hansen's Disease Center, Carville, LA, USA. Depending upon the nature of the study and the procedure used, the pH of the incubation mixture is adjusted accordingly. For maximum oxidation of ^{14}C-palmitate and subsequent release of ^{14}C-CO_2, a pH of 6·2 has been described.[7] Additionally, a pH of 5·1 has been determined to be optimal for the assimilation of ^{14}C-palmitic acid into PGL-I.[12]

In this study, we employed a unique incubation system to assess the effect of pH on the utilization of ^{14}C-palmitate substrate for metabolic activities of human-derived *M. leprae*. A pH of 4·8 was optimal for the oxidation of ^{14}C-palmitic acid releasing ^{14}C-CO_2, whereas maximum assimilation of ^{14}C-palmitate into PGL-I and PDIM of *M. leprae* occurred at pH 6·8. When compared to nude mouse-derived *M. leprae*, there are discrepancies in the pH requirements for optimal metabolism of ^{14}C-palmitate by human-derived *M. leprae*. It is recognized that further experiments using human-derived *M. leprae* are needed to verify these results.

Our findings demonstrate that human-derived *M. leprae* is competent to use ^{14}C-palmitic acid as a substrate for metabolic activity. Furthermore, a 7-day incubation period is ample for the distribution of radioactivity from palmitate into CO_2 and the

major lipid and glycolipid fractions of *M. leprae*. Although 2×10^8 AFB were used in each reaction vessel, the appreciable amount of radioactivity measured in each fraction suggests that lower numbers of *M. leprae* might also yield satisfactory results.

Drug effectiveness and the emergence of resistant organisms are two important factors that must be confronted in the treatment of leprosy. Until a medium capable of inducing multiplication and sustaining growth of *M. leprae* in axenic culture is developed, studies related to metabolism and drug sensitivity will of necessity depend upon tissue-derived organisms. The ease in detectability of the oxidation of palmitic acid to CO_2 and the specificity ascribed to the assimilation of palmitate into the complex lipids of *M. leprae* provide assays for the assessment of the metabolic integrity of the bacillus in a given culture environment. The ability to integrate both of these assays in a single incubation procedure provides a valuable tool for the investigator.

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Compétence de *Mycobacterium leprae* d'origine humaine pour utiliser l'acide palmitique dans la synthèse de phénol-glycolipide-I et de phthiocérol dimycocérosate et pour dégager du CO_2 en culture axénique

E J Shannon, E B Harris, H S Haile-Mariam, M Guebre-Xavier et D Frommel

Résumé Jusqu'à présent *Mycobacterium leprae* viable n'a pas été disponible en quantité suffisante, ce qui a entravé les études de métabolisme utilisant des souches de *M. leprae* d'origine humaine. Dans cette étude, nous avons obtenu des quantités suffisantes de *M. leprae* sur un patient lépromateux non traité pour titrer les effets du pH sur le métabolisme de l'acide ^{14}C-palmitique par *M. leprae*.

Le métabolisme catabolique (oxydation de l'acide ^{14}C-palmitique et dégagement de $^{14}CO_2$) atteint son maximum lorsque *M. leprae* a été incubé à 33°C et mis en suspension dans le milieu de Middlebrook 7H9 additionné d'ADC et tamponné pour maintenir un pH de 4,8. Le métabolisme anabolique (synthèse de ^{14}C-phénol glycolipide-I et de son précurseur, ^{14}C-phthiocérol dimycocérosate) a atteint son maximum lorsque le pH a été maintenu à 6,8.

Competencia *de Mycobacterium leprae* de origen humano en el uso del ácido palmítico en la síntesis de glicolípido-I fenólico y dimicocerosato de ftiocerol y la liberación de CO_2 en un cultivo axénico

E J Shannon, E B Harris, H S Haile-Mariam, M Guebre-Xavier y D Frommel

Resumen Hasta ahora, han habido insuficientes cantidades de *Mycobacterium leprae* viables, lo cual ha impedido los estudios metabólicos con *M. leprae* de origen humano. En este estudio, se obtuvieron suficiente cantidad de un paciente lepromatoso sin tratar para titular los efectos del pH sobre el metabolismo del ácido ^{14}C-palmítico por *M. leprae*.

El metabolismo catabólico (oxidación del ácido ^{14}C-palmítico y la liberación de $^{14}CO_2$) alcanzó un maximo cuando se incubó *M. leprae* a 33°C y se suspendió en un medio Middlebrook 7H9 suplementado con ADC y tamponado para mantener un pH de 4,8. El metabolismo anabólico (síntesis de glicolípido-I ^{14}C-fenólico y su precursor, dimicocerosato de ^{14}C-ftiocerol) llegó a un máximo cuando se mantuvo el pH en 6,8.

Lepr Rev (1992) **63,** 108–116

Activity of sparfloxacin against *Mycobacterium leprae* inoculated into footpads of nude mice

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Summary The antileprosy activity of a new quinolone, sparfloxacin, was examined in the nude mouse footpad model. By serial dosing (once a day, 5 or 6 times per week, during the 3rd–5th months postinoculation), 10 mg/kg of sparfloxacin displayed bactericidal-type activity and bacteriostatic activity was present at daily doses of 5 and 2 mg/kg. By intermittent dosing (once a day, twice weekly at daily doses of 10 and 20 mg/kg or once weekly at a daily dose of 30 mg/kg, during the 3rd–5th months postinoculation), sparfloxacin markedly inhibited the growth of leprosy bacilli with slight remultiplication at later stages. Sparfloxacin seems to be worth studying clinically as a novel antileprosy drug.

Introduction

At present, the most reliable chemotherapy for the treatment of leprosy is the multidrug therapy that uses dapsone, clofazimine and rifampicin. However, resistance of *Mycobacterium leprae* to each of these agents has been reported,[1] and the inhibitory action of dapsone is bacteriostatic, and clofazimine has an unfavourable side-effect, namely, skin pigmentation. Rifampicin is a reliable bactericidal drug, but expensive. Therefore it is necessary to develop new agents which are not cross-resistant with existing antileprosy drugs, are bactericidally effective, less toxic and less expensive than rifampicin.

Sparfloxacin[2] (Figure 1) is a novel quinolone with broad and potent antibacterial activity *in vitro* and *in vivo*.[3] Previously we found that sparfloxacin was more potent than ofloxacin in growth-inhibitory activity against *M. leprae* in the nude mouse footpad model, and its activity seemed to be the bactericidal-type when it was given orally once daily, 6 times a week, 3–5 months postinoculation at doses of 15 and 30 mg/kg.[4] Such an encouraging result caused us to examine the antileprosy activity of sparfloxacin in more detail.

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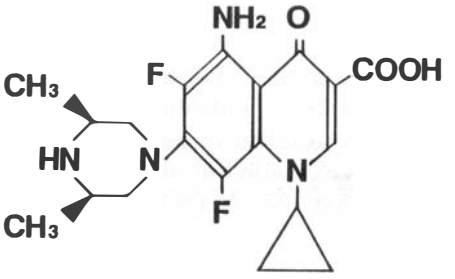

Sparfloxacin (SPFX)

Figure 1. Chemical structure of sparfloxacin.

Materials and methods

DRUG ADMINISTRATION

Sparfloxacin was provided by Research Laboratories, Dainippon Pharmaceutical Co. Ltd, Osaka, Japan. It was homogenized in distilled water containing 0·001% Tween 80, sterilized for 25 min at 121°C, and kept at −80°C until use. The drug suspension, in doses of $\frac{1}{10}$ ml, was given orally to each nude mouse through a mouse catheter. The treatment followed the Shepard's kinetic method.[5] In the first experiment, sparfloxacin was given continuously, 5 or 6 times a week, at doses of 2, 5 and 10 mg/kg, and in the second experiment it was given intermittently, 2 times a week at doses of 10 and 20 mg/kg, or once a week at a dose of 30 mg/kg.

MICE

BALB/c (nu/nu) female mice, aged 5 weeks, were purchased from Clea Japan Inc., Tokyo, Japan. They were randomly grouped into 10 mice per group (5 mice per cage) in a vinyl isolator (Sanki Scientific Arts Co., Tokyo, Japan) and kept at 22 ± 1°C, being fed on a sterilized heat-stable pellet form diet, MB-6E (Funabashi Farm Co., Chiba, Japan), and sterilized drinking water.

M. LEPRAE INFECTION

We used the *M. leprae* strain Thai-53, which had been isolated from a subcutaneous leproma of a Thai lepromatous patient in 1980[6] and passed through the nude mouse footpads 7 or 8 times. Inocula were prepared according to the method of Nakayama *et al.*[7] Several infected swollen footpads were aseptically homogenized with chilled physiological saline (PS), and centrifuged at $330 \times \mathbf{g}$ for 3 min at 4°C. The supernatant was treated with alkali and centrifuged. The precipitated bacilli were suspended in 0·1% Tween 80-containing PS (pH 3)[7] and washed. The washed bacilli were suspended in PS at a cell density $> 2 \times 10^8$ bacilli/ml. A 0·05-ml portion was inoculated into each of both hind footpads of nude mice.

COUNTING OF ACID-FAST BACILLI

We took 4 or 6 footpads of 2 or 3 mice at specified time points, homogenized with PS, centrifuged at 330 × **g** as described above, and diluted the supernatant appropriately with PS. Acid-fast bacilli (AFBs) were counted in duplication according to the method of Shepard and McRae.[8] AFBs were counted in more than 40 microscopic fields with a Nikon microscope, Model Optiphoto XF-21 (Nikon Corp., Tokyo, Japan).

DETERMINATION OF HIND FOOTPAD VOLUME

The weight of water removed by the soaking from below the *malleolus lateralis* of the hind footpad was measured by a digital volume meter, Model MK-550 (Muromachi Kikai Co., Tokyo, Japan).

Results

Efficacy with serial treatment. Antileprosy activity of sparfloxacin was examined in nude mice inoculated with 10^7 leprosy bacilli per footpad and given sparfloxacin orally, once a day, 5 or 6 times a week, between 60 and 152 days postinoculation on daily doses of 2, 5, and 10 mg/kg. As shown in Figure 2, the average AFBs in 4 footpads of 2 untreated nude mice reached above 10^9 AFBs per footpad on day 1 of month 8 and 9 postinoculation, gradually increased thereafter and reached nearly 10^{10} bacilli per footpad 11 months postinoculation. The average numbers of AFBs in the sparfloxacin 2-mg/kg group were 3×10^7 and above 10^9 AFBs per footpad at 8 and 11 months after inoculation, respectively, suggesting that growth of leprosy bacilli was inhibited by sparfloxacin but that the regrowth occurred when medication was stopped. The average numbers of AFBs in the sparfloxacin 5-mg/kg group were below the inoculated level (10^7 bacilli per footpad) until 9 months but increased about 10 times at both 10 and 11 months after inoculation, suggesting a delayed growth of leprosy bacilli. In contrast, no increase in the average numbers of AFBs was observed throughout the observation period in the sparfloxacin 10-mg/kg group, demonstrating that the drug action was bactericidal-type against leprosy bacilli at this dosage. The average mouse footpad volume of the untreated control markedly increased with time, while that of the sparfloxacin 2-mg/kg group showed a slight swelling only at 10 and 11 months postinoculation and no swelling was detected in the sparfloxacin 5- and 10-mg/kg groups (Figure 3).

Efficacy with intermittent treatment. In order to assess the influence of dose regimens upon the efficacy of sparfloxacin, nude mice were inoculated with 10^7 leprosy bacilli per footpad and orally treated with sparfloxacin, once a day, twice a week, with doses of 10 and 20 mg/kg, or once a week with 30 mg/kg, between 61 and 154 days postinoculation. The untreated control showed a marked increase of 2 or 3 orders of magnitude in the average numbers of AFBs from 8 months after inoculation (Figure 4). The average numbers of AFBs in the sparfloxacin 10-mg/kg-twice-a-week group increased about 10 times at 10 and 11 months postinoculation and those of the sparfloxacin 20-mg/kg-twice-a-week and 30-mg/kg-once-a-week groups rose several times only at 11 months postinoculation. All the medicated groups showed only slight mouse footpad swelling at

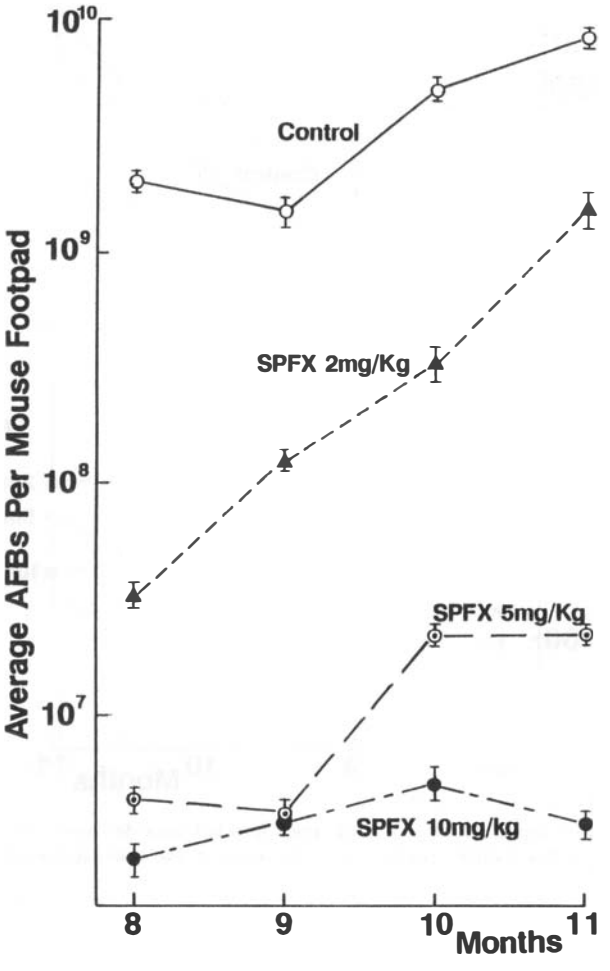

Figure 2. Growth inhibition of leprosy bacilli inoculated into nude mouse footpads by serial medication with sparfloxacin. Groups of 10 nude mice were infected with the strain Thai-53 of *M. leprae* by injecting 10^7 bacilli into each of both hind footpads, and orally treated with sparfloxacin (SPFX) once a day, 5 or 6 times a week, between 60 and 152 days postinfection at daily doses of 0, 2, 5 and 10 mg/kg. In total, 4 or 6 footpads of 2 or 3 mice were taken at indicated months postinfection and acid-fast bacilli (AFBs) in the footpads were counted.

10 and 11 months postinoculation (Figure 5). These results suggested that sparfloxacin did not kill all the leprosy bacilli by these 3 intermittent regimens and allowed some of them to remultiply when medication was stopped.

Discussion

In a previous paper,[4] we found that sparfloxacin orally given at doses of 15 and 30 mg/kg once a day, 5 or 6 times a week, for 3 months starting from month 3 postinfection completely inhibited the growth of *M. leprae* in the footpads of nude mice throughout the

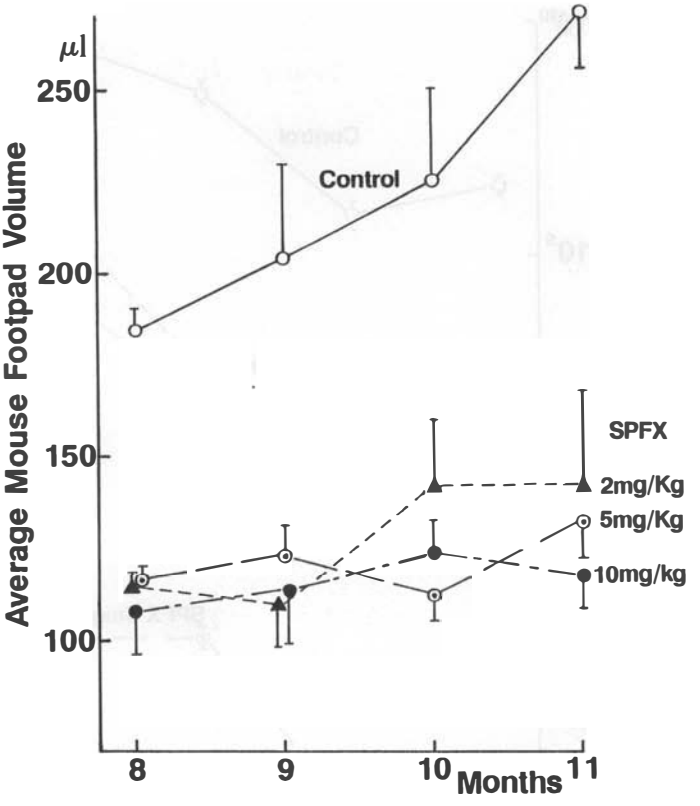

Figure 3. Inhibition of footpad swelling of nude mice infected with *M. leprae* by serial medication with sparfloxacin (SPFX). Mouse footpad volumes were measured in the mice used in the experiment shown in Figure 2; mean ± SD.

11 months postinfection, while ofloxacin at the same dosages showed only slight temporary growth inhibition. This result was of interest because ofloxacin had been considered to be the most effective among quinolones on the *M. leprae* infection in mice.[9] So, we repeated similar experiments with lower dosages of sparfloxacin to confirm the present result.

As shown in the Results section, 10 mg/kg of sparfloxacin given orally once a day, 5 or 6 times a week, for 3 months starting from month 3 postinfection completely inhibited the growth of *M. leprae* throughout the 11 months postinfection. This suggests that in this case the drug action was the bactericidal type. On a dose of 5 mg/kg, administered as above, sparfloxacin completely inhibited the bacterial growth till month 9 postinoculation, but a slight remultiplication occurred at 10 and 11 months, suggesting that the drug action was no more than bacteriostatic at this dosage. A suppressed but continued growth of *M. leprae* was observed in mice given 2 mg/kg of sparfloxacin indicating that it has less bacteriostatic drug action at this dosage. These results, when combined with the previous ones,[4] show that sparfloxacin was more potent than ofloxacin[9] in activity against *M. leprae* in nude mice, and are consistent with the findings of Franzblau and White[10] that sparfloxacin is more potent than ofloxacin in activity against *M. leprae in vitro*.

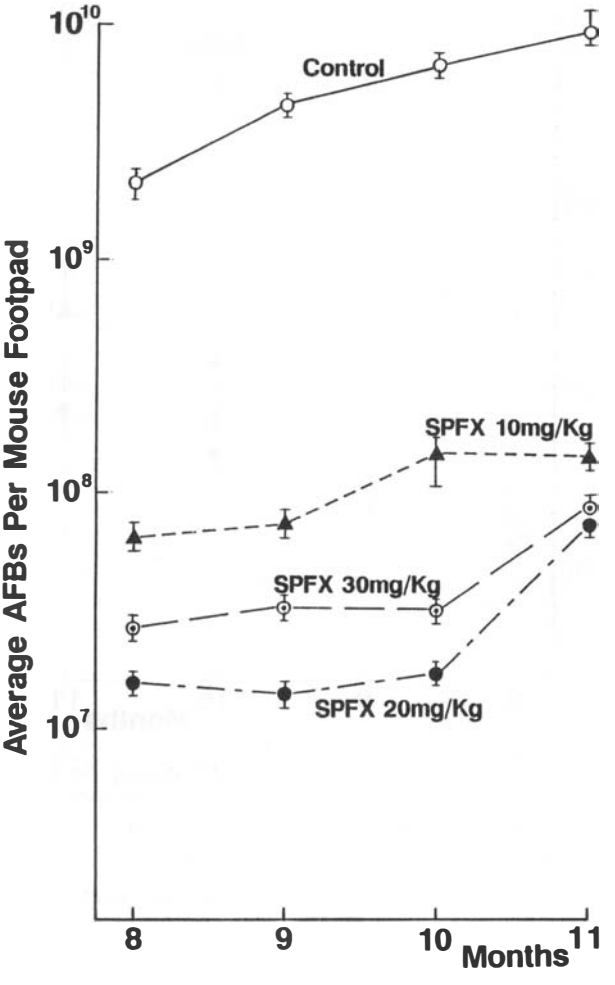

Figure 4. Growth inhibition of leprosy bacilli inoculated into nude mouse footpads by intermittent medication with sparfloxacin. Groups of 10 nude mice were infected with the strain Thai-53 of *M. leprae* by injecting 10^7 bacilli into each of both hind footpads, and orally treated with sparfloxacin (SPFX) once a day, twice a week, at a daily dose of 10 and 20 mg/kg, or once a week at a dose of 30 mg/kg, between 61 and 154 days postinfection. In total 4 or 6 footpads of 2 or 3 mice were taken at indicated months postinfection and acid-fast bacilli (AFBs) in the footpads were counted.

We next examined what the effect of sparfloxacin was when administered intermittently. The growth of *M. leprae* was completely inhibited till 10 months postinfection when sparfloxacin was given orally once a day, twice a week at doses of 10 and 20 mg/kg, or once a week at a dose of 30 mg/kg for 3 months starting from month 3 postinfection, but slight remultiplication was observed in all of the groups at month 11 postinfection. Therefore, the growth-inhibitory activity of sparfloxacin seems to be bacteriostatic when used intermittently in these dosing regimens.

We have reported that the level of sparfloxacin in a pooled serum specimen taken from 10 nude mice by the puncture of their carotid arteries at 2 hours after a single oral

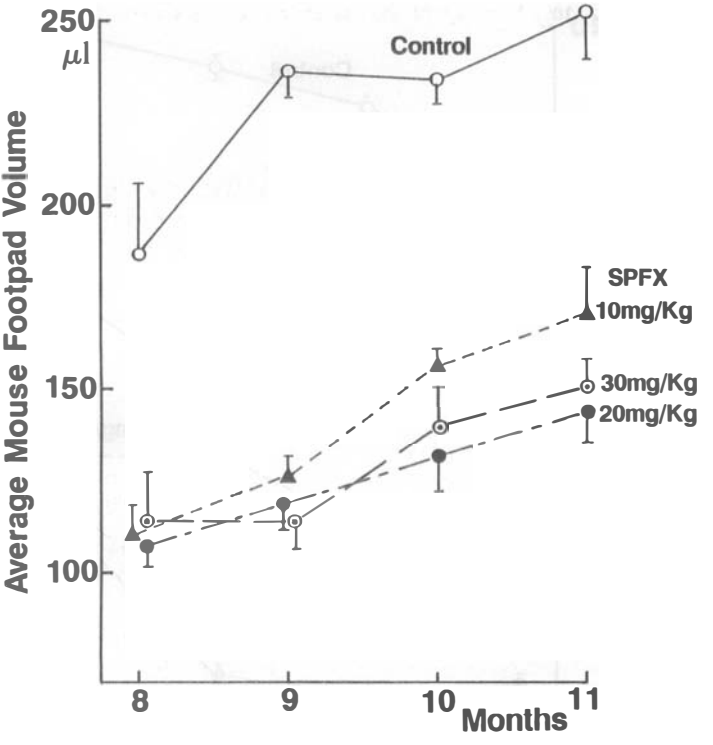

Figure 5. Inhibition of footpad swelling of nude mice infected with *M. leprae* by intermittent medication with sparfloxacin (SPFX). Mouse footpad volumes were measured in the mice used in the experiment shown in Figure 4; mean ± SD.

administration of 30 mg/kg sparfloxacin was 0·54 μg/ml, when it was measured by an HPLC system.[4] Nakamura *et al.*[11] have reported that C_{max} of sparfloxacin in plasma and muscle are 0·19 μg/ml and 0·42 μg/g, respectively, with half-lives of about 3 hours in normal mice orally given 5 mg/kg. Kanamaru *et al.*[12] disclosed in the phase I study that the C_{max} of sparfloxacin were 0·44, 0·65 and 1·39 μg/ml of serum at a single oral dose of 100, 200 or 400 mg per person (1·5, 3·1 and 6·3 mg/kg, respectively), with $t_{\frac{1}{2}}$ of 16·8, 16·3 or 16·0 h.[12] These results show that sparfloxacin might be applicable to leprosy in humans.

The strain Thai-53 of *M. leprae* was derived from a virgin case and susceptible to the present main antileprosy drugs. Taking the risk of monotherapy into consideration, activities by combined regimens with sparfloxacin against this strain are now being examined in the same nude mouse footpad model. The use of the infected nude mouse as an LL-animal model[13,14] greatly reduced the hinderance due to stained tissue debris in microscopic counting of AFBs and the volumetry of the footpad swelling made a palpable onset semi-quantitatively realizable.

Sparfloxacin is an antibacterial agent under development in Europe, the USA and Japan. Clinical efficacies of sparfloxacin on various bacterial infections have been reported to be excellent with acceptable side-effects in Japan (New Drug Symposium for sparfloxacin, The 38th General Meeting of the West Branch of Japan Society of Chemotherapy, 7 December 1990, Gifu, Japan). Therefore, based on our ongoing

research it seems reasonable to suggest that sparfloxacin is worth studying clinically as a novel antileprosy drug.

Acknowledgments

We are grateful to Drs S Nakamura and J Matsumoto, Research Laboratories, Dainippon Pharmaceutical Co. Ltd. for supplying sparfloxacin and their helpful discussion. We are also indebted to Dr K Kohsaka of this Institute for supplying the strain Thai-53 of *M. leprae*, and for his kind suggestions regarding this publication.

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Activité de la sparfloxacine contre *Mycobacterium leprae* inoculée dans la plante du pied de la souris 'nude'

M Gidoh et S Tsutsumi

Résumé Nous avons examiné l'activité antilépreuse d'une nouvelle quinolone, la sparfloxacine, sur la plante du pied de la souris 'nude'. Administrée en traitement en série (une fois par jour, 5 ou 6 fois par semaine, du 3 ème au 5 ème mois suivant l'inoculation) la sparfloxacine a présenté une activité de type bactéricide à la dose de 10 mg/kg, et une activité bactériostatique aux doses journalières de 5 et 2 mg/kg. En traitement intermittent (une fois par jour, deux fois par semaine aux doses de 10 et 20 mg/kg, ou bien une fois par semaine à la dose journalière de 30 mg/kg du 3 ème au 5 ème mois suivant l'inoculation), la sparfloxacine a nettement inhibé la croissance du bacille de la lèpre avec une légère reprise de la multiplication vers la fin du traitement. L'étude clinique de la sparfloxacine en tant que nouveau médicament contre la lèpre parait justifiée.

La actividad de sparfloxacina contra *Mycobacterium leprae* inoculada en las almohadillas de los pies de ratones desnudos

M Gidoh y S Tsutsumi

Resumen Se examinó la actividad contra la lepra de una nueva quinolona, sparfloxacina, en el modelo de la almohadilla del ratón desnudo. Por administración en serie (una vez por día, 5 o 6 veces por semana, durante el 3o hasta 5o mes postinoculación), 10 mg/kg de sparfloxacina presentó actividad antibacteriana, y presentaba bactividad bacteriostática con dósis diarias de 5 y 2 mg/kg. Por medio de dósis intermitentes (una vez por día, dos veces por semana con dósis diaries de 10 y 20 mg/kg, o una vez por semana con una dósis diaria de 30 mg/kg, durante el 3o hasta 5o mes postinoculación), sparfloxacin inhibió positivamente el crecimiento de los bacilos de la lepra con leve multiplicación durante las fases posteriores. Parece que la sparfloxacina merece un estudio clínico como una droga nueva contra la lepra.

Lepr Rev (1992) **63,** 117–124

Evaluation of *Mycobacterium leprae* particle agglutination test, using eluates of filter paper blood spots

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Summary A comparison of the ELISA test with the newly-developed MLPA test was carried out, using eluates of blood spots from filter paper for the detection of the anti-PGL-I antibody. A very good positive correlation was observed between these two tests. The concordance rate was found to be 92·6%, ranging from 71·4% to 100%. This nonconcordance was not found when freshly-collected samples were used. The MLPA test is simple and reliable. The use of eluates from blood spots collected on filter paper further simplifies the test in the collection and transportation of blood samples. This accurate and rapid method makes the MLPA test logistically feasible for large-scale screening. With our modification of MLPA with eluates more samples can be screened with the kit than with sera.

Introduction

Since the introduction of ELISA using phenolic glycolipid-I[1,2] (PGL-I) serodiagnosis of leprosy has undergone changes over many years. Because many synthetic glycoconjugates of PGL-I with terminal disaccharide-[3–6] or trisaccharide-based antigens are available,[4,7,8] ELISA for anti PGL-I has been refined for serodiagnosis of leprosy. A Latex agglutination test has also been developed for rapid serodiagnosis of leprosy.[9]

There has recently been developed a novel gelatin agglutination test named the *Mycobacterium leprae* particle agglutination (MLPA) test that uses sensitized gelatin particles.[10] This test was found to be simple, and had a sensitivity and specificity comparable to those of conventional anti-PGL-I ELISA, and was further found to be useful in the field in leprosy-endemic countries. We present here our experiences with this simple test and our attempt to further simplify the test by using eluates of blood spots, collected on filter paper.

Materials and methods

SOURCE OF BLOOD SAMPLES

We used a total of 217 samples in this study, collected from 65 leprosy patients who

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attended the Outpatient Department of the Central Leprosy Teaching and Research Institute (both treated and untreated, classified according to the Ridley–Jopling scale (LL-28, BL-14, TT-13, BT-5, PN-5)), 49 household contacts and 61 noncontacts who resided in the field operation area of CLT & RI, 33 healthy persons who worked in different sections of CLT & RI and 9 pregnant women attending the Obstetric & Gynaecology Department of Chengalpattu Medical College Hospital.

COLLECTION OF BLOOD SAMPLES

Blood samples were collected by venepuncture and finger prick. In the latter method blood oozing out of the finger tip cut by a lancet was absorbed on a strip of Whatman chromatography filter paper, No. 3 (2·0 × 7·5 cm). About 50 μl of blood was collected by this method. After air-drying, the filter paper strips and sera were placed in plastic self-sealing bags, and the samples were kept at −20°C until further use.

ELUTION OF BLOOD SPOTS

Two small discs of 7-mm diameter were cut from the dried blood spots on filter paper and eluted in 225 μl of phosphate-buffered saline (pH 7·2) with 0·05% Tween-20 (PBST) containing 1% bovine serum albumin (BSA). The elution was carried out at room temperature for 1 hour, which gave a serum dilution of 1:20.

ELISA

ELISA was done using the same procedure as reported earlier.[11] Briefly ND-0-BSA antigen supplied by IMMLEP/WHO was diluted in carbonate bicarbonate buffer (CBCB) pH 9·6 and 50 μl per well was added to half of a 96-well flat-bottom polysterene microtitre plate (Dynatech Micro-ELISA system, Germany). The remaining wells were coated with 50 μl per well of BSA in CBCB. After overnight incubation at 37°C blocking was done with 1% BSA in PBST. Sera (1:300 dilution) and eluates of blood (1:40 dilution) were added to both antigen and BSA coated wells in duplicate. After 1 hour incubation at 37°C peroxidase conjugated anti-human IgM (Dako, Denmark) at 1:2000 dilution was added to all wells and incubated at 37°C for 1 hour. A substrate solution (O-phenylenediamine and H_2O_2) in citrate buffer pH 5·0 was added. The reaction was stopped with 5 N H_2SO_4. The optical density was read at 492 nm in an ELISA reader (MR 600 microplate reader, Dynatec). The difference in OD values between the antigen and BSA coated wells was calculated for each sample. The mean value of duplicate wells was taken. A mean difference of more than 0·2 OD was considered positive.

MLPA (*MYCOBACTERIUM LEPRAE* PARTICLE AGGLUTINATION TEST)

The serodia-leprae microtitre particle agglutination test kit for detection of anti-PGL antibody was supplied as a gift by Fujirebio Inc., Japan. (The gelatin particles were sensitized with NT-P-BSA, a semi-synthetic antigen.) The lyophilized unsensitized and sensitized particles were reconstituted with a reconstitution solution supplied with the kit 30 minutes before starting the test.

PROCEDURE FOR THE MLPA WITH DIRECT SERA

A serum diluent of 75 μl was added to the first well and 25 μl of the diluent was added to the second and subsequent wells of a 96 U bottom microtitre plate, 25 μl of test serum were added to the first well (1:4 dilution). After mixing, 25 μl of diluted serum from the first well were transferred to the second well (1:8 dilution) and this doubling dilution was carried out from the second well to the third well and so on. Unsensitized particles totalling 25 μl were added to the second well only (1:16 dilution) and 25 μl of sensitized particles were added to the third and subsequent wells (dilutions 1:32, 1:64 up to 1:512). The plates were covered and thoroughly mixed on a rotator at 160 cpm for 1 minute, and then incubated at 37°C in a moist chamber. The reading of the results was carried out visually. Agglutination with sensitized particles was read in comparison with unsensitized particles as negative, +, ++, +++. The highest dilution at which the agglutination seen was taken as the end point titre for that sample. As suggested by the manufacturer, and also from our further standardization, it was decided to use a titre of 1:64 as the cut-off dilution for positivity for this test.

PROCEDURE FOR THE MLPA WITH ELUATES OF BLOOD

Serum diluent (30 μl) were added to the third well and subsequent wells, and 30 μl of eluates (1:20 dilution) were added to the first, second and third wells. From the third well after mixing, 30 μl of diluted serum were transferred to the fourth well and this doubling dilution was continued for subsequent wells.

Unsensitized particles totalling 15 μl were added to the first well only (1:30 dilution) and 15 μl of sensitized particles were added to the second, third and subsequent wells (1:30, 1:60, 1:120 up to 1:480 dilution). The rest of the procedure was the same as for the test using direct sera. After standardization it was decided to have 1:60 as the cut-off dilution for this test.

Results

To establish the reproducibility of the MLPA test with eluates of blood, 81 samples were initially screened. The MLPA test was done with both eluates and direct sera. They belonged to 39 leprosy patients (LL-19, BL-6, TT-5, BT-4, PN-5), 9 pregnant women and 33 occupational contacts. We found an excellent positive correlation between the MLPA test done with eluates and direct sera. The concordance rate was found to be 97·5% (Table 1). Reading the result as positive or negative in both methods was found to be easy. The MLPA test done with the sera showed a positivity in 76% (19/25) of MB cases, 79% (10/14) of PB cases and 3·03% (1/33) of occupational contacts, whereas the MLPA test done with eluates showed a positivity in 80% (20/25) of MB cases, 64% (9/14) of PB cases and 3·03% (1/33) of occupational contacts.

Using 217 samples, we compared MLPA with ELISA using eluates from blood spots on filter paper as described above (Table 2). The samples comprised of 65 leprosy patients (LL-active 14, LL-inactive-14, BL active-7, BL inactive-7 TT-13, BT-5, PN-5), 49 household contacts, 61 noncontacts, 33 occupational contacts and 9 pregnant women. We found a good positive correlation between the results obtained with the ELISA and

Table 1. Concordance between MLPA with sera and with eluates of filter paper

Group	No. of specimens tested	No. of specimens with test results*				% Concordance
		S+F+	S+F−	S−F+	S−F−	
Lepromatous (LL)						
Active	10	10	0	0	0	100
Inactive	9	6	0	1	2	88·9
Borderline lepromatous (BL)						
Active	2	2	0	0	0	100
Inactive	4	1	0	0	3	100
Tuberculoid (TT)	5	4	0	0	1	100
Borderline tuberculoid (BT)	4	3	0	0	1	100
Pure neuritic (PN)	5	2	1	0	2	80
Pregnancy	9	0	0	0	9	100
Occupational contacts	33	1	0	0	32	100
	81	29	1	1	50	97·5

*S, MLPA done with sera. F, MLPA done with eluates of filter paper.

Table 2. Concordance between IgM anti-PGL-I ELISA and MLPA using eluates of filter paper

Group	No. of specimens tested	No. of specimens with test results*				% Concordance
		E+M+	E+M−	E−M+	E−M−	
Lepromatous (LL)						
Active	14	12	1	0	1	92·9
Inactive	14	10	2	0	2	85·7
Borderline lepromatous (BL)						
Active	7	6	0	0	1	100·0
Inactive	7	2	2	0	3	71·4
Tuberculoid (TT)	13	7	2	0	4	84·6
Borderline tuberculoid (BT)	5	4	0	0	1	100·0
Pure neuritic (PN)	5	2	0	1	2	80·0
Household contacts (HHC)	49	0	3	0	46	93·9
Noncontacts (NC)	61	1	5	0	55	91·8
Pregnancy	9	0	0	0	9	100·0
Occupational contacts	33	1	0	0	32	100·0
	217	45	15	1	156	92·6

* E, ELISA; M, MLPA.

MLPA tests. The concordance rate was found to be 92·6% (ranging from 71·4% to 100%). ELISA showed a positivity in 83·3% (35/42) of MB cases, 65·2% (15/23) of PB cases, 6·1% (3/49) of household contacts, 9·8% (6/61) of noncontacts and 3·03% (1/33) of occupational contacts. MLPA showed a positivity in 71·4% (30/42) of MB cases, 60·9% (14/23) of PB cases, 1·6% (1/61) of noncontacts and 3·03% (1/33) of occupational contacts. The efficiency of both these tests was found to be comparable (Table 3). The MLPA positive samples had a mean ELISA value of $0{\cdot}561 \pm 0{\cdot}314$ (0·175 to 1·131), while the MLPA negative samples had $0{\cdot}133 \pm 0{\cdot}111$ (0·00 to 0·53).

Table 3. Comparison between ELISA and MLPA using eluates of filter paper

	ELISA (%)	MLPA (%)
* Specificity	93·4	98·7
† Sensitivity	76·9	67·7

* MLPA is more specific than ELISA ($\chi^2 = 4{\cdot}25$, $p = 0{\cdot}03$)

† MLPA is as sensitive as ELISA ($\chi^2 = 1{\cdot}37$, $p = 0{\cdot}24$)

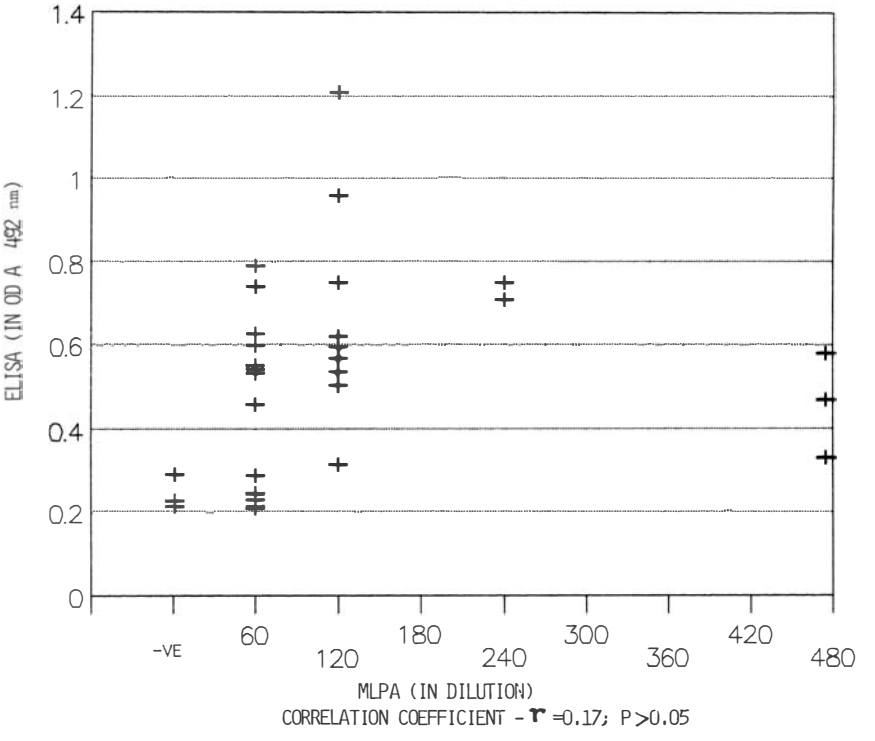

Figure 1. Correlation between results of anti-PGL-1 ELISA and MLPA.

Of the 217 samples, 16 samples showed a lack of concordance, 15 of which (6·9%) were only ELISA positive. They consisted of LL active-I, LL inactive-2, BL inactive-2, TT-2, HHC-3 NC-5. One sample (PN) was only positive by MLPA (0·5%) (Table 2). The OD values by ELISA for these samples ranged from 0·20 to 0·53 ($0{\cdot}309 \pm 0{\cdot}125$). All these sera were stored at $-20°C$ between 2 and 10·5 months ($7{\cdot}6 \pm 2{\cdot}5$ months). The nonconcordance was not observed when freshly collected samples were used for MLPA.

Further the attempt to correlate the result of ELISA (expressed as OD) with the titre

Table 4. Interobserver variation in reading MLPA results

		Person-B			
	1+	1+	2+	3+	Neg.
		59	03	0	11
	2+	14	19	09	0
Person A					
	3+	0	04	02	0
	Neg.	06	0	0	184

Agreement in reading the result positive or negative = Kappa = 0·88.

Agreement in reading the grade (+, + +, + + +) of the result = Kappa = 0·48.

Kappa more than 0·75—excellent, Kappa between 0·40 and 0·75—Fair to Good, Kappa below 0·40—poor agreement.[18]

of MLPA (expressed in dilution) revealed that there was no statistically significant correlation between these results (Figure 1, $r = 0{\cdot}17$).

When we analysed the interobserver variation in reading the MLPA result, it showed that the agreement for reading the result as positive or negative between the observers was excellent (Kappa = 0·88), whereas the agreement for reading the grade of the results (+, + +, + + +) between the observers was found to be fair to good (Kappa = 0·48). The variation was found to be in the range of 1+ (Table 4).

Discussion

Since the development of anti-PGL ELISA,[1,2] the serology of leprosy has changed a lot with the introduction of many synthetic glycoconjugates of PGL-I.[3–8] The antibody response to PGL-I is predominantly IgM. The antibody level increases from TT to LL across the spectrum of leprosy. In recent years studies using ELISA have reported a significant proportion of subjects in endemic areas showing a high positive antibody response to PGL antigen without any clinical signs of leprosy.[12,13] Many studies have shown the possible use of anti-PGL ELISA as a monitor for chemotherapy, as the antibody level was shown to be decreased by effective chemotherapy.[14–16]

Recently a much simpler and less time consuming MLPA test was introduced.[10] The comparative study of MLPA and ELISA for detection of IgM anti-PGL antibody titre proved that both the methods basically have identical sensitivity and specificity. MLPA, however, cannot detect IgG antibody, because of the poor agglutination capacity of IgG anti-PGL-I antibody. We proposed to compare these two methods and further attempted to simplify the test by using samples from eluates of blood spots from filter paper. Anti PGL-I ELISA using eluates from blood spots collected on filter paper is routinely done in our laboratory. It is found to be a suitable method for the large scale screening of samples, which was observed by other workers.[17] Initially we compared the MLPA test using direct sera with the MLPA test using eluates of blood from filter paper. We found an excellent positive correlation between these two methods, with a concordance rate of 97·5%. As the amount of antigen used is less, 50% more tests can be done with the same amount of the eluates of blood.

When we compared MLPA with ELISA using eluates from blood spots on filter paper, we found a very good positive correlation between these two methods. The concordance rate was found to be 92·6%. This is in agreement with the observations of other workers.[10] Of the 217 samples, 16 showed nonconcordance (7·5%), of which 15 samples were positive by ELISA only. These samples showed OD in ELISA, ranging from 0·20 to 0·53. All these sera were stored at $-20°C$ between 2 and 10·5 months ($7·6 \pm 2·5$ months). This nonconcordance was not found when freshly collected samples were used for MLPA. The serological test with eluates should be done as soon as possible after collection, an important fact that was also observed by other workers.[17] Further we attempted to correlate the activity of ELISA with that of MLPA. It revealed that there was no statistically significant correlation between the results of these two methods ($r = 0.17$). Although we used ND-0-BSA antigen in ELISA, the correlation with NT-P-BSA in MLPA was good—this was observed by other workers,[9] as was a good correlation between PGL-I and ND-0-BSA in latex agglutination tests.

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Lepr Rev (1992) **63,** 117–124

Évaluation du test d'agglutination des particules de *Mycobacterium leprae*, utilisant les éluats de taches de sang sur papier filtre

B Sekar et L D Anandan

Résumé Nous avons comparé le test ELISA au test récemment développé MLPA en utilisant les éluats de taches de sang d'un papier filtre pour la détection des anticorps anti-PGL-I. Nous avons observé une très bonne corrélation positive entre ces deux tests. Le taux de concordance observé a été de 92,6%, variant entre 71,4% et 100%. Cette non-concordance n'a pas été observée sur les échantillons fraîchement recueillis. Le test MLPA est simple et fiable. L'utilisation des éluats de taches de sang recueilli sur papier filtre simplifie encore le test en facilitant le prélèvement et le transport des échantillons de sang. Avec cette méthode précise et rapide, la logistique du test MLPA devient réalisable dans les campagnes de dépistage à grande échelle. Notre modification de MLPA avec les éluats permet de traiter un plus grand nombre d'échantillons avec le kit qu'avec les serums.

Evaluación de la prueba de aglutinación de partículas de *Mycobacterium leprae*, utilizando eluatos de manchas de sangre en papel de filtro

B Sekar y L D Anandan

Resumen Se realizó una comparación entre la prueba ELISA con la recién desarrollada prueba MLPA, utilizando eluatos de manchas de sangre en papel de filtro para la detección del anticuerpo anti-PGL-I. Se obtuvo una muy buena correlación positiva entre las dos pruebas. El coeficiente de concordancia obtenido fue 92,6%, con una escala de 71,4% a 100%. No se obtuvo esta falta de concordancia cuando se usaron muestras frescas. La prueba MLPA es sencilla y fiable. El uso de eluatos de manchas de sangre en papel de filtro simplifica la prueba aun más en cuestión de la recolección y el transporte de muestras de sangre. Este rápido y exacto método hace que la prueba MLPA sea factible logísticamente para estudios en gran escala. Nuestra modificación de la MLPA usando eluatos y el kit permite el estudio de más muestras que usando sueros.

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Double-blind evaluation of BACTEC and Buddemeyer-type radiorespirometric assays for *in vitro* screening of antileprosy agents

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Summary Two radiorespirometric assays, the BACTEC 460 and Buddemeyer-type $^{14}CO_2$ detection systems, were evaluated in a double-blind manner for their ability to discriminate between authentic antileprosy agents and inactive compounds. Freshly harvested, nude-mouse derived *Mycobacterium leprae* were incubated in axenic media in the presence of coded test solutions prepared in a remote laboratory. Activity was assessed by comparing the rate of $^{14}CO_2$ evolution from [1-^{14}C]palmitic acid to controls. Breaking the code revealed that both systems demonstrated a dose response to ethionamide, pefloxacin and rifampicin as well as sensitivity to dapsone. Most of the water, ethanol, sucrose, dabsyl chloride and riboflavin negative-control samples failed to effect a significant reduction in radiorespirometric activity. This study confirms the ability of the radiorespirometric assays to function as a primary drug screening system in leprosy.

Introduction

Historically, the screening of compounds for activity against *Mycobacterium leprae* has had to utilize the mouse footpad model[1–3] because of the failure to cultivate the leprosy bacillus *in vitro*. The high cost, the length of time (6–12 months per experiment), the requirement for gram quantities of drug and the dependence on non-human pharmacokinetics[4] have all motivated investigators to develop rapid *in vitro* systems which measure bacterial metabolism (following exposure to antimicrobial agents) as an index of viability.[5–7]

The ability of *M. leprae* to oxidize rapidly palmitic acid to carbon dioxide[8–10] has been exploited by Franzblau *et al.*[10–17] when screening for new antileprosy drugs, using two related assay systems: a Buddemeyer-type, liquid scintillation based, two-compartment system[10] and an adaptation of the commercial BACTEC 460 system.[11] These systems are very similar in that they both quantitate the rate of $^{14}CO_2$ evolution from ^{14}C-labelled

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substrates. Both are 'automated' systems which do not require host cells, subsampling, extraction, filtration or other processing following the incubation of bacilli with drugs.

The present WHO-sponsored, double-blind study was undertaken to evaluate objectively the utility of these systems in screening for antileprosy drugs. Coded samples of compounds with known antileprosy activity, and control samples with no activity, were prepared in the London laboratory and sent to the Carville laboratory where they were tested in the two *in vitro* assays. In this way we were able to assess the reliability and reproducibility of the assays in screening for antileprosy activity.

Methods

The drug solutions were composed of stock solutions of rifampicin (RMP; 2·5 mg/ml in ethanol), ethionamide (ETH), dapsone (DDS; 5 mg/ml in ethanol), and pefloxacin (PEF; 5 mg/ml in water) and were prepared at NIMR (London). Triplicate 0·1 ml aliquots of these stock solutions, together with 2·5-fold, 5-fold and 10-fold dilutions were provided for a subsequent 100-fold dilution in the test media following filter sterilization. Negative control solutions consisted of distilled water, absolute ethanol, 1% sucrose, riboflavin (0·5 mg/ml), and dabsyl chloride (0·1 mg/ml). These last two acted as colour controls for ethionamide and rifampicin, respectively. The 70 test samples were coded, randomized, stored at −20°C and shipped on dry ice to the Carville laboratory where they were held at −20°C until used.

M. LEPRAE INOCULUM

M. leprae was harvested from the footpads of athymic nu/nu mice when the footpads had reached a bacillary load of approximately 10^{10} AFB. Footpads were surface decontaminated with iodine and ethanol, minced and homogenized in 7H12 medium (Middlebrook 7H9 broth, 0·1% casitone (Difco), 1% w/v albumin and 5 μg/ml catalase). The bulk of tissue debris was removed by slow-speed centrifugation ($108 \times g$, 5 min, 10°C) and the bacilli pelleted ($2710 \times g$, 45 min, 10°C) and resuspended in 7H12 medium to approximately 10^9/ml. Cell counts were determined by the method of Shepard & McRae.[18] The suspensions were treated with 50 μg/ml ampicillin and 2·5 μg/ml amphotericin B for 4–5 h to eliminate contaminants. These agents have repeatedly been shown to be inactive against *M. leprae*.[10,19] Aliquots of the bacillary suspension were inoculated into Middlebrook 7H11 and Lowenstein–Jensen slants, tryptic soy and thioglycollate broths and blood agar to check for contaminants.

BACTEC

The *M. leprae* suspension was diluted to 10^8/ml in 7H12 medium and 0·1 ml aliquots (10^7 AFB) delivered via tuberculin syringe to BACTEC 12B media (4 ml in 20 ml serum vials) supplemented with 50 μg/ml ampicillin and 2·5 μg/ml amphotericin B. The controls were 16 cultures that had received 0·1 ml 7H9 broth. Other cultures received 0·1 ml of coded test solutions in quadruplicate. All vials were flushed with 2·5% oxygen, 10% carbon dioxide, balance nitrogen using the BACTEC 460 instrument and were then incubated at 33°C. The growth index (GI, $^{14}CO_2$ evolution) was determined at weekly intervals for 3 weeks in

the BACTEC 460 by flushing with the above gas mixture. Readings from week 2 were used in evaluating activity.

BUDDEMEYER

The *M. leprae* suspension was diluted to 10^6/ml in 7H12 medium and 1 ml aliquots (10^6 AFB) dispensed to 6 ml screw-capped vials (Wheaton, Millville, NJ, USA). The controls were 16 cultures who received 10 μl 7H9 broth. Other cultures received 10 μl of coded test solutions in quadruplicate. Vials, with loose caps, were then incubated for 2 weeks at 33°C under an atmosphere of 2·5% oxygen, 10% carbon dioxide in an incubator with automatic oxygen and carbon dioxide control capability, and 1 microCurie of [1-^{14}C] palmitic acid (58 mCi/mmole; New England Nuclear, Boston, MA, USA) was added to each vial in a volume of 10 μl ethanol. The glass vials, with loose caps, were then placed within wide-mouth scintillation vials (Poly-Q; Beckman, Brea, CA) containing a 2 × 4 cm strip of Whatman No. 42 filter paper which had previously been dipped into a mixture of 20 ml Liquifluor concentrate (New England Nuclear), 15 g PPO, 5 ml Triton-X 100 and 5 ml 2N NaOH (in MeOH). The entire assembly was incubated at 33°C and $^{14}CO_2$ evolution determined at daily intervals for 1 week by placing the double vial assemblies in a liquid scintillation counter. Cumulative counts per minute from the day 7 reading were used in evaluating activity.

STATISTICAL EVALUATION

Statistical significance was determined by the Student's *t*-test.

Results

BACTEC

Using a *p* value of 0·05 as a cut-off for active substances, there were 6 false positives out of 22 non-antileprosy substances (Table 1). While 11 of 12 DDS samples were active, there was little, if any, dose-response over the entire range of 0·1–5·0 μg/ml. Both ETH and PEF displayed no activity at 0·1 μg/ml; 2 of 3 samples were active at 0·5 μg/ml and all 2·0 and 5·0 μg/ml samples effected significant reductions compared to controls. The dose response was more apparent with PEF than with ETH. All RMP concentrations demonstrated highly significant activity and effected a clear dose-response.

BUDDEMEYER

Only 1 of the 22 non-antileprosy substances appeared active, possibly due to the large SD obtained with this sample (A20) (Table 2). Results with DDS were variable, although 2 of 3 samples were positive at 0·5, 2·0 and 5·0 μg/ml. Both ETH and PEF gave inconclusive results at 0·1 μg/ml and significant dose-responsive activity at the 3 higher concentrations. All concentrations of RMP again demonstrated highly significant, dose-dependent activity.

Table 1. BACTEC system

Coded sample	De-coded sample and concentration (μg/ml)	Mean	SD	p	Rating
Control		746	113		
Heat killed		2	1	$<0{\cdot}001$	
A13	Water	670	39	0·212	Inactive
A18	Water	684	63	0·315	Inactive
A22	Water	574	108	0·014	Active*†
A25	Water	613	48	0·036	Active*†
A32	Water	643	37	0·094	Inactive
A65	Water	576	27	0·010	Active*†
A10	Sucrose	639	50	0·088	Inactive
A37	Sucrose	654	35	0·192	Inactive
A08	Ethanol	633	31	0·068	Inactive
A12	Ethanol	732	44	0·808	Inactive
A23	Ethanol	626	49	0·057	Inactive
A36	Ethanol	648	45	0·113	Inactive
A39	Ethanol	642	25	0·100	Inactive
A59	Ethanol	752	51	0·926	Inactive
A04	Dabsyl Cl	725	9	0·724	Inactive
A52	Dabsyl Cl	807	32	0·308	Inactive
A61	Dabsyl Cl	736	38	0·864	Inactive
A69	Dabsyl Cl	614	21	0·035	Active*†
A20	Riboflavin	698	77	0·437	Inactive*
A26	Riboflavin	591	37	0·017	Active*†
A38	Riboflavin	703	117	0·513	Inactive
A70	Riboflavin	528	76	0·002	Active*†
A03	DDS 0·1	564	12	0·006	Active
A34	DDS 0·1	516	12	0·001	Active*
A57	DDS 0·1	611	18	0·032	Active*
A02	DDS 0·5	501	48	0·001	Active
A48	DDS 0·5	669	41	0·204	Inactive*
A56	DDS 0·5	599	3	0·021	Active
A01	DDS 2·0	512	26	0·001	Active
A31	DDS 2·0	462	24	$<0{\cdot}001$	Active*
A67	DDS 2·0	480	15	$<0{\cdot}001$	Active
A27	DDS 5·0	476	13	$<0{\cdot}001$	Active
A50	DDS 5·0	588	2	0·014	Active*
A68	DDS 5·0	425	32	$<0{\cdot}001$	Active
A16	ETH 0·1	651	43	0·123	Inactive*
A44	ETH 0·1	775	47	0·630	Inactive
A55	ETH 0·1	759	19	0·824	Inactive
A43	ETH 0·5	635	165	0·129	Inactive*
A62	ETH 0·5	570	22	0·007	Active
A64	ETH 0·5	570	17	0·007	Active
A07	ETH 2·0	537	46	0·002	Active
A40	ETH 2·0	469	56	$<0{\cdot}001$	Active
A41	ETH 2·0	551	70	0·005	Active
A14	ETH 5·0	449	36	$<0{\cdot}001$	Active
A30	ETH 5·0	395	50	$<0{\cdot}001$	Active
A47	ETH 5·0	503	43	0·001	Active
A19	PEF 0·1	728	48	0·758	Inactive*
A42	PEF 0·1	816	49	0·316	Inactive
A49	PEF 0·1	ND			

Table 1. (*Contd.*)

Coded sample	De-coded sample and concentration (μg/ml)	Mean	SD	p	Rating
A11	PEF 0·5	643	61	0·100	Inactive*
A15	PEF 0·5	616	79	0·047	Active
A29	PEF 0·5	604	22	0·025	Active
A17	PEF 2·0	536	50	0·002	Active
A28	PEF 2·0	457	35	<0·001	Active
A45	PEF 2·0	561	64	0·006	Active
A09	PEF 5·0	362	29	<0·001	Active
A53	PEF 5·0	418	5	<0·001	Active
A66	PEF 5·0	318	46	<0·001	Active
A24	RMP 0·05	458	32	<0·001	Active
A33	RMP 0·05	440	41	<0·001	Active
A63	RMP 0·05	ND			Active
A06	RMP 0·25	394	26	<0·001	Active
A35	RMP 0·25	290	37	<0·001	Active
A54	RMP 0·25	395	28	<0·001	Active
A21	RMP 1·0	204	35	<0·001	Active
A58	RMP 1·0	262	27	<0·001	Active
A60	RMP 1·0	258	14	<0·001	Active
A05	RMP 2·5	226	10	<0·001	Active
A46	RMP 2·5	222	37	<0·001	Active
A51	RMP 2·5	212	8	<0·001	Active

For controls, $n = 16$; for test samples, $n = 4$.
Rating criteria: active = $p < 0{\cdot}05$; inactive = $p > 0{\cdot}05$ *vs.* controls.
*, Apparent disagreement with results of Buddemeyer assay.
ND, not determined; †, false positive result.

Discussion

This double-blind, 2-laboratory evaluation of these *in vitro* radiorespirometric systems confirms previous reports on the ability of these assays to detect activity of established antileprosy drugs at concentrations below peak obtainable plasma levels.[10–12] All of the known antileprosy compounds were found to be active at the concentrations which they would be predicted to be active and there was good concordance between replicate samples. Results from earlier studies and this report suggest a correlation between degree of drug activity in the mouse footpad[19–24] and radiorespirometric systems.[11,12,14,16] In general, highly active, potent drugs such as RMP produced lower levels of $^{14}CO_2$ than bacteriostatic agents such as DDS. Since all concentrations of RMP were active in both Buddemeyer and the BACTEC systems, we were unable to determine an MIC. The MIC of ethionamide, as measured by the *in vitro* systems, appeared to be between 0·1 and 0·5 μg/ml (compared to 0·05 μg/ml as estimated by the mouse footpad system). All concentrations of DDS were active in the BACTEC system, whereas in the Buddemeyer system occasional samples at all concentrations were found to be inactive, making it difficult to compare the MIC *in vitro* with that estimated using the mouse footpad technique (approximately 0.003 μg/ml). Pefloxacin appears to have an MIC of approximately 0·5 μg/ml *in vitro*.

Table 2. Buddemeyer system

Coded sample	De-coded sample and concentration (μg/ml)	Mean	SD	p	Rating
Control		7213	992		
Heat killed		148	10	<0.001	
A13	Water	6704	331	0·333	Inactive
A18	Water	6671	552	0·313	Inactive
A22	Water	6731	982	0·395	Inactive*
A25	Water	6833	243	0·465	Inactive*
A32	Water	7325	958	0·842	Inactive
A65	Water	6963	987	0·656	Inactive*
A10	Sucrose	7257	605	0·935	Inactive
A37	Sucrose	6501	533	0·188	Inactive
A08	Ethanol	6693	758	0·343	Inactive
A12	Ethanol	7384	435	0·745	Inactive
A23	Ethanol	6361	603	0·174	Inactive
A36	Ethanol	7316	1300	0·876	Inactive
A39	Ethanol	7444	1251	0·696	Inactive
A59	Ethanol	7879	306	0·210	Inactive
A04	Dabsyl Cl	6272	1496	0·141	Inactive
A52	Dabsyl Cl	6548	466	0·215	Inactive
A61	Dabsyl Cl	6896	1003	0·575	Inactive
A69	Dabsyl Cl	8143	1165	0·122	Inactive*
A20	Riboflavin	5399	1971	0·023	Active*†
A26	Riboflavin	7092	268	0·814	Inactive*
A38	Riboflavin	6760	681	0·403	Inactive
A70	Riboflavin	7252	544	0·941	Inactive*
A03	DDS 0·1	5623	648	0·007	Active
A34	DDS 0·1	6258	330	0·078	Inactive*
A57	DDS 0·1	6310	213	0·093	Inactive*
A02	DDS 0·5	5543	100	0·004	Active
A48	DDS 0·5	5392	804	0·003	Active*
A56	DDS 0·5	5746	781	0·014	Active
A01	DDS 2·0	5439	828	0·004	Active
A31	DDS 2·0	6621	414	0·265	Inactive*
A67	DDS 2·0	6080	814	0·050	Active
A27	DDS 5·0	5805	1204	0·025	Active
A50	DDS 5·0	6268	1076	0·110	Inactive*
A68	DDS 5·0	5193	290	0·001	Active
A16	ETH 0·1	5884	1235	0·034	Active*
A44	ETH 0·1	6501	335	0·181	Inactive
A55	ETH 0·1	7035	854	0·746	Inactive
A43	ETH 0·5	5038	1131	0·001	Active*
A62	ETH 0·5	5791	456	0·013	Active
A64	ETH 0·5	5296	1626	0·007	Active
A07	ETH 2·0	1699	460	<0.001	Active
A40	ETH 2·0	1953	570	<0.001	Active
A41	ETH 2·0	ND			Active
A14	ETH 5·0	1086	39	<0.001	Active
A30	ETH 5·0	1163	237	<0.001	Active
A47	ETH 5·0	1270	85	<0.001	Active
A19	PEF 0·1	5789	1252	0·025	Active*
A42	PEF 0·1	ND			
A49	PEF 0·1	8480	550	0·026	Inactive

Table 2. (*Contd.*)

Coded sample	De-coded sample and concentration (μg/ml)	Mean	SD	*p*	Rating
A11	PEF 0·5	5206	644	0·001	Active*
A15	PEF 0·5	4732	469	<0·001	Active
A29	PEF 0·5	5527	961	0·007	Active
A17	PEF 2·0	3319	430	<0·001	Active
A28	PEF 2·0	3438	264	<0·001	Active
A45	PEF 2·0	3136	717	<0·001	Active
A09	PEF 5·0	2506	187	<0·001	Active
A53	PEF 5·0	2458	19	<0·001	Active
A66	PEF 5·0	2608	307	<0·001	Active
A24	RMP 0·05	4179	557	<0·001	Active
A33	RMP 0·05	4423	922	<0·001	Active
A63	RMP 0·05	5346	389	0·002	Active
A06	RMP 0·25	2174	388	<0·001	Active
A35	RMP 0·25	2266	348	<0·001	Active
A54	RMP 0·25	2082	57	<0·001	Active
A21	RMP 1·0	453	139	<0·001	Active
A58	RMP 1·0	832	122	<0·001	Active
A60	RMP 1·0	802	168	<0·001	Active
A05	RMP 2·5	633	77	<0·001	Active
A46	RMP 2·5	696	47	<0·001	Active
A51	RMP 2·5	631	87	<0·001	Active

For controls, $n = 16$; for test samples, $n = 4$.
Rating criteria: active = $p < 0{\cdot}05$; inactive = $p > 0{\cdot}05$ *vs.* controls.
*, Apparent disagreement with results of BACTEC assay.
ND, not determined; † false positive result.

Up to now the radiorespirometric systems evaluated in this report have been used to screen 6 macrolides,[14] 17 clofazimine derivatives,[15,17] 20 fluoroquinolones,[16] 1 tetracycline,[11] 5 aminoglycosides, 3 rifamycins and 2 lincosamides[12] for activity against *M. leprae*. Thus, 2 agents, clarithromycin[14] and sparfloxacin,[16] were first recognized as being the most active clinically relevant agents in their respective classes and are currently in clinical trials in leprosy. Another potential antileprotic identified by radiorespirometry is fusidic acid,[13] an established antibiotic which has poor pharmacokinetics in mice (in contrast to humans) and is inactive against *M. leprae* in the mouse footpad model (Colston, unpublished results).

There was fairly good agreement (79%) between the BACTEC and Buddemeyer systems, especially considering that the two assays were evaluated in separate experiments at different times using different nude mouse-derived inocula. The BACTEC system requires approximately 10 times more bacilli than the Buddemeyer-type system to obtain usable readings. This relatively lower sensitivity also results in smaller differences observed between control and drug-treated samples than that observed in the Buddemeyer system. The BACTEC system, however, appears to be more sensitive to weakly-active agents such as DDS and results in lower variance among replicate samples. This may be due to the ability to produce efficiently and maintain the desired (microaerophilic) environment using the BACTEC 460 instrument, which appears optimal for maintenance of *M. leprae* viability *in vitro*.[25] With either test (consisting of approximately 300 vials—70

samples in quadruplicate plus 4 heat-killed and 16 drug-free controls), the numbers evaluated in the present study can be read within a normal 8 hour working day.

Conclusion

Radiorespirometry, using either the BACTEC 460 or Buddemeyer $^{14}CO_2$ detection systems, is capable of differentiating between antileprosy agents and inactive substances following a 2-week incubation of freshly harvested, viable leprosy bacilli under appropriate incubation conditions.

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Lepr Rev (1992) **63,** 125–133

Évaluation en double-aveugle des tests radiorespirométriques BACTEC et type Buddemeyer pour le triage *in vitro* des agents antilépreux

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Résumé Nous avons comparé deux essais radiorespirométriques, le système BACTEC 460 et le système type Buddemeyer de détection de $^{14}CO_2$, en double-aveugle, pour évaluer leur aptitude à différencier entre les agents antilépreux authentiques et les composés inactifs. *Mycobacterium leprae* provenant de souris "nude", fraîchement récolté, a été incubé en milieu axénique en présence des solutions à tester identifiées par code et préparées dans un laboratoire éloigné. L'activité a été déterminée en comparant le contôle du taux d'évolution de $^{14}CO_2$ partir de l'acide (1-^{14}C) palmitique. En décodant, nous avons observé que les deux systèmes présentaient une résponse proportionnée à la dose à l'éthionamide, la pefloxacine et la rifampicine, de même qu'une sensibilité à la dapsone. La plupart des échantillons témoins-négatifs eau, éthanol, sucrose, chlorure de dabsyl et riboflavine n'ont produit aucune réduction significative de l'activité radiorespirométrique. Cette étude confirme l'aptitude des essais radiorespirométriques à fonctionner comme un système de triage primaire des agents antilépreux.

La evaluación doble-ciego de las pruebas radiorespirométricos BACTEC y de tipo Buddemeyer en los estudios *in vitro* de los agentes contra la lepra

S G Franzblau, A N Biswas, P Jenner y M J Colston

Resumen Dos pruebas radiorespirométricas, los sistemas de detección de $^{14}CO_2$ BACTEC 460 y el tipo Buddemeyer, fueron evaluados de un modo doble-ciego para su habilidad de discriminar entre agentes verdaderamente antileprosos y los compuestos inactivos. *Mycobacterium lepræ* recién obtenido de ratones desnudos fue incubado in medios axénicos, en la presencia de soluciones de prueba codificadas, preparadas en un laboratorio remoto. Se evaluó la actividad comparando la velocidad de evolución de $^{14}CO_2$ del ácido [1-^{14}C]palmítico. Después de revelar el código, ambos sistemas mostraron una respuesta de dósis a la etionamida, pefloxacina y rifampicina, además de sensibilidad a la dapsona. La mayoría de muestras de control negativo, de agua, etanol, sucrosa, cloruro de dabsilo y riboflavina no lograron una reducción significativa de actividad radiorespirométrica. El estudio confirma la manera en que las pruebas radiorespirométricas pueden funcionar como un sistema de examen primario para drogas contra la lepra.

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Clinical observations on leprosy patients with HIV1-infection in Zambia

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Summary The clinical observations carried out on 10 leprosy patients with HIV1-infection, admitted between 1.1.1986 and 1.5.1988 to the Salvation Army Hospital at Chikankata, Mazabuka, Zambia are described. A total of 8 of this group were newly-diagnosed borderline leprosy patients.

Their clinical data were compared with those of 34 newly-diagnosed borderline leprosy patients, admitted in the same period—50% were men, 50% women.

The clinical presentation, with respect to leprosy, on admission, did not differ very much in both groups. The incidence of neuritis in both groups was 50% (respectively 5 and 17). The outcome of specific therapy of neuritis was worse in the HIV1 patients than in the other group: only partial recovery in 4 out of 5 and no response in 1, compared with a complete recovery in 10 cases, and a partial recovery in 7 cases in the other group.

A total of 6 patients of the HIV1-group admitted to have had multiple heterosexual contacts, 5 had a history of sexually transmitted disease, 7 had generalized lymphadenopathy and 4 presented with another disease in addition to leprosy.

While in hospital the group of 10 HIV1-infected patients suffered 17 episodes of intercurrent disease against none in the other group; 1 patient (male) died with generalized dermatitis and sepsis; 1 woman died with fulminant hepatitis.

Introduction

Human immunodeficiency virus type 1 (HIV1) was confirmed in Zambia in 1983.[1] In this study we report clinical observations on 10 leprosy patients infected with HIV1, admitted to the Leprosy Department of the Salvation Army Hospital, Chikankata, Mazabuka, Zambia between January 1986 and May 1988. This hospital serves as a leprosy referral hospital for the Southern Province of Zambia.

Serological testing for HIV1-antibody was made available for the district hospitals in Zambia at the Microbiology/Pathology Laboratory of the University Teaching Hospital in Lusaka after January 1986. After August 1987 the testing was also done at the medical laboratory of Chikankata Hospital.

Between January 1986 and May 1988 12 leprosy patients were found to be infected

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with HIV1; 7 were tested because of clinical suspicion and 5 were found during a survey.[2] We describe here the 10 available clinical observations—8 of this group were newly-diagnosed borderline leprosy patients. The findings in this group were compared with those in a group of 34 newly-diagnosed patients with the same classification, admitted in the same period.

Material and Methods

There were 291 admissions to the Leprosy Department of Chikankata Hospital between January 1986 and May 1988: 82 were newly-diagnosed cases; the remaining 209 were referrals for treatment of complications, leprosy having been diagnosed earlier.

Of the 82 new cases, 68 were newly-diagnosed borderline-leprosy patients (including 8 HIV1 patients). The files of 34 were readily available for analysis.

The findings in the group of 8 patients with HIV1-infection and with newly-diagnosed borderline leprosy were compared with 34 new borderline cases admitted in the same period. From both groups sex, mean age, family history of leprosy, and the time lapsed between the onset of symptoms and reporting for medical attention were compared.

Relevant data concerning their leprosy status and clinical history were compared. The effect of specific therapy was analysed, as were episodes of intercurrent disease other than leprosy reactions.

All the leprosy patients described here were put on multidrug therapy. Those patients found to have active neuritis were treated for the first 2 weeks with 40 mg prednisolone then for 4 weeks with 30 mg prednisolone, and thereafter the prednisolone dosage was reduced by 5 mg every 4 weeks until it was zero. The prednisolone was administered once daily, in the morning. Other drugs, e.g. antibiotics, were prescribed as necessary when indicated.

The serological test used to demonstrate the presence of HIV1-antibodies was the Wellcozyme-anti HTLVIII competitive enzyme-linked immunoassay VK51, the same test as is used in the Microbiology/Pathology Laboratory of the University Training Hospital, Lusaka. All the positive results found at our laboratory were reconfirmed in Lusaka.

Results

The mean age in the group of 8 patients with newly-diagnosed borderline leprosy and HIV1-infection (group 1) and the group of 34 newly-diagnosed borderline leprosy patients (group 2) did not differ significantly (respectively 42·3 and 41·2 years).

More than 50% of the patients had a family member who suffered from leprosy. Group 1 patients reported somewhat sooner to the hospital than group 2, respectively within 5 months and 9 months after the start of their symptoms. These differences are because the men in group 2 reported on average 12·8 months after the onset of their symptoms.

In both groups 25% of the patients had positive skin smears. About 50% of the patients in both groups reported with active neuritis. In group 2, 10 recovered after specific treatment and 7 improved only partially. The outcome for this complication in

Table 1.

Newly-diagnosed borderline leprosy + HIV infection (Group 1)			Newly-diagnosed borderline leprosy (Group 2)		
Men (4)	Women (4)	Total (8)	Men (17)	Women (17)	Total (34)
Mean age (years)					
43·7	41	42·3	38·2	43·8	41·2
Family history positive for leprosy					
+3	3	6	8	11	19
Time from onset of symptoms (months)					
4·5	6	5·5	12·8	5	9·3
Positive skin smears					
1	1	2	5	4	9
Irreversible neural damage at first examination*					
—	—	—	3	—	3
Active neuritis†					
3	2	5	6	11	17
Complete recovery after corticosteroids					
—	—	—	4	6	10
Partial recovery after corticosteroids					
2	2	4	2	5	7
No response					
1	—	1	—	—	—
Episodes of icd‡					
9	5	14	—	—	—
Death					
1	1	2	—	—	—

* Irreversible neural damage: neural damage existing longer than 6 months before first examination.

† Active neuritis: signs and symptoms of active neural inflammation, and/or impairment of neural function for a period shorter than 6 months before first examination.

‡ Intercurrent disease.

group 1 was much worse: 4 recovered only partially and 1 did not respond at all. Many episodes of intercurrent disease (other than leprosy reactions) were observed in group 1; 2 patients in group 1 died.

The findings are described in more detail in Table 1. Further clinical details in all the group of 10 HIV1-positive were analysed. Table 2 describes their leprosy assessments, classification, specific therapy and treatment outcomes.

Table 3 describes the history of and physical examinations relating to HIV1-infection. None of these patients admitted to drug abuse or to having any homosexual contact. In all, 6 admitted multiple heterosexual contact; 5 had had sexually transmitted diseases (STD) in the past; 7 reported with a generalized lymphadenopathy; 1 with splenomegaly, 1 had hepatomegaly; 2 had active STD on admission; and 4 patients presented themselves with 1 or more afflictions in addition to leprosy.

Table 4 describes the observed episodes of intercurrent disease other than reversal reaction and their outcomes; 17 episodes in 7 patients are noted; 1 male patient (BB, 48 yr)

Table 2. Leprosy patients with positive HIV1-serology leprosy assessment

Sex/age	Presentation	Duration symptoms (m)	Family leprosy	Class	Skin smears	Therapy	Result
M/48	Reversal reaction	5	+	BB	—	DT*/C†	Died
M/51	Mild E NL. icd‡	3	+	LL	+	TT[4]§	Settled
M/58	Neuritis	6	+	BT	—	DT/C	Improved
M/38	Neuritis	6	+	BL	+	TT/C	Improved
M/31	Patches	1	?	BT	—	DT	Stable
F/29	icd	3	+	BL	+	TT	Stable
F/49	Patches mild RR	2	?	BT	—	DT	Settled
F/35	Neuritis	8	+	BT	—	DT/C	Improved
F/30	Neuritis	7	+	BT	—	DT/C	Improved
F/50	Patches	7	?	BB	—	DT	Died

* Double therapy:
600 mg rifampicin once per month supervised.
100 mg dapsone daily.
† Corticosteroids.
‡ icd, intercurrent disease.
§ Triple treatment:
600 mg rifampicin once per month supervised.
300 mg clofazimin once per month supervised.
100 mg dapsone daily.
100 mg clofazimin three times weekly
BB, borderline leprosy; BT, borderline–tuberculoid leprosy; BL, borderline–lepromatous leprosy; LL, lepromatous leprosy; RR, reversal reaction.

Table 3. History and other clinical findings on admission

Sex/age	Multiple sexual partners	Sexually transmitted disease (STD)	Lymphadenopathy	Other
M/48	Yes	Yes	Yes	—
M/51	Yes	Yes	Yes	Splenomegaly gonorrhoea
M/58	Yes	Yes	Yes	—
M/38	—	Yes	Yes	Chancroid
M/31	Yes	Yes	Yes	
F/29	Yes	No	Yes	Bronchitis oral candidiasis
F/49	No	No	No	—
F/35	No	No	No	—
F/30	Yes	No	Yes	Hepatomegaly abscess occiput
F/50	?	No	No	—

died with generalized dermatitis and sepsis; 1 female (BB, 50 yr) died with fulminant hepatitis.

Discusssion

The group described in this study is very small: studies on larger groups should follow soon. On presentation the group of 8 newly-diagnosed borderline leprosy patients with

Table 4. Leprosy patients with positive HIV1-serology episodes of intercurrent disease during admission and outcome

Sex/age	Illness	Outcome
M/58	Tonsillitis, multiple abscesses, toxic hepatitis, malaria, generalized dermatitis + sepsis	Died
M/51	Gonorrhoea, macrocytic anemia (folic acid deficiency), urinary tract infection	Recovered
M/58	None	
M/38	Chancroid	Recovered
M/31	None	
F/29	Bronchitis, oral candidiasis	Recovered
F/49	None	
F/35	Herpes zoster	Recovered
F/30	Abscess occiput, septic tendovaginitis	Recovered
F/50	Pneumonia, fulminant hepatitis	Died

HIV1-infection did not differ very much from the other group of 34 newly-diagnosed borderline leprosy patients in terms of age and presenting signs/symptoms of their leprosy. The only clinical difference was that the group of HIV1-positive patients had poorer outcomes in the treatment of active neuritis.

HIV1 infects neural macrophages, neural multinuclear cells, microglial cells and sometimes neurones. It can also cause peripheral neuropathy.[3] HIV1 virus readily infects T4 helper cells, which play a key role in cell-mediated immunity. The leprosy bacillus is known to invade macrophages and Schwann cells.[4] The way the individual handles the leprosy bacillus determines the clinical picture and the outcome of the leprosy infection.[5] The observations in this group suggest that HIV1-infection and leprosy infection enhance each other in terms of development of more fulminant neuritis in a relatively short time. More observations, also with histopathological studies, will be required to verify this matter. Otherwise, HIV1-infection in these leprosy patients presented itself as it does in patients without leprosy.

The history and equal distribution among women and men points to the pattern of mainly heterosexual transmission of the disease, as earlier observed in Zambia.[6] The high incidence of generalized lymphadenopathy (7 out of 10) and the many episodes of intercurrent disease (16 × infection, 1 × generalized dermatitis) are evidence of compromised immunity. The group is too small to allow conclusions that HIV1-infection tends to be clinically worse than in other HIV1-positive nonleprosy patients, or that the leprosy is more downgraded, even though it is likely that our patients were already having longer established HIV1-infection with advanced immunological disturbance. Observations on more patients in the near future will hopefully clarify this issue.

Conclusions

HIV1-infection does occur in leprosy patients in Zambia and possibly causes early irreversible neuritis, and HIV1-infection in leprosy patients presents clinically in a similar way to HIV1-infection in nonleprosy patients apart from the observations on neuritis.

Acknowledgments

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This work was carried out at the Salvation Army Hospital, Chikankata, Mazabuka, Zambia.

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Lepr Rev (1992) **63,** 134–140

Observations cliniques de patients lépreux infectés par HIV1 en Zambie

ANNA E M VREEBURG

Résumé Nous décrivons les observations cliniques de 10 patients lépreux infectés par HIV1, admis à l'Hopital de l'Armée du Salut à Chikankata, Mazabuka, Zambie, entre le 1.1.1986 et le 1.5.1988. Sur ce groupe, 8 au total étaient des cas-limite de lèpre récemment diagnostiqués,

Leurs dossiers cliniques ont été comparés avec ceux de 34 cas-limite de lèpre, récemment diagnostiqués, admis au cours de la même période, 50% hommes et 50% femmes.

Le tableau clinique à l'admission, en ce qui concerne la lèpre n'était pas très différent dans les deux groupes. L'incidence des névrites, dans les deux groupes, était de 50% (respectivement 5 et 17). Le résultat de la thérapeutique spécifique de la névrite était plus mauvais chez les patients HIV1 que dans l'autre groupe: seulement 4 guérisons partielles chez 4 de 5 patients traités, et pas de réponse chez 1; en comparaison, l'autre groupe présentait une guérison complète dans 10 cas, et une guérison partielle dans 7 cas.

Six patients au total dans le groupe HIV1 ont admis avoir eu des contacts hétérosexuels multiples, 5 avaient une histoire de maladie transmise sexuellement, 7 avaient une lymphadénopathie généralisée et 4 avaient une autre maladie en plus de la lèpre.

Pendant leur séjour à l'hopital, les patients du groupe de 10 porteurs de HIV1 ont souffert 17 épisodes de maladie intercurrente tandis que l'autre groupe n'en avait aucun; 1 patient est mort de dermatite généralisée et septicémie; une patiente est morte d'hépatite fulminante.

Observaciones clínicas de pacientes leprosos con infección HIV1 en Zambia

ANNA E M VREEBURG

Resumen Se describen las observaciones clínicas efectuadas en 10 pacientes leprosos con infección HIV1, recibidos en el Salvation Army Hospital en Chikankata, Mazabuka, Zambia entre el 1.1.1986 y el 1.5.1988. Ocho miembros de este grupo eran pacientes con lepra incierta recién diagnosticada.

Se compararon sus datos clínicos con aquellos de otros 34 pacientes con lepra incierta recién diagnosticada, admitidos durante el mismo período; 50% de los pacientes eran hombres, 50%, mujeres.

La presentación clínica con respecto a la lepra al ser admitidos no difería muchos entres los dos grupos. La incidencia de neuritis en ambos grupos era 50% (5 y 17 respectivamente). El resultado de la terapia específica para la neuritis fue peor en el grupo con HIV1 que en el otro; solamente hubo una recuperación parcial en 4 de 5 casos y ninguna reacción en 2; comparado con una recuperación total en 10 casos, y una parcial en 7, en el otro grupo.

Un total de 6 pacientes del grupo HIV1 admitió contactos heterosexuales múltiples, 5 tenía antecedentes de una enfermedad transmitida sexualmente, 7 tenía linfadenopatía y 4 presentó síntomas de otra enfermedad además de lepra.

Minetras estuvo en el hospital, el grupo de 10 pacientes infectados con HIV1 sufrió 17 episodios de enfermedad intercurrente comparado con ninguno en el otro grupo; 1 paciente (varón) murió con dermatitis generalizada y sepsis; 1 mujer murió con hepatitis fulminante.

Lepr Rev (1992) **63,** 141–144

Diagnostic exploration of enlarged peripheral nerves in suspected cases of leprosy. An analysis of 55 cases

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Summary In 55 cases presenting with enlarged peripheral nerves without any skin lesions, a rice grain-sized biopsy of the nerve lesion was taken for histopathological examination. As a result definitive diagnoses could be established: leprosy was diagnosed in 32 cases. In 23 cases the cause of nerve enlargement was not leprosy: post-traumatic neuritis 9, cysts 5, hypertrophic neuritis 3, nonspecific 4, neurofibroma 1, and amyloidosis 1. In all of these cases there was a deficit of the nerve function and postoperatively there were no complications. The authors, as a result of this experience, believe that surgical exploration and biopsy is a harmless diagnostic tool for establishing a definitive diagnosis of leprosy in cases presenting with enlarged peripheral nerves without any skin lesions. In 23 out of 55 such cases the nerve enlargement was proved to be other causes than leprosy.

Introduction

The enlargement of peripheral nerves is one of the most important criteria for the diagnosis of leprosy. However, similar enlargements can also be caused by other peripheral nerve disorders, and this causes a problem in differential diagnosis in the absence of any other clinical manifestation of leprosy. We performed explorative surgery on the nerves of 55 such cases, and careful observations of the exposed nerve and histopathological examination of a very small biopsy of the nerve lesion established the correct diagnosis in all cases. This method and the results are presented and analysed in this communication.

Materials and methods

All the 55 patients studied had enlargement of peripheral nerves with a functional disturbance such as loss of superficial sensitivity, anhidrosis, muscle atrophy, clawed

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fingers or toes, footdrop and plantar ulcers. There were no skin lesions. Their ages ranged from 12 to 72 years (43 males and 12 females). The nerves involved were: 19 ulnar nerves, 8 median, 2 radial, 12 common peroneal, 1 posterior tibial and 15 cutaneous nerves, and 2 cases had bilateral enlargement of the ulnar nerves. The cutaneous nerves involved were the greater auricular (5), the superficial peroneal (5), the sural (2) and the antibrachial cutaneous (1), the infrapatellar branch of the saphenous (1), and the lateral cutaneous branch of the same nerve (1).

METHOD OF SURGICAL EXPLORATION AND BIOPSY

We explored the elbow for ulnar and median, the carpel tunnel for median, the radial groove in the upper arm for radial, around the neck of the fibula for common peroneal, the tarsal tunnel for the posterior tibial, and the sites of enlargement of the various cutaneous nerves.

Under local infiltration anaesthesia a longitudinal incision was made overlying the affected nerve, and the nerve exposed. Detailed observations were made on the shape and size of the nerve swelling; the appearance, colour, and thickness of the nerve sheath and its adhesions to the surrounding tissues and the condition of the surrounding structures. Any coexisting conditions such as injuries or other diseases causing deformity of bones, joints, fascia and nerve tunnel were specially looked for. Then a longitudinal incision was made in the nerve sheath. Observations were made on any change in internal pressure, adhesions between the epineurium and perineurium, the presence of any caseation, necrosis or fibrosis. A 'rice-grain' sized biopsy was taken from the nerve lesion through the epineurium and perineurium and examined histopathologically.

Operative findings

Caseation was found in 5 nerves, the elbow tunnel showed obvious marrowing in 5, while cysts were found in 5. The fluid in the cysts was milky white. The shape of enlargement of the nerve was fusiform in the majority, beaded in some and uniform in others; 1 nerve had within it a neurofibroma. In all nerves there were adhesions between the epineurium and adjacent tissue, the extent being variable. There were 2 ulnar nerves showing dislocation at the elbow. Some nerves showed cysts distributed longitudinally.

Histopathological findings

The 32 cases diagnosed as leprosy by histopathology consisted of 10 cases of tuberculoid leprosy, 21 cases of borderline leprosy and 1 indeterminate case. In 12 of these cases AFB were demonstrated. The cyst wall in the 5 cases with neurilemmal cysts was made of collagen. In 3 nonleprosy cases the nerve showed hypertrophic neuritis. All cases showed a degeneration of the nerve to a varying extent. Amyloid change was seen in 1 case.

Results

The detailed results are shown in Table 1, and 32 (58·2%) out of 55 cases were diagnosed as leprosy. In 23 cases the causes of nerve enlargement varied from post-traumatic neuritis to neurilemmal cysts. Thus nerve exploration and a rice-grain-sized biopsy could establish diagnosis.

Table 1.

Nerve	Ulnar	Median	Radial	Common peroneal	Posterior tibial	Cutaneous nerves including greater auricular and superficial peroneal	Total
Disease							
Leprosy	8	6	1	6	1	10	32 (58·2%)
Post-traumatic neuritis	7			2			9
Neurile-mmal				5			5
Nonspecific neuritis				1		3	4
Hypertrophic neuritis		2	1				3
Neurofibroma	1						1
Nerve amyloidosis	1						1
Total	17	8	2	14	1	13	55

Discussion

One of the most important features of *M. leprae* is its predilection for peripheral nerve trunks. After entering the host through the skin or mucous membrane, the organisms probably spread centripetally from nerve ends to the nerve trunks. Specific interstitial mononeuritis or polyneuritis develops as a consequence. It may affect the nerve trunk, its primary branches or finer branches. The main clinical manifestation is nerve enlargement and disturbance of nerve function. Many cases of 'pure neuritic' leprosy occur where skin manifestations of the disease are absent. In these cases one or more nerves are enlarged with a variable amount of nerve dysfunction in its distribution. Often the diagnosis is in doubt. Exploration of the enlarged nerve together with biopsy is needed to establish diagnosis. Our results have shown that such an exploration and a rice-grain-sized biopsy indeed establishes diagnosis and has no harmful effect on the patient, because the biopsy is small and is taken from an already grossly affected portion of the nerve. In 23 of 55 cases reported here the cause of nerve enlargement was not leprosy. This is important to remember in order to avoid any wrong diagnosis. Diagnosis of leprosy often causes an adverse socioeconomic and psychological effect on the patient and his family. Wrong diagnosis is a calamity, an avoidable calamity.

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Exploration des nerfs périphériques hypertrophiés dans le diagnostic de cas suspectés de lèpre. Une analyse de 55 cas

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CHEN JIAKUN, GU DAXIN, WANG ZAIMING ET PENG JINHU

Résumé Dans 55 cas présentant une hypertrophie des nerfs sans lésions cutanées, une biopsie de la lésion nerveuse, de la taille d'un grain de riza été prélevée pour examen histopathologique. Des diagnostics définitifs ont pu ainsi être établis: la lèpre a été diagnostiquée dans 32 cas. Dans 23 cas, la cause de l'hypertrophie du nerf n'a pas été la peste, mais: névrite post-traumatique 9 cas, kystes 5 cas, névrite hypertrophique 3 cas, non spécifique 4 cas, neurofibrome 1 cas, et amyloïdose 1 cas. Dans tous ces cas, un déficit de la fonction du nerf a été observé, et il n'y a pas eu de complication post-opératoire. Les auteurs, par suite de cette expérience, estiment que l'exploration chirurgicale et la biopsie constituent un outil de diagnostic sans danger pour établir un diagnostic de lèpre définitif dans les cas présentant une hypertrophie des nerfs periphériques sans lésions cutanées. Dans 23 des 55 cas présentant ces caractères, l'hypertrophie nerveuse s'est révélée être dûe à d'autres causes que la lèpre.

La exploración diagnóstica de los nervios periféricos aumentados en los casos sospechados de lepra. Un análisis de 55 casos

DONG LIWEN, LI FUTIAN, GU ZHANGJING, ZHANG JIALIN,
CHEN JIAKUN, GU DAXIN, WANG ZAIMING Y PENG JINHU

Resumen En 55 casos en que se ha presentado nervios periféricos aumentados sin lesiones dérmicas, se tomó una biopsia del tamaño de un grano de arroz de la lesión del nervio, para un examen histopatológico. Por consecuencia, se pudieron establecer diagnósticos definitivos: se diagnosticó la lepra en 32 casos. En 23 casos, la causa del aumento de los nervios no fue leprosa: neuritis postraumática 9, quistes 5, neuritis hipertrófica 3, no específicos 4, neurofibroma 1 y amiloidosis 1. En todos estos casos, hubo un déficit de la función neurológica, y no hubieron complicaciones postoperativas. Como consecuencia de esta experiencia, los autores creen que la exploración quirúrgica y biopsia es un procedimiento diagnóstico inofensivo para el establecimiento de un diagnóstico definitivo de la lepra en aquellos casos que presentan nervios periféricos aumentados sin lesiones dérmicas. En 23 de 55 de tales casos, el aumento de los nervios resultó ser por razones distintas a la lepra.

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An application of the LePSA methodology for health education in leprosy

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Summary This paper describes how the innovative LePSA technique can be used by community health workers to appropriately educate and increase compliance among leprosy patients. A lesson plan illustrating the interactive nature of the technique in a hypothetical Third World community is presented. The lesson plan, using MDT default, shows how the technique can elicit individual participation in a group setting and serve as both an educational and a behaviour change tool.

Introduction

In leprosy, early diagnosis and patient compliance with drug therapy are critical for control of the disease.[1] With respect to compliance, there is a large literature on the problems encountered with leprosy and other chronic diseases.[1–6] In addition, efforts have been made by health educators as well as other social scientists to reduce noncompliance.[7] McDougall & Georgiev state, however, that although there are good educational materials for health workers, little exists for patients; they present an outline of basic information needed by leprosy patients to improve compliance with drug regimens.[7]

We propose here the application of a new interactive health education/training method (called 'LePSA') to enable community health workers (CHW's) to improve knowledge and compliance among leprosy patients.

The LePSA Method

Leprosy control should ideally be accomplished through small groups in the community, including family/household groups, as well as through individual counselling. There are many techniques for accomplishing health education in groups but the best are 'interactive' involving the client or patient and eliciting his/her attitudes and involvement

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throughout the educational process. A very effective technique of this type is the LePSA method. LePSA is a culturally sensitive, community-based methodology easily learned and used by health workers. As formulated by Dr Roy Shaffer in Kenya, LePSA stands for:

Le, Learner-centred; P, Problem-posing; S, Self-discovery; A, Action-oriented.[8]

Learner-centred refers to a focus on the beliefs, needs and concerns of the participants. Empirically, this is facilitated by group formation of 5–12 participants in a circle. The community health worker or facilitator does not sit above or away from others and does not appear to control the session. Everyone has eye contact. People are made to feel at home among friends after appropriate introductions and small talk. Each participant is tactfully but directly requested to participate. The CHW allows a great deal of latitude and time for expression of each participant's views. Structure and control is maintained primarily by prior agreement to discuss a single problem.

The problem-posing phase emphasizes the presentation of a single problem as facilitated by the CHW.[8] The problem may be presented in a variety of ways, i.e. a story, a picture or most effectively through role play with the assistance of the participants. It is important that the CHW does not suggest a solution to the problem. This problem-posing role play is called the 'starter'. After the starter is completed, the CHW asks 3 questions:

What specific things or people did you see in the starter?
What was happening? (Was the specific, posed problem recognized as a problem by those gathered?)
Does this problem happen in our place or situation?[8]

In addition, the CHW or facilitator may probe for specific effects of the problem on the participants and their community. This discussion is ended by reaching a consensus on the nature of the problem as it occurs locally.

The discussion then enters the self-discovery phase, whereby, through dialogue, the participants discover and verbalize root causes. Shaffer says 'such a discovery lesson should result in the learner exclaiming "AHA!!!", and having a positive "aha-attitude" towards the posed problem.' That is, each learner contributes sufficiently to the dialogue so as to feel like an active, valuable group member. During the self-discovery phase the following questions guide discussion:

Why does it happen—what are the causes of this problem?
What are the side-effects or complications?
What are the possible solutions which we ourselves can carry out in the community?[8]

The self-discovery stage is designed to clarify the participant's knowledge as well as stimulate feelings of competence through active involvement in defining the problem and discovering solutions or answers. This leads to the action phase. At this point there is a consensus on a given solution(s) or strategy(ies) and specific means are devised for implementation with contributions from each participant.[8]

The LePSA method is highly flexible and can be used to communicate specific information of virtually any kind through lesson plans or training modules. In addition, it can be integrated with other health education techniques like those emphasizing audiovisual tools or social marketing. With respect to leprosy, modules can be developed for topical areas such as leprosy identification, sociocultural aspects of stigma, side-effects

such as darkening of the skin that may occur with some drugs, such as clofazimine, leprosy patient defaulting and deformity prevention. The choice of a specific problem to be covered may be left to the participants or suggested by a health worker. Other important topics are not ignored when they spontaneously arise, i.e. the relationship of leprosy to other health problems, sanitation, and hygiene practices. The CHW, however, is trained to redirect the group back to the original problem.[8] Below is a summary of how the LePSA technique might be applied.

A LEPSA LESSON PLAN FOR LEPROSY HEALTH EDUCATION

Group

The group in this theoretical example is made up of residents from an area of high leprosy concentration. Participants may include both leprosy patients, family and nonleprosy neighbours. Ideally the group size should be no more than twelve.

Subject

The problem of multidrug therapy (MDT) defaulters

Objectives

1 To promote early diagnosis and regular use of drug therapy among leprosy patients.
2 To demonstrate the dangers of discontinuing antileprosy medication.

Materials

A couple of 'actresses' (chosen from the group), with 2 towels or some clothes used for a simulated clothes washing.

Method—Role Play

Scene One: 2 women, both afflicted with leprosy, are washing clothes together. The first woman says, 'I have not seen you in the clinic for a while to receive your medicine along with us.' The second woman replies, 'Oh, I stopped taking the medicine when it caused a lot of pain in my arms. Maybe it's just my fate. I'm not sure what to do.'

Scene Two: 6 months later the 2 women are washing clothes again. The second woman says, 'You are looking fine.' The first woman responds, 'Thank you. I've been taking my medicine when I should even when it's hard for me. But now I am much better. How do you feel?' The second woman responds, 'Well not so good, my arm and fingers have been somewhat numb lately. I just haven't been able to take the medicine as I should.'

The role play stops.

Questions

The CHW, as facilitator, asks 'starter' and 'self-discovery' questions to initiate and maintain discussion.

Concepts/Knowledge

The discussion should lead to the following consensus.

1 The cause of leprosy is not necessarily sin or hereditary.[9] It is caused by *Mycobacterium leprae* or germs. Leprosy and the associated pain and numbness can best be arrested by early diagnosis and taking the right drugs for a certain length of time. The need for adherence is emphasized. Problems with adherence, such as the following, may be discussed:
   a One should continue medication if there is pain or inflammation.
   b Other drugs such as analgesics or anti-inflammatories may be taken if there is pain or neuritis.
   c One should go to the clinic or health post if there are any side-effects.[10]
2 Consensus is also reached that it is important to begin early MDT. Ways to increase feasibility of regular MDT are discussed.
3 Consensus is reached about the dangers of defaulting.
   a A slower cure.
   b Increased skin and nerve damage.
   c Increased potential for muscle wasting.[10]

Action point

At this stage the participants are asked to share at least one new insight about MDT defaulting with at least one other person in the community. Those with leprosy or those related to or knowledgeable about someone with leprosy are asked to return to a new meeting to discuss how MDT participatation can be increased or facilitated. Clinical referrals or appointments are also made at this point if requested. These measures will help reduce the transmission of leprosy in the community.

Evaluation (optional)

At a specified time depending on resources and need, participants can be tested with respect to knowledge and behaviour changes. A study by Matthews in India emphasized the importance of using behavioural objectives to estimate the success of any leprosy health education programme.[11]

Other modules or lession plans utilize the same LePSA format. This example utilizes the case of leprosy default, but there are various reasons for defaulting and thus various potential topics for this problem.[12,13]

Discussion

The LePSA method has the potential for utilization with a wide range of health problems associated with leprosy. The first author has witnessed the use of the LePSA method in Kenya, where it was developed, and has used it for a variety of health problems in the Philippines. It is particularly promising for teaching leprosy control cross-culturally at the community level because of its simplicity, adaptability to activities of every-day living, ease of integration with other educational techniques and the involvement of participants

in the learning process. Von Parjis says, 'health workers have difficulty formulating advice, instructions and explanations from the patient's or the public's point of view. . . . Such communication is ineffective.[14] The LePSA method helps the CHW overcome this barrier because he or she communicates information by requiring the learner to discover, discuss and select locally relevant ideas about the nature of the problem as well as solutions. The method is applied at the learner's pace and takes more time than simple instruction. However, it increases the probability of real understanding and provides a framework for immediate action.

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Lepr Rev (1992) **63,** 145–150

La méthodologie LePSA appliquée à l'éducation sur la lèpre

J L LENNON ET D W COOMBS

Résumé Ce document décrit comment la technique innovatrice LePSA peut être utilisée par les travailleurs sociaux pour éduquer les malades et en amener le plus grand nombre à accepter. On y présente un projet pédagogique illustrant la nature interactive de la technique dans une communauté imaginaire du tiers monde. Le projet pédagogique, faisant appel à une médication mixte, montre comment cette technique peut susciter la participation de chaque individu dans un groupe et servir aussi bien pour former que pour faire changer les comportements.

Una aplicación de la metodología LePSA en la educación sanitaria de la lepra

J L LENNON Y D W COOMBS

Resumen Esta publicación resume cóma los que trabajan en la salud comunitaria pueden usar la técnica innovadora LePSA para capacitar adecuadamente y aumentar la conformidad de los pacientes con lepra. En un plan de lecciones se presenta el caracter interactivo de la técnica en una comunidad hipotética del Tercer Mundo. El plan, que utiliza MDT por defector, demuestra cómo la técnica puede estimular la participación de individuos en un ambiente de grupo, y servir de herramienta tanto educacional como relativa al compartamiento,

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Attitudes towards leprosy in the outpatient population of dermatology clinics in Trinidad

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Summary We interviewed a total of 92 dermatology clinic patients using a brief questionnaire to determine their knowledge, attitudes and beliefs about leprosy. This small survey helped to confirm our suspicions that some knowledge of leprosy is lacking and that much stigma still remains.

Introduction

In Trinidad and Tobago patients with leprosy have been cared for on a domiciliary basis since 1969, when admissions to the leprosarium at Chacachacare (an island off the north-western coast of Trinidad) were discontinued. Leprosy control has been partially integrated with dermatology services since 1986 and patients are seen mainly as outpatients at skin clinics held at peripheral health centres, where both general skin patients and leprosy patients attend.

Methods

Patients were chosen at random from the skin clinic population at peripheral health centres and at 1 general hospital skin clinic. Patients under 18 years of age and those attending for leprosy were excluded. Anyone who might have had more than an average experience of leprosy, for example from nurses' training, or employment at Chacachacare, were also excluded. The interviewer was a medical social worker with a 3-year experience in dealing with leprosy patients. A set 12-item questionnaire was used.

Results

There were 92 respondents—72 female (78%) and 20 male (22%). (Percentages throughout are represented to the nearest whole digit). The predominance of females

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Table 1. Source of information about leprosy

Source	Number	Percent
Parents and other relatives	33	36
Know of persons suffering from leprosy	17	18
Media	16	17
School	9	10
Posters at health centres	7	8
Reading books	4	4
Did not remember	3	3
Never heard of leprosy	6	6

appears to hold for the clinic population as a whole and this may be due to the fact that women are more likely to notice and present for the treatment of skin complaints.

When questioned on the information sources concerning leprosy, the responses were sometimes vague, and people were unable to say with certainty where they had acquired their information. The results are summarized in Table 1. The posters referred to had been recently displayed in Health Centres. Contrary to our expectations, most people did not relate leprosy to the biblical description.

Ideas about cause are shown in Table 2. Again, contrary to what we had experienced most people admitted ignorance, and only 4 (about 4%) had concepts of a curse or punishment as the cause of leprosy.

Respondents were questioned about their level of education in an attempt to determine whether this had any bearing on their knowledge of the cause of leprosy. About half had completed primary school (see Table 3). Of the 19 who knew that leprosy was caused by a germ, 9 had reached secondary school level and the remaining 10 had attended primary school only. Of the 7 who thought it to be heredity, 5 had reached secondary level and 2 primary education. All of those who blamed a curse or punishment had completed primary school. Of those who knew nothing, 20 had secondary education, 36 primary education, 4 had no schooling and 2 had only preschool education.

Respondents were asked what leprosy looked like, and 37 respondents (40%) knew that leprosy was associated with skin rashes. The responses included remarks such as 'skin with light patches', 'bumps on face', 'sores on the body'. However, only 1 person knew that the spots were sometimes associated with numbness; 31 respondents (34%) had no idea how the disease presented; 16 (17%) thought that deformities were present and their comments included 'fingers and feet clawed', 'eating away of fingers and toes',

Table 2. Causation of leprosy

Response	Number	Percent
Do not know	62	67
Germ	19	21
Heredity	7	8
Curse or punishment	4	4
Total	92	100

Table 3. Educational level

Source	Number	Percent
Primary school	52	57
Secondary school	34	37
Pre-school	2	2
No schooling	4	4
Total	92	100

Table 4. Curability of leprosy

Response	Number	Percent
Curable	45	49
Incurable	14	15
Do not know	33	36
Total	92	100

Table 5. Reaction to leprosy in self

Response	Number	Percent
Seek medical attention	69	75
Do not know what to do	17	19
'Prayers'	2	2
'Bush medicine'	1	1
Seek attention but avoid people	1	1
Does not believe it could happen	1	1
'Will die if it happens'	1	1
Total	92	100

'Deformities', 'disfigurement', 12 (13%) believed that deformities accompanied the skin changes. We did not attempt to distinguish between presenting signs and stigmata.

About 50% of those questioned believed that leprosy is curable (see Table 4). We do not know whether their concept of cure related to resolution of skin lesions or deformities, and whether it related to their knowledge that a particular form of treatment is available.

Most people (75 = 81%) claimed no contact with anyone with a diagnosis of leprosy. Of the 17 who knew of someone with leprosy, 12 claimed to have a friend or family member with leprosy; the remaining 5 had casual knowledge of 'someone in the neighbourhood'.

The reaction to contracting leprosy in the individual or a close friend or relative was positive in the majority of cases, with similar proportions seeking and accepting medical advice and supporting and encouraging friends to do the same (see Tables 5 and 6). However, they did not appear to expect friends and family to be as supportive of them (see Table 7).

Only 4 respondents considered leprosy a differential diagnosis for their own (non-

Table 6. Response to family and friends contracting leprosy

Response	Number	Percent
Supportive	64	70
Do not know	17	18
Shun	8	9
'Prayers'	2	2
'Bush medicine'	1	1
Total	92	100

Table 7. Response of family and friends to respondent's diagnosis of leprosy

Source	Number	Percent
Dont know	39	43
Supportive	34	37
Shun	15	16
Family supportive, friends shun	3	3
Will support but still shun	1	1
Total	92	100

leprosy) skin complaints, 43 (47%) felt they could contract leprosy, 22 (24%) thought not and 30 (33%) did not know.

The majority of individuals (60 = 66%) did not know where leprosy patients are cared for; 18 (20%) thought patients were still on the island of Chacachacare. Of the 14 who knew that they were in the community, 7 were definite about it, but the remaining 7 gave vague responses, e.g. 'some clinic', 'somewhere in Port of Spain'.

Discussion

We concluded that the general knowledge of leprosy was deficient. The receiving of secondary school education did not appear to influence that knowledge as is shown by questions about the cause.

Individuals seemed more likely to recall childhood memories. In some cases there had been recent viewing of leprosy on television and possibly some had heard a recent radio interview involving staff of the Leprosy Control Unit.

Contrary to our previous notions, the Bible did not feature as a significant source of knowledge, although we have had many queries in the past from people who believe that biblical leprosy is the same as that we see today.

There is one study from the English-speaking Caribbean (performed in Guyana) with which we can compare some of our results. Cook[1] reported that 61% of her respondents believed that leprosy was incurable. This is significantly greater than our 14%. Her survey was performed before embarking on an educational programme. In Trinidad and Tobago, education about leprosy started receiving greater emphasis during the 1970s and

so perhaps our group had an advantage—52% of Cook's respondents associated leprosy with skin changes (our study—40%), and 29% spoke of deformities or loss of extremities (our study—17%). Our group therefore was only minimally more knowledgable about the signs. The knowledge of sensory loss in this disease was lacking. In our experience those who present with loss of feeling in their extremities sometimes believe that this is due to 'nerves', 'arthritis' or 'something lacking in the blood'. The notion of leprosy as a cause is usually absent.

While the majority suggested that they would respond favourably to the diagnosis of leprosy in themselves, in friends or relatives, by seeking medical attention and being supportive, they did not seem to expect the same response if the positions were reversed, in effect 64% of the respondents claimed that they would be supportive of friends and relatives who contracted leprosy, but only 50% of them expected support from others if they had the disease.

It is our experience that a common response to the diagnosis is to question the patients as to how they contracted leprosy and they are keen that other people should not know. In addition, patients are sometimes reluctant to tell other members of the immediate family, including spouses, that they have leprosy. In-laws seem to be particularly difficult to approach and contact examination sometimes becomes a ticklish issue. This reinforces our suspicion that the stigma still exists, although to a lesser extent than Cook demonstrated in Guyana.

As in Guyana, there is a persistent ignorance about the cause of leprosy, its symptoms, signs, and curability, which is an obstacle to the process of eradication. We believe that there must be a greater educational thrust beginning, perhaps, at primary school level. Emphasis must be placed on bacterial causation, the efficacy of modern chemotherapy, which quickly renders patients non-infectious,[2] and the fact that early diagnosis and treatment may prevent deformities. Although leprosy seems to be less of a problem now in the Caribbean we must still not lose sight of its continued presence and importance.

Reference

[1] Cook, Anne. An urban community's thoughts about leprosy; a survey in Guyana. *Lepr Rev*, 1982; **53:** 285–296.

[2] Jopling WH, McDougall AC. *Handbook of Leprosy*, 4th Edn. Oxford: Heinemann Professional Publishing, 1988, p. 4.

Lepr Rev (1992) **63,** 151–156

Attitudes a l'égard de la lèpre chez la population visitant la consultation externe de dermatologie à Trinidad

M Suite èt C Gittens

Résumé Nous avons interrogé un total de 92 patients de la clinique de dermatologie en leur présentant un bref questionnaire pour déterminer leur connaissance, attitude et convictions au sujet de la lèpre. Cette petite enquète a contribué à confirmer nos soupçons, à savoir que la lèpre n'est pas suffisamment connue et qu'elle reste très stigmatisée.

Actitudes a la lepra en la población externa de las clínicas dermatológicas en Trinidad

M Suite y C Gittens

Resumen Entrevistamos un total de 92 pacientes de clínicas dermatológicas por medio de un cuestionario breve, para determinar los conocimientos, actitudes y creencias respecto a la lepra. Este pequeño estudio nos ayudó confirmar nuestras sospechas de que faltan algunos conocimientos y que persiste mucho dell estigma.

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Attitudes of rural people in central Ethiopia towards leprosy and a brief comparison with observations on epilepsy

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Summary To find out public attitudes toward leprosy a door-to-door survey was carried out in 1546 sampled households in the rural farming community of Meskan and Mareko in central Ethopia, where the prevalence of leprosy is estimated to be 1 : 1000. Attitudes toward leprosy were compared with attitudes to epilepsy, studied in a previously performed survey in the same community. Eighty-seven per cent of the respondents were above the age of 25, and 59·5% were females. There were slightly more Muslims (54%) than Christians. The majority of the interviewees (87%) were farmers, with an illiteracy rate of 84%. Ninety-five per cent and 83%, respectively, were not willing to employ or work with a person having the disease. Seventy-five per cent would not allow their children to associate with a playmate suffering from leprosy. Comparative analysis of attitudes in the same community showed that negative attitudes toward leprosy were stronger than those toward epilepsy, particularly with regard to matrimonial associations, sharing of accommodation, and physical contact with an affected person. The reasons for these differences appear to be the community's deeply entrenched belief that leprosy is both hereditary and contagious, expressed respectively by 48% and 53% of the respondents. In order to minimize the perpetuation of negative attitudes, there is a need to educate and impress on the population that leprosy is a treatable infectious disease which is not congenitally acquired, and that it is even curable if detected early. The study reinforces previously proposed suggestions that, in developing countries such as Ethiopia, leprosy care should be integrated into the general health services.

Introduction

About 10 million people in the world, mainly in developing countries, are infected by

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leprosy; 12% are found in Africa.[1] Situated in the north-eastern part of Africa, Ethiopia covers an area of 1·25 million sq km and has a population of 46,000,000.[2] It belongs to the leprosy-endemic regions of the African continent. A review of the leprosy control programmes in the country (1976–89) revealed that the cumulative national average prevalence rate was 2·6 per thousand.[3] Although a decline in the detection rate has been noticed since 1982, coinciding with the introduction of multiple drug therapy (MDT), leprosy remains a serious public health problem in the country.

Besides the physically disfiguring and disabling effects of the disease, its victims and their families suffer a great deal from social prejudices and isolation. The situation in Ethiopia is similar to that recorded from other developing countries. As Giel wrote in 1968, 'Among the outcasts of the society, concentrated around the churchyards and cemeteries of Ethiopia, lepromatous lepers are the most easily recognized'.[4]

The objective of the present study is to evaluate the knowledge and traditional beliefs and attitudes toward leprosy in a rural Ethiopian community. An attempt will also be made to compare the attitude toward leprosy with that previously recorded for epilepsy in the same community.[5]

Subjects and methods

Between 1986 and 1988 an epidemiological study of neurological disorders was carried out in the rural subdistrict of Meskan and Mareko (population 181,883) in the Shoa Administrative Region of central Ethopia. At the time of the survey, the subdistrict comprised 6 town-dwellers' associations and 82 peasant associations. There was a total of 40,000 households in the subdistrict, with an average family size of 4·5 members. The study was undertaken in a random selection of 30% of the associations, involving 60,820 inhabitants. The majority of the inhabitants (89%) were from the Gurage ethnic group, while the rest were from the Oromo, Amhara, Tigre and Kembata ethnic groups. In the survey, trained lay health workers were employed to administer specially designed questionnaires to detect neurological symptoms and signs;[6] the questionnaires were those used for a community-based study of neurological disorders in the same area.

Concomitant with this survey, the lay health workers were also trained to interview adults, mainly heads of households, on their opinions of common neurological disorders that may carry significant negative and unfavourable attitudes in the community. These disorders included mental retardation, physical handicap, leprosy and epilepsy. In order to avoid confusion, every fourth household of all the randomly selected villages in the study area was interviewed on each of the disorders. This resulted in the inclusion of 1546 households each for the attitudinal surveys of leprosy and epilepsy.

The questionnaire used for this study and shown in the Appendix was translated into Amharic, the 'official' Ethiopian language. Local dialects were used in the interviews whenever required. Before the administration of the questionnaire, the aims and purpose of the study were clearly explained to the respondents, and their consent was obtained. There was a 94% and 95% participation in the interviews on epilepsy and leprosy respectively.

The chi-square test (with Yates' correction) was used as a test of independence between two variables.

Results

As summarized in Table 1, the characteristics of the respondents for the leprosy and epilepsy interviews were very similar. Taking those who responded to the questionnaire on leprosy, 85% were above the age of 25, and the majority (87%) were farmers. There were slightly more Muslims (54%) than Christians. Eighty-two per cent were married, and of those 89% had children. The rate of illiteracy were very high (84%). As the men in the community were often in the fields during the door-to-door visits of the lay health workers, there was a slight preponderance of females (59·6%) among the respondents to the interview on leprosy, similar to that experienced in the study of epilepsy.

Those who were literate obtained their skill from church and regular schools, as well as through participation in the literacy campaign. Less than 2% had received secondary school education. The vast majority in the community (94%) had incomes at subsistence level ($US 120 per annum), and only 1% could be classified as well-to-do.

Table 1. Characteristics of respondents

	Epilepsy		Leprosy	
Characteristics	No.	%	No.	%
Age (years)				
14–25	206	14·2	195	13·4
26–35	377	26·0	420	29·0
36–45	338	23·3	368	25·4
46+	531	36·5	468	32·2
Sex				
Male	606	41·6	586	40·3
Female	850	58·4	865	59·6
Religion				
Christian	674	46·3	666	45·9
Moslem	781	53·7	785	54·1
Marital status				
Married	1147	78·8	1183	81·5
Widow/Widower	162	11·2	125	8·6
Single	76	5·2	84	5·8
Divorced	70	4·8	59	4·1
Level of education				
Illiterate	1240	85·2	1223	84·3
Read and write	120	8·2	93	6·4
Grade 2–8	75	5·2	109	7·5
Grade 9 and above	21	1·4	26	1·8
Occupation				
Farmer	1267	87·0	1265	87·2
Housewife	75	5·1	85	5·9
Merchant	37	2·5	40	2·7
Labourer	29	2·0	15	1·0
Dependant	27	1·9	20	1·4
Student	13	0·9	12	0·8
Government employee	9	0·6	14	1·0

In Ethiopia leprosy is commonly referred to as qumtina, an Amharic word denoting 'the state of amputation or mutilation'. Likewise, a person with leprosy is called qwomata. These terms were used by 70% of the respondents, in spite of the fact that only 7% of them were from the Amhara ethnic group. The preferred term for leprosy in Amharic is sega dewe, which literally translates as 'the disease of the flesh'; this term was used by only 0·3% of the respondents. Other less commonly-used terms for leprosy within the study population were buska, gegehu yelegode and yajamoy in the Mareko, Meskan and Silti dialects of the Gurage language, and shishera was used by the Hadiya language-speakers. All these terms have equivalent meanings and connotations similar to the Amharic word qumtina.

As shown in Table 2, the proportion of respondents that had heard of, or, in a few cases, read about leprosy and epilepsy was equal. However, a higher percentage of respondents had seen a sufferer from leprosy. Interestingly, a significantly higher proportion of respondents believed that leprosy is hereditary and contagious, as compared to epilepsy. The negative attitude towards leprosy is further demonstrated by the unwillingness or intolerance of the respondents to employ, work or live with a person

Table 2. Public response to attitudinal questions

Question	Response number	Answer (%) Yes	No	Don't know	*p* value
Have you heard or read about leprosy?	1365	90·3	9·7		
. . . . . epilepsy?	1441	89·0	11·0	—	>0·10
Have you seen someone with leprosy?	1351	95·9	4·1		
. . . . . epilepsy?	1338	86·2	13·8	—	<0·001
Do have a family member with leprosy?	1347	2·3	97·7		
. . . . . epilepsy?	1332	14·3	85·7	—	<0·001
Is leprosy hereditary?	1328	47·8	52·2		
Is epilepsy hereditary?	1274	4·9	95·1	—	<0·001
Is leprosy contagious?	1324	53·1	43·8	3·1	
Is epilepsy contagious?	1269	44·6	53·4	2·0	<0·001
Is leprosy a form of insanity?	1321	1·0	99·0		
. . . . . epilepsy?	1265	1·9	98·1	—	0·01<0·05
Would you employ a leper?	1316	3·8	95·1	1·1	
. . . . . an epileptic?	1254	25·0	75·0	—	<0·001
Are you willing to work with a leper?	1317	15·6	83·3	1·1	
. . . . . an epileptic?	1257	52·7	46·1	1·2	<0·001
Would you house a person with leprosy under pressure?	1314	0·4	98·9	0·7	
. . . . . epilepsy?	1260	67·2	32·2	0·6	<0·001
Do you think a person with leprosy should be hidden from public view?	1314	3·6	96·4		
. . . . . epilepsy?	1262	1·8	98·2	—	0·001<0·01
Would you allow a leper to use public transport?	1314	97·2	2·8		
. . . . . an epileptic?	1262	90·1	9·1	0·8	<0·001
Would you shake hands with a leper?	1314	22·5	77·5		
. . . . . an epileptic?	1262	90·8	9·2	—	<0·001
Would you have a person with leprosy as a friend?	1308	9·3	90·7		
. . . . . epilepsy?	1259	40·6	58·3	1·1	<0·001
Would you allow your child to play with a child having leprosy?	1311	25·2	74·8		
. . . . . epilepsy?	1254	65·1	33·9	1·0	<0·001

Table 3. Question: Would you allow someone from your family to marry a person with epilepsy/leprosy?

	Respondents				
	Epilepsy 1257		Leprosy 1313		
Results	No.	%	No.	% *p*	Value
Yes	327	26·0	39	3·0	<0·001
Would not tolerate (reason not specified)	422	33·6	213	16·2	<0·001
No, the sufferer is unable to earn a living	292	23·3	185	14·0	<0·001
No, contagious	148	11·8	302	23·0	<0·001
No, genetically inadvisable	49	3·9	563	42·9	<0·001
Don't know	18	1·4	11	0·8	

having the disease. Similarly, fewer respondents were willing to be friends with or allow their children to be associated with a person suffering from leprosy; 78% of the interviewees were unwilling to shake hands with a leprosy sufferer, compared with 9% that expressed the same attitudes to a patient with epilepsy.

When asked if they would accept a successfully treated and cured case of leprosy, nearly 42% of the interviewees responded with 'once a leper, always a leper'.

When the attitudes to marriage were evaluated (Table 3), only 3% expressed probable consent to a family member undertaking a matrimonial relationship with a person affected by leprosy. On the other hand, there was a 26% positive response on the same question concerning epilepsy. The main factors contributing to the strong reluctance concerning marriage with a leprosy sufferer were the fear of contagion and hereditary considerations, as well as the feeling that a person with leprosy is incapable of being gainfully employed. Whereas 38% of those interviewed on epilepsy thought that evil spirits and punishment from God were responsible for the disorder, only 13% of respondents implicated these reasons for leprosy. The respondents considered genetic

Table 4. Question: What do you think is the cause of epilepsy/leprosy?

	Respondents				
	Epilepsy 1270		Leprosy 1329		
Results	No.	%	No.	%	*p* value
Don't know	655	51·6	266	20·0	<0·001
Evil spirit	381	30·0	97	7·3	<0·001
Punishment/curse from God	102	8·0	70	5·3	<0·001
Physical contact	64	5·0	333	25·0	<0·001
Born with it	63	5·0	514	38·7	<0·001
Febrile disease	3	0·2	44	3·3	
Accident	1	0·1	5	0·4	
Lightning	1	0·1			

Table 5. Question: How should society take care of persons with epilepsy/leprosy?

	Respondents				
	Epilepsy 1214		Leprosy 1314		
Results	No.	%	No.	%	*p* value
Don't know	554	45·6	175	13·3	
Give alms	415	34·2	877	66·7	<0·001
Medicine to be provided	199	16·4	184	14·0	<0·001
Let own family help	20	1·6	25	1·9	<0·001
Government to take care	18	1·5	47	3·6	
Pray for them	6	0·5	1	0·1	
Give sacrifices to the spirits	2	0·2	1	0·1	
Employ them to be independent	—	—	4	0·3	

transmission and contagion as the factors most commonly associated with the causation of leprosy. This was significantly different ($p < 0·001$) from the beliefs found with epilepsy (Table 4).

The respondents' attitude on what society should do for the sufferers of leprosy and epilepsy was very revealing (Table 5). The need to provide conventional treatment was expressed by a modest 14–16% of respondents in both interviews. However, more interviewees (67%) thought that victims of leprosy should be dealt with by the offer of alms, as compared with 34% who had the same belief for the epileptics ($p < 0·001$).

Discussion

The study population in the rural sub-district of Butajira consists of mainly illiterate farmers who have very little exposure to scientific knowledge on diseases like leprosy and epilepsy. The prevalence of leprosy in the community was found to be 1/1000.[6] It is also an interesting point that 2·3% of the respondents in this survey admitted that a family member or a relative suffered from leprosy.

Less than 15% of the interviewees possess radios, the only means of access to mass media available to the community. It must also be pointed out that the Ethiopian mass media offer only limited programmes on health education. Thus, the views that the respondents express on leprosy and epilepsy represent largely the beliefs and practices which are indigenous and prevalent in the rural community, without much outside or foreign influence. It is quite obvious from this study that the rural community has stronger and more negative feelings toward leprosy compared with those toward epilepsy, particularly on such matters as physical contact and marriage with victims. What is indeed at the root of this strong social stigma toward leprosy?

The Ethiopian Amharic word qumtina used for leprosy is very similar in concept to the Arabic word judham derived from jadham, with the literal meaning of 'cutting', denoting the outcome of the disease.[7] The Amharic terms for leprosy the disease, and for the person with the disease, although widely used in the country, have derogatory and deeply entrenched discriminatory and stigmatizing connotations. For what it is worth,

the less pejorative new terminology sega dewe, 'the disease of the flesh', is fortunately gaining wider acceptance. In this connection it is worth mentioning that, as part of the programme of destigmatization, Dogliotti proposed the replacement of the 'opprobrious term—leprosy' with the eponym 'hanseniasis',[8] though we are all aware that changing the name is not certain to change an attitude.

Nevertheless, in the rural farming community surveyed, it was our experience that leprosy patients do not in fact face outright segregation and ostracism. They seem in general to get a sympathetic reaction from their community. In a survey undertaken in the same community to detect neurological cases including leprosy,[6] we were impressed by the way leprosy patients were mixing and intermingling freely with others who did not openly discriminate against or reject them. This is very unlike the unfriendly reception that leprosy patients receive in the big towns and cities in Ethiopia.

It is also a common practice that in the peasant associations farmers with leprosy are allocated pieces of land equal to those of other peasants: they can cultivate these on their own or, if unable to do so, hire others to do the work for them. Like all other farmers, they can build their huts within the allocated village boundaries without any restriction or segregation. These conditions and observations suggest that leprosy patients in the rural community are better accepted or tolerated than in the towns, where they are invariably treated as outcasts.

In this attitudinal study on leprosy 13% of the respondents were from Butajira, the main small rural town, and from two other satellite towns within the study area. The attitudes of the respondents from these semiurban centres to different aspects of leprosy was not statistically different from that recorded in the rural villages.

As evidence in Table 5, the majority of the respondents are convinced that leprosy sufferers should depend on alms, which may explain why we find so many of leprosy sufferers among the multitudes of beggars around places of worship.

In a *Leprosy Review* editorial of 1977, Antia appropriately referred to leprosy as the 'disease which affects the body of the patient and the morale of the public'.[9] Indeed, leprosy has a profound effect on the patient, and carries a strong stigma in all cultures and societies.

In his analysis of the psychological aspects of leprosy, Davey identified the following main sources of stress in the leprosy patients: the stress of inherited idea, the stressful experience of leprosy related to its physical disabilities; and the stress of home and family life emanating from the threat of unemployment and problems of marriage.[10]

As evidenced in this study, there is a widely held concept that leprosy is congenital. Nearly half of the respondents in this survey thought that the disease was inherited, as compared to 5% who expressed the same belief about epilepsy. Such congenital transmission of leprosy is believed to extend through several generations, very similar to what has been documented among Hong Kong Chinese.[11] Traditionally, in many parts of Ethiopia, marriage with a leprosy sufferer would be allowed only after the families of each of the partners have independently convinced themselves that leprosy has not occurred for seven generations. Although this study did not address itself to the attitudes of the leprosy patients to their own disease, it was quite clear from our experience in the study area that those with leprosy face both rejection and isolation, particularly if they exhibit obvious amputations, ulcerations and disfigurement.

Edwards proposed that the origin of the social stigma of leprosy was a primitive fear evoking a guilt complex in both the sufferer and the observer, a rational fear of contagion, and the religious fear of divine punishment.[12]

In previous studies of leprosy within the religious context, we come across persistent allegations of mistranslation and misinterpretations of writings on leprosy in holy scripture. References to leprosy are certainly made in the Bible. However, Browne, for one, argues that leprosy, as the currently well-defined clinical entity, is not explicitly or beyond doubt referred to in the Bible, although the word 'leprosy' and its cognates occur in translations from the original scriptures in Western languages.[13] In his review of the same subject, Mohamed in 1985 found that leprosy is also not mentioned in the Quran. What was erroneously translated from the Quran as leprosy was vitiligo. He further argues that the medieval type of persecution, isolation and segregation of leprosy patients, still practised in many Moslem communities, has no religious justification.[7]

Similarly, Skinsnes has cast serious doubts on the suggestion that the negative social reaction to leprosy is the result of biblical teachings, including possible mistranslation. Based on our experience and as confirmed by this study, we tend to agree with his conclusions that the negative social reactions encountered are largely derived from a 'wrongly perceived picture of a contagious, incurable disease which progresses and eventually results in deformities and mutilation'.[14]

In Zambia, witchcraft was believed to be an important cause of leprosy, and the disease was often believed to be a punishment, reminiscent of the beliefs in medieval Europe.[15] Yet these beliefs were not very prevalent in the Ethiopian rural community we surveyed. Only 12·6% implicated evil spirits and punishment from God as the cause of the disease. On the other hand, as mentioned earlier, the hereditary factor was considered very important. The fear of contagion was expressed by 48% of the respondents. Direct contact was believed to be the main method of transmission, while a minority also considered sexual contact to be a means. Similar strong fears of contagion have been documented in studies from communities in Mangalore, in south-west India.[16]

The conclusion to draw from this study is that the rural community as a whole needs to be provided with correct information on the cause and outcome of leprosy. There is a real need to impress on the public that the disease is not genetically transmitted. This necessitates intensive health education to convince the population that, as an infectious disease, leprosy can be cured, and if detected very early can be cured without deformities. The absence of strong negative religious beliefs, and the observed tolerance and understanding of the community toward leprosy sufferers would certainly contribute positively to the success of such health education. A campaign of education should, as Dogliotti suggested, extend to medical, paramedical, social, religious and educational institutions.[8] It is emphasized that the education of those in the medical profession should precede that of the general public.

The integration of leprosy care into the general health services would help to reduce the segregation of leprosy patients. In this connection, we subscribe to the views of Antia that the specialized treatment of leprosy patients in isolation encourages the perpetuation of the stigma in the minds of the public and the medical profession.[9] The present existing leprosy control programmes, with better resources and trained manpower, should therefore help to strengthen the basic health delivery centres in the country, and also actively participate in the health stations in order to ensure that the follow-up of leprosy patients is not neglected.

While we educate communities in endemic areas to avoid being victims of the disease and to report when they experience the first sign of leprosy, it is absolutely vital that we also find ways of re-integrating those that have been successfully treated. In the context of

developing countries, it is common knowledge that a disabled person with a skill has better chances of overcoming prejudices and getting social acceptance. As Frist has emphasized, attention must be given to create integrated vocational rehabilitation opportunities for leprosy patients.[17]

Acknowledgment

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APPENDIX

Attitude Questionnaire

Date Farmers/Urban Association House No. Interviewer

TO BE ANSWERED BY ONE MEMBER OF THE HOUSEHOLD, PREFERABLY BY THE HEAD OR WIFE

Name of informant..... Age..... Sex.....
Marital status: Married..... Single..... Divorced..... Widow.....
Number of children: Male..... Female..... Total.....
Occupation..... Income per month:.....
Education: Illiterate..... Read and write..... Grade.....
Religion: Christian..... Moslem..... Other.....

ATTITUDES TO LEPROSY

Have you heard or read about leprosy? Yes..... No.....
If yes, where? .....

How would you recognize a person with leprosy? .....

Is there in your language/dialect another name for a person with leprosy?
Yes..... No..... If yes, specify: .....

After giving a full description of the different manifestations of leprosy (skin lesions, deformities and amputations due to nerve damage), the enumerator tells the respondent: WE CALL THIS *LEPROSY (SEGA DEWE)* AND THAT IS THE TERM WE WILL USE IN THE QUESTIONS TO FOLLOW.

Have you ever seen a person with leprosy? Yes..... No.....

Have you among your relatives anyone with leprosy?
Yes..... No..... If yes, specify relationship .....

Do you think you know the cause of leprosy? Yes..... No.....
If yes, explain .....

Do you think that leprosy is inherited? Yes..... No.....
If yes, how? .....

Do you think that leprosy is contagious? Yes..... No.....
If yes, how? .....

Do you think leprosy is a form of insanity? Yes..... No.....

Do you know what to do for a person with leprosy?
Yes..... No..... If yes, how? .....

If a person with leprosy has been treated and his disease has been cured will you consider him/her to be an ordinary healthy person?
Yes..... No..... If no, why? .....

If you had the opportunity, would you employ someone with leprosy?
Yes..... No..... If no, why? .....

Are you willing to work with a person having leprosy?
Yes..... No..... If no, why? .....

Would you allow your child to play with a child having leprosy?
Yes..... No..... If no, why? .....

What would you do if you were forced to share accommodation with someone with leprosy?

.....

Do you have a friend who has leprosy? Yes..... No.....

Would you be a friend of someone with leprosy?
Yes..... No..... If no, why? .....

May anyone in your family marry someone with leprosy?
Yes..... No..... If no, why? .....

Are you afraid of someone who has leprosy?
Yes..... No..... If yes, why? .....

Should a family having a member with leprosy hide him/her from outsiders?
Yes..... No..... If yes, why? .....

Do you think a person with leprosy should use public transport?
Yes..... No..... If no, how should he/she travel? .....

Would you shake hands with a person known to have leprosy? Yes..... No.....

How should society take care of persons with leprosy?

.....

At the end of the interviews health education on leprosy is given to the respondent and his/her family by the enumerator.

Lepr Rev (1992) **63,** 157–168

Attitude des populations rurals à l'égard de la lèpre dans le centre de l'Ethiopie et brève comparaison avec certaines observations sur l'épilepsie

R Tekle-Haimanot, L Forsgren, A Gebre-Mariam, M Abebe, G Holmgren, J Heijbel et J Ekstedt

Résumé Pour connaître la réaction du public face à la lèpre, un sondage porte à porte a été effectué auprès de 1546 foyers dans les communautés rurales d'agriculteurs de Meskan et de Mareko dans le centre de l'Ethiopie, où la fréquence des cas de lèpre est estimée à 1 pour 1000. Les attitudes à l'égard de la lèpre ont été comparées aux attitudes vis-à-vis de l'épilepsie, étudiées lors d'une précédente enquête dans la même communauté. Quatre-vingt-sept pour cent des personnes interrogées ont plus de 25 ans, et 59,5% sont des femmes. Le groupe étudié se compose d'un peu plus de musulmans (54%) que de chrétiens. La majorité des personnes interrogées (87%) sont des fermiers, et le taux d'analphabétisme est de 84%. Respectivement 95% et 83% ne souhaitent pas employer ou travailler avec une personne souffrant de la maladie. Soixante-quinze pour cent ne permettraient pas à leurs enfants de fréquenter un camarade de jeu atteint de la lèpre. Une analyse comparative, dans la même communauté, a montré que les attitudes négatives à l'égard de la lèpre étaient plus marquées que celles à l'égard de l'épilepsie, notamment en ce qui concerne les relations matrimoniales, le partage du logement et le contact physique avec une personne atteinte. Il semble que ces différences s'expliquent par le fait que la communauté croit profondément que la lèpre est à la fois héréditaire et contagieuse, opinion exprimée par 48% et 53% des personnes interrogées, respectivement. Pour mettre un terme à ces attitudes négatives, il faut éduquer la population et lui inculquer que la lèpre est une maladie infectieuse que se soigne, qu'elle n'est pas congénitale et qu'elle est guérissable si elle est décelée tôt. Cette étude renforce les propositions déjà formulées pour intégrer le traitement de la lèpre aux programmes généraux de santé, dans les pays en développement comme l'Ethiopie.

Actitudes de los habitantes rurales de Etiopía Central a la lepra, y una breve comparación con la epilepsia

R Tekle-Haimanot, L Forsgren, A Gebre-Mariam, M Abebe, G Holmgren, J Heijbel y J Ekstedt

Resumen Se realizó un estudio de las actitudes públicas a la lepra, de casa en casa en 1546 residencias muestreadas en las comunidades agrícolas rurales de Mesken y Mareko, en Etiopía Central, en donde se calcula la frecuencia de la lepra en 1 por 1000. Se compararon las actitudes a la lepra con las actitudes la epilepsia determinados en un estudio anterior en la misma comunidad. 87% de las personas interrogadas tenían más de 25 años, y un 59,5% eran mujeres. Habían pocos más Musulmanes (54%) que Christianos. La mayoría de personas entrevistadas eran agricultores, con un nivel de analfabetismo de 84%. 95% y 83% respectivamente no estaban dispuestos emplear ni trabajar con una persona que padecía de la enfermedad. Un 75% no permitía que sus hijos se asocien con un compañero que sufría de la lepra. Un análisis comparativo de las actitudes en la misma comunidad indicó que las negativas a la lepra erán más fuertes que las contra la epilepsia, especialimente respecto a las asociaciones matrimoniales, la distribución de acomodación y los contactos físicos con un enfermo. Las razones por estas diferencias parecían ser debidas a la creencia intensa que la lepra era tanto hereditaria como contagiosa, expresada por 48% y 53% de los entrevistados respectivamente. Para reducir a un mínimo la perpetuación de las actitudes negativas, es necesario educar y convencer la población que la lepra es una enfermedad infecciosa tratable, que no se adquiere por razones congenitales, y que es hasta curable si se detecta temprano. El estudio refuerza las sugerencias propuestas anteriormente que en los países en desarrollo, como la Etiopía, se debe integrar el cuidado de la lepra a los servicios sanitarios generales.

Lepr Rev (1992) **63,** 169–172

Appraisal of the knowledge and attitude of Nigerian nurses toward leprosy

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Summary The attitudes of nurses toward leprosy are studied and in this paper The findings show that their knowledge of leprosy is lacking and that they also fear leprosy. This study recommends that leprosy should be included in the basic nursing curriculum in order to increase awareness and to decrease the stigma of leprosy.

Introduction

'When a country has a problem of leprosy, all professional and auxillary staff in their basic training should be given an understanding of the disease'.[1]

Nurses are the largest group of health professionals in Nigeria. While it is possible to run a primary health care centre without a doctor, it would be unrealistic to operate one without a nurse on the staff list.

With about 200,000 registered leprosy cases in Nigeria the Nigerian Government is rightly giving control of leprosy the priority it needs, and has therefore decided to implement leprosy control using the primary health care approach.

For this strategy to succeed, the personnel who form the pivot of primary health care, i.e. nurses, should possess sufficient knowledge and a positive attitude vis-á-vis leprosy if effective health care delivery is to be assured for the patients suffering from this disease.

Because of this, a study was undertaken to discover how much was known about, and the attitudes of Nigerian nurses towards leprosy patients.

Materials and methods

Having obtained approval for the study from the National Council of Nigerian Nurses and Midwives, letters and a sample of the questionnaire were sent to 1 nursing school in each of the 21 states of the Federation and the Federal Capital territory, Abuja. Those interested in contributing to the study were requested to supply information using the form provided and return it to the medical officer in charge of Kaduna State Leprosy

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Table 1.

School code	School name	Average score out of 30 questions
1	School of Nursing, Kano, Kano State	13·2 (44)*
2	School of Nursing, FTC, Abuja	16·4 (55)
3	School of Nursing, Portharcourt, Rivers State	14·0 (47)
4	School of Nursing, UNTH, Anambra State	16·7 (56)
5	School of Nursing, ABUTH, Kaduna State	16·1 (54)
6	School of Nursing, Wusasa, Kaduna State	15·0 (50)
7	School of Nursing, Sokoto, Sokoto State	13·2 (44)
8	School of Nursing, Ikot Ekpene, Akwa Ibom State	14·3 (48)
9	School of Nursing, Maiduguri, Borno State	14·5 (48)
10	School of Nursing, Abeokuta, Ogun State	16·2 (54)

* Numbers in parentheses are percentages.

Control Services. There were positive responses from 14 nursing schools and 30 sets of questionnaires were sent to each of these schools to be filled in by their final year students. However, only 10 schools returned the filled-in questionnaires (Table 1).

A total of 278 filled-in questionnaires from these 10 nursing schools were then analysed to discover the knowledge and attitude of Nigerian nurses.

There were 45 questions—30 were used to appraise knowledge and 15 were used to appraise the nurses' attitude vis-à-vis leprosy.

Results (Tables 1 and 2)

Tables 1 and 2 show the results of the questionnaires.

Discussion

Leprosy is a disease adversely affecting the body of the patient and the mind of the unaffected public. But the caring professions cannot blame the public for this when the majority of the medical profession, especially nurses, continues to treat leprosy as a disease that is apart from all the others.

The present study reveals a below-average basic knowledge and a largely negative perception of leprosy by most of the respondents in this study— findings that leave a lot to be desired.

Any leprologist of experience will agree that the effect on the lay public of a qualified nurse, posted to a primary health care centre, who knows nothing about leprosy, and is obviously afraid to touch a leprosy patient—which could describe about 65% of the respondents in this study—would be very negative.

Empirical evidence reveals that fortunately the younger members of the nursing profession do not suffer the intense fear of leprosy which still prevails amongst the older generation. This group of younger medical workers forms a vast and important 'captive

Table 2. Response

Comment	Strongly agree	Agree	Indifferent	Disagree	Strongly disagree
1 Leprosy is highly infectious	71 (26)*	108 (39)	15 (6)	56 (20)	28 (10)
2 Many nurses would wish to work in leprosy hospitals	23 (8)	21 (8)	83 (30)	76 (27)	75 (27)
3 Nursing of leprosy patients is a dirty job	124 (44)	83 (30)	3 (1)	49 (18)	19 (7)
4 There are no career prospects as far as nursing practice in leprosy hospitals is concerned	64 (23)	51 (18)	91 (33)	50 (18)	22 (8)
5 The children of leprosy patients invariably become lepers themselves	102 (37)	82 (30)	8 (3)	63 (23)	23 (8)
6 Patients with leprosy should ideally be isolated	87 (31)	123 (44)	16 (6)	38 (14)	14 (5)
7 Most workers in leprosy hospitals usually contract the disease	48 (17)	64 (23)	46 (17)	89 (32)	31 (11)
8 The commonest presentation of leprosy is deformed limbs	72 (26)	115 (41)	8 (3)	56 (20)	27 (10)
9 It would be better to treat leprosy patients in general hospitals instead of 'special' leprosy hospitals	40 (14)	52 (19)	38 (14)	102 (37)	46 (17)
10 Deformities are an inevitable consequence of leprosy	101 (36)	82 (30)	24 (9)	60 (22)	11 (4)
11 If one had a choice, it is better to contract leprosy than the acquired immune deficiency syndrome (AIDS)	50 (18)	63 (23)	41 (15)	46 (17)	78 (28)
12 Health workers in leprosy hospitals are mediocre with no hope of alternative employment	22 (8)	46 (17)	54 (19)	123 (44)	33 (12)
13 Nurses should be given extra allowances for taking the risk of working in leprosy hospitals	96 (35)	84 (30)	11 (4)	40 (14)	33 (12)
14 It may be difficult to find a suitable husband if a spinster nurse works in a leprosy hospital	121 (44)	69 (25)	25 (9)	38 (14)	25 (9)
15 Working in a leprosy hospital is one of the best ways of exhibiting a humanitarian nature	88 (32)	123 (44)	52 (19)	12 (4)	3 (1)

* Numbers in parentheses are percentages.

audience'. They *must* receive a basic training in leprosy that should include the formation of positive attitudes to the disease and clinical contacts with the patients.

Officials of the National Council of Nigerian Nurses and Midwives should liaise with officials of the National Tuberculosis and Leprosy Control Programme in order to review the basic nursing curriculum and include lectures and practical training on leprosy. The inclusion of simple facts about leprosy in the nursing curriculum will not only help in the early detection of leprosy, but would also help to destigmatize the disease. This aspect is particularly important as the lay public see nurses as role models vis-à-vis attitudes to all diseases.

Acknowledgment

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Reference

[1] Who Expert Committee (1976).

Lepr Rev (1992) **63,** 169–172

Estimation des connaissances et de l'attitude des infirmièrs nigériens envers la lèpre

N Awofeso

Résumé Les attitudes des infirmièrs envers la lèpre sont étudiées et, dans cette communication, les résultats obtenus montrent que leurs connaissances de la lèpre sont insuffisantes et qu'en plus, ils ont peur de la lèpre. Cette étude recommande que la lèpre soit inscrite au curriculum de base de la formation des infirmièrs, afin de les rendre plus conscients de la maladie, et de réduire le stigma attaché à la lèpre.

Una apreciación de los conocimientos y actitudes de las enfermeras nigerinas a la lepra

N Awofeso

Resumen Las actitudes de enfermeras en Nigeria a la lepra han sido estudiadas en esta publicación y los resultados demuestran que sus conocimientos de la lepra es deficiente y que temen la lepra. Este estudio recomienda la inclusión de la lepra en el programa básico de estudios para enfermeras, para aumentar la conciencia y reducir el estigma de la lepra.

Lepr Rev (1992) **63,** 173–182

SPECIAL ARTICLE

Relationship problems between doctors and paramedical professionals working in leprosy with reference to a possible solution

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Summary An empirical investigation was conducted on the in-group dynamics of health personnel working in leprosy. The sample populations were taken from the National Leprosy Eradication Programme (NLEP) employees of two state governments in India. They consisted of 21 doctors and 335 paramedicals, the former constituting a formal group and the latter a semiformal group. Two separate scales were developed for each of these groups to elicit information on five potential areas of intergroup relationships.

The results indicated that there was very poor acceptance of the out-group and its roles, i.e. poor acceptance of the paramedicals by the doctors and vice versa. Three reasons were elicited from this study. First, doctors held their professional standing to be on a higher level than the paramedicals, leading to excessive social distancing between doctors and paramedicals. Second, multiprofessional involvement in NLEP work has increased the trend of professional overlapping, leading to a significant apprehension of the encroachment of skills. Third, there was a mutual lack of trust of each others professional skills. Despite these problems the otherwise more severe human relationship problems, such as domineering behaviour and prejudiced perception against the out-group were found to be significantly less in this study.

In order to improve working relationships between these groups a method that has been used at Karigiri is recommended. The method has two parts. The first is aimed at intrapersonal understanding and the second at the development of interpersonal skills. Role play that mimics their original work situation and an analysis of case histories were the methods of teaching that were found to be more advantageous in internalizing these skills.

Introduction

To control leprosy, the National Leprosy Eradication Programme (NLEP) in India has employed a significant number of professionally trained health personnel, such as medical

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officers and paramedical professionals. These employees are directly involved in patient care activities that consist of prevention, treatment, education and rehabilitation of leprosy patients.

Medical officers are identified as a recognized prestigious occupational group. Paramedical staff are also adequately trained in their area of health, however they are of a lower power professional group in comparison to doctors. Among these two groups, medical officers are formal, while paramedicals are semi-formal in nature and each belongs to their own professional group on the basis of economic and intellectual needs. The study considers this as in-group dynamics. Anyone who does not share these needs is seen as 'out-group' by the 'in-group'.

Good intrapersonal relationships between these two major professional groups will open up a two-way communication, and provide support to each others professional skills, utimately facilitating an environment that is conducive for ideal leprosy control work. This study has focused on five potential areas which can assist or affect intergroup relationships amongst medical and paramedical professionals. The relevant data to analyse these aspects was obtained from the health professionals by asking them to evaluate their own role and the role of the other professional group, with the assistance of two scales developed for this purpose.

Materials and methods

SAMPLE

The health care system taken for analysis was the NLEP of two state governments in India. The health personnel of NLEP were selected from one district in Andhra Pradesh (AP), and one in Tamil Nadu (TN), consisting of a total sample population of 356. For the analysis of inter-group behaviour, the sample population was divided up in one or two of the following ways, on the basis of the social identity construction of Rey-Kowshiki.[1]

The total sample population of 356 NLEP health personnel formed one group from the sample districts.

2 The sample population was also split into two groups depending on whether they had professional medical qualifications (21) or allied health professional qualifications (335). The allied health professionals included nurses, laboratory technicians (LT), leprosy physiotherapy technicians (PT), health educators (HE), non-medical supervisors (NMS), pharmacists (Pharm) and the leprosy field workers known as leprosy inspectors (LI) in TN and nonmedical assistants (NMA) in AP.

Cluster sampling was used in this study by selecting the whole of each of the above two districts as clusters. The reason being that at the district level the NLEP consists of units such as leprosy control units, survey–education–treatment centres and temporary hospitalization wards. Collecting data from all these units is possible through cluster sampling, which results in a uniform pattern of information and recording.

SCALE OF ASSESSMENT

Two scales of assessment were constructed to evaluate mutual perception of medical and paramedical professionals. The data were collected using a scale developed by the

researcher based on the perception–attitude–behaviour (PAB) concept. The scale consisted of 19 variable test items (Table 1). Mutual perception of medical and paramedical professionals was one of the variables. This consisted of two scales of 5 statements each, to elicit PAB responses from doctors and the same number for paramedicals (Appendix 1 and 2). Two statements in it were phrased positively and the remaining 3 negatively. A specific prepilot analysis of the NLEP organizational climate conducted by the researcher helped to identify the following 5 potential areas which can assist or affect intergroup relationships between medical and paramedical professionals:

1 Professional overlapping: paramedicals, encroaching on the doctors area of specalization and vice versa.
2 Social distancing due to occupational prestige.
3 Mutual trust or mistrust towards each others professional skills.
4 Mutual professional support or prejudiced behaviour.
5 Participative attitude or a domineering attitude towards the out-group.

To elicit the attitude of the sample population in the above-mentioned areas, appropriate statements in accordance with their job descriptions were used (Appendices 1 and 2).

Table 1. Coefficient ranking of variables

S. No.	Variables	N	Mean	SD	Coefficient of variations	Position
1	Mutual perception of doctors and paramedics	356	2·43	0·72	29·63	19
2	Interaction of health professionals with admin staff	356	2·49	0·63	25·30	9
3	Supervisory behaviour	62	2·83	0·76	26·86	16
4	Health professionals—leprosy patients relationship	356	2·58	0·71	27·52	17
5	Autonomy	356	2·95	0·62	21·01	2
6	Subordinate description of supervisory, behaviour	356	2·39	0·67	28·03	18
7	Pay satisfaction	356	2·70	0·72	26·67	14
8	Skill utilization	356	2·77	0·69	24·91	8
9	Organizational climate	356	2·84	0·63	22·18	6
10	Job significance within the community	356	2·57	0·68	26·46	12
11	Promotion satisfaction	356	2·91	0·78	26·80	15
12	Adjustment pattern to the disease	356	2·30	0·59	25·65	13
13	Organizational commitment	356	3·06	0·67	21·90	5
14	Skill variety	356	3·03	0·66	21·78	4
15	Adjustment pattern to the nature of work	356	2·43	0·62	25·51	11
16	Skill development	356	3·09	0·52	16·82	1
17	Job significance within the organization	356	2·71	0·69	21·46	10
18	Interdepartmental relations	356	2·95	0·63	21·36	3
19	Technical satisfaction	356	2·74	0·66	24·09	7

SCORING SYSTEM

The content analysis of the responses from the sample served as the source of data pool. The intercorrelation of factors to this variable with other variables was $r = 0{\cdot}001$. The internal consistency of the PAB scale was obtained by correcting r with the 'KR-21 formula' $r = 1{\cdot}00$.

The Likert scale as modified by Vasudeva[2] was used in scoring the PAB scale. It consists of a 6-point response instead of the 5-point response of the original Likert scale. These were: strongly agree (SA); agree (A); mildly agree (MA); mildly disagree (MD); disagree (D), and strongly disagree (SD). Thus it eliminated the possibility of the undecided response of the 5 point Likert scale, forcing the candidate to either accept or reject the statement. One study[3] has stated that the 'Don't know' category has been a source of difficulty and controversy in many fields of psychological research. The scoring for the 2 positive statements were as follows: SD—0, D—1, MD—2, MA—3, A—4 and SA—5. For the 3 negative statements this scoring was reversed.

Results were obtained by using three tests, namely: (a) the co-efficient of variation test; (b) the two-tail test for the level of significance; and (c) the computation of frequency of response.

Results

1 Mutual perception of medical and paramedical professionals was rated last (19th) in the coefficient ranking of the variable test (N = 356; mean = 2·43; SD = 0·72 and coefficient of variations = 23·63) (Table 1). It indicated that there was a very poor acceptance of the out-group and their roles.

2 Further analysis was made to find out whether there was any significant difference betwen the medical and paramedical professionals in the in-group and out-group discriminatory behaviour (Table 2). The results showed no significant difference. This indicated that the level of discriminatory behaviour between the two groups was similar.

3 The computation of frequency of response revealed that three potential areas of intergroup relationships were significantly affected (Table 3). These were (a) social distancing by doctors due to occupational prestige (71·4%); (b) mutual lack of trust toward each others professional skills (62·1%); and (c) mutual perception of professional

Table 2. Comparison of mutual perception of medical and paramedical professionals

							Pooled variance estimate			
Profession	N	Mean	SD	SEr	F	P	t	df	2-tail	Significant/ not significant
Doctor	21	2·69	0·35	0·076	4·48	0·000*	1·67	354	0·095	NS
Paramedical	335	2·41	0·74	0·040						

* Significance level of F value is large. Therefore pooled variance 2-tail probability estimate was used in this analysis.

Table 3. Frequency of response

Nos	Statement No. in the schedule	Among the total sample							Among doctors							Among paramedicals						
		0	1	2	3	4	5	Total	0	1	2	3	4	5	Total	0	1	2	3	4	5	Total
1	18	33	81	24	42	111	65	356	0	3	4	5	6	3	21	33	78	20	37	105	62	335
2	36	28	97	25	56	111	35	356	0	5	1	0	10	5	21	28	92	24	56	101	30	331
3	54	31	127	60	33	64	36	351	1	8	7	2	2	0	20	30	119	53	31	62	36	331
4	72	22	79	15	49	155	33	353	1	0	1	3	14	2	21	21	79	14	46	141	31	332
5	90	67	167	54	8	41	16	353	3	11	3	1	3	0	21	64	156	51	7	38	16	332

overlapping (61·2%). However, a domineering attitude and prejudiced behaviour toward the out-group were significantly less (18·3% and 32·8%, respectively).

Discussion

The above finding is not surprising and has been reported earlier by members of the medical professions in general practice.[4–7] Therefore, in this discussion an attempt has been made to explain the three problem areas in human relationships as elicited in this study, in comparison with earlier works.

As far as paramedicals are concerned one study[8] has pointed out that working beside a physician may be acceptable to paramedicals, but working in a subsidiary relationship to a physician is not. A further study[9] is also of the same opinion and pointed out that the new generation of allied health professionals expect to be treated with the respect that their professional training has earned for them. They are less likely to carry out doctor's orders without question than was formerly the case. For example, physiotherapy education emphasizes a cooperative team approach to physical treatment.[10] It has been noted[11] that pharmacists hold similar expectations. New curricula in nursing particularly stresses the importance of nurses being able to meet a patient's psychosocial needs, solve clinical problems, generate problem-oriented nursing plans and act as patients' advocates.[12] Such a trend elevates the allied health professional from the level of an ancillary staff to a therapist status.

At the same time, paramedicals were aware of the existing norms of belonging to a lower professional group in comparison to the doctors. Second, professional ethics forced them to accept the doctor to be the leader of the team. For any professional, interference or orders from an out-group can become a sensitive issue. This conflict between their actual role and their group expectations leads to an attitude of less trust of doctors.

Looking at the problem from the doctors point of view, their professional standing leads them to maintain a certain level of social distance from allied health professionals in the work situation, when both these groups interact in leader–subordinate roles. However, excessive social distancing affects the social ties that draw both these groups together. The results of this study showed that a significant percentage (71·4) of doctors were strongly inclined toward maintaining such a social distance. At the same time a significant number of allied health personnel perceived such distancing negatively (56·5%).

Also, to a certain extent the comparison of work experience between these health

professionals explains the lack of trust doctors have toward paramedicals. Most of the paramedicals in NLEP were exclusively recruited to work in leprosy, whereas the medical officers were transferred from general medical care to work in leprosy. Among the sample population, only 35% of doctors in comparison to 46% of paramedicals had more than 5 years experience in the field of leprosy. Similarly, only 20% of doctors had more than 10 years of experience in NLEP, whereas 47% of paramedicals had more than 10 years. In such a situation, the experienced paramedicals let the doctors know that they do not appreciate them meddling in their area of work because they feel that they have far more experience of leprosy than the doctors. This results in a passive attempt not to accept the domination of the high-powered group. When doctors find it difficult to exercise the 'team leader approach', it leads to frustration and results in a lack of trust in paramedicals.

Regarding professional overlapping in the NLEP, seven paramedical professionals and a doctor are involved in a patient care activities. With so many professionals being involved together in leprosy work the situation of overlapping can very easily be perceived. It can naturally produce apprehension among doctors if they feel that paramedicals are encroaching upon their specialization and vice versa.

Despite these relationship problems, it is heartening to note that the NLEP organization is less significantly affected by the other two more severe forms of human relation problems, such as a domineering attitude and prejudiced behaviour towards an out-group.

AN ALTERNATE PERSPECTIVE

In recent times attempts have been made to promote and strengthen the relationship between the health personnel and the community. Similarly, the relationship amongst health workers is also equally important. Improved relationships will positively affect worker performance and programme implementation. One study[13] pointed out that not teaching about working relationships during medical training led to management by imitation, with the younger physicians mimicking the behaviour of their more experienced peers.

Since 1987 the researcher has been conducting sessions on 'working relationships' during the management and health education modules. These were conducted for health professionals, as part of their postbasic training in leprosy at the Schieffelin Leprosy Research and Training Centre, Karigiri, India. The sessions were conducted in a homogeneous group situation. The participants were either medical officers or non-medical supervisors.

The content of these sessions were divided into two parts. The first aimed at intrapersonal understanding; a 2-hour session was marked for this in the management module. In this session attempts were made to uncover the basis of out-group bias. For this purpose, feedback about profession-based self-concept was elicited by administering the PAB rating scale developed for this study on the participants (Appendix 1 and 2). Profession based self-concept is the most important single factor that affects communication with others. They scored themselves with the key given by the trainer. This exercise was followed by lecture/discussion to further develop intraunderstanding about themselves and to perceive accurately how others are reacting to one's own behaviour.

The second part was on development of interpersonal skills. It involved listening, understanding and communicating.[14] The main objective of the health education module is to learn these three skills and to apply them in their patient and community work. These

principles also apply to interpersonal relationships with colleagues, subordinates and supervisors. Two methods of teaching were used, namely, role play and analysis of case histories. The feedback from the role play was used to create awareness about their own style of listening and communication. Initially we used a rating scale for this purpose. Along with the rating scale, we have introduced video recordings, which were taken during the role play and these were used for further recall, thus developing performance.

To understand why the patient and community decide to behave the way they do, analysis of case histories were used. This can also produce awareness in understanding certain behaviour in the other professional group. This session was conducted as group work and the members do group reporting. In the plenary session desirable and undesirable behaviour are analysed and attempts are made to understand these from the psychosocial perspective of the patient and community. Approximately 10 hours were allotted for developing interpersonal skills. These sessions progressed at a speed set by the participants. There is no long-term follow-up report on the outcome of such sessions; however, the postmodule feedback session showed that there was initial uncertainty and anxiety when their intrapersonal and interpersonal styles were exposed in the feedback. Gradually most of the participants settled down and found the exercise useful.

We do recognize the limitations of the above relearning processes as relationship building is controlled by several environmental factors, such as organizational climate and the basic personality of the individuals. The personnel are also controlled by behaviour pattern set by the 'in' and 'out' professional groups and are subjected to pressure exerted by these groups. To change this group behaviour, we recommend that the issue of mutual interdependence and respect of other health professional skills should be addressed at a basic level in medical and allied education. This process may need to be relearned from time to time as part of refresher or postbasic training. In this way it will become an established norm, thus creating an ideal working environment.

Acknowledgment

This study is a part of the doctoral thesis of Mr R Premkumar, submitted to the Faculty of Social Sciences, Nagpur University, Nagpur, India.

We wish to thank Mrs Judy Satish and Dr Sujai Suneetha for their assistance in the preparation of the manuscript and Mrs Glory Davidson for typing.

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APPENDIX 1

Mutual perception of medical and paramedical professionals (MPMP) scale

Statement to all the medical professionals in the sample

S. No.	Factor	Statement loaded with factor	Statement No. in the schedule	Kind of statement
1	Fear behaviour about the paramedicals encroaching upon their job.	PMWs and NMS develop inflated ideas of their own capacity and try to do the doctor's job.	18	Negative
2	Attitude of maintaining social distance.	A medical officer is a medical officer everywhere. He should maintain his official dignity always.	36	Negative
3	Trust behaviour towards the skills of the paramedicals.	Doctors can trust the smear reports given by the technicians.	54	Positive
4	Prejudiced perception about paramedicals.	PMWs are capable of detecting leprosy and handling the condition when it is not complicated.	72	Positive
5	Domineering attitude towards paramedicals.	Paramedical professions can only have a limited influence on the final decision of patient management.	90	Negative

APPENDIX 2

Mutual perception of medical and paramedical professionals (MPMP) scale

Statement to paramedical professionals

S. No.	Factor	Profession to whom the statement is directed to	Statement loaded with factor	Statement No. in the schedule	Kind of statement
1	Attitude of the paramedicals wanting to encroach upon MO's specialization.	NMS	Consulting a doctor in leprosy is not essential, because NMS can classify and treat leprosy effectively.	18	Negative
		HE	Consulting the MO regarding health education activities is not essential because health educators can decide and conduct programmes.		
		LI (TN)	Consulting a doctor in leprosy is not essential because LIs can classify and treat leprosy effectively.		
		NMA (AP)	Consulting a doctor in leprosy is not essential because NMAs can classify and treat leprosy effectively.		
		PT	Prescription for physiotherapy by MO is not essential because physios can decide themselves what treatment to give.		
		LT	Consulting the MO regarding repeat smears is not essential because lab. technicians can decide.		
		Nurse	Consulting the MO regarding patient care is not essential because nurses can decide effectively		
		Pharm	Consulting the MO in leprosy is not essential because pharmacists can easily prescribe these medicines.		
2	Trust behaviour towards the skills of the MOs	NMS	Compared with NMS, the MOs know leprosy very well and are capable people.	54	Positive
		HE	Compared with HE the MOs know leprosy very well and are capable people		
		LI (TN)	Compared with LI, the MOs know leprosy very well and are capable people.		
		NMA (AP)	Compared with NMA, the MOs know leprosy very well and are capable people.		
		PT	Compared with physios, the MOs know leprosy very well and are capable people.		
		LT	Compared with Lab. Technicians, the MOs knows leprosy very well and are capable people.		
		Nurse	Compared with nurses, the MOs know leprosy very well and are capable people.		
		Pharm	Compared with pharmacists, the MOs know leprosy very well and are capable people.		

Appendix 2 (continued overleaf)

Appendix 2 (*continued*)

S. No.	Factor	Profession to whom the statement is directed to	Statement loaded with factor	Statement No. in the schedule	Kind of statement
3	Perception about social distance of MOs.	NMS	The MOs are proud people who maintain a certain distance from NMS.	36	Negative
		HE	The MOs are proud people who maintain a certain distance from health educators.		
		LI (TN)	The MOs are proud people who maintain a certain distance from LIs		
		NMA (AP)	The MOs are proud people who maintain a certain distance from NMAs		
		PT	The MOs are proud people who maintain a certain distance from Physios.		
		LT	The MOs are proud people who maintain a certain distance from Lab. Technicians.		
		Nurse	The MOs are proud people who maintain a certain distance from nurses.		
		Pharm	The MOs are proud people who maintain certain distance from pharmacists.		
4	Prejudiced percetion about MOs.	ALL	At times it is difficult to think that doctors in a control unit are equal to doctors in general practice	72	Negative
5	Domineering attitude towards MOs	NMS	The MOs should seek suggestions from NMS when classifying leprosy	90	Negative
		HE	The MOs should seek suggestions from health educators when arranging health education.		
		LI (TN)	The MOs should seek suggestions from LI when classifying leprosy.		
		NMA (AP)	The MOs should seek suggestions from NMA while classifying leprosy.		
		PT	The MOs should seek suggestions from physios regarding deformity assessments.		
		LT	The MOs should seek suggestions from lab. technicians when reading smear reports.		
		Nurse	The MOs should seek suggestions from nurses when treating in-patients.		
		Pharm	The MOs should seek suggestions from pharmacists when prescribing medicines.		

Lepr Rev (1992) **63,** 183–186

Letters to the Editors

A SUGGESTED NEW METHOD TO MEASURE PATCH AREA IN PAUCIBACILLARY LEPROSY

Sir,

Medical personnel usually depend on clinical parameters to judge the regression of lesions in order to assess the effect of treatment in paucibacillary leprosy where the BI is zero. Mitsuda reaction is almost always positive in PB cases and has a limited role. Periodic histopathological examination of PB lesions would be a useful parameter for the assessment of therapy but may not always be practicable under field conditions. However, because the usual techniques of clinical evaluation are subjective and prone to inter-personnel variations they cannot be used for research purposes.

During the Phase III immunotherapy trials with the ICRC vaccine, we have attempted to use the reduction in area of the patch as an objective parameter, as follows:

1 A piece of polythene transparency (used for overhead projection) measuring 10 mm × 10 mm (i.e. 100 mm^2) was weighed on an electronic balance (METTLER® Model AE 240, which has an accuracy of up to 10^{-4} grammes) to obtain the known weight of 100 mm^2 of transparency.
2 The margin of the patch was traced onto the transparency described above, with a microtip sketch pen, while the patient was supine or prone. The transparency was cut along the outlined border using a Tuc's knife (as used in cataract surgery).
3 This cut-out was weighed on the same electronic balance. The weight of the cut-out was divided by the known weight of 100 mm^2 of transparency (as recorded above) to calculate the area of the patch.
4 In each case, the outline on the transparency was traced on to millimetre squared graph paper and the number of millimetre squares were counted to calculate the area of the patch.

The area of the patch measured by this technique correlated with the standard technique of counting millimetre squares on graph paper.

This suggested method is simple, less time-consuming and is thus an improvement on the more tedious graph method, the only drawback being that a sophisticated electronic balance is necessary.

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COMMENT: REVERSAL REACTIONS IN LEPROSY AND THEIR MANAGEMENT

Sir,

As members of the medical profession, we were very pleased to read your editorial: 'Reversal Reactions in Leprosy . . .', by Dr Patricia Rose and Dr M. F. R. Waters (Volume 62, no. 2, June 1991). The subject has long demanded the attention it was given in this authoritative article. However, we would like to make the following comments:

We agree that early diagnosis of nerve damage is very important. Nevertheless, we also think that it is also very important to include an early nerve damage detection test, i.e. sensation tests (ST). We feel it should receive attention with voluntary muscle tests (VMT), and before a motor-conducted velocity test (MCV).

We think that both STs and VMTs, in hospital and field settings should be researched, because, providing techniques are accurate, these tests have proved reliable measures of changing nerve function. Naturally, examining techniques and record-keeping should be as objective as possible, but, in our experience, we have noticed they are particularly prone to error in field settings. We agree that increased awareness should be brought to leprosy control staff as we believe reversal reactions (RR) are most effectively managed using a team approach. Prevention of disability (POD) staff should have specific repeated training, with emphasis placed on keeping regular, accurately recorded results using individual patient forms. In this way, changes can be measured and appropriate treatment regimens carried out accordingly.

After the acute phase has passed, appropriate management of early nerve damage usually necessitates the strengthening and re-education of weakened muscles. We feel it is important to mention this in the area of RR management because, even though nerve function may partially or completely recover, the patient who does not receive adequate advise regarding exercises for hypertrophy specific muscle fibres may still be left with a useless, atrophic hand.

We hope you agree with our comments and we wait with anticipation for your 'reversed reaction'!

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FIONA McCUSKER
P A M SCHREUDER

REPLY: REVERSAL REACTIONS IN LEPROSY AND THEIR MANAGEMENT

Sir,

We welcome the comments by Miss McCusker and Dr Schreuder on the Editorial 'Reversal Reactions in Leprosy . . .' (*Lepr Rev* 1991; **62:** 113–121). Of course, sensory testing is important and should be performed routinely, with VMTs, to enable the field worker to monitor change and detect the early signs of nerve damage. Although sensory tests are not specifically mentioned by name, they are implied in the 'clinical' paragraph (page 114) where the need for careful records to detect new skin anaesthesia is mentioned (before VMTs!). Such regular sensory testing is an integral part of the ILEP reversal reaction protocols.

They are also correct in drawing attention to the need for continual and appropriate exercise, at the right time, to strengthen weakened muscles. Some patients will require more encouragement than others in this respect, but it is remarkable how much may be achieved.

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PATRICIA ROSE*
M F R WATERS†

TREATMENT OF SMEAR NEGATIVE MB PATIENTS WHO HAD RECEIVED PREVIOUS DAPSONE MONOTHERAPY

Sir,

With reference to the correspondence on the above subject (*Lepr Rev*, 1991; **62:** 339–40) I would like to make the following comments:

1 The article on the same subject by Cartel *et al.* (*Lepr Rev* (1991) **62,** 186–192) highlights the problems of a high relapse rate (27·5%) in MB cases who had previous monotherapy with dapsone. The references given in the paper also point this out.
2 During my WHO/STC to Fiji in 1983 it was seen that out of the 441 active cases, 63 (14%) were old MB cases treated with dapsone monotherapy who had relapsed. Of the 105 MB patients currently under treatment (January 1991) 24 (22·9%) were patients who had relapsed after previous treatment with dapsone monotherapy.
3 In countries like Fiji where the incidence of leprosy is falling, a high proportion of cases newly-requiring treatment will probably emerge as MB cases relapsing after previous treatment with dapsone monotherapy.
4 If this occurs, as the data suggests, these cases could be a new source of infection in the community and pose a challenge to progress made in leprosy control with MDT.
5 I feel that not enough attention has been paid to this issue and I would like to suggest the following:

Data be collected urgently to assess the magnitude of this problem.

Wherever possible all MB cases previously treated with dapsone monotherapy should be put on MDT in a phased manner.

In all new programmes, all MB cases should receive the benefit of MB MDT.

In countries where this may be difficult a strict surveillance of all MB cases previously treated with monotherapy should be undertaken.

In the long run it would probably be cheaper, more cost effective and scientifically sound to treat all MB cases (who had previously been treated with monotherapy) with MDT.

Provision must be made in budgets of National Leprosy Programmes to address this issue.

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K JESUDASAN

'3 PS' IN SCHOOL SURVEYS—'PRIMING', PRIVACY AND A PERSONALIZED APPROACH

Sir,

The degree of exposure of the body in most school medical surveys in India depends on the age, sex and the community of the children being examined. In our field area, which is endemic for leprosy, we have attempted to compare surveys conducted at school with a near-total examination of the same children in the privacy of their homes.

The initial examination was conducted, as per usual practice, at school. The whole body except the upper thigh, groin and buttocks (about 80% of body surface) was examined in the case of all boys and primary school girls (6–9 years old). A female paramedical worker trained in leprosy examined the face, neck, upper limbs, abdomen, lower back and lower extremities below the knee (about two-thirds of body surface) in older girls (10–15 years old). In all, 24 out of 3,129 children examined (7·6/1000) were found to be suffering from leprosy. All had single lesions.

A week later, health education sessions were organized and community leaders, parents/

Table 1. Distribution of single lesions

Site	Males		Females		Total	
	N	%	N	%	N	%
Face and neck	2	11·11	2	15·38	4	12·90
Upper extremities	5	27·78	3	23·78	8	25·80
Chest and abdomen	1	5·56	1	7·69	2	6·45
Back	2	11·11	1	7·69	3	9·67
Thighs and buttocks*	4	22·22	3	23·08	7*	22·59
Legs and feet	4	22·22	3	23·08	7	22·59
Total	18	100	13	100	31	100

* Lesions on thighs and buttocks were detected only during near-total body examination.

guardians and school children were told facts about leprosy using audio-visual aids. The importance of early detection was emphasized.

Subsequently, the same children were re-examined thoroughly in the privacy of their homes, by the same personnel. The degree of exposure of the body varied for sociocultural reasons, but on average, a near-total examination of the body (except genitalia) was carried out on all boys and primary school girls while approximately 80% of body surface was examined in older girls. All the children were highly cooperative, possibly because of the team's personal approach and the reassuring presence of their family. In all, 31 cases (all with single lesions) were detected, as against 24 cases detected by the routine method of the school survey. The prevalence rose from 7·6/1000 to 9·8/1000.

The site where the lesion appears first is significant and can be easily ascertained in patients with single lesions. The commonest sites in this study were the upper limbs (25·80%), thighs and buttocks (22·59%), and legs and feet (22·59%) (Table 1). We had reported a similar distribution of single lesions in an earlier study conducted in an urban slum.[1] The thighs and buttocks are among the regions that receive maximum trauma and friction and are common sites for leprosy lesions,[2] which may escape detection in the absence of maximum exposure of the body. In this study, all the additional 4 boys and 3 girls detected during near-total body examination had lesions on these regions.

School children are a 'captive' and easily accessible subset of the population wherein surveys can be carried out with maximum exposure of the body provided parents and children are 'primed' with health education and the survey team uses a personal approach in which their privacy is ensured.

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Lepr Rev (1992) **63,** 187–189

Teaching Materials and Services

30 techniques for the care of leprosy patients; TLMI, London

Dr John Harris (formerly of Zaire, Africa) of the Leprosy Mission International, 80 Windmill Road, Brentford, Middlesex, London TW8 0QH, U.K., has produced a 30-page booklet describing 30 techniques for the care of leprosy patients. These range from history taking and skin examination through to reports and case-finding, covering virtually all the most important tasks relating to the care of leprosy patients. The format is based on a checklist of activities or tasks, against which the reader can put a tick when each one has been understood. Another column can be marked when the activity has been carried out and there is provision for checking by a supervisor. The book is very well printed and the format is easy to follow; it should be of great value and deserves wide circulation.

The Heiser Program now includes tuberculosis

The Heiser Program for Research in Leprosy, initiated at The New York Community Trust in 1974, has awarded over 125 postdoctoral fellowships and research grants over the past 17 years. The Program's scope has now been extended to include research in tuberculosis. A number of factors influenced this decision.

Tuberculosis, for long a major infectious disease in the developing world, causing three million deaths each year, is now sharply on the rise in the industrial nations. Furthermore, much of this disease is being caused by bacteria that are resistant to the commonly used antibiotics. It is now clear that the bacterial agents, *Mycobacterium leprae* and *Mycobacterium tuberculosis*, are closely related and have similar antigenic components. Thus, the search for effective means of immunization may well follow a common path for the two diseases. In the light of these developments, a number of laboratories concerned with leprosy research are concurrently engaged in work on tuberculosis, and it seems logical to foster this combined attack.

The Heiser Program will thus continue its support of leprosy research, and at the same time will accept applications for the support of research on tuberculosis.

The Awards

In accordance with Dr Heiser's stipulation at the time that he set up his fund in The New York Community Trust, the income is used not for treatment of patients but for basic laboratory research directed at a better understanding of the diseases and their bacterial agents. The ultimate aim is to find measures for the prevention and cure of these diseases that will serve to bring them under control. Two types of awards have been established to foster these objectives: (1) postdoctoral fellowships, designed to attract qualified and highly motivated young biomedical scientists to train in the relevant fields of research; and (2) small research grants that will support the training efforts of laboratories involved in research on leprosy and/or tuberculosis, or that will provide funds for the initiation of new research projects in the field.

Enquiries to Mrs Barbara M. Hugonnet, Director, Heiser Program for Research in Leprosy and Tuberculosis, 450 East 63 Street, New York, New York 10021, USA.

Bitter facts about drugs: PACE, Pakistan

This book takes a critical look at the range of drugs available in Pakistan. The author concludes that about 800 of the brand drugs (in an estimated 2000 dosage forms) widely sold in Pakistan are of questionable value or unsafe. Yet they account for 50% of the total drug sales in the country. The book includes a review of a large number of these drugs, classified in pharmacological groups with introductory pharmacological information on each group.

To promote its products, the pharmaceutical industry spends an estimated US$455 annually per physician in Pakistan. The author draws attention to this fact and appeals to all parties involved to accept their responsibility for developing a national drug policy and ensuring the rational use of drugs.

The book is available at US$25, including postage, from the distributor: PACE Distribution Company, 5th Floor, Press Trust House, I.I. Chundrigar Road, Karachi 74200, Pakistan.

Eye-care programmes in developing countries

Published by the Norwegian Association of the Blind and Partially-Sighted (NABP), this comprehensive resource manual deals with the principles, planning, implementation, and evaluation of eye-care programmes in developing countries. Based on the NAPB's field experience worldwide, the book stresses the community-based, participatory approach.

Available in English at US$30 to individuals in developed countries and NGOs and free of charge to individuals in developing countries at the following address: Director, Norwegian Church Aid, P.O. Box 52802, Nairobi, Kenya.

International Agency for the Prevention of Blindness, *Newsletter*

The *IAPB News* is produced from the Secretariat, P.O.B. 191, Haywards Heath, West Sussex RH16 4YF, UK, and distributed free of charge. The December 1991 issue, No. 15, covers cataract operations; strategies for Ivermectin distribution through primary health care systems; eye care in the Cameroon; the prevention of blindness in Latin America; and the setting up of an international agency of opportunities and services by the American Academy of Ophthalmology to, '. . . link organisations and educational institutions which need professional personnel with health care professionals interested in providing education and clinical eye-care services to the international community'.

American Association for the Advancement of Science

The AAAS Sub-Saharan Africa Journal Distribution Programme provides subscriptions to more than 200 scientific, engineering, and other scholarly journals to some 175 university and research institute libraries in 35 countries. As a result of the AAAS effort, over 3500 subscriptions reach African institutions that do not have easy access to current literature.

The programme is funded by the Carnegie Corporation of New York, the Ford Foundation, and the US Agency for International Development (USAID). Recipient institutions are identified through in-country needs inventories, supplemented by advice from donor societies and from experts on research conditions in Africa.

Journal titles in the biomedical field included in the distribution programme are *JAMA*, *Annals of Internal Medicine*, *Pediatrics*, the journals of the American Society of Microbiology, American Physiological Society, etc.

The focus of the AAAS Journal Distribution Programme is beginning to expand. Because an important factor in the high price of overseas subscriptions is postage, new technologies are being explored, such as CD-ROM (Compact Disc Read-Only-Memory), that can supplement hard copy.

The *New England Journal of Medicine* may be made available on CD-ROM to a number of African libraries.

For further details on AAAS programmes, please contact Ms L. Levey, AAAS, 1333 H Street NW, Washington, DC 20005, USA.

Voluntary Health Association of India (VHAI)

The need for a national apex organization in the voluntary health sector based on secular principles was strongly expressed in a meeting of leaders of voluntary hospitals and health care institutions of India in a meeting held in Bangalore in 1969. This started a process which culminated in the formation of Voluntary Health Association of India in 1974 based in Delhi with a clear mandate to promote the concept of community health in the country in order to correct the prevailing imbalances in the health care delivery system due to overemphasis on expensive hospital oriented curative health services. In its 15 years of existence VHAI has established links with more than 3000 health and development organizations spread all over the country.

VHAI works to promote social justice in the provision and distribution of health. Its major activities are aimed at achieving the following objectives:

helping to create the atmosphere for building up a people's health movement through effective networking, lobbying, campaigning and public affairs related activities;

helping in the evolution of low-cost, appropriate and people oriented health programme in harmony with the traditional knowledge and skills of the community;

providing support services to community health programmes taken up by members and associates; and

researching, training and educating on various aspects of (primary) health care.

For further details contact: Voluntary Health Association of India, 40, Institutional Area (Near Qutub Hotel), New Delhi 110 016. Ph.: 668071, 668072, 665018, 655871, 652953. Grams: 'VOLHEALTH'. Fax: 011-676377.

Intermediate Technology, UK, *Newsletter*

When Intermediate Technology (IT) was first registered in 1966 with a grant of £100, it was tiny: a band of 6 highly committed people with a network of supporters and contacts working out of very cramped offices in London. Fritz Schumacher, who by then was an internationally-renowned economist, advisor to governments, and economic advisor to the British coal industry, stuffed envelopes and licked stamps along with the rest of the IT staff in the early days.

After 25 years, the offices in Rugby, London, Peru, Sri Lanka, Zimbabwe and Bangladesh are still cramped, but now IT has nearly 200 people working for it world-wide, a budget of more than £6m each year, and more than 38,000 supporters in Britain alone.

The organization has worked in more than 60 countries in its first 25 years, and has learnt much about appropriate technologies and techniques from those communities.

Throughout its life, Intermediate Technology has initiated many new ideas, both in Britain and overseas. In Britain, Intermediate Technology helped initiate Local Enterprise Trusts—now called Local Enterprise Agencies—providing skills and knowledge to would-be small business people. In addition, the group has spawned a number of 'breakaway' groups specializing in specific fields of appropriate technology; for example IT Power, IT Transport and AHRTAG (Appropriate Health Resources and Technology Action Group).

After 25 years, the group has a number of wholly-owned subsidiaries which help with information and influencing work. IT Consultants markets the group's expertise and experience world-wide and IT Publications publishes a wide range of practical books on appropriate technology and development issues.

For further details write to: Intermediate Technology, Myson House, Railway Terrace, Rugby CV21 3HT, U.K.

Lepr Rev (1992) **63,** 190–191

News and Notes

'Can leprosy be eradicated from India?'

This is the title of an interesting and provocative publication by Prakash Kotecha and Trudy Harpham, respectively from the Medical College, Baroda, Gujarat, India and the Health Policy Unit, the London School of Hygiene and Tropical Medicine, London. It appears in *Health Policy and Planning* **6** (1), 82–5 (1991) and draws attention to an 'overzealous political commitment' to the eradication of leprosy in India, in the face of numerous medical, technical and operational constraints. Recommendations are made for a more realistic concept of controlling rather than eradicating leprosy from India.

TDR and IDRC prize for a paper on 'Women and tropical diseases'

'Leprosy in women: characteristics and repercussions' was the title of the paper that won for its team the first US$5000 prize offered by TDR and Canada's International Development Research Centre (IDRC) for the best paper on women and tropical diseases.

The members of the winning team, all women and all from the Instituto de Biomedicina in Caracas, were Marian Ulrich, Ana Maria Zulueta, Gisela Caceres-Dittmar, Celsa Sampson, Maria Eugenia Pinardi, Elsa M. Rada and Nacarid Aranzazu. A total of 35 papers were submitted from 20 countries; over half of the first authors were female and over two-thirds were from developing countries.

The selection committee chose the Venezuelan team's paper because it covered several aspects—physiological, social and biomedical. It outlined risk factors not only in pregnancy but at all stages of a woman's life; described the impact of the disease on the overall quality of her life; and was extremely well written.

The Centre also highly commended 4 other papers: 'Adam's rib awry: women and schistosomiasis' by Edward H Michelson of Bethesda (MD), USA; 'Women and malaria by R Reubin of Madurai, India; 'Women, tropical diseases: leprosy' by Elizabeth Duncan of Edinburgh, Scotland, U.K.; and 'A synoptic inventory of needs for research on women and tropical parasitic diseases with an application to schistosomiasis' by Hermann Feldmeier and Ingela Krantz of Göteborg, Sweden. Of the 'TDR diseases' the most popular were malaria, leprosy and schistosomiasis. Only 1 paper stressed the social and economic factors that oppress women and contribute to their poor health.

Medical students survey eye damage in Calcutta

Leprosy sufferers, totalling 750,000, are blinded by the disease through paralysis of the muscles controlling the eyelids. This is a dreadful complication as sightless people usually compensate by relying on other senses, but leprosy patients who have lost their sensation in hands and feet find themselves doubly disadvantaged.

Since 1983 a World Health Organization survey on eye damage in leprosy patients has been carried out in many countries with the aim of detecting problems and preventing blindness. This has been co-ordinated by Timothy ffytche, Consultant Ophthalmic Surgeon at St Thomas's Hospital, London. Until now this survey work has not been conducted in Calcutta—but in November 1992 two students from St Thomas's Hospital Medical School will be carrying out initial research there.

Mohua Jain and Aparna Prinja have been sponsored by LEPRA's Elective Student Programme (where grants are made, generally to cover air fare, to about 30 students per year engaged in leprosy work). They will be based at the Greater Calcutta Leprosy Treatment and Health Education Scheme Centre. Difficulties in communicating with patients should be largely overcome as both women have a good knowledge of Bengali/Hindi languages. This may also mean that they will be able to discover more detailed information about patients than might otherwise be possible.

It is hoped that follow-up surveys may be arranged for Calcutta in future, but in the meantime Aparna and Mohua's findings are awaited with great interest.

Second Conference on AIDS in Asia and the Pacific

The Second International Congress on AIDS in Asia and the Pacific will take place in New Delhi, India, 8–12 November 1992.

The theme of the conference is 'The Reality, the Challenge and the Opportunity'.

The conference will emphasize that the reality is that there are a number of countries, such as Thailand and India, that are already experiencing major epidemics and that many other countries have rapidly increasing numbers of HIV infected individuals. It will also emphasize the obvious challenge, not only to learn from what has happened in the rest of the world but to implement strategies to minimize the spread of HIV. Finally the conference will highlight the unique opportunities many countries in the region have that may enable them to avoid being embroiled in this tragic epidemic. It is sponsored by The Government of India, and The All India Institute of Medical Sciences, together with The World Health Organization and The AIDS Society for Asia and the Pacific (ASAP). Further information can be obtained from: Professor John M Dwyer, Chairman, AIDS Society for Asia and the Pacific, Prince of Wales Hospital, Randwick, NSW 2031, Australia (FAX-612 398 9887).

International Colloquium on Integration of traditional and modern methods in the control of leprosy and in the study of mycobacterial taxonomy, Antwerp, Belgium, 16–19 December 1992

The above International Colloquium will be held at the Institute of Tropical Medicine Prince Leopold in Antwerp, 16–19 December 1992. It is organized in conjunction with the 13th conference of the IWGMT (International Working Group on Mycobacterial Taxonomy) and has 2 parts:

(1) 16 December: Integration of traditional and modern methods in the Control of Leprosy;
(2) 17–19 December: IWGMT Conference on Integration of traditional and modern methods in the study of Mycobacterial Taxonomy.

The official language of the Colloquium will be English.

Persons who wish to attend the Colloquium and authors who wish to present a paper on Wednesday 16 December, or a poster on Friday afternoon, 18 December, are invited to register their name and address, and to submit a title as soon as possible. A very limited number of short presentations may also be accepted for the plenary sessions of the IWGMT on 17 and 18 December. These will be restricted to papers relating to the following themes in mycobacterial systematics: 1 Phylogenetic relationships, 2 Identification methods and strategies, and 3 Ecology and epidemiology. More details will be sent to those who have indicated their intention to participate.

The organizing committee is composed of Professor L Eyckmans, Professor F Portaels (Antwerp, Belgium) and Dr L G Wayne (Long Beach, USA).

Secretariat of the Colloquium: Miss A F Smeets, Institute of Tropical Medicine, Nationalestraat 155, B-2000 Antwerp, Belgium. Tel: 32 3 247 62 06; Fax: 32 3 216 14 31.

The All-Africa Leprosy and Rehabilitation Training Centre (ALERT)

seeks a

DIRECTOR OF TRAINING

and a

DEPUTY DIRECTOR OF TRAINING

to plan, organize and manage our programme of leprosy and related courses at the Centre in Addis Ababa and elsewhere across Africa

ALERT is an international training centre, recognized by the WHO as a Collaborating Centre for leprosy training, which operates a national referral hospital and a large field control programme in the Shoa Province for the purposes of training, demonstration and research in optimal levels and strategies of patient care and treatment.

We are looking for two experienced professionals with complementary skills to work together to help achieve ALERT's international training goals. One of the positions should be filled by a well-qualified medical specialist who has a comprehensive experience not only in clinical leprosy but also preferably dermatology as well. The other position would be filled by an educational specialist, with qualifications and experience of such educational specializations as curriculum development, distance learning and educational management.

Considerable travel is involved in the job, and fluency in French and/or other languages relevant to Africa an advantage.

Detailed CVs and the names and contact details of three referees should be sent, within 2 months of the appearance of this advertisement, to:

The Executive Director, ALERT, P.O. Box 165, Addis Ababa, Ethiopia. Telephone: +251 1 71 11 10. Telex: 21821 ALERT ET. Fax: +251 1 71 11 99.

Internationally competitive salaries and benefits are available for the right candidates for these challenging and demanding positions. Free furnished accommodation is available on ALERT's own attractive campus, within easy reach of Addis Ababa's many international amenities.

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. Once manuscripts have been accepted a copy on disk that matches the hard copies exactly would be very much appreciated.

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.

Proofs are submitted to authors for immediate return by air.

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