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Leprosy Review

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LEPRA

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

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

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Editorial

LEPROSY CONTROL AND THE IMPLEMENTATION OF MULTIPLE DRUG THERAPY: TO WHAT EXTENT CAN THE OPERATIONAL STRATEGY BE SIMPLIFIED FOR PRIMARY HEALTH CARE?

Since the publication of the recommendations of the World Health Organisation (WHO) on the use of regimens of multiple drug therapy (MDT) of relatively short duration for all cases of leprosy,[1] remarkable progress has been made, not only in the implementation of such regimens, but also in the development of leprosy control programmes in many parts of the world. In the first few years, the implementation of MDT was slow, reaching a coverage of only 8·8% in 1986, but thereafter increasing rapidly to 55·7% in 1990. From a total of 5·4 million registered cases in 1985, the figure dropped to 3·7 in 1990 (a reduction of about 31%), attributable mainly to the implementation of MDT and the release from treatment (and eventually from surveillance) of very large numbers of patients. Disability and child rates have come down, relapse rates are remarkably low, and the incidence of toxic (drug) reactions or immunological reactions based on either cell-mediated or humoral mechanisms, has been no greater (and possibly less) than with dapsone monotherapy. Given time, it is expected that some early reports of reduction in incidence rates following MDT will be confirmed. By 1987, speaking at a meeting in New Delhi on the evaluation of MDT through Primary Health Care (PHC), Dr SK Noordeen, Chief, Leprosy, Division of Control of Tropical Diseases, WHO, drew attention to the major changes in technology brought about by MDT, the improved outlook, virtually worldwide, towards the disease, and the immense opportunities to reduce leprosy in the next decade.[2] In 1988, a widely circulated WHO publication bore the title *Multidrug therapy for leprosy: an end in sight*,[3] and this was followed by a second in 1991, entitled *Towards elimination of leprosy*,[4] drawing attention to the progress being made in many endemic countries and to the possibility of reducing prevalence to an elimination level of less than 1 case per 10,000 of the population by the year 2000. New estimates by WHO for the number of cases worldwide have recently been published, revising the previously quoted figure of 10–12 million cases to 5·5 million.[5]

The overall pace and extent of MDT implementation worldwide

Despite these encouraging results, concern has been expressed in recent years about the

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overall pace and extent of MDT coverage worldwide. A recent WHO report[6] draws attention to considerable regional variations with regard to prevalence and MDT implementation between 1986 and 1990; the South-East Asia Region (SEARO) and the Western Pacific Region (WPRO) have achieved satisfactory levels, but elsewhere this is not the case. Progress in the development of control programmes and the implementation of MDT has been distinctly weak in Brasil, Nigeria, Myanmar and Indonesia. In Africa (AFRO Region), the overall rate at the end of 1990 was only 18·4% (compared, for example, with 66·2% for South-East Asia), with some notably low figures in Burkina Faso, Cape Verde, Chad, Congo, Côte d'Ivoire, Guinea, Madagascar, Mali, Mozambique, Niger, Reunion, Rwanda, São Tomé, Senegal, Swaziland, Togo and Uganda. Figures for the Americas are also unsatisfactory. The reasons which lie behind this situation vary greatly from one country to another, or even in different regions of the same country, but they include—(1) lack of political commitment and motivation, (2) constant, even increasing pressure to allocate time, money and personnel to health problems other than leprosy (for example, AIDS/HIV infection, tuberculosis, malaria, immunization, population control), (3) poorly developed infrastructure and lack of trained personnel, (4) absence of a proper plan of action, (5) shortage of money, (6) lack of laboratory facilities, notably for slit-skin smears, (7) poor referral facilities for complications and (8) inadequate resources, including regular supplies of dapsone, clofazimine and rifampicin for MDT.

We are now well into 1992 and the goal, whether in terms of 'control', 'elimination', 'eradication' or 'MDT for all' is almost universally directed at the year 2000. Despite the progress described above, it is clearly disconcerting that many leprosy endemic countries, especially in Africa, have barely started to implement MDT, or have achieved only single figure percentage results in their cases on treatment.

Integration with primary health care and the district health programme

Various proposals have been made through the years[7,8,9] to overcome these problems, for the most part based on the wider use of PHC, including the District Health Programme (DHP), the latter being defined as '. . . a geographical area that is small enough for its health and related social and economic problems to be properly understood and for appropriate action to be taken in response, but large enough to permit the deployment of essential technical and managerial skills for planning and management of the health programme.' Writing in 1978, before the development of MDT as we now know it, Buchmann reviewed the entire subject of PHC in relation to leprosy control in great detail,[10] concluding that it was not only advisable, but clearly the most obvious strategy for the full development of leprosy control programmes, including treatment delivery. Since the publication of the Declaration of Alma Ata on PHC in 1978,[11] all Who documents and publications on leprosy (and tuberculosis[12]) have accepted the principle of integrating leprosy control into the general health services wherever possible, whilst at the same time underlining the importance of maintaining a vertical, specialized element at various levels of the programme, for supervision, referral facilities, drug supply and financing. *The International Federation of Anti-Leprosy Associations* (ILEP), representing over 20 independent, voluntary organizations working in the field of leprosy, has also strongly affirmed its commitment to the use of the general health services based on PHC,

whilst at the same time describing the basic, rather than optimal, requirements for implementation[13]—a most valuable step in the direction of simplification. The principle of using PHC/DHP in leprosy control seems to have been accepted by most agencies working in leprosy as the only operational technology likely to have a progressive epidemiological impact, but in practice, its application continues to present problems. These are basically similar to those which have been described for tuberculosis[12]—planning, training, provision of supplies and supervision.

The possibility that the pace and extent of MDT implementation are unsatisfactory and unlikely to improve in the foreseeable future, unless new strategies are introduced, has recently been reviewed in depth by Yuasa in the *International Journal of Leprosy*.[14] He outlines the main problems which have so far been encountered and makes a plea for the involvement of *all* members of the health services, in *all* leprosy-endemic countries, to bring the benefits of MDT to *all* patients in need, without delay. He emphasizes that '. . . the MDT program must be simple, so that any leprosy-endemic country, with whatever the current state of health services, can adopt it'. His approach gives great emphasis to the use of PHC and DHP personnel in detecting, diagnosing and treating leprosy cases (but without any expectation that they will routinely participate in the prevention and management of disability or deformity—a somewhat unconventional view, which is discussed in more detail below). The strategy described seems to have worked well in the Philippines, where it has to a large extent been carried out by 'barangay' midwives, with facilities for supervision and the referral of problem cases, and including the provision of MDT for both pauci- and multi-bacillary cases in blister calendar packs. This account of a successful programme is by no means unique. In 1982 an entire number of this *Journal* was devoted to the subject of leprosy and PHC,[15] with accounts of experiences from Tanzania, the Sudan, Kenya, Indonesia, Sri Lanka and India. Some reservations were expressed, particularly about the timing of integration in relation to the treatment of all known cases, but in general the views recorded were positive and encouraging. In 1986, an important report from WHO[16] described a consultation on leprosy control and PHC, with contributions from the Gambia, Malawi, Vietnam, Malaysia, Ethiopia, Brasil and Thailand. Some failures and a number of problems were reported, but in general it was agreed by participants that the approach had great advantages over the continued use of vertical, specialized systems.

PHC and leprosy control in India

Despite encouraging progress in the implementation of MDT in the National Leprosy Eradication Programme in India, the Leprosy Division recently identified an area of difficulty in extending MDT services to 66 of their endemic districts. The problem had been accentuated by the large numbers of patients in need and the lack of trained personnel, coupled with the impossibility of training them in the foreseeable future. A decision of potentially great interest and importance, not only for India, but for control programmes elsewhere, was therefore taken by the Leprosy Division late in 1990, when *Guidelines for Modified MDT Scheme in Selected Districts* were drawn up and circulated to appropriate regions, accompanied by training manuals for various grades of health staff. This 66-page document is reviewed in greater detail elsewhere in this *Journal*;[17] it describes the administrative and technical steps which must be taken in order to

implement MDT through the general health services, using PHC and DHP (as opposed to using the specialized staff of the NLEP). The 14-day period of intensive therapy at the outset, used hitherto by the NLEP, will be discontinued; the WHO regimen will be used instead. Health education activities are to be intensified and the bacteriological examination of skin smears will be limited to multi-bacillary cases, or suspected multi-bacillary cases. This initiative should clearly be monitored with great care; it represents, at least in concept, a significant simplification of the existing operational strategy in India (estimated to have 3 million cases), thus affording an opportunity for the collection of date and an assessment of feasibility, presumably within a relatively short period of time. Inherent in the modified approach is the continued use of NLEP staff wherever possible and it bears repetition that this is in keeping with the advice which has been given by WHO and other agencies advocating this approach, to the effect that integration with PHC does *not* imply that all specialized elements should disappear from the scene; on the contrary, a specialized element, wherever it is available, should be retained at various levels.

Further simplification

In recent years, either from WHO or ILEP, several modifications which undoubtedly simplify the approach needed at PHC level, have been made. They include the following—(1) for the treatment of multi-bacillary patients, 24 months' treatment (rather than extending, wherever possible, until skin smears are negative, as in the original recommendations of 1982) is acceptable, particularly if there are resource constraints, (2) the supervision of monthly doses of rifampicin (pauci-bacillary cases) or rifampicin and clofazimine (multi-bacillary cases) should ideally be carried out by a health worker, but if this is difficult or impossible, responsibility may be delegated to other members of the community (teacher, village leader, family member, etc.), (3) provided they are reliable, skin smears are valuable and should be made available, but they are no longer regarded as an absolute prerequisite for initiating MDT, since in most cases it is possible to diagnose leprosy and distinguish between multi- and pauci-bacillary cases on clinical grounds. Two further aspects of the subject call for more serious investigation in the context of simplifying MDT at PHC level. The *first* concerns the use of systems which take note of the number of skin, or skin and nerve lesions, or of the number of 'body areas' affected, in order to allocate patients to either pauci- or multi-bacillary groups for treatment. A number of publications recording experience from different parts of the world[18,19,20,21] suggest that this approach may be preferable in certain circumstances to reliance on skin-smear results. The *second* relates to the use of blister-calendar packs for MDT drugs[22] and to the need for an objective assessment of their value, particularly in programmes using the PHC/DHP approach. If found useful and potentially cost-effective, efforts should be made to set up local production thus avoiding the main impediment to their wider use at the present time, which centres on the additional cost of packs manfactured by drug companies. Finally, the proposal by Yuasa, in the editorial referred to above,[14] that disability management should realistically be separated from the public health activities of staff who are engaged in case detection and chemotherapy, giving responsibility to a separate agency, or to non-government organizations, calls for serious consideration. This is partly because current (and past) efforts to combine case detection and

chemotherapy with disability prevention and management have been, in general, unsuccessful and partly because the proposed separation could, if properly planned and executed, very considerably simplify the work of PHC/DHP personnel.

Conclusion

The principle of using PHC/DHP in leprosy control appears to have been widely accepted by WHO and other agencies. Some progress has been made in its application, but in many countries where control programmes and MDT are particularly weak no systematic attempt has so far been made to develop its potential. The success of MDT under a wide range of circumstances, including some which, at least at the outset, had sub-optimal personnel and other resources, suggests that PHC/DHP should be considered more widely. Some important simplifications for this purpose have already been made; others could be developed quite quickly. Particularly for those who have identified the year 2000 for elimination, time may be short, unless new strategies are used. Is this perhaps the moment to look more closely at what is needed and what is possible, and to use PHC/DHP to close the gap, thus bringing the benefits of MDT to a much wider segment of patients?

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Evaluation of four semi-synthetic *Mycobacterium leprae* antigens with sera from healthy populations in endemic and non-endemic areas

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Summary In order to determine the frequency of occurrence of antibodies to semisynthetic antigens of *Mycobacterium leprae* in clinically healthy nonpatient populations and to establish a 'baseline' for comparison with antibody frequencies in both patients with a history of leprosy and their contacts, ELISAs were conducted using representative sera from two areas: a leprosy endemic area, Cebu City, Philippines and a nonendemic area for leprosy Chicago, Illinois, USA. These sera were tested, by an indirect IgM ELISA, for the presence of antibodies reacting with four semisynthetic antigens based on the phenolic glycolipid I antigen of *M. leprae*: ND-O-BSA (natural disaccharide with octyl linkage to bovine serum albumin), NT-O-BSA (natural trisaccharide with octyl linkage to BSA), ND-P-BSA (natural disaccharide with phenolic ring linkage to BSA) and NT-P-BSA (natural trisaccharide with phenolic ring linkage to BSA). Using an OD reading $\geqslant 0{\cdot}16$ as positive, the antigen with the lowest background seroreactivity was ND-O-BSA, which reacted with 5/398 (1·3%) sera from Cebu, and 3/426 (0·7%) sera from Chicago. A total of 10 (2·5%) of 398 sera from the endemic area reacted with at least one antigen and 5 (1·3%) sera reacted with all four semisynthetic antigens. Of the 426 sera from Chicago, 12 (2·8%) were reactive with at least one antigen and 3 (0·7%) were reactive with all four semisynthetic antigens. Mean ELISA values for the 22 positive sera for each antigen ranged from 0·17 to 0·3 OD units, while the mean values for all sera in

[1]Deceased 30 January 1990
[2]Deceased 8 January 1988

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each area ranged from 0·01 to 0·04 OD units for all four antigens. Reactivity of 14 of the positive sera to some antigens, but not all four semisynthetic antigens, indicated that the carrier and linker arms might be associated with this background reactivity. Investigation of alternative linker arms and carriers is warranted. We conclude that nonspecific background reactivity to the semisynthetic antigens representing the PG-I molecule of *M. leprae* is 0·7–1·3%, based on a $\geqslant$0·16 OD cutoff value. From these data it was concluded that reactivity in individuals free of leprosy was low enough to warrant use of these antigens in a diagnostic setting, such as screening household contacts and highly endemic populations. When incidence and prevalence of leprosy are low, testing with these antigens would not be cost effective, unless applied to high risk individuals. Serological screening with these antigens might be useful in detecting and differentiating bacteriological relapse, type 1 or 2 reactions, early detection of leprosy, and monitoring treatment in endemic areas.

Introduction

The incubation period for leprosy has been estimated to vary between 2·9 and 5·3 years for tuberculoid leprosy and 9·3 and 11·6 years for lepromatous leprosy.[1] The disease may be transmitted to others during this long incubation period. Therefore, serological assays, which would indicate infection by detecting *Mycobacterium leprae* antibodies in asymptomatic individuals could facilitate the initiation of appropriate chemotherapy and assist control programmes by identifying potentially infectious individuals. Knowledge of background levels of antibody in the healthy endemic populations can also provide a baseline of reactivity to evaluate the prevalence of subclinical infection. Serological assays may be useful in patients with a history of leprosy, in evaluating the success of therapy, and in evaluating bacteriological relapse. Candidate antigens for such an assay include the semisynthetic neoglycoproteins, which mimic the sugar determinants of the phenolic glycolipid (PGL-I) of *M. leprae*.[2–7]

While these semisynthetic glycoprotein antigens have been studied in paients with disease, comparative survey results of reactivity among large numbers of healthy individuals in endemic and nonendemic areas have not been reported.[8–15] Information on the specificity and background levels of antibody in ELISA (enzyme-linked immunosorbent assay) with these antigens is needed to evaluate the serological prevalence of response to the PG-I synthetic analogues. This information must be derived from healthy populations in endemic areas. As suggested by Harboe, the controls used in antibody studies should be individuals with the same ethnic and socioeconomic background as the leprosy patients but who lack epidemiologic exposure to infectious cases.[16] However, establishing the specificity of a serological assay for a disease with such a long incubation period becomes problematic. It requires being able to follow a cohort of healthy individuals for many years after obtaining their sera to verify who does and who does not develop the disease. While the probability of becoming infected is negligible in a nonendemic area, there is a risk in an endemic area. Furthermore, healthy individuals in an endemic area without an epidemiological history of exposure may remain asymptomatic. Even if members of a cohort later developed disease, it would be unclear if they were infected at the time of the serum collection or if they became infected sometime after the sample was collected. Not being able to establish accurately when someone actually becomes infected and correlate this with the serological results complicates calculations of

test specificity. To adjust for this difficulty a nonendemic population with a near zero risk of developing disease was included in this study to assure a disease-free background level of antibody reactivity to these semisynthetic antigens.

The frequencies of antibody reactivity to 4 semisynthetic antigens of *M. leprae* in the endemic and the nonendemic populations are presented in this paper from data generated by an IgM specific indirect ELISA. The 4 semisynthetic antigens are compared for degree of reactivity in the study populations. The nonendemic population sera were obtained from health care personnel and obstetric patients from Chicago, Illinois, USA. The seroreactivity rate in this group could then be compared to the seroreactivity rate among healthy individuals in an endemic population. The endemic population was selected from healthy individuals residing in Cebu City, Philippines, who attended the Cebu Skin Clinic for conditions other than leprosy and who did not have a leprosy case in their household.

Materials and methods

STUDY POPULATIONS

The Chicago population sample consisted of 426 healthy young adults (predominantly nursing students, medical students and obstetrical patients). None of these subjects had a history of residence in a leprosy endemic area or contact with a patients with active leprosy. In the Chicago population, 82% of the subjects were females and 18% were males. The Chicago females ($n = 351$) were between 11 and 81 years old, with a median age of 23 years. The Chicago males ($n = 75$) were between 17 and 58 years old, with a median age of 28 years (Table 1).

In the Cebu population of 398 persons, the sex distribution was even, with 199 males and 199 females. These individuals were selected from those people who came into the Cebu Skin Clinic for diseases other than leprosy, mostly for ordinary skin diseases such as eczema, fungal infections, bacterial and viral infections, acne vulgaris, and numerous other skin diseases. Those who were selected for the study did not have a leprosy case in their household and had no clinical evidence of leprosy at the time the blood was

Table 1. Age and sex distribution of the 2 study populations

Age category (Years)	Leprosy endemic (Cebu)		Leprosy nonendemic (Chicago)	
	Male	Female	Male	Female
11–20	45	35	1	110
21–30	70	66	48	186
31–40	30	44	21	48
41–50	20	22	4	5
51–60	18	19	1	0
61–70	10	11	0	1
71–80	6	2	0	0
81+	0	0	0	1
Total	199	199	75	351

collected. The females were between 13 and 77 years old, with a median age of 30 years. The males were between 13 and 78 years old, with a median age of 28 years (Table 1).

Antigens

Immulon II 'u' bottom plates (Dynatech Laboratories, Alexandria, VA 22314, USA) were coated with antigen in a volatile buffer as previously described.[17] The antigens, based on the phenolic glycolipid-I antigen of *M. leprae*, were: ND-O-BSA [natural disaccharide with ocytl linkage to bovine serum albumin (BSA)], NT-O-BSA (natural trisaccharide with octyl linkage to BSA), ND-P-BSA (natural disaccharide with a phenolic ring linkage to BSA) and NT-P-BSA (natural trisaccharide with phenolic ring linkage to BSA).[5–7] Microtitre plates were coated by applying 50 microlitres of a given antigen at a concentration of 0·2 micrograms/ml (based on the weight of the sugars). Unmodified BSA (Cat. No. A-7030, Sigma Chemical Co., St Louis, MO 63178, USA) was used as a control antigen and coated at a concentration of 0·32 μg/ml. The octyl linked antigens were provided under NIH contract (NO1 AI-52582) by Dr P. Brennan, Colorado State University, USA. The phenol-linked sugars were provided by Dr T. Fujiwara of Nara University with funding provided by the Western Regional Office of the Pacific area of the World Health Organization.

SERA

The sera were separated from blood collected by venipuncture and aliquots stored at $-70°$C until ready for use.

ELISA

The assay was performed as previously described.[18] Plates coated with the specified antigen were first blocked with 75 microlitres of 10% skimmed milk in phosphate-buffered saline with 0·1% Tween-20 (PBS), pH 7·4, and incubated for 1 hour at 37°C. The sera were diluted 1:500 in 10% skimmed milk in PBS, pH 7·4. Control sera (positive: lepromatous sera; negative: normal sera) were diluted similarly. Each plate included the same control sera: a high positive control (OD of $1{\cdot}30 \pm 0{\cdot}08$), a low positive control (OD of $0{\cdot}3 \pm 0{\cdot}04$) and 4 negative sera (1, a pooled sample and 3 from individuals with OD values less than 0·10).

Peroxidase conjugated goat anti-human IgM (μ-chain specific, Cappel Laboratories) was diluted 1:6000 in blocking buffer and incubated in the wells for 45 min at 37°C. Any study serum sample yielding an optical density of 0·10 or higher was retested twice in duplicate and the values of the 4 OD values were averaged. The conjugate background values were subtracted from all sera values prior to recording.

Results

COMPARATIVE ENDEMIC AND NON-ENDEMIC IgM REACTIVITIES BY SEX

The mean OD values ranged from $0{\cdot}02 \pm 0{\cdot}03$ to $0{\cdot}04 \pm 0{\cdot}05$ and the sex of the study subjects made no difference in either the endemic or nonendemic populations. We detected no significant differences in reactivity to the various antigens when the subjects

were stratified by age and sex. The NT-O-BSA antigen had slightly higher background (0·01 to 0·02 OD units greater) than the other antigens in both populations. Also females in the 21–30 and 31–40-year-old age groups were slightly more reactive than males and other age groups with OD values of 0·01–0·02 units higher.

Comparisons by population and sex were also made for those samples which were positive to at least one of the antigens. Positive sera were those with reactivity greater than 0·15 OD units. The means ± SD for the positive tests were: 0·21 ± 0·02 for ND-O-BSA, 0·23 ± 0·03 for NT-O-BSA, 0·17 ± 0·01 for ND-P-BSA, and 0·2 ± 0·01 for NT-P-BSA. For the endemic population (Table 2), 4 males had sera which were reactive to at least 1 of the antigens. For the females, 6 of the sera were reactive to at least 1 of the antigens, and those means ± SD for positive reactions were: 0·24 ± 0·08 for ND-O-BSA, 0·23 ± 0·07 for NT-O-BSA, 0·23 ± 0·09 for ND-P-BSA, and 0·23 ± 0·04 for NT-P-BSA.

For the nonendemic population (Table 3), only 1 male had a serum sample that was reactive. It was reactive to NT-P-BSA at an OD value of 0·16. A total of 6 females were reactive to at least 1 of the antigens. The means ± SD of positive values for these samples were: 0·27 ± 0·13 for ND-O-BSA, 0·3 ± 0·14 for NT-O-BSA, 0·23 ± 0·05 for ND-P-BSA, and 0·25 ± 0·06 for NT-P-BSA. These values are similar to the values of the endemic positive reactive tests. The mean positive OD values for ND-O-BSA (0·27) and NT-O-BSA (0·3) appear to be higher than those to the other antigens. However, this is due to 1 sample which had high OD values of 0·46 and 0·55, respectively.

A total of 22 sera from the endemic and non-endemic populations, which were positive with at least 1 or more antigens, were retested with the unmodified BSA carrier

Table 2. ELISA IgM optical density values* for sera reactive to semisynthetic *M. leprae* antigens from an endemic area (Cebu, Philippines)

Serum No. (Sex/Age)	BSA only	Semisynthetic antigens				Number positive
		ND-O-BSA	NT-O-BSA	ND-P-BSA	NT-P-BSA	
146 (F/22)	0·04	**0·20**	**0·19**	**0·17**	**0·19**	4
190 (F/31)	0·03	**0·19**	**0·20**	**0·21**	**0·21**	4
300 (M/72)	0·00	**0·22**	**0·22**	**0·16**	**0·19**	4
519 (M/21)	0·03	**0·19**	**0·26**	**0·18**	**0·20**	4
815 (F/62)	0·04	**0·34**	**0·35**	**0·35**	**0·27**	4
693 (F/50)	0·04	0·14	**0·18**	**0·17**	0·11	2
105 (F/37)	0·03	0·08	**0·30**	0·08	**0·25**	2
297 (M/61)	0·03	0·13	**0·20**	0·08	0·07	1
341 (F/35)	0·04	0·09	**0·18**	0·04	0·06	1
514 (M/37)	0·04	0·12	**0·22**	0·12	0·10	1
No. positive (%†)		5 (1·3)¶	10 (2·5)	6 (1·5)	6 (1·5)	27
Strong positive‡		1 (0·25)	2 (0·5)	1 (0·25)	0 (0)	
Weak positive§		4 (1·0)	8 (2·0)	5 (1·25)	6 (1·5)	

* Average values resulting from 4 assays; positive values (OD ≥ 0·16) in **bold** type. Control OD values were: high positive control = 1·30 ± 0·08, low positive = 0·3 ± 0·04 and negative sera = 0·04 ± 0·04.

† % = Number positive/398 tested × 100%.

‡ Strong positive = $OD_{492} \geqslant 0{\cdot}30$.

§ Weak positive = $0{\cdot}16 \leqslant OD_{492} \leqslant 0{\cdot}29$.

¶ Numbers in parentheses are percentages.

(Tables 2 and 3). None of the sera was found to be positive to BSA. The mean ± SD of the OD values for these sera was 0·03 ± 0·02.

IgM REACTIVITY IN AN ENDEMIC AREA

Table 2 presents ELISA values for all the Cebu sera that were reactive to at least 1 antigen according to the antigen(s) to which the sera were reactive. While serum no. 815 gave the highest reading, other sera tested did not yield strongly positive results, i.e. OD values ⩾0·30. Overall, 10 of the 398 sera (2·5%) were reactive to at least 1 of the 4 antigens, and all ten were reactive with NT-O-BSA; 5 sera (1·3%) had OD values of at least 0·17 to all 4 antigens and 2 sera (0·5%) were reactive to 2 antigens and 3 sera (0·7%) were reactive to only 1 antigen. In comparing only the samples with positive OD values, the average OD values were not significantly different between the antigens.

Table 2 also summarizes the positive serological reactivity of 398 people from Cebu City to each of the 4 semisynthetic antigens. A sample was considered to be a high positive if it yielded an OD value of ⩾0·30, was low positive if it gave an OD of 0·16–0·29, and was negative if the OD was ⩽0·15. The fewest number of sera (5/398) reacted to ND-O-BSA, the largest number of sera reacted to NT-O-BSA (10/398), and 6/398 sera reacted to both ND-P-BSA and NT-P-BSA.

Table 3. ELISA IgM optical density values* for sera reactive to semisynthetic *M. leprae* antigens from a non-endemic area (Chicago, USA)

Serum No. (Sex/Age)	BSA only	Semisynthetic antigens				Number positive
		ND-O-BSA	NT-O-BSA	ND-P-BSA	NT-P-BSA	
R10109 (F/25)	0·02	**0·21**	**0·22**	**0·23**	**0·20**	4
R10225 (F/18)	0·01	**0·46**	**0·55**	**0·30**	**0·31**	4
R10251 (F/17)	0·02	**0·23**	**0·30**	**0·21**	**0·18**	4
R9923 (F/19)	0·05	0·03	**0·21**	0·02	**0·20**	2
R9916 (F/37	0·01	0·01	0·01	**0·27**	**0·28**	2
R10190 (F/22)	0·02	0·13	0·14	**0·17**	0·09	1
R10121 (F/22)	0·07	**0·16**	0·14	0·15	0·04	1
R9996 (F/21)	0·03	0·00	**0·33**	0·05	0·04	1
R9984 (F/32)	0·03	0·02	0·00	**0·20**	0·06	1
R9800 (F/20)	0·00	0·00	0·01	0·00	**0·32**	1
No. 88 (F/33)	0·01	0·13	**0·16**	0·04	0·01	1
No. 37 (M/39)	0·02	0·02	0·06	0·00	**0·16**	1
No. positive (%†)		4 (0·9)¶	6 (1·4)	6 (1·4)	7 (1·6)	23
Strong positive‡		1 (0·2)	3 (0·7)	1 (0·2)	2 (0·5)	
Weak positive§		3 (0·7)	3 (0·7)	5 (1·2)	5 (1·2)	

* Average values resulting from four assays; positive values (OD ⩾0·16) in **bold** type. Control OD values were: high positive control = 1·30 ± 0·08, low positive = 0·3 ± 0·04 and negative sera = 0·04 ± 0·04.

† % = Number positive/398 tested × 100%.

‡ Strong positive = OD_{492} ⩾0·30.

§ Weak positive = 0·16 ⩽ OD_{492} ⩽0·29

¶ Numbers in parentheses are percentages.

IgM REACTIVITY IN A NON-ENDEMIC AREA

Of the 426 sera tested from Chicago, 12 (2·8%) were reactive to at least 1 antigen (Table 3), 3 of the samples (0·7%) were reactive to all 4 antigens, 2 sera were (0·5%) reactive to 2 antigens, and 7 sera (1·6%) were each reactive to only 1 of the antigens. Only serum R9923 was reactive with the 2 trisaccharide antigens but not with the 2 disaccharide antigens. As with the Cebu sera, if only the positive OD values are compared, the average OD values were not significantly different between the antigens.

The positive serological responses of 426 people from Chicago to the 4 semi-synthetic antigens are also summarized in Table 3. As with the Cebu data, ND-O-BSA produced the lowest frequency of reactive sera (4/426) compared to NT-O-BSA (6/426), ND-P-BSA (6/426), and NT-P-BSA (7/426). The seropositivity rates of the Chicago sera were not significantly different from those from Cebu.

Discussion

We have studied the seroprevalence in IgM ELISAs of 4 semisynthetic *M. leprae* antigens in 2 populations, 1 endemic and 1 nonendemic for leprosy. This study allowed us to evaluate and compare the specificity of these 4 semisynthetic antigens as markers for subclinical infection.

The overall rates of sera reactive to at least 1 of the antigens were comparable between the endemic population (2·5%) and the nonendemic population (2·8%). More than half (7/12) of the nonendemic sera were reactive to only 1 of the antigens. For sera which reacted to all 4 antigens, the positive rate in the endemic area was 1·3% (5/398). Although this was almost double the rate of 0·7% (3/426) in the nonendemic area, these rates are not statistically significant.

The possible reaction of the sera with BSA has been questioned, but we found that when similar assay conditions were employed using BSA as the antigen, all the sera were nonreactive (Tables 2 and 3). The contributions of the 3rd sugar, the phenol linker arms, octyl linker arms and BSA were evaluated. The dominant sugars were the terminal and penultimate sugars and 8 of 832 sera reacted with all 4 antigens; 2 sera out of 836 individuals reacted only to the trisaccharide antigens (NT-O-BSA and NT-P-BSA): these were serum no. 105 from the endemic sera and serum R9923 from the nonendemic population; 1 serum, R9916, from the nonendemic group reacted only with the antigens containing the phenol linker arm. There was no indication that the BSA carrier was recognized by itself; 4 of the endemic sera and 7 of the nonendemic sera reacted with single antigens. Thus, 12 of the 22 reactive sera from 836 tested were responding to structures beyond the sugar epitopes. This may be due to the recognition of unique conformational structures formed between the BSA, linker arm and the sugar determinants. The antigen to which the most sera reacted was NT-O-BSA (16/22) and the least reactive was ND-O-BSA (9/22). From these data we conclude that improvements could be made with this family of antigens. Further development of other linker arms and carriers could reduce the reactivity in healthy individuals to the semisynthetic antigens representing the PG-I antigen.

A limitation of the study was that, since it was designed as a cross-sectional study, we did not follow-up serologically positive healthy individuals. In our previous studies of

leprosy patients we were able to follow up individual cases since the patients were being treated medically and followed in a clinic. It was not possible to follow up individuals in either of the present populations. This was because the participants in the endemic area were not under medical care, while the population from the nonendemic area was transient. These problems limited our ability to follow up and observe the serological conversion and reversion in healthy populations. However, the nonendemic group did provide baseline data in a population which allowed us to estimate the specificity of the various serological assays.

In one of our previous studies, we showed that the correlations between NT-O-BSA and ND-O-BSA ranged from $r = 0{\cdot}963$ to $0{\cdot}998$ ($p < 0{\cdot}001$) for 31 lepromatous patients in an endemic area, Cebu, PI.[14] In another study, we found that the reactivity rates of the patient sera from 35 lepromatous patients in an endemic area (Cebu, PI) to ND-O-BSA, and NT-O-BSA were highly correlated ($r = 0{\cdot}866$, $p < 0{\cdot}001$).[15] However, the seroprevalence to ND-P-BSA with patient sera was found to be lower than the other antigens.[19] Our findings in this and previous work with sera from patients with clinical leprosy have led us to concentrate on the use of ND-O-BSA antigen, since it provides better specificity and sensitivity than the NT-O-BSA and NT-P-BSA antigens. The NT-P-BSA antigen is similar in reactivity to ND-O-BSA. Of the 4 semi-synthetic antigens, ND-O-BSA appears to be the antigen of choice for the detection of subclinical disease or asymptomatic infections in this endemic population because of its lower background reactivity, i.e. greater specificity.

This report did not evaluate the D-BSA antigen described by Gigg *et al.*[3] However, the ND-O-BSA antigen and D-BSA antigens were compared in a report by Engers *et al.*[20] They found that the 2 antigens were similar in reactivity with 20 lepromatous sera and 7 control sera.

No significant differences could be found when the subjects were stratified by age and sex. This finding is not in agreement with those reported by Fine *et al.*[21] We found a slight increase, though not significant, in ELISA values for females compared to males in the 21–30 and 31–40-year-old age groups. The difference in findings with others may be explained by the dilution of sera in our test to 1:500, which could result in lowering of natural levels of IgM in the test sample. This seems reasonable since the dilutions from eluted blood imprenated paper in the report by Fine *et al.* were equivalent to 1:20 dilution of serum.[21] In another report, Izumi *et al.*, describing a particle agglutination test using the NT-P-BSA as antigen, reported a higher than expected rate of reactivity among normal pregnant women.[22] When the sera from the pregnant women was diluted 1:32, 12/120 were found to be positive. This reactivity could be eliminated by continuing the dilution of sera to 1:64.

In summary, this study has allowed us to estimate the specificity of 4 semisynthetic glycoconjugate *M. leprae* antigens in an endemic and a nonendemic population. Our data suggest that the specificity of these antigens is quite high, i.e. 98·7% in the leprosy endemic area. It is possible that the difference between the rate of false-positive tests (0·94%) in a nonendemic area and the rate of positive tests in seropositive healthy individuals in the endemic area reflects subclinical infection. In terms of practical application, we concluded that seropositivity in individuals free of leprosy was low enough to warrant use of these antigens in diagnostic settings, and in screening household and other contacts for subclinical leprosy infections. The specificity of the antigens may be improved by developing new carriers and/or linker arms for the synthetic sugar epitopes. Where the

risk, or incidence and prevalence of leprosy is low, it would not be cost effective to use these antigens in screening general populations, since the rate of false positives would greatly exceed the numbers of new cases detected.

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Évaluation de quatre antigènes semi-synthétiques de *Mycobacterium leprae* avec les serum de populations saines dans des régions d'endémie et de non-endémie

J T Douglas, L M Steven, D S Hirsch, T Fujiwara, K E Nelson, M G Madarang et R V Cellona

Résumé Notre but était de déterminer la fréquence de l'apparition d'anticorps aux antigènes semi-synthétiques de *Mycobacterium leprae* dans des populations de non-malades en bonne santé clinique et d'établir une base pour la comparaison de la fréquence des anticorps chez les patients avec une histoire de lèpre d'une part, et leurs contacts d'autre part. Nous avons donc exécuté des tests ELISA sur des serum représentant deux régions: une région où la lèpre est endémique, Cebu City, Philippines et une régon où la lèpre n'est pas endémique, Chicago, Illinois, USA. Ces serum ont été testés, par indirect IgM ELISA, pour rechercher la présence d'anticorps réagissant avec quatre antigènes semi-synthétiques basés sur l'antigène phénolique glycolipidique I de *M. leprae*: ND-O-BSA (disaccharide naturel lié par un octyl à la serum albumine de boeuf BSA), NT-O-BSA (trisaccharide naturel lié par un octyl à BSA), ND-P-BSA (disaccharide naturel lié par un noyau phénolique à BSA). En prenant 0,16 comme lecture OD positive, l'antigène avec la séroréactivité de fond la plus basse était ND-O-BSA, qui réagissait avec 5/398 (1,3%) serum provenant de Cebu, et 3/426 (0,7%) serum provenant de Chicago. Au total 10 des 398 serum (2,5%) provenant de la région d'endémie ont réagi avec au moins un antigène et 5 serum (1,3%) ont réagi avec tous les quatre antigènes semi-synthétiques. Des 426 serum provenant de Chicago, 12 (2,8%) ont réagi avec au moins un antigène et 3 (0,7%) avec tous les quatre antigènes semi-synthétiques. Les valeurs moyennes de l'ELISA pour les 22 serum positifs pour chaque antigène ont varié entre 0,17 et 0,3 unités OD, tandis les valeurs moyennes pour tous les serum dans chaque régione ont varié entre, 0,01 et 0,04 unités OD pour tous les quatre antigènes. La réactivité de 14 des serum positifs à certains antigènes, mais pas à tous les quatre antigènes semi-synthétiques, indique que le porteur et le lieur pourraient être associés à cette réactivité de fond. Il serait justifié de chercher à remplacer les lieurs et porteurs. Nous concluons que la réactivité de fond aux antigènes semi-synthétiques représentant la molécule PG-I de *M. leprae* est de 0,7–1,3% basée sur 0,16 comme valeur positive. A partir de ces données nous avons conclu que la réactivité chez les individus non lépreux était assez basse pour justifier l'usage de ces antigènes dans les opérations de diagnostic, telles que le dépistage des contacts de l'entourage et les populations très endémiques. Lorsque l'incidence et la fréquence de la lèpre sont basses, l'emploi de ces antigènes pour les tests ne se justifie pas économiquement, sauf chez les individus à haut risque. Le dépistage sérologique avec ces antigènes pourrait être utile pour la détection et l'identification de la rechute bactérienne, les réactions de type 1 ou 2, la détection précoce de la lèpre, et le suivi du traitement dans les régions d'endémie.

La evaluacion de cuatro antigenos *Mycobacterium leprae* semi-sinteticos con sueros de populaciones sanas en zonas endemicas y no endemicas

J T Douglas, L M Steven, D S Hirsch, T Fujiwara, K E Nelson, M G Madarang y R V Cellona

Resumen Para poder determinar la frecuencia de ocurrencia de los anticuerpos en los antígenos semi-sintéticos de *Mycobacterium lepræ* en populaciones clínicamente sanas que no son pacientes, y para establecer una 'línea de base' para comparar las frecuencias de anticuerpos en los pacientes con antecedentes de lepra y sus contactos, se realizaron ELISAs usando sueros representativos de dos zonas: una de lepra endémica, Cebu City, Islas Filipinas, y una zona no endémica, Chicago, Illinois, EE.UU. Se probaron estos sueros por medio de ELISA IgM indirecta, para la presencia de anticuerpos que reaccionan con cuatro antígenos semisintéticos basados en el antígeno fenólico glicolípido I de *Mycobacterium lepræ*: ND-O-BSA (disacárido natural con enlace octílico con albumina sérica bovina), NT-O-BSA (trisacarido natural con enlace octílico con albumina sérica bovina), ND-P-BSA (disacarido natural con enlace fenólico con albumina sérica bovina), y NT-P-BSA (trisacarido natural con enlace fenólico con albumina sérica bovina). Usando una lectura OD $\geqslant$0,16 como positiva, el antígeno con la seroactividad de fondo más bajo fue ND-O-BSA que reaccionó con 5/398 (1,3%) de los sueros de Cebu, y 3/426 (0,7%) de los sueros de Chicago. Un total de 10 (2,5%) de los 398 sueros de la zona endémica reaccionó con al menos un antígeno y 5 (1,3%) de los sueros reaccionaron con los cuatro antígenos semi-sintéticos. De los 426 sueros de Chicago, 12 (2,8%) eran reactivos con al menos un antígeno y 3 (0,7%) reaccionaban con los cuatro antígenos semi-sintéticos. Los valores medios ELISA para los 22 sueros positivos de cada antígeno variaban entre 0,17 y 0,3 unidades OD, y los promedios para todos los sueros en cada zona variaban entre 0,01 y 0,04 unidades OD para todos los antígenos. La reactividad de 14 de los sueros positivos con algunos de los antígenos, pero no todos los antígenos semi-sintéticos, indica que el portador y los enlaces pueden ser asociados con esta reactividad de fondo. Se justifica la investigación de otros portadores y enlaces. Concluimos que la reactividad de fondo no específica con los antígenos semi-sintéticos que representa la molécula PG-I de *Mycobacterium lepræ* es 0,7 a 1,3%, valor basado en un valor de corte de $\geqslant$0,16 OD. Estos datos nos permiten concluir que la reactividad de individuos libres de lepra fue suficientemente bajo para justificar el uso de estos antígenos en un ambiente diagnóstico, por ejemplo el control de contactos familiales y en populaciones muy endémicas. Cuando la incidencia y frecuencia de la lepra son bajas, pruebas que usan estos antígenos no serían rentables, al menos que se les aplicará a individuos muy expuestos a riesgo. El control serológico por medio de estos antígenos podría ser útil en la detección y diferenciación de los relapsos bacteriológicos, las reacciones de tipo 1 o 2, la detección temprana de la lepra y para controlar el tratamiento en zonas endémicas.

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Leprosy in French Polynesia. Epidemiological trends between 1946 and 1987

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Summary The analysis of computerized data (OMSLEP system) on patients from French Polynesia followed since 1940 has shown a decrease in the mean annual detection rates for leprosy, all forms combined, from 24.73 per 100,000 inhabitants in 1946 to 8·1 per 100,000 in 1987 ($y = -0.49\,x + 45.83$; $p < 0.05$). In fact, the decrease was significant ($y = -1{\cdot}18\,x + 83{\cdot}54$; $p < 0{\cdot}05$) during the first half of the study period (1946–66), but not during the second half (1967–87). Similarly, a significant decrease in all of the specific mean annual detection rates (according to the form of leprosy and to the sex and age of patients), in the proportion of multibacillary patients among the total of newly detected cases, and in the proportion of all patients with disabilities at the onset of leprosy was observed only during the first half of the study period (1946–66). Nevertheless, when comparing age-specific cumulative detection rates, calculated by 10-year age groups over the period 1946–66, to those of the period 1967–87, an ageing of the leprosy population was noted. Finally, the decrease of mean annual detection rates was greater in the smaller populations of remote islands than in the population of Tahiti, the main island, where 70% of the total population were living during the study period. This decline was shown to correspond to an effective improvement of the leprosy situation which could be attributed, among other factors (such as economic development and systematic BCG vaccination), to the implementation of a control programme for leprosy in 1950. The introduction in 1982 of multidrug therapy for all patients suffering active leprosy has raised the hope of a subsequent decline of leprosy in French Polynesia in the near future.

Introduction

Up to now, leprosy control has been based on the adequate treatment of patients detected as early as possible. The knowledge and understanding of the evolution of epidemi-

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ological indicators for leprosy are essential for evaluating and monitoring control strategy. Therefore, the collection and analysis of epidemiological data is a most important part of leprosy control programmes. However, reliable epidemiological data on leprosy are difficult to collect in most countries, especially for operational reasons. In French Polynesia, an area where the population is of a relatively small size and where medical infrastructures are considerable, a control programme for leprosy was implemented by the end of the 1940s. In 1986–7, computerization of data on leprosy patients registered from 1940 onwards was initiated according to the OMSLEP[1] system and reliable information on leprosy for the past 40 years has now become available. This enabled us to analyse the evolution of the main epidemiological indicators for leprosy in French Polynesia for the period 1946–87.

Background

French Polynesia is made up of about 130 islands (88 usually inhabited), with a land surface of only 4000 km^2, scattered over an oceanic area of 4 million km^2. The 130 islands are divided into 5 archipelagoes (Society, Australes, Tuamotus, Gambiers and Marque-

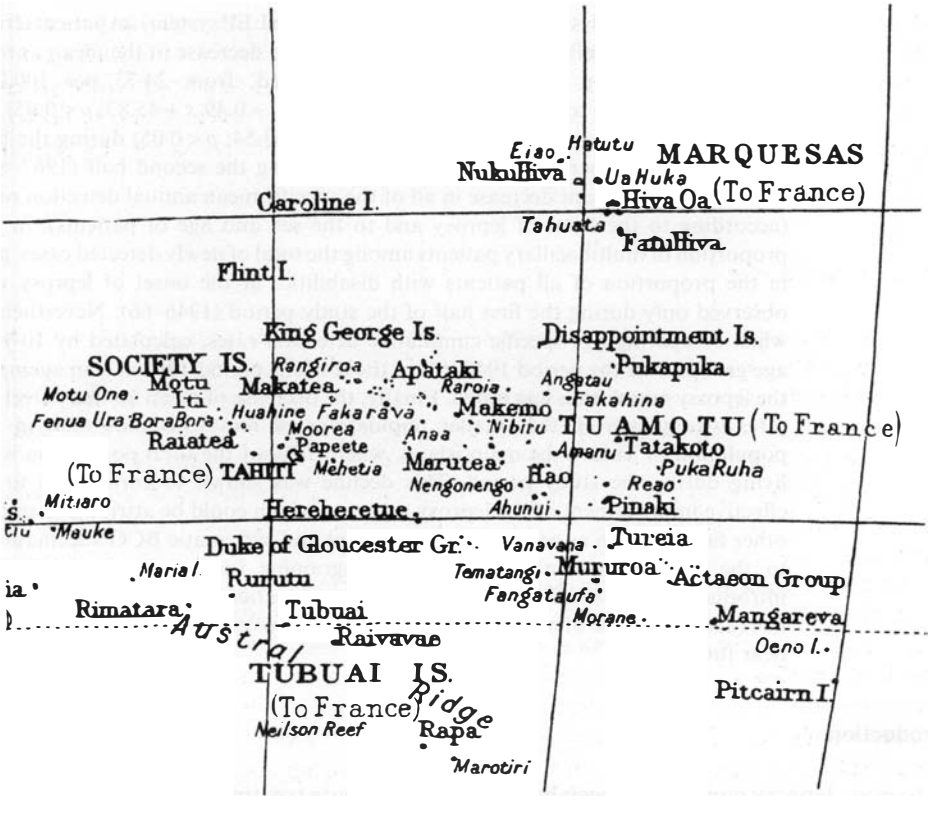

Figure 1. Archipelagoes of French Polynesia.

sas); Papeete, the main town, where administrative authorities are concentrated, is located on Tahiti, the main island of the Society archipelago (Figure 1). The population increased dramatically between 1946 and 1987; according to the IT Stat.[2] records, there were 56,601 inhabitants in 1947 (18,462 < 15 years of age and 38,139 > 15 years of age), and 181,862 in 1986 (69,077 < 15 years of age and 112,785 > 15 years of age). For each year of the study period, the population was calculated from the results of 8 censuses (1946, 1951, 1957, 1962, 1967, 1971, 1977 and 1983) assuming a linear increase between two censuses. It is important to note that, between 1946 and 1987, about 75% of the total population of French Polynesia were living in Tahiti while only 50% were born on that island.

As in many countries, the leprosy control programme started with the construction of leprosariums, the first two in Tahiti and in a remote valley of the Southern Marquesas (1500 km north of Tahiti) in 1914; a third one was opened in 1934 in Reao, one of the easternmost islands of the Tuamotu archipelago. Since 1902, notification of all cases of leprosy to the Health Authority by the diagnosing physician has been compulsory. For each new case of leprosy, a patient form is filled out indicating name, sex, date and place of birth, date and place of detection, as well as the results of clinical, microbiological and pathological examinations, and the nature and duration of treatment. Each month assessment of drug intake and of clinical evolution is performed and the form updated. All data on leprosy patients living in the 3 leprosariums are centralized in Tahiti where a central leprosy register is kept. In 1950, the 'Louis Malardé' Institute was created and was given direction of the leprosy control unit. This unit organizes active case-finding among household contacts of known leprosy patients, and passive case-finding; it is responsible for the prescription, distribution, supervision and evaluation of chemotherapy. Today the Institute is still in charge of the leprosy control programme and keeps the territorial leprosy register.

Materials and methods

The data analysed in this study comes partly from the territorial register and partly from the medical files of patients followed from 1946 to 1987. The diagnosis of leprosy was based on the clinical examination of patients (including examination of the skin and the large nerve trunks) supplemented by biological tests: the lepromin intradermal reaction, the search for acid-fast bacilli in nasal mucosa and skin (earlobes and skin lesions) and biopsy for pathological examination. Clinical examination and biological tests also permitted the assignment of cases retrospectively into paucibacillary and multibacillary categories.

Between 1951 and 1982 the basis of treatment for leprosy was dapsone monotherapy, which was prescribed lifelong for multibacillary patients and for an average of 10 years for paucibacillary patients. Rifampicin (RMP) was prescribed occasionally and over short periods of time from 1973 to 1982. After January 1982, multidrug therapy, including daily administration of 10 mg/kg RMP, has been implemented in French Polynesia. All drugs are distributed free of charge every month to patients, either at the Institute, or in non-specialized public health clinics (in this latter case the drugs are provided by the leprosy control unit).

The annual prevalence rates for leprosy were calculated according to the definition

given by Lechat and Vanderveken,[3] i.e. taking into account all known leprosy cases (on treatment as well as under surveillance after treatment). Because important variations in the number of newly detected leprosy cases were observed from year to year, the following indicators were calculated for 3-year periods: crude, type-specific, sex-specific, and age-specific (<15 years, >15 years) detection rates; proportion of multibacillary patients among the total number of cases, and with disabilities[4] of grade >2. Also, cumulative detection rates, specific for 10-year age groups, and mean annual detection rates according to the place of birth were calculated for the two consecutive 21-year periods, 1946–66 and 1967–87.

All data from the medical files of the patients were anonymously entered on the OMSLEP record card and analysed by computer. For statistical analysis, Pearson's χ^2 test and the Student's t test were used.[5] Regression curves were established using a computer statistical package (Chart 3 Microsoft).

Results

PREVALENCE RATE

In 1946, 133 leprosy patients, all on treatment, were recorded in the territorial register, giving a prevalence rate of 2·4/1000; in 1987, the number of registered patients was 291 (88 on treatment and 203 under surveillance after treatment) and the prevalence rate was 1·57/1000, not significantly different ($p>0·05$) from that of 1946. If taking into account only the patients requiring treatment for the calculation of the prevalence rate, as recommended by WHO in 1988,[6] then the prevalence rate in 1987 was 0·48/1000, significantly lower ($p<0·01$) than that of 1946.

CRUDE DETECTION RATES

Between 1946 and 1987, 520 new leprosy cases were detected, 233 (45%) were multibacillary and 287 paucibacillary cases; 306 (59%) were males and 214 were females (Table 1).

During the first 3-year period of the study (1946–48), the number of newly-detected patients was 42 and the mean annual detection rate for leprosy (all forms combined) was 24·73/100,000 (Table 1). The corresponding figure was 44 during the last 3-year period (1985–87) but, given the dramatic increase of the population to 181,862 inhabitants, the mean annual detection rate for leprosy was 8·1/100,000, significantly lower than that for the period 1946–48. The regression curve, plotted on the basis of mean annual detection rates for all 3-year periods (Figure 2) indicates a significant decrease ($y=-0·49\,x+45·83$; $r=-0·80$; $p<0·05$). In fact, the regression was not constant between 1946 and 1987; the detection rate fell dramatically from 24·73 in 1946–48 to 8·6/100,000 in 1964–66 ($y=-1·18\;x+83·54$; $r=-0·89$; $p<0·05$); conversely, between 1967 and 1987, no significant decrease ($p>0·05$) was observed in the detection rates of the 7 3-year periods.

SPECIFIC DETECTION RATES

With respect to the type of leprosy (Table 1), during the first 3-year period of the study, 25 of the 42 newly-detected cases were multibacillary (14·7/100,000 mean annual detection

Table 1. Mean annual detection rates for leprosy according to (a) type, (b) sex and (c) age by 3-year periods between 1946 and 1987

	(a) Type						(b) Sex				(c) Age			
	Total		Paucibacillary		Multibacillary		Males		Females		< 15 Years		> 15 Years	
3-year periods	No.	Rates*	No.	Rates*	No.	Rates*	No.	Rates*	No.	Rates*	No.	Rates*	No.	Rates*
1946–48	42	24·73	17	10·01	25	14·72	25	28·04	17	21·07	10	18·05	32	27·96
1949–51	60	33·19	27	14·93	33	18·25	31	32·08	29	33·06	12	16·97	48	43·60
1952–54	43	21·44	19	9·47	24	11·96	25	24	18	18·07	19	22·45	24	20·70
1955–57	33	14·75	19	8·49	14	6·25	23	20	10	9·22	8	8·23	25	19·75
1958–60	35	14·63	17	7·10	18	7·52	21	17·01	14	12·04	5	4·80	30	22·18
1961–63	28	10·98	17	6·67	11	4·31	16	12·02	12	9·07	6	5·42	22	15·24
1964–66	24	8·61	14	5·02	10	3·59	15	10·32	9	6·75	3	2·49	21	13·27
1967–69	24	7·75	15	4·84	9	2·90	15	9·18	9	6·15	3	2·22	21	12·00
1970–72	30	8·53	15	4·26	15	4·26	16	8·58	14	8·48	5	3·21	25	12·77
1973–75	37	9·67	22	5·75	15	3·92	21	10·04	16	8·85	8	4·83	29	13·34
1976–78	37	8·94	21	5·07	16	3·86	16	7·36	21	10·07	4	2·30	33	13·72
1979–81	37	8·11	22	4·82	15	3·28	28	11·73	9	4·13	1	0·55	36	13·10
1982–84	46	9·19	29	5·79	17	3·39	28	10·74	18	7·52	6	3·14	40	12·92
1985–87	44	8·06	33	6·04	11	2·01	26	9·15	18	6·88	14	6·75	30	8·86
Total	520	—	287	—	233	—	306	—	214	—	104	—	416	—

* Per 100,000 inhabitants.

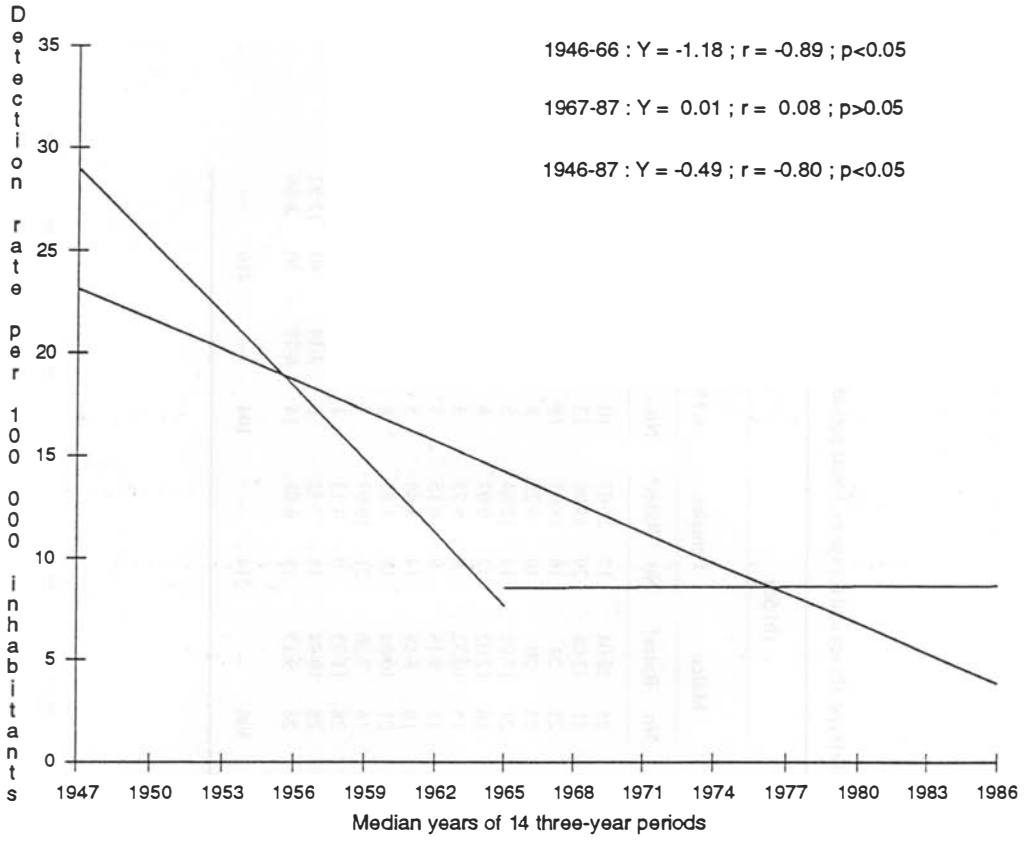

Figure 2. Evolution of mean annual detection rates for leprosy (all forms) by 3-year periods between 1946 and 1987.

rate) and 17 were paucibacillary patients (10/100,000) whereas, during the last one, of the 44 newly detected patients, 11 were multibacillary (2·01/100,000) and 33 were paucibacillary (6·04/100,000). The regression curve plotted on the basis of the 14 specific 3-year detection rates showed a significant ($p < 0{\cdot}05$) decline for both multibacillary and paucibacillary detection rates. The decline was significant for multibacillary as well as for paucibacillary detection rates between 1946 and 1966 ($p < 0{\cdot}05$), but not between 1967 and 1987 ($p > 0{\cdot}05$).

With respect to sex of the patients (Table 1), a significant decrease ($p < 0{\cdot}01$) of the detection rate was observed between 1946 and 1987, from 28·04 to 9·15/100,000 in males and from 21·07 to 6·88 in females. Again, the regression was significant in males ($p < 0{\cdot}01$) as well as in females ($p < 0{\cdot}05$) between 1946 and 1966, but not between 1967 and 1987 ($p > 0{\cdot}05$).

With respect to age (Table 1), of the 42 newly detected patients during the first 3-year period of the study (1946–48), 10 were less than 15 years of age (mean annual detection rate: 18·05/100,000) and 32 were 15 years of age or more (27·96/100,000). The regression curves plotted on the basis of all 14 age-specific detection rates showed a significant

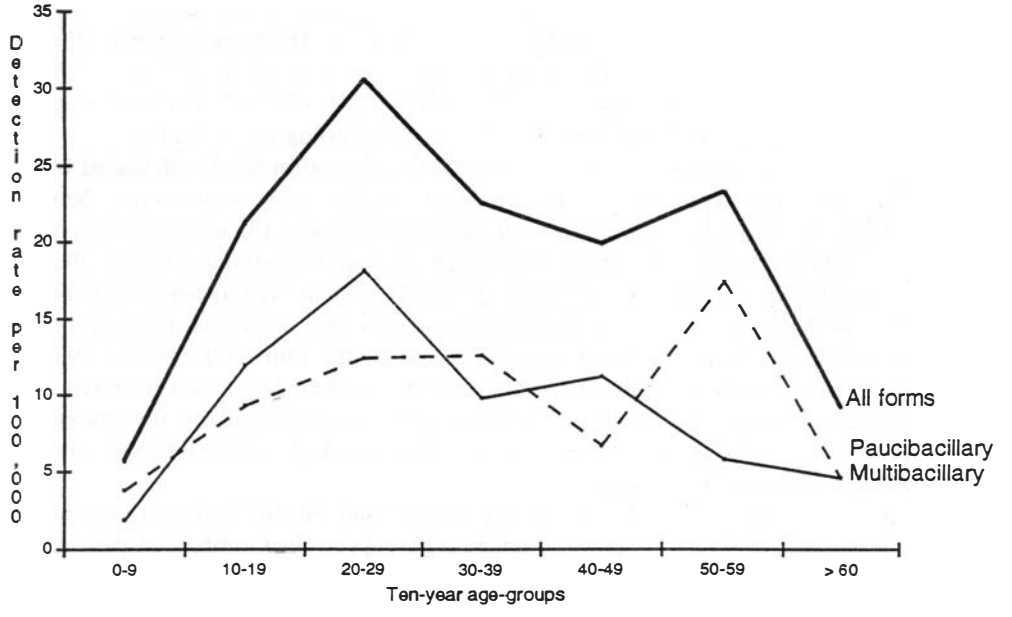

Figure 3. Age-specific detection rates of leprosy between 1946 and 1966.

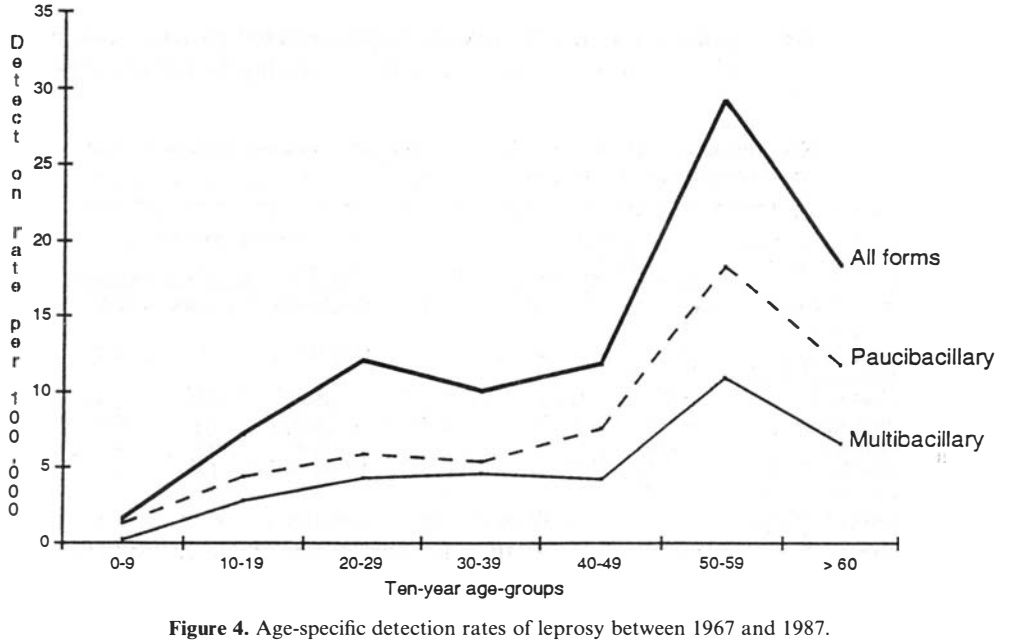

Figure 4. Age-specific detection rates of leprosy between 1967 and 1987.

decrease ($p < 0{\cdot}05$) for both < 15 years of age and > 15 years of age detection rates; as observed for previously reported epidemiological indicators, the regression was effective ($p < 0{\cdot}05$) during the period 1946–66, but not during the period 1967–87 ($p > 0{\cdot}05$).

This led us to consider two study periods, 1946–66 and 1967–87, for analysing our results concerning detection rates as well as other epidemiological indicators.

When considering age-specific, 21-year cumulative detection rates, calculated by 10-year age groups, more pertinent data became available for analysis of results. Between 1946 and 1966, 265 new cases of leprosy (130 paucibacillary and 135 multibacillary) were detected; as shown in Figure 3 the highest detection rates were observed in the 20–29 years age groups for leprosy, all forms combined (30·5/100,000), as well as for multibacillary cases (18·1/100,000); whereas, for paucibacillary patients, detection rates were not significantly different in the 7 10-year age groups ($p > 0{\cdot}05$). During the period 1967–87 (Figure 4), 255 new cases (157 paucibacillary and 98 multibacillary) were detected, with the highest detection rates being observed in the 50–59 years age groups for leprosy (all forms combined, 29·2/100,000), as well as for paucibacillary (10·9/100,000) and for multibacillary patients (18·3/100,000).

With respect to place of birth, during the period 1946–66, the highest mean annual detection rates were observed in remote islands, especially in the Gambier islands, and in the Northern and Southern Marquesas islands, where they were 198, 72 and 49 per 100,000, respectively (Table 2); during the same period, the detection rate was 9·2/100,000 in the Society archipelago (where 70% of the population were living). During the 1967–87 period, the mean annual detection rates decreased dramatically to 54 and 12/100,000 in the Gambier and Northern Marquesas islands, respectively, while they remained stable in the Southern Marquesas (49/100,000) as well as in the Society archipelago (7/100,000).

PROPORTION OF MULTIBACILLARY PATIENTS AMONG NEWLY-DETECTED CASES

The proportion of multibacillary patients among newly-detected patients was 59·5% during the first 3-year period (1946–48) of the study and 25% during the last one (1985–7);

Table 2. Mean annual detection rates for leprosy according to place of birth in French Polynesia by 21-year periods between 1946 and 1987

	1946–66 period			1967–87 period		
Place of Place of birth	Mean* population	Mean* No. of cases	Mean* rate	Mean population	Mean No. of cases	Mean rate
Society islands	58,388	5·4	9·2	97,405	7	7·2
Marquesas islands						
Northern	2505	1·8	72·2	4600	0·6	12·4
Southern	1356	0·8	49·6	2824	1·4	49
Australes islands	4206	0·9	22·1	7036	0·7	9·5
Tuamotu islands	6530	2·2	34·3	9655	1·4	14·3
Gambier islands	552	1·1	198·4	870	0·5	54·7
Outside of FP†	9708	0·42	4·4	18,239	0·7	3·6

* Annual mean population, number of cases and detection rates (per 100,000 inhabitants).

† Patients born outside of French Polynesia, but detected in French Polynesia.

the regression curve plotted on the basis of the 14 3-year proportions ($y = -109{\cdot}8\ x + 114$) indicates a significant decrease ($p < 0{\cdot}05$). As was noted for other indicators previously reported, the decrease was significant between 1946 and 1966 but not significant between 1967 and 1987.

PROPORTION OF PATIENTS WITH DISABILITIES OF GRADE > 2 AT DETECTION

In 1946–8, among the 42 newly-detected patients, 22 (52%) presented disabilities of grade > 2 at the moment of detection; this percentage fell dramatically to reach 6·8% in 1985–7; for the whole study period, the regression curve ($y = -0{\cdot}51\ x + 79{\cdot}5$) indicates a significant decrease ($p < 0{\cdot}05$). Again, the decrease was significant ($p < 0.05$) during the first period of the study (1946–66), but not during the second one (1967–87).

Discussion

As mentioned above, the number of newly-detected patients differed greatly from year to year during the whole study-period. Such a phenomenon may be due either to the small number of cases and random fluctuations, or to a lack of continuity in the active case finding performed in the islands. Therefore, to validate detection rates as estimates of incidence, we examined the evolution of 2 indicators: the proportion of newly-detected patients with deformities of grade > 2 and the proportion of multibacillary patients among the total number of newly-detected patients (though the use of the latter indicator may be controversial). The proportion of patients with deformities among the newly-detected cases should tend towards zero if detection rates approach incidence rates and the proportion of multibacillary patients (who are usually detected first when control schemes are initiated) should decrease steadily some years after the implementation of a leprosy control programme.[3] In fact, we observed a reduction of these 2 proportions, along with the decrease of the detection rates. This suggests that, 20 years after the implementation of the control programme, the 3-year detection rates reported in our study closely approximated the true incidence of leprosy.

The next point to emerge from our data is the consistant decrease in the leprosy detection rates. The fact that it is limited to the period 1946–66, that is, during the period following the introduction of dapsone, must be considered very carefully. The evolution of the epidemiological situation may not always be attributed to the efficacy of a control programme,[7] and the declining incidence of leprosy coincident with the implementation of a leprosy control programme is difficult to interpret because of other possible influencing factors, such as a change in control programme efforts, economic development of the country and the natural decline of the disease.[8] After 1946 the main change in leprosy control in French Polynesia was the closure of leprosariums in the remote islands of the Marquesas and Tuamotu archipelagoes, and, in 1950, the centralization at the Louis Malardé Institute of the activities of the leprosy control unit. In fact, this operational change resulted in the strengthening and the standardizing of the activities of the control unit and treatment measures. Thus, the reduction of detection rates is likely to reflect an improvement in the epidemiological situation rather than a failure of the control strategy, and it may be assumed that an actual decline in leprosy has occurred since 1946. A period of important economic development occurred in French Polynesia but, because

this only commenced after 1962,[9] it is unlikely to be the only cause of the improvement in the leprosy situation between 1946 and 1966. Moreover, this economic improvement affected remote islands much less and much later than Tahiti; thus, it is not likely to be responsible for the decrease of the detection rates for leprosy in the remote archipelagoes. Though several reports have suggested that control programmes only resulted in improvement of the leprosy situation in a few areas,[10] some of our findings suggest that improvement in the leprosy situation noted in French Polynesia could be attributed, among other factors, to the efficacy of the control programme implemented in 1950. The most important is the decline in the proportion of newly-detected patients with disabilities, which has been demonstrated in other countries[11] to be the main effect of a control strategy. Another point is that the most important decrease in detection rates was observed in remote islands. This suggests that control programmes, including not only standardized treatment and the follow-up of patients, but also active case-finding among household contacts, are easier to manage, and, thus, are more effective in small size populations. That such a decrease was not observed in the South Marquesan population, which is also of a small size, remains difficult to explain.

Regarding the second study period of 1967–87, the stability in detection rates might suggest, as reported in a previous study,[12] that no change occurred in the leprosy situation. It must be emphasized that, during that period, the highest detection rates were observed in the oldest age groups (in terms of age at detection) whereas, during the first period (1946–66), they were observed, at least for multibacillary leprosy, in the 20–9 year age group. In fact, the difference between age at onset and age at detection was probably longer during the first period than during the second, due to the delay in case finding. Thus, the difference in age at onset between the two periods was most likely greater than what we have reported. However, the ageing of the leprosy population may have several explanations, among them the introduction in French Polynesia by the mid-1960s of systematic BCG vaccination for all new-born children. As reported by Bagshawe, BCG should afford protection against leprosy, more particularly in vaccinated children under 15 years of age.[13] Also, it is known that the efficacy of a leprosy control programme should result in a more marked decrease in children,[14] and that increase in the mean age of patients at the onset of leprosy reflects a decrease in the risk of infection in a community. However, it should be kept in mind that increasing mean age of patients has been considered as an indicator of long-term decreasing trends irrespective of any control strategy.[8] Why detection rates for leprosy remained stable during the period 1967–87 is difficult to explain. It is assumed that, theoretically, effective treatment of all patients with overt disease (known prevalence) together with the reduction to zero of the reservoir of undetected cases (unknown prevalence) should interrupt transmission, and that after a period of latency, no new cases should appear.[15] In that assumption, a most important point is that treatment should be effective: in French Polynesia, nearly half of the multibacillary patients on dapsone monotherapy have relapsed and have become additional sources of transmission.[16] Therefore, it might be speculated that an additional reservoir of infection, consisting of all relapsing multibacillary patients since 1946, has contributed to the emergence of new cases of leprosy and to a slowing down of the decrease in detection rates which was observed during the previous period. Whatever the explanation and despite the stability in detection rates for leprosy during the period 1967–87, our results suggest that the leprosy situation also improved during the last 21 years of the study. Finally, it should be noted that, ever since multidrug therapy was implemented

in French Polynesia in 1982, no relapses have been detected;[17] whereas, as mentioned above, during the time of dapsone monotherapy, cumulative relapse rates of 30–50% were observed in multibacillary patients.[16] It seems reasonable to hope that, by suppressing or greatly reducing the occurrence of relapse, the implementation of MDT in French Polynesia will reduce the risk of transmission of the disease, and that a subsequent fall in detection rates should be observed in the near future.

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Lèpre en Polynésie Française. Tendances épidémiologiques entre 1946 et 1987

J-L Cartel, J-P Boutin, A Spiegel, Ph Glaziou, R Plichart, R Cardines et J-H Grosset

Résumé L'analyse des données informatiques (système OMSLEP) sur des patients de Polynésie française suivis depuis 1940 a révélé une diminution des taux annuels moyens de détection de toutes les formes de lèpre, de 24,73 pour 100 000 habitants en 1946 jusqu'a 8,1 pour 100 000 en 1987 ($y = -0{,}49\,x + 45{,}43$; $p < 0{,}05$). En réalité, la diminution était significative ($y = -1{,}18\,x + 83{,}54$; $p < 0{,}05$) pendant la première moitié de la période d'étude (1946–66), mais ne l'était pas pendant la seconde (1967–87). De même, on a observé seulement au cours de cette même première moitié (1946–66) de la période d'étude une diminution significative dans tous les taux de détection annuels moyens spécifiques (selon la forme de lèpre, le sexe et l'age des patients), dans la proportion des patients multibacillaires sur le total des nouveaux cas détectés, et dans la proportion de tous les patients souffrant d'infirmités au début de leur lèpre. Pourtant, lorsque les taux de détection cumulatifs par age, calculés par groupe d'age de 10 ans, au cours de la période 1946–66, ont été comparés à ceux de la période 1967–87, on a noté un vieillissement de la population lépreuse. Enfin, la diminution des taux de détection annuels moyens était plus importante dans les plus petites populations des iles isolées que dans la population de Tahiti, l'ile principale, où 70% de la population totale vivait pendant la période de l'étude. On a montré que ce déclin correspondait à une amélioration réelle de la situation quant à la lèpre, que l'on pourrait attribuer, entre autres facteurs, (tels que le développement économique et la vaccination BCG systématique), au programme de contrôle de la lèpre exécuté en 1950. L'introduction en 1982 d'une thérapeutique multidrogue pour tous les patients atteint de lèpre évolutive a fait naître l'espoir d'un nouveau déclin de la lèpre en Polynésie française dans un avenir prochain.

La lepra en la Polinesia Francesa. Las tendencias epidemiologicas entre 1946 y 1987

J-L Cartel, J-P Boutin, A Spiegel, Ph Glaziou, R Plichart, R Cardines y J-H Grosset

Resumen El análisis de datos informatizados (sistema OMSLEP) sobre pacientes de la Polinesia Francesa desde 1940 ha indicado una reducción del promedio anual de detección de la lepra, en una combinación de todas sus formas, de 24,73 por 100 000 habitantes en 1946 a 8,1 por 100 000 en 1987 ($y = -0{,}49\,x + 45{,}83$); $p < 0.05$). En efecto, la reducción durante la primera mitad del período del estudio (1946–66) fue significativa ($y = -1{,}18\,x + 83{,}54$; $p < 0{,}05$), pero no durante la segunda mitad (1967–87). Igualmente, se observó una reducción significativa de todos los promedios anuales específicos de frecuencia de detección (según la forma de la lepra y el sexo y edad de los pacientes), en la proporción de pacientes multibacilares en el total de casos recién detectados, y en la proporción de todos los pacientes con incapacidades al inicio de la lepra, durante el la primera mitad del período de estudio (1946–66). No obstante, cuando se compara la frecuencia de detección cumulativa para edades específicas, calculada en grupos de 10 años durante el período 1946–66, con la frecuencia para 1967–87, se notó un aumento de la población leprosa. Finalmente, la reducción del promedio anual de frecuencias de detección fue más grande en las poblaciones más pequeñas de las islas remotos que en la población de Tahiti, la isla principal, donde vivía 70% de la población total durante el período del estudio. Se mostró que la disminución correspondía a una mejora efectiva de la situación leprosa que se podía atribuir a, entre otros factores (como el desarrollo económico y la vacunación antituberculosa sistemática), debida a la implementación de un programa de control de la lepra en 1950. La introducción en 1982 de una terapia multi-droga para todos los pacientes que sufrían de lepra activa ha creado la esperanza de una reducción posterior de la lepra en la Polinesia Francesa en un futuro próximo.

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Leprosy in French Polynesia. The possible impact of multidrug therapy on epidemiological trends

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Summary In 1982, following the recommendations of a WHO study group, multidrug therapy (MDT) was introduced into French Polynesia to treat all patients suffering from active leprosy, and—only on request—those still on dapsone monotherapy. After 5 years, a clear-cut decrease of prevalence and mean annual detection rates for leprosy (except for detection rates among children aged less than 15 years, many of such cases being detected early by increased household contact training) has been observed. There was also a decrease in the proportion of newly detected cases with disabilities. During the 21-year period preceding the introduction of MDT into the control programme, mean annual detection rates for leprosy had remained stable, and this led to the consideration that such a decrease was due neither to the natural decline of the disease nor to the economic improvement of the country. Our results, together with the fact that, to date, the relapse rate was nil in the Polynesian patients put on MDT, strongly suggest that the implementation of MDT has resulted in a decrease of detection rates for leprosy which may be a consequence of a decrease in the transmission of the disease.

Introduction

From the early 1950s, dapsone monotherapy was the basis of the treatment for leprosy in French Polynesia, prescribed to paucibacillary patients for an average of 10 years and for life to multibacillary patients. In November 1982, following the recommendation of the WHO study group,[1] multidrug therapy (MDT) was introduced to treat all patients suffering from active leprosy. These included newly-detected patients as well as those detected before 1982 and suffering a relapse; patients detected before 1982 and still on dapsone monotherapy without signs of active leprosy were put on MDT only on request. The aim of this study is to discuss if changes in the epidemiological trends of leprosy have

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been observed after MDT was introduced and to determine if this could be attributed to the introduction of MDT into the control programme. Because the results of a previous study have indicated that detection rates for leprosy remained stable between 1967 and 1983,[2] the epidemiological indicators were analysed over the period 1967–83 (pre MDT) and 1983–90 (post MDT).

Patients and methods

As shown in Table 1, the population increased dramatically in French Polynesia between 1967 and 1990; according to I.T.Stat.[3] records, there were 98,378 inhabitants in 1967 and 197,061 in 1990. For each year of the study period, the population was calculated from the results of 5 censuses (1967, 1971, 1977, 1983 and 1988) assuming a linear increase between 2 censuses. During the entire period 1967–90 about 75% of the total population were living in Tahiti although only 50% were born on that island.

The data analysed in the study came partly from the territorial register and partly from the medical files of patients followed from 1967 to 1990. The diagnosis of leprosy was

Table 1. Annual population and prevalence rates* for leprosy in French Polynesia between 1967 and 1990

Year	Population	Prevalence Rates*	No. of patients on treatment			
			Total	DDS	MDT	Other†
1967	98,378	3·21	315	315	0	0
1968	103,199	3·09	319	319	0	0
1969	108,020	2·94	318	318	0	0
1970	112,842	2·57	290	287	0	3
1971	117,663	2·47	291	285	0	6
1972	120,949	2·36	286	272	0	14
1973	124,236	2·28	283	271	0	12
1974	127,522	2·26	288	276	0	12
1975	130,808	2·21	289	277	0	12
1976	134,095	2·13	286	283	0	3
1977	137,381	2·1	288	282	0	6
1978	142,276	1·98	281	269	0	12
1979	147,172	1·95	287	266	0	21
1980	152,067	1·76	267	251	0	16
1981	156,962	1·66	260	234	0	16
1982	161,858	1·45	234	181	1	52
1983	166,753	1·25	209	141	14	54
1984	169,778	1·1	186	98	60	28
1985	174,141	0·96	141	55	67	19
1986	178,619	0·59	105	51	44	10
1987	183,232	0·48	88	35	43	10
1988	187,841	0·25	46	19	21	6
1989	192,451	0·18	35	19	14	2
1990	197,061	0·14	28	17	11	0

* Per 1,000 inhabitants.

† Rifampicin added to dapsone monotherapy (patients diagnosed before 1983).

based on the clinical examination of the patients (including examination of the skin and the large nerve trunks) supplemented by biological tests: the lepromin intradermal reaction, the search for acid-fast bacilli in the nasal mucosa and the skin (earlobes and skin lesions) and biopsy for pathological examination. Clinical examinations and biological tests permitted the diagnosis of leprosy and, retrospectively, the assignment into paucibacillary and multibacillary categories.

From 1951, dapsone monotherapy has been the basis of treatment for leprosy; from 1970 to 1984, rifampicin (RMP) was prescribed occasionally and over short periods to patients on dapsone monotherapy. After November 1982, the multidrug therapy for paucibacillary patients has consisted of the daily administration for 6 months of 100 mg of dapsone (DDS) and 10 mg per kg of RMP. For multibacillary patients MDT has consisted of the daily administration for 24 months of DDS and RMP in the same doses as for paucibacillary with a daily supplement of 100 mg of clofazimine (CLO) during the first 12 months and of 5 mg per kg ethionamide (ETH) for the first 2 months. All the drugs are distributed free of charge every month to the patients, either in the Leprosy Control Unit or in non-specialized Public Health Clinics.

Annual prevalence rates for leprosy were calculated according to the definition given by the WHO Expert Committee in 1988,[4], i.e. taking into account only leprosy patients on treatment. Because of the annual variations in the number of newly-detected leprosy patients, the following epidemiological indicators were calculated on 3-year periods: mean annual detection rates, proportion of multibacillary patients among the total number of cases and the proportion of patients with disabilities[5] of grade $\geqslant 2$.

All data from the medical files of the patients were anonymously entered on the OMSLEP record card and analysed by computer. For statistical analysis, Pearson's χ^2 test and the Spearman test were used.[6] Regression curves were established using a computer statistical package (Chart 3 Microsoft).

Results

PATIENTS ON MDT

Between November 1982 and December 1990, 141 leprosy patients were given multidrug therapy—86 were newly-detected cases and 55 were patients diagnosed before November 1982 and still on dapsone monotherapy (including 2 multibacillary patients who relapsed while on dapsone monotherapy).

PREVALENCE RATE

The number of patients on treatment decreased steadily from 315 in 1967 (prevalence rate 3·20/1,000) to 209 in 1983 (prevalence rate 1·25/1,000)—that is a 61% reduction over 17 years (Table 1). The regression curve plotted on the basis of the 17 annual prevalence rates indicates a significant decrease ($y = -0{\cdot}10\ \chi + 208{\cdot}43$; $r = -0{\cdot}97$; $p < 0{\cdot}001$). After the introduction of MDT into the control programme, the number of patients on treatment decreased from 209 in 1983 to 28 in 1990 (prevalence rate 0·14/1,000)—that is a reduction of more than 89% over 7 years. The regression curve plotted on the basis of the 7 annual prevalence rates indicates a significance decrease ($y = -0{\cdot}17\ \chi + 346{\cdot}12$; $r = -0{\cdot}97$; $p < 0{\cdot}001$).

DETECTION RATES

Between 1967 and 1990, 276 leprosy patients were detected in French Polynesia of whom 107 (38·8%) were multibacillary and 169 paucibacillary; 44 (16%) were less than 15 years old and 232 were 15 years old or more (Table 2 and 3).

As shown in Table 2, the mean annual detection rate for all forms of leprosy was 7·75/100,000 during the 1st 3-year period of the study (1967–1969) and remained roughly stable up to the 7th 3-year period (1985–1987); no significant difference ($r = 0{\cdot}10$, $p > 0{\cdot}05$) could be demonstrated between the 7 detection rates. During the 8th 3-year period of the study (1988–1990), the mean annual detection rate fell to 3·46/100,000 and was significantly lower ($p < 0{\cdot}01$) than those of the previous period.

According to the type of leprosy, the mean annual detection rate for multibacillary leprosy remained roughly stable between the 1st and 6th 3-year period of the study, and

Table 2. Mean annual detection rates for leprosy according to type by 3-year periods between 1967 and 1990

	Total		Paucibacillary		Multibacillary	
3-year periods	No.	Rates*	No.	Rates*	No.	Rates*
1967–69	24	7·75	15	4·84	9	2·90
1970–72	30	8·53	15	4·26	15	4·26
1973–75	37	9·67	22	5·75	15	3·92
1976–78	37	8·94	21	5·07	16	3·86
1979–81	37	8·11	22	4·82	15	3·28
1982–84	46	9·19	29	5·79	17	3·39
1985–87	44	8·06	33	6·04	11	2·01
1988–90	21	3·63	12	1·9	9	1·39
Total	276	—	169	—	107	—

* Per 100,000 inhabitants.

Table 3. Mean annual detection rates for leprosy according to age by 3-year periods between 1967 and 1990

	Total		< 15 Years old		⩾15 Years old	
3-year periods	No.	Rates*	No.	Rates*	No.	Rates*
1967–69	24	7·75	3	2·22	21	12·00
1970–72	30	8·53	5	3·21	25	12·77
1973–75	37	9·67	8	4·83	29	13·34
1976–78	37	8·94	4	2·30	33	13·72
1979–81	37	8·11	1	0·55	36	13·10
1982–84	46	9·19	6	3·14	40	12·92
1985–87	44	8·06	14	6·75	30	8·86
1988–90	21	3·63	3	1·45	18	4·80
Total	276	—	44	—	232	—

* Per 100,000 inhabitants.

subsequently decreased to 2·01 in 1985–87, and reached 1·39/100,000 in 1988–90 (Table 2). No significant difference could be demonstrated between the first 7 mean annual detection rates ($r = -0{\cdot}10$, $p > 0{\cdot}05$); conversely, the 1·39 mean annual detection rate during the 3-year period 1988–90 was significantly lower ($p < 0{\cdot}05$) than the mean detection rate over the previous 7 3-year periods (3·32/100,000). Similarly, annual mean detection rates for paucibacillary leprosy remained roughly stable during the first 7 3-year periods of the study ($p > 0{\cdot}05$) and decreased suddenly during the last period to reach 1·9/100,000, significantly lower ($p < 0{\cdot}001$) than the mean detecton rate over the previous 7 3-year periods (5·32/100,000).

According to age, the mean annual detection rates for leprosy patients 15 years old or more remained stable during the first 6 3-year periods of the study ($r = 0{\cdot}49$, $p > 0{\cdot}05$) then decreased to 8·86/100,000 in 1985–87 to reach 4·80/100,000 in 1988–90 (Table 3). Both these last 2 mean annual detection rates (8·86 and 4·80/100,000) were significantly lower ($p < 0{\cdot}05$ and $p < 0{\cdot}001$) than the mean annual detection rate (13·03/100,000) over the previous 6 3-year periods. Conversely, no significant difference could be evidenced ($p > 0{\cdot}05$) between the 8 mean annual detection rates for leprosy patients less than 15 years.

PROPORTION OF MULTIBACILLARY PATIENTS AMONG NEWLY DETECTED CASES

During the 8 3-year periods of the study, the proportion of multibacillary patients among the newly detected patients ranged from 25 to 50%. No significant decrease ($p > 0{\cdot}05$) of that proportion occurred between the 1st and 8th 3-year periods (Table 4).

PROPORTION OF PATIENTS WITH DISABILITIES OF GRADE $\geqslant 2$ AT DETECTION

During the first 5 3-year periods of the study (1967–81), the proportion of patients with disabilities of grade $\geqslant 2$ among newly detected patients remained stable, ranging from 29·2% to 32·6% (Table 5), average value 31·5%. By contrast, it was on average 11·7% during the last 3-year periods of the study (1982–90), significantly lower ($p < 0{\cdot}01$) than during the preceding period.

Table 4. Proportion of multibacillary patients among newly-detected cases by 3-year periods between 1967 and 1990

	Total		Paucibacillary		Multibacillary	
3-year periods	No.	%	No.	%	No.	%
1967–69	24	100	15	62·5	9	37·5
1970–72	30	100	15	50	15	50
1973–75	37	100	22	59·5	15	40·5
1976–78	37	100	21	56·7	16	43·3
1979–81	37	100	22	59·5	15	40·5
1982–84	46	100	29	63	17	37
1985–87	44	100	33	75	11	25
1988–90	21	100	12	55	9	45
Total	276	100	169	61·2	107	38·8

Table 5. Proportion of patients with disabilities at detection by 3-year periods between 1967 and 1990

3-year periods	Total newly detected	Newly detected cases with disabilities	
		No	%
1967–69	24	7	29·27
1970–72	30	10	33·33
1973–75	37	11	29·72
1976–78	37	12	32·43
1979–81	37	12	32·43
1982–84	46	7	15·21
1985–87	44	3	6·81
1988–90	21	3	14·3
Total	276	65	23·6

Discussion

The main finding of this study is that, in French Polynesia, a clear-cut decrease of leprosy prevalence and mean annual detection rates has been observed in the 3-year period 1988–90. There was also a decrease in the proportion of newly-detected cases with disabilities. However no significant decrease occurred in the detection rate among children less than 15 years old. The crucial question is to determine if such findings are related to the implementation of MDT from 1982.

A gradual decline in the prevalence rate was observed between 1967 and 1983, before the implementation of MDT into the control programme, but this decline was much more marked in the years after this, obviously because of the increasing number of patients who were released from the active file on completion of treatment. More important, from the epidemiological point of view, is the reduction in the detection rates. Following the introduction of MDT into any control programme, a decline in new-case detection is only expected after 5 years;[7] this was effectively observed in the current study. The fact that such a decline was observed in all specific detection rates except in that for leprosy in children less than 15 years old is not surprising. Active case-finding, which is only performed in household contacts in French Polynesia, has been more intensive in the years following the introduction of MDT, which has resulted in an increase in the number of new cases among children. As a matter of fact, this number was 14 (of which 11 were detected among household contacts) over the period 1985–87, approximately twice as high during this period as during the 6 preceding 3-year periods. Similarly, intensive active case-finding should permit the detection of new cases at an earlier stage of the disease, thus resulting in a decrease of the proportion of patients with disabilities at detection; this was also noted in the present study.

When assessing the decrease in detection rates for leprosy, it might be questioned if it reflects an improvement of the leprosy situation due to the implementation of MDT or whether it is caused by other possible influencing factors, such as a change in the control programme efforts, the economic improvement of the country and the natural decline of

the disease. Since detection rates remained stable during the period 1967–87, that is over 21 years, one is led to assume that the subsequent decrease observed after 1987 is more likely to be due to other causes than natural evolution. Moreover, even in the case of natural decline, it is known that the decrease in detection rates, which has effectively been observed in some countries before MDT was introduced, has been very gradual.[8] With respect to the organization of the Leprosy Control Unit, no change occurred during the past 24 years except for the implementation of MDT, which has resulted in intensifying active case-finding and in improving the management and follow-up of patients, newly-detected as well as 'old' ones still on dapsone monotherapy and who were put on multidrug therapy on request. The only other factor which could have possibly influenced the evolution of the disease might be the economic improvement which started in the early 1960s in French Polynesia.[9] Nevertheless, if such a factor has to be taken into account, again, one would expect a faster improvement in the leprosy situation: in the present study the improvement began to be noted only after 25 years. Also, the rapid decrease in detection rates observed between 1988 and 1990 does not fit well with the possible long-term effect of economic improvement; such a result is much more consistent with the conclusions of theoretical calculations on what is expected from the implementation of MDT.[7] Finally, the small number of cases detected over the whole study-period might be considered to represent a possible limitation in the intepretation of our findings. In fact, precisely because detection rates for leprosy were already low before MDT was implemented, it may be assumed that any significant decrease should be more difficult to prove and, if proved, that decrease should be considered even more significant.

From the results reported here it may be suggested that, together with the improvement of the economic situation of the country, the implementation of MDT has resulted in French Polynesia in a decrease of detection rates for leprosy, which may be a consequence of a decrease in transmission of the disease. This finding, and the fact that, to date, the relapse rate was nil in the Polynesian patients put on MDT,[10] strengthens the hope that total control of leprosy might be obtained through MDT in the next decade(s).

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La lèpre en Polynésie Française. Impact possible d'une thérapeutique multidrogue sur les tendances épidémiologiques

J-L Cartel, A Spiegel, L Nguyen Ngoc, J-P Moulia-Pelat, P M V Martin et J-H Grosset

Résumé En 1982, suivant les recommandations d'un groupe d'étude du WHO, la thérapeutique multidrogue (MDT) a été introduite en Polynésie française pour traiter tous les patients souffrant de lèpre évolutive, et, à leur demande seulement, les patients recevant encore un traitement par la dapsone. Cinq ans après, on a observé un abaissement net des taux de fréquence et de détection annuelle moyenne des cas de lèpre (excepté les taux de détection chez les enfants de moins de 15 ans, beaucoup de ces étant décelés tôt grâce à une meilleure formation des contacts de l'entourage). On a constaté également une réduction dans la proportion des nouveaux cas présentant des infirmités. Au cours des 21 années précédant l'introduction de MDT dans le programme de contrôle, les taux annuels moyens de détection de la lèpre étaient restés stables, et ceci amène à penser qu'une telle réduction n'est dûe ni à un déclin naturel de la maladie, ni à l'amélioration de l'économie du pays. Nos résultats, en plus du fait que, jusqu'à présent, le taux de rechutes a été nul chez les patients polynésiens traités au MDT, suggèrent fortement que l'introduction de MDT a abouti à un abaissement des taux de détection de la lèpre qui peut être la conséquence d'une réduction dans la transmission de la maladie.

La lepra en la Polinesia Francesa. El impacto que puede tener la terapia multidroga sobre las tendencias epidemiologicas

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Resumen En 1982, a consecuencia de las recomendaciones del grupo de estudio de la OMS, se introdujo el uso de la terapia multidroga (TMD) a la Polinesia Francesa para el tratamiento de todos los pacientes que sufrían de lepra activa, y (sobre pedido solamente) de aquellos que continuaban con monoterapia con dapsona. Se observó una reducción muy marcada de la frecuencia y del promedio anual de detección, de la lepra (excepto en el caso de la detección en los niños con menos de 15 años de edad, frecuentemente realizada temprano por un aumento de entrenamiento por medio de contacto familial directo). Durante el período de 21 años antes de la introducción de la TMD al programa de control, el promedio anual del nivel de detección de la lepra ha permanecido estable y ésto nos ha hecho creer que tal reducción se debe ni a una disminución natural de la enfermedad ni a mejoras económicas del país. Neustros resultados, en conjunto con el hecho que hasta ahora la tasa de relapso fue nula en los pacientes polinesios con TMD, sugieren marcadamente que la implementación de TMD ha resultado en una reducción de los nivales de detección de la lepra, que puede ser una consecuencie de una reducción de la transmisión de la enfermedad.

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The allocation of leprosy patients into paucibacillary and multibacillary groups for multidrug therapy, taking into account the number of body areas affected by skin, or skin and nerve lesions

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Summary In Nepal, the setting up and maintaining of reliable services for slit-skin smears has proven difficult. A clinical classification system for leprosy has therefore been developed to assist in the allocation of patients to either paucibacillary or multibacillary groups for the purposes of multiple drug therapy (MDT), using 9 body areas: head (1), arms (2), legs (2), trunk (4). Patients with more than two areas of the body affected are grouped as multibacillary (MB) and those with only one or two areas affected are paucibacillary (PB). Using a computer simulation model and the data of 53 patients registered at Green Pastures Hospital (GPH) in Pokhara and 703 field patients from the Western Region, different clinical classification systems were evaluated with regard to their sensitivity, specificity, and predictive value for MB or PB classification, as compared with the histological classification for the GPH cases and the bacteriological classification for the field patients. The sensitivity and specificity of the body area system in present use were 93% and 39%, respectively. The low specificity is due to MB overclassification. The sensitivity of the WHO classification system without skin smear facilities is 73% (the difference with the body area system is significant: $p < 0{\cdot}05$, McNemar's test). Our histology findings confirm previous publications indicating that, while some borderline–tuberculoid (BT) patients may outwardly have a 'PB appearance' and be skin-smear negative, their nerve biopsy and sometimes skin biopsy may show a 'MB' picture. This is the first publication discussing a 'body area system' for the purpose described, including diagrams of the areas used. In Nepal it has proved easy to use and teach and its use may be justified in other control programmes which implement MDT, particularly if slit-skin smear services are unreliable or nonexistant.

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Introduction

Leprosy control in Nepal has peculiar difficulties—mountainous terrain, long distances between treatment centres and patients, poorly developed communications and limited financial resources. It was noticed several years ago that in Nepal a considerable proportion of ostensibly borderline–tuberculoid patients have a 'BT' appearance, are skin-smear negative, but have widespread skin and nerve lesions and therefore give a 'multibacillary impression' (see case reports below). Partly because of these considerations, but also because of the difficulty of establishing and maintaining reliable slit-skin smear services, the International Nepal Fellowship (INF)/German Leprosy Relief Association (DAHW) supported Leprosy Control Project (LCP) in the Western and Mid-Western Regions of Nepal and the Netherlands Leprosy Relief Association (NSL) supported Eastern Leprosy Control Project (ELCP) accepted the policy in 1986[1] of allocating patients to either paucibacillary (PB) or multibacillary (MB) World Health Organization (WHO) treatment regimens,[2] taking account of the number of body areas involved by skin lesions, skin and nerve lesions, or any type of secondary damage attributable to leprosy. A number of recent publications have stressed the need for a simple and reliable classification system that is based on clinical parameters,[3–7] as opposed to a system which depends on the availability of a reliable skin-smear service.

This paper describes experience with the use of this system during the past 5 years in two different centres in Nepal and discusses its possible value in relation to other systems which have the same objective, but which are based on counts of the number of skin, or skin and nerve lesions. The effects on different parameters of increasing or decreasing the number of body areas as a cut-off point for MB classification are also discussed.

Methods

CASE SELECTION

Case-finding in both projects is based on voluntary presentation, encouraged by multimedia health education. The average disability proportion (at least WHO grade 2)[8] among new cases in the Western Region is 22%,[9] so there is still a considerable case-finding delay with many patients. The diagnosis 'leprosy' is based on finding either acid-fast bacilli in the slit-skin smear, a definitely enlarged peripheral nerve trunk or a definitely anaesthetic skin lesion. Despite the operational difficulties, 98% of newly registered cases have skin smears taken,[9] but the result in the field may be delayed for 2–3 months. The quality of the smear taking often leaves much to be desired, despite frequent refresher courses.

Out of 377 patients registering as new cases at Green Pastures Hospital (GPH) in Pokhara between January 1987 and June 1991, 53 consecutive cases were enrolled in the study. Similarly, 703 consecutive cases, newly registered between January 1990 and June 1991 at the Western Regional mobile clinic, were included for analysis. The cases were random in that all GPH patients registered after September 1990 were included whose histology results were already available by August 1991. For the field cases all new registrations with skin-smear results were included. Cases for whom the body area score was not available were excluded from the analysis.

CLASSIFICATION

In 1985, the INF published a Manual for the Implementation of Multidrug Therapy in the Leprosy Control Programme of Nepal.[1] It included the proposal that the allocation of patients to PB or MB groups, for the purpose of MDT, could be based on a count of the number of body areas involved by skin, or skin and nerve lesions. Between the different agencies operating in leprosy control in Nepal there has been some variation in the application of this system in practice, notably with regard to the precise demarcation of the body areas. The INF LCP in the West have used a total of 9, while in the East the ELCP used a total of 7. The diagrams in Figure 1 represent a consensus view of what has been used, for the head, arms, legs and trunk. In the ELCP the trunk is only divided into back and front, there being 2 areas less. It was advised that any patient with skin, or skin and nerve lesions on more than two areas of the body should be grouped as MB for the purpose of MDT. Thus any patients with only one or two areas involved would be grouped as PB. The precise definition of 'nerve lesions' or 'nerve involvement' has proved

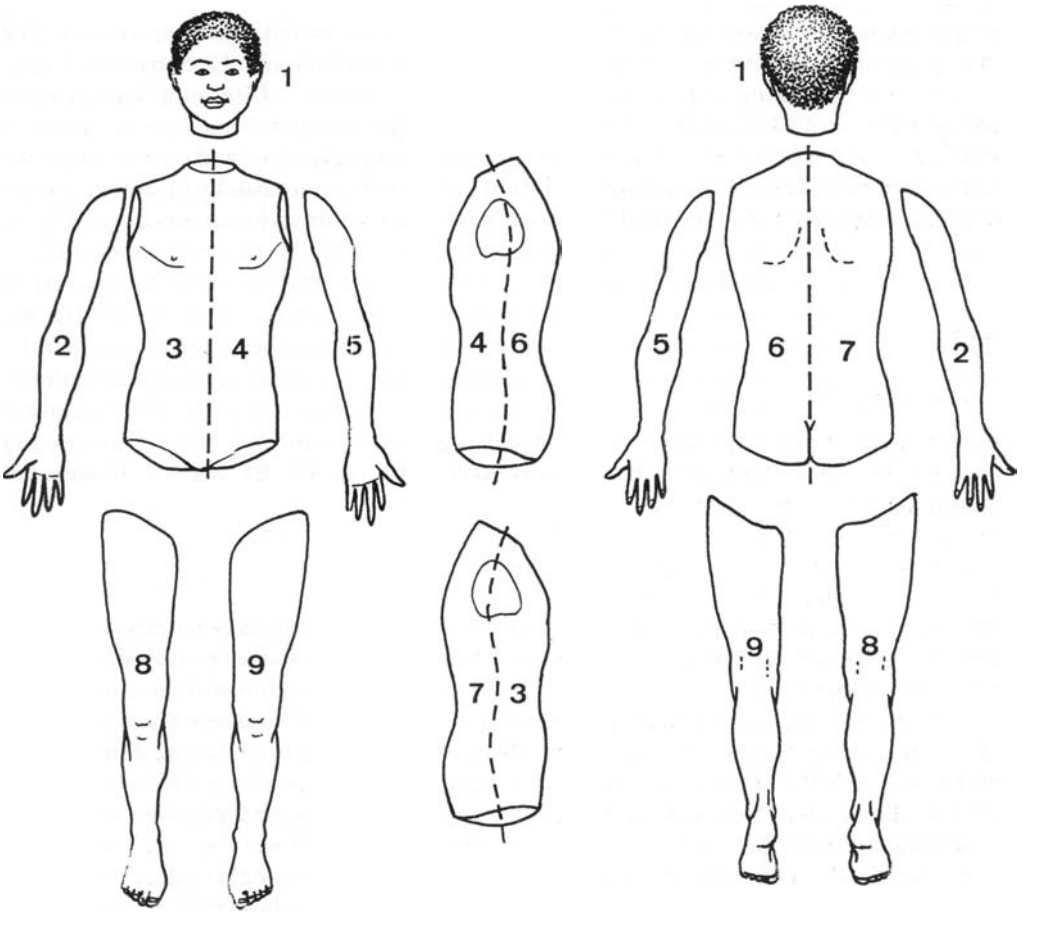

Figure 1.

somewhat difficult, but our policy has been to accept sensory and/or motor defects due to lesions of the facial, ulnar, radial, median, lateral popliteal, posterior tibial, sural and superficial peroneal nerves as being due to leprosy, especially if associated with typical skin lesions. Patients with nerve defects only are routinely referred to a supervisor and if necessary to a medical officer. The staff are trained in the recognition of deformity due to conditions other than leprosy, such as poliomyelitis, birth injury and trauma. In practice the term 'nerve involvement' has included claw hand, drop foot, lagophthalmos, absorption of the extremities, and ulceration of the hand or foot.

In addition to this system, the Ridley–Jopling classification[10] was also used, looking at clinical appearance and skin-smear results for the final classification. The clinical appearance was assessed using a classification chart as described by Jopling.[11] Correlation of the clinical and histological classification was found to be good ($r = 0{\cdot}72$, see Table 7). All newly registered cases had skin smears taken from 3 routine sites (earlobe, elbow and knee) and from one or two of the most active looking skin lesions. All the skin smears of the cases described below were processed and read at the same reference laboratory at GPH in Pokhara. Since September 1990 all newly registered cases at GPH have also had a skin biopsy taken from an active looking skin lesion and/or a nerve biopsy taken from, when possible, an enlarged sensory nerve (usually one of the radial cutaneous nerves). The biopsy specimens were fixed in FMA and sent to a histopathologist (Dr Sebastian Lucas, London) for processing and reading. Along with the specimen, information was also sent on the clinical classification, appearance of the lesions biopsied and the presence or absence of any leprosy reactions. When the clinical classification and a skin smear or histology result were not in agreement, the clinical classification usually prevailed, unless the BI or histology result revealed MB disease while the clinical classification was PB. In that case the final classification was changed to agree with the bacterial index (BI) or histology result. At GPH any positive BI is considered MB, while in the histology a BI of more than 1 and/or a histological classification of BB, BL or LL is taken to be MB. We realize that the definitions of 'MB', particularly the histological one of 'BI more than 1', need further scientific validation, but we accepted them as current working definitions.

The WHO classification referred to in this paper is as described in the 1988 Technical Report Series,[8] namely that skin-smear negative patients with I, TT and BT disease are paucibacillary and patients with a positive skin smear or BB, BL and LL disease are multibacillary.

COMPUTER SIMULATION

An analysis was done using the data of a sub-set of 53 cases newly registered at GPH and 703 patients newly registered in the Western Regional mobile clinic. The number of body areas involved in the disease was recorded and, along with other clinical data, entered into a computer database, using Epi Info software, version 5.01.[12] Classification according to the number of body areas involved in the disease was then simulated, taking different cut-off points for MB classification (BC2 = 2 or more body areas involved, BC3 = 3 or more areas involved, etc.). Also a clinical classification system (CCS) used in India[13] (where the paucibacillary regimen is advised for indeterminate, tuberculoid (TT) and borderline–tuberculoid (BT) cases with less than 10 skin/nerve trunk lesions only) was simulated, as well as the current WHO classification recommendations, using the GPH case data. In the model used, the effects of the absence or availability of skin-smear results could also be

studied among the GPH cases. The MB or PB classifications obtained using the different CCSs were then compared with the histology classification for the GPH cases and the bacteriological classification for the field cases. The latter is based on the current WHO recommendation that all skin-smear positive patients should be treated with MB MDT.[8] Thus the sensitivity, specificity and predictive values for MB and PB classification could be calculated for each of the different classification systems.

STATISTICS

The significance of the difference between the various proportions was tested with McNemar's paired Chi-squared test (Armitage, p. 121).[14] The difference between 2 unpaired sample means was tested using the standardized normal deviate (SND or z-test, Armitage, p. 106).[14] A p-value of less than 5% was used as the level of statistical significance. The correlation coefficient used (Table 8) is as in Armitage, p. 150 ff.[14] Of the most important proportions the 95% confidence interval is given in brackets behind the proportion, e.g. 14% ($\pm$12%) means that there is 95% chance that the proportion actually lies between the values 2% and 26%.

Case reports

CASE NO. 20 (see Table 10)

A 33-year-old male patient had had symptoms of paraesthesia and anaesthesia for 2 years. He had not yet received any treatment. On examination, many (>20) hypopigmented dry macules of varying sizes were found, mainly on his limbs and face. Some were anaesthetic, but not all. Some were well defined and others were not. Both ulnar and lateral popliteal nerves, the left radial cutaneous and posterior tibial nerve and the right greater auricular nerve were enlarged and he already had anaesthetic areas on his hands and feet. His voluntary muscle test (VMT) showed ulnar nerve function loss. There were a total of 9 body areas involved and his disability grade was 2. Skin smears from 4 sites were negative for acid-fast bacilli (AFB). He was classified as MB–BT and put on MB MDT. The biopsies revealed the skin and nerve specimens to be borderline with a skin BI of 3 and a nerve BI of 4.

CASE NO. 28

A 32-year-old male patient came to GPH with symptoms of 3 years duration. He was concerned about the increasing number of patches on his skin. Examination showed many (>20) hypopigmented, mainly large and well-defined, nonanaesthetic macules all over his body. The left ulnar, radial cutaneous, lateral popliteal and superficial peroneal nerves were enlarged. He showed nerve function loss of both ulnar nerves. Nine body areas were involved and his disability grade was 1. The skin smear for AFB was negative at 4 sites but his classification was MB–BT and the patient was started on MB MDT. The result of the skin biopsy was BT with a BI of 2 and the biopsy of the nerve was florid tuberculoid leprosy, but with a BI of 4.

CASE NO. 33

A 31-year-old male patient gave a history of having had symptoms for only 1 month, starting with parasthesia in his right hand. On examination there were fifteen, mostly ill-defined, anaesthetic, hypopigmented macules of different sizes, mainly on the arms, legs and buttocks. Both ulnar, radial cutaneous, lateral popliteal and superficial peroneal nerves were enlarged, as well as the right posterior tibial nerve. There was also nerve function loss of both ulnar nerves and the left lateral popliteal nerve. There were 6 body areas involved and the disability grade was 1. Skin smears for AFB were negative at 4 sites. Our classification according to the body area system was MB–BT and therefore MB MDT was started. The biopsy result of the nerve indicated BT leprosy with a BI = 3·5, while the skin biopsy showed BT disease with no AFB.

CASE NO. 38

A 36-year-old male patient presented mainly for the treatment of a complicated ulcer on his right foot. Although he had already had the disease for 10 years he had not previously received treatment. The clinical examination showed many (>20) hypopigmented, mostly anaesthetic and well-defined macules with a dry and rough surface of differing sizes. Both ulnar, supra orbital and greater auricular nerves were enlarged. His hands and feet were anaesthetic with some shortening of fingers and toes. There were 9 body areas involved and his disability grade was 2. Skin smears for AFB were negative at 5 sites. The classification, according to the body area system, was MB–BT and treatment with MB MDT was started. The biopsy result of the skin indicated BT leprosy with a BI of 2. The nerve biopsy showed mainly fibrous tissue with few nerve fibres. There were no AFB and no specific label was able to be given.

Results

Tables 1 and 2 describe the age and sex distribution of the study cases. Although in all 3 groups the age peak falls in the 30–44 age group, the average age of the field patients is younger than the GPH patients. The male:female ratio is higher in GPH than in the field

Table 1. Age distribution of the study cases

Age group	GP all		GP histology		Field	
	Freq.	%	Freq.	%	Freq.	%
0–14	14	3·7	2	3·8	45	6·4
15–29	72	19·1	6	11·3	162	23·0
30–44	138	36·6	24	45·3	225	32·0
45–59	92	24·4	14	26·4	186	26·5
60–74	54	14·3	7	13·2	74	10·5
75–95	7	1·9	0		11	1·5
Total	377	100·0	53	100·0	703	100·0

Table 2. Sex distribution of study cases

Sex	GP all		GP histology		Field	
	Freq.	%	Freq.	%	Freq.	%
F	111	29·4	19	35·8	259	36·8
M	266	70·6	34	64·2	444	63·2
Total	377	100·0	53	100·0	703	100·0

(2·4 and 1·7 respectively), stressing the fact that field-based health services are more easily accessible for women, than referral centres. Table 3 shows the differential classification of the study cases, according to the Ridley–Jopling classification. No indeterminate cases were registered, but there is a striking difference between the proportion of tuberculoid (TT) cases found in the field (16·5%) and in GPH (0·8%). The lepromatous proportion (borderline–lepromatous and lepromatous or BL–LL) is 27·7% against 43·4% respectively. This emphasizes the general observation that referral centres tend to see a higher proportion of more advanced cases. Table 4 shows the distribution of body areas involved in each of the study groups. There is significant difference ($p < 0{\cdot}001$, SND test for difference between sample means)[14] between the average number of body areas involved in field patients and in GPH patients. This again supports the finding that less advanced cases more readily register for treatment in field clinics.

Tables 1–4 show that the 'histology sub-group' of the GPH cases, although small in number ($n = 53$), is a representative sample of the whole group of GPH cases. Table 5 shows a breakdown of the cases in this sub-group, comparing MB–PB classification according to the different computer simulated clinical classifications with the MB–PB classification found histologically. The results for BT group are shown separately, since this is a significant sub-group (see Table 3), which originally led to the development and implementation of the body area system. Table 6 shows the same among field cases with the outcome of skin smears, where cases with BI = 0 are PB and all others are MB. The results of the calculations of sensitivity, specificity and predictive values of MB–PB are shown in Table 7. Table 8 shows the correlation of the classification of the GPH cases, with the histological classification of the same cases. The correlation of bacteriological index with the clinical (Ridley–Jopling) classification among the field cases is shown in Table 9. Details of the 'BT sub-group' of the GPH cases are given in Table 10.

Figure 1 shows the demarcation of the body areas as used in GPH. Figure 2 shows the cumulative percentage of sensitivity and predictive value of a PB classification for GPH cases. Figure 3 shows the same for the field cases. The specificities of the different CCSs for GPH and field cases are shown in Figure 4.

Table 3. Classification of study cases according to the Ridley–Jopling system

	GP all		GP histology		Field	
Class	Freq.	%	Freq.	%	Freq.	%
TT	3	0·8			116	16·5
BT	192	51·1	26	50·0	305	43·4
BB	8	2·1	1	1·9	26	3·7
BL	124	33·0	19	36·5	112	15·9
LL	39	10·4	3	5·8	83	11·8
NL	9	2·4	3	5·8	61	8·7
NC	1	0·3				
Total	376	100·0	53	100·0	703	100·0

NC, not classified.

Table 4. Distribution of body area involvement in the study cases

	GP all		GP histology		Field	
Body areas	Freq.	%	Freq.	%	Freq.	%
1	44	11·7	6	11·3	139	19·8
2	35	9·3	5	9·4	72	10·2
3	27	7·2	7	13·2	91	12·9
4	24	6·4	1	1·9	95	13·5
5	25	6·6	5	9·4	97	13·8
6	18	4·8	1	1·9	66	9·4
7	37	9·8	2	3·8	47	6·7
8	15	4·0	3	5·7	29	4·1
9	151	40·2	23	43·4	67	9·5
Total	376	100·0	53	100·0	703	100·0
Mean =	6·02		5·98		4·24	
SD =	3·05		3·17		2·54	

Table 5. Comparison of histological classification with different clinical classification systems in 53 patients registered as new cases at Green Pastures Hospital since August 1990

Clinical classification	Histological classification					
	All			BT		
	MB	PB	Total	MB	PB	Total
bc2						
MB	30	17	47	7	15	22
PB	0	6	6	0	5	5
bc3						
MB	28	14	42	7	13	20
PB	2	9	11	0	7	7
bc4						
MB	27	8	35	6	7	13
PB	3	15	18	1	13	14
bc5						
MB	27	7	34	6	6	12
PB	3	16	19	1	14	15
who1						
MB	22	1	23	0	0	0
PB	8	22	30	7	20	27
who						
MB	24	4	28	1	3	4
PB	6	19	25	6	17	23
India						
MB	25	5	30	6	4	10
PB	5	18	23	1	16	17
gp						
MB	30	16	46	7	15	22
PB	0	7	7	0	5	5

bc2, cases with 2 or more body areas involved are classified as 'MB'; bc3, cases with 3 or more body areas involved are classified as 'MB'; bc4, cases with 4 or more body areas involved are classified as 'MB'; bc5, cases with 5 or more body areas involved are classified as 'MB'; who1, WHO-recommended classification criteria,[8] without skin-smear services; who, same, but with skin-smear services; India, Indian CCS: > 10 lesions (skin + nerve) = MB; gp, classification system used in GPH: BC3 + skin-smear services.

Table 6. Comparison of the bacteriological classification with different clinical classification systems in 703 patients registered as new cases since January 1990 in the Western Regional Field Programme (for all cases and BT cases separately)

Clinical classification	Bacteriological classification					
	All			BT		
	MB	PB	Total	MB	PB	Total
bc2						
MB	178	386	564	25	254	279
PB	8	131	139	1	25	26
bc3						
MB	173	319	492	24	232	256
PB	13	198	211	2	47	49
bc4						
MB	164	237	401	23	165	188
PB	22	280	302	3	114	117
bc5						
MB	146	160	306	18	106	124
PB	40	357	397	8	173	181
who1						
MB	150	71	221	0	0	0
PB	36	446	482	26	279	305

bc2–who1: see Table 5.

Discussion

The method described above was used in the assessment of patients in Pokhara with regard to relapses after MDT for leprosy.[15] All 22 relapse cases had more than 2 body areas involved in the disease on initial examination. The fact that many skin-smear negative patients showed clinically extensive disease, especially among BT patients, was also recognized by the WHO Expert Committee in 1988.[8] In GPH, 68% of BT cases show signs of leprosy in more than 2 body areas. These findings, along with the difficulties in

Table 7. Comparison of clinical classification systems with the histological classification for GPH cases and with bacteriological classification for the field cases

	bc2 (%)	bc3 (%)	bc4 (%)	bc5 (%)	who1 (%)	who (%)	india (%)	gp (%)
Sensitivity								
GPH	100	93	90	90	73	80	83	100
BT	100	100	86	86	0	14	86	100
Field	96	93	88	78	81			
Specificity								
GPH	26	39	65	70	96	83	78	30
BT	25	35	65	70	100	85	80	25
Field	25	38	54	69	86			
False negative ratio								
GPH	0	7	10	10	27	20	17	0
BT	0	0	14	14	100	85	14	0
Field	4	7	12	22	19			
False positive ratio								
GPH	74	61	35	30	4	17	22	70
BT	75	65	35	30	0	15	20	75
Field	75	62	46	31	14			
Predictive value MB								
GPH	64	67	77	79	96	86	83	65
BT	32	32	46	50		25	60	32
Field	32	35	41	48	68			
Predictive value PB								
GPH	100	82	83	84	73	76	78	100
BT	100	100	93	93	74	74	94	100
Field	94	94	93	90	93			

bc2–gp, see Table 5. GPH, new cases from Green Pastures Hospital, for whom histology results were available ($n = 53$). BT, BT sub-group of GPH cases ($n = 27$). Field, new cases from the Western Regional Field ($n = 703$).

Table 8. Cross tabulation of clinical classification and histological classification in 53 new cases in Green Pastures Hospital

Clinical classification	Histological classification							
	NO	I	TT	BT	BB	BL	LL	Total
NL	1	0	1	1	0	0	0	3
BT	4	1	3	17	1	1	0	27
BB	0	0	0	0	0	1	0	1
BL	0	0	0	3	1	10	5	19
LL	0	0	0	0	0	0	3	3
Total	5	1	4	21	2	12	8	53

Correlation coefficient (r) = 0·72, $p < 0{\cdot}001$; (95% conf. limits: $0{\cdot}56 < r < 0{\cdot}83$).

NO, No signs of leprosy in the skin and/or nerve biopsy.

NL, neural leprosy (no skin lesions).

Table 9. Cross tabulation of clinical classification with bacteriological index (highest value) for field cases

BI	Clinical classification						Total
	NL	TT	BT	BB	BL	LL	
0	54	113	279	19	36	16	517
1	3	3	10	4	3	1	24
2	3	0	2	2	9	2	18
3	1	0	6	0	18	7	32
4	0	0	4	1	28	18	51
5	0	0	4	0	17	27	48
6	0	0	0	0	1	12	13
Total	61	116	305	26	112	83	703

NL, neural leprosy.

Table 10. Details of the BT cases in the GPH histology group

Pt No.	Age	Sex	Class	BI	Body areas	Skin hist. class.	Skin BI	Nerve hist. class.	Nerve BI	Hist. MB/PB Class	BC3	GP
1?	36	F	BT	0	3	BT	.	.	.	PB	MB	MB
2*	50	M	BT	1	9	.	.	NO	.	PB	MB	MB
3	27	M	BT	0	1	BT	0	NO	.	PB	PB	PB
5?	60	M	BT	0	5	.	.	NO	.	PB	MB	MB
6?	36	F	BT	0	3	NO	.	NO	.	PB	MB	MB
8*	50	F	BT	3	2	BT	0	.	.	PB	PB	MB
11*	37	M	BT	1	2	BT	1	.	.	PB	PB	MB
14†	39	F	BT	0	9	BT	2	NO	.	MB	MB	MB
17?	56	M	BT	0	9	BT	1	NO	0	PB	MB	MB
20†	33	M	BT	0	9	BB	3	BB	4	MB	MB	MB
22?	68	M	BT	0	5	NO	.	.	.	PB	MB	MB
28†	32	M	BT	0	9	BT	2	BT	4	MB	MB	MB
30*	27	M	BT	2	3	BT	2	.	.	MB	MB	MB
33†	31	M	BT	0	6	BT	0	BT	4	MB	MB	MB
34?	55	M	BT	0	5	TT	0	BT	1	PB	MB	MB
37	27	F	BT	0	1	NO	.	BT	0	PB	PB	PB
38†	36	M	BT	0	9	BT	2	NO	0	MB	MB	MB
39?	41	F	BT	0	4	TT	0	NO	.	PB	MB	MB
41	9	M	BT	0	1	TT	0	NO	.	PB	PB	PB
43†	60	M	BT	0	8	BT	1	BL	4	MB	MB	MB
44?	55	F	BT	0	3	BT	1	NO	0	PB	MB	MB
46?	36	M	BT	0	9	.	.	BT	0	PB	MB	MB
49	51	M	BT	0	1	BT	0	NO	0	PB	PB	PB
50?	51	M	BT	0	3	I	0	NO	0	PB	MB	MB
51	55	M	BT	0	1	TT	0	NO	0	PB	PB	PB
52?	57	M	BT	0	3	BT	0	NO	0	PB	MB	MB
53?	55	F	BT	0	3	BT	1	NO	0	PB	MB	MB

* Would have been misclassified as PB in the absence of skin smears (15%).
† Would have been misclassified as PB without the body area system (22%).
? Possibly overclassified as MB (37%).
BI, bacteriological index of the skin smear (highest reading); skin BI, bacteriological index of the skin biopsy; nerve BI, bacteriological index of the nerve biopsy; GP, final classification at GPH, taking into account the BC3 system + the skin-smear result.

obtaining reliable smear results in the field, led to the development of the new criteria for MB classification in Nepal.

In a recent publication[4] Becx-Bleumink describes an elaborate classification system based on a score that takes into account the number and appearance of the skin lesions, as well as the number of nerves that are enlarged. In well-trained hands, this system proved remarkably reliable for correctly classifying patients into PB or MB categories.

Comparison of the system of 9 body areas, as used in Pokhara, with the 7 body area system used in Biratnager, showed no significant difference in the final MB/PB classification between the two groups. As shown earlier in Table 7, the choice of the cut-off point for MB classification considerably affects the sensitivity and specificity of the system.

The following considerations may be important in deciding which criteria for MB classification to use:

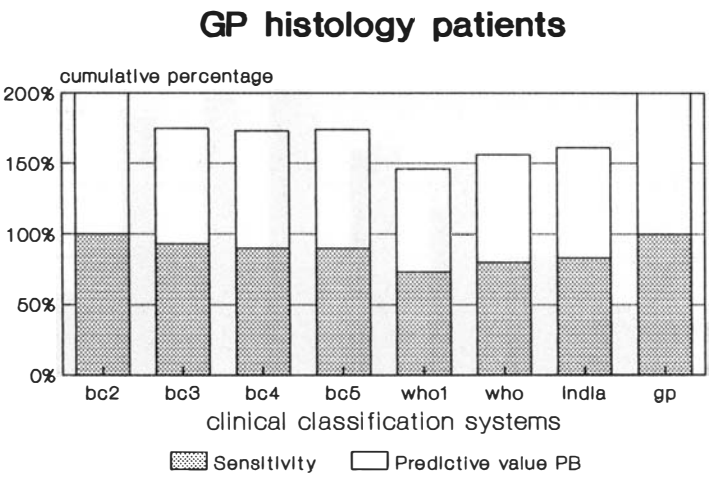

Figure 2. $n = 53$. bc2, cases with 2 or more body areas involved are classified as 'MB'; bc3, cases with 3 or more body areas involved are classified as 'MB'; bc4, cases with 4 or more body areas involved are classified as 'MB'; bc5, cases with 5 or more body areas involved are classified as 'MB'; who1, WHO-recommended classification criteria,[8] without skin-smear services; who, same, but with skin-smear services; india, Indian CCS: > 10 lesions (skin + nerve) = MB; gp, classification system used in GPH: BC3 + skin-smear services.

1 Ability of the system to correctly identify MB cases, minimizing the number of 'false negative cases'. These are the cases classified as PB, which are, in fact, MB. This is represented by the sensitivity and the predictive value of a MB classification.
2 Ability of the system to minimize the number of 'false positive cases', who are classified MB but are in fact, PB. This can be an important economical consideration since false positive cases are treated unnecessarily with MB MDT. This ability is represented by the specificity of the system.
3 Ability of the system to correctly identify PB cases, i.e. the predictive capacity to say that cases diagnosed as PB are in fact PB and not MB. This is represented by the predictive value of a PB classification.

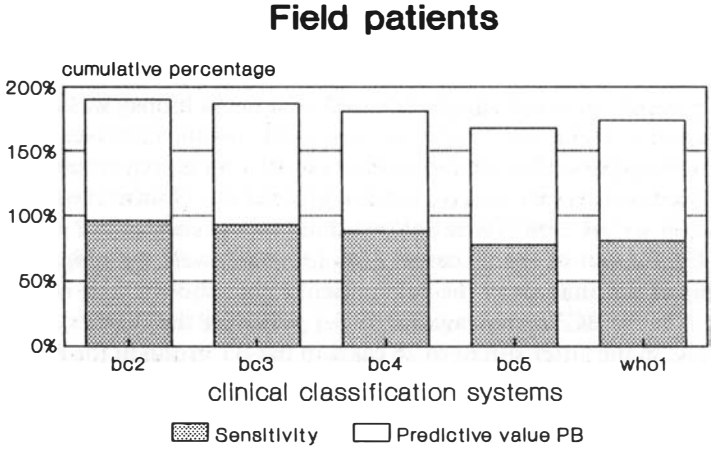

Figure 3. $n = 703$. For MB criteria see Figure 2.

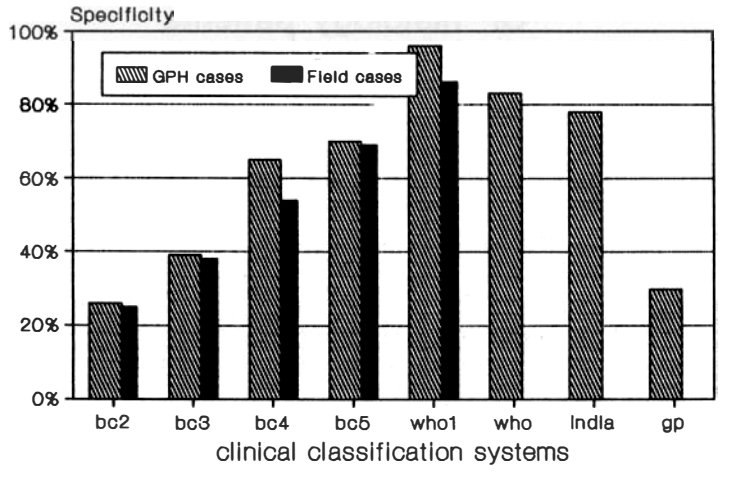

Figure 4. For MB criteria see Figure 2.

Which of the three takes priority may well vary from country to country or project to project. Since the danger of relapse is associated with 1 and 3, we feel that the sensitivity of the system and predictive value of the PB classification should have higher priority than the specificity. Although the relapse rates in trials with reliable skin-smear facilities have been very low,[8] this situation may be quite different under circumstances where skin-smear services are either absent or unreliable. The computer simulation model shows that, using the current WHO classification criteria, the sensitivity drops from 80% to 73% in the absence of skin-smear results. In other words, the proportion of 'false negative cases' increases from 20% (±14%) with skin smears, to 27% (±16%) without skin smears, as shown in Table 7. Among the group of BT patients ($n=27$) in GPH, 7 (26% (±17)) are misclassified as PB using the WHO system in the absence of skin smears. This improves to 22% (±16%) when skin smears are available. For our present body area system (BC3), these proportions are only 4% (±5%) for all patients and 0% for BT patients respectively. The difference in false negative MB proportions between the simulated WHO results and the GPH results is statistically significant ($p<0{\cdot}05$, McNemar's paired chi-square test).

Our results confirm the findings of other authors,[16–19] that in a considerable proportion of patients the classification based on a nerve biopsy was MB, while the skin smear was negative or the skin biopsy showed a PB classification (see Table 10). Typical examples of a discrepancy between skin-smear result and biopsy results are given in the 4 case reports cited earlier. One might question whether our clinical classification 'MB–BT' is not in fact 'BB' or 'BL', but Table 8 shows that this was only so in 2 out of 27 cases (case nos 20 and 43). Six out of the 27 cases (22% (±16%)) were histologically 'MB–BT'.

The results of the analysis of the field patient's data show a false negative proportion of 7% (±4%) for the BC3 system against 19% (±6%) for the WHO system without skin-smear facilities. In the latter situation 26 cases in the BT group in the field (8·5% (±3%)) would have been (mis)classified as PB, while in fact their skin smear was positive. Only 2 of those (0·7% (±0·9%)) would have been misclassified using the BC3 system.

Table 9 shows that 71 MB cases (19 BB, 36 BL and 16 LL, which is 32% of all BB, BL

and LL cases), who should have been skin-smear positive, have in fact a negative BI. This may be due to inadequate smear taking techniques, laboratory mistakes (which is unlikely in such numbers, because of regular quality control), or re-registration of old, already treated patients, who were unsatisfied with their previous treatment result. There are indications that the latter may be the most likely explanation. If these cases had either been excluded from the analysis, or had been skin-smear positive, the false positive MB proportions would all have been 6% lower.

These results certainly need verification using data from a larger group of patients, preferably using data of field patients as well as referral centre patients. But there is in our opinion sufficient indication to say that, in the absence of reliable skin-smear services, that use of the present WHO criteria for MB classifcation may not be 'safe' enough. We realize, of course, that they were never intended to be used without skin smear facilities, but the difficulty of establishing good skin-smear services has nowadays been widely recognized.[4–7] It is our experience in the field programme that the weakest link lies with the smear taker, rather than with the laboratory. Despite repeated efforts to improve the quality of smear taking, the results have generally remained poor.

The weakness of the body area system compared to, for instance, the score system introduced in Ethiopia by Becx-Bleumink[4] clearly lies in the high proportion of cases that are over-classified as MB (10·5% in the Ethiopian score system against 61% for the BC3 system). It does seem necessary to develop the body area system further to increase its specificity. But it should be noted that the Ethiopian results are based on skin-smear results and not on histology. Nilsen *et al.*,[16] also in Ethiopia, reported that 8 out of 44 (18%) patients with leprosy whom they studied, showed a PB histology picture in the skin, while the nerve histology revealed a BI thought to be compatible with MB leprosy. It might therefore be that the false negative proportion of the Ethiopian system is much higher in reality, than the reported 4·9%. Becx-Bleumink considers classification should be done by leprosy supervisors, we agree that this is desirable, but it is not feasible if we consider integrated leprosy control such as in Nepal, where diagnosis and classification will often have to be done by general health staff. We therefore need a system which is easy to teach and use and which in relatively inexperienced hands will produce MB overclassification rather than underclassification.

Counts of lesions have been used extensively in the Indian National Leprosy Eradication Programme.[13] All active BT cases with more than 10 lesions receive the multibacillary regimen. In the computer model this system produces considerably fewer 'false positive cases' than the body area system (22% ($\pm$17%) against 61% ($\pm$20%) respectively), but the 'false negative proportion' is much higher, particularly in the BT group (17% ($\pm$13%) against 7% ($\pm$9%) for all cases; 14% ($\pm$26%) against 0% for BT cases—see Table 7).

In Pakistan[20] the PB regimen is only given to TT cases, with 1–5 lesions, including skin and nerve lesions and the MB regimen is given to all others.

A recent publication from the Medical Commission of the International Federation of Anti-Leprosy Associations (ILEP)[21] states that reliable skin smears are essential for diagnosis, classification and the allocation of patients to PB or MB groups. However, a recent WHO report[22] has emphasized that multidrug therapy may in fact be started before the establishment of reliable smear services, whilst at the same time advising that they should nevertheless be established as soon as possible.

Where reliable skin-smear facilities are available a decrease in the use of 'routine sites', while including more active skin lesions in the smear taking, could considerably increase the operational value of skin smears.

In clinical classification systems the definition of nerve 'involvement' needs further study, as do variations in the number of lesions currently in use to demarcate pauci-facillary and multibacillary leprosy. Considering additional clinical signs, as used in Ethiopia[4] and Papua New Guinea,[7] may increase the sensitivity and specificity of the system. Safeguards are needed to ensure the availability of expert opinion in cases of doubt, so that no patient is undertreated.

While we have used 3 or more body areas out of a total of 9 as main MB criterium, some may feel that the BC2 system is 'better', since it is even safer in terms of the false negative MB proportion. Increasing the cut-off point to 4 body areas (BC4) decreases the MB overclassification from 61% ($\pm$20%) to 35% ($\pm$19%) (Table 7), but the proportion of false negative MB cases increases from 7% ($\pm$9%) to 10% ($\pm$11%) (not statistically significant, due to the small number of cases). In the BT group the increase is significant (0% to 14% ($\pm$12%), $p < 0{\cdot}05$, McNemar's test). Further increase of the cut-off point shows no advantages. Despite considerable MB overclassification, the body area system described here has worked well in practice and may prove of value in other leprosy control programmes as an aid to the more expedient implementation of multiple drug therapy, particularly if slit-skin smear services are unreliable or nonexistent.

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Répartition des patients lèpreux entre le groupe paucibacillaire et le groupe multibacillaire en vue d'une thérapeutique multi-médicaments, en tenant compte du nombre des parties du corps affectées par des lésions de la peau ou de la peau et des nerfs

W H van Brakel, R de Soldenhoff et A C McDougall

Résumé Au Népal, il s'est révélé difficile d'organiser et de maintenir des services fiables capables de faire des frottis de peau fendue. Un système de classification clinique pour la lèpre a donc été mis au point pour faciliter la répartition des patients entre le groupe paucibacillaire et le groupe multibacillaire en vue d'une thérapeutique multi-médicaments (TMM); 9 parties du corps sont utilisées: tête (1), bras (2), jambes (2); tronc (4). A l'aide d'un modèle de simulation informatisé et des données de 53 patients enregistrés à Green Pasture Hospital (GPH) à Pokhara et de 703 patients externes de la Région Ouest, plusieurs systèmes de classification clinique ont été évalués quant à leur sensibilité, spécificité, et valeur de prédiction pour la classification en MB ou PB, par comparaison avec la classification histologique pour les patients du GPH et la classification bactériologique pour les patients externes. La sensibilité et la spécificité du système par parties du corps utilisé actuellement ont été de 93% et 39% respectivement. La faible spécificité est dûe à une classification excessive en MB. La sensibilité du système de classification de l'OMS, sans service de frottis cutanés est de 73% (la différence avec le système des parties du corps est significative: $p < 0,05$, test de McNemar). Nos observations histologiques confirment les publications antérieures qui indiquent que, tandis que certains cas-limites tuberculoïdes (LT) peuvent de l'extérieur avoir une 'apparence multibacillaire' et être négatif au frottis cutané, la biopsie des nerfs et parfois la biopsie de la peau peut présenter un tableau multibacillaire. Cette communication est la première à discuter du 'système parties du corps' dans l'objectif décrit, avec les diagrammes des parties utilisées. Au Népal, ce système s'est révélé facile à utiliser et à enseigner et son emploi se justifierait dans d'autres programmes de contrôle impliquant une thérapeutique multi-médicaments, en particulier lorsque les services pratiquant les frottis de peau fendue ne sont pas fiables ou n'existent pas.

La asignación de pacientes con lepra a grupos paucibacilares y multibacilares para una terapia multidroga, que toma en cuenta el número de zonas del cuerpo afectadas por lesiones de la piel, o de la piel y nervios

W H van Brakel, R de Soldenhoff y A C McDougall

Resumen En Nepal, el establecimiento y mantenimiento de servicios fiables para espécimenes por incisión de la piel han resultado difíciles. Por lo tanto, se ha desarrollado un sistema de clasificación clínica para la lepra que ayude en la asignación de pacientes a grupos paucibacilares o multibacilares para propósitos de terapia multidroga (TMD), utilizando 9 zonas del cuerpo: cabeza (1), brazos (2), piernas (2), tronco (4). Pacientes con más de dos zonas del cuerpo afectadas se asignan al grupo multibacilar (MB) y los afectados por solamente una o dos zonas se asignan al paucibacilar (PB). Utilizando un modelo de simulación informática y los datos de 53 pacientes registrados en la Green Pastures Hospital (GPH) en Pokhara, y 703 pacientes externos de la Región Occidental, se evaluaron diferentes sistemas de clasificación clínica con respecto a su sensibilidad, especificidad y valor pronóstico para la clasificación MB o PB, comparados con la clasificación histológica de los casos GPH y la clasificación bacteriológica de los pacientes externos. La sensibilidad y especificidad del sistema de superficie de cuerpo que se usa actualmente fueron 93% y 39% respectivamente. La baja especificidad se debe a la sobreclasificación MB. La sensibilidad del sistema de clasificación de la OMS sin facilidades de espécimen de piel es 73% (la diferencia con el sistema de superficie del cuerpo es significativa: $p < 0,05$, prueba de McNemar). Nuestros resultados histologicos confirman publicaciones anteriores que indican que, aunque algunos pacientes Tuberculoides Incierta (BT) pueden tener una 'apariencia externa PB' y ser negativos a la prueba de espécimen de piel, su biopsia de nervios, y a veces la de piel, puede presentar un cuadro 'MB'. Esta es la primera publicación que discute un 'sistema de superficie de cuerpo' para el propósito descrito, incluyendo diagramas de las zonas empleadas. En Nepal, ha resultado fácil usar y enseñar, y se puede justificar su uso en otros programas de control que implementan TMD, especialmente si los servicios para espécimenes por incisión de la piel ha resultado no fiables o si no existen.

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Leprosy control in 7 districts of South Sulawesi, Indonesia, 1986–91

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Summary This paper describes the leprosy control programme in 7 districts of the South Sulawesi Province in Indonesia. This province is reported to have the highest prevalence of leprosy in the country. The programme started in 1986 with re-registration of all patients on the cumulative registers. Strict criteria for admission of patients to MDT were initially applied. In 1990 it appeared that these criteria had been too strict, thus necessitating a second re-registration of patients still on DDS monotherapy. More flexible criteria for admission to MDT led to an increase in MDT coverage from 45% to 78% within 6 months.

By April 1991, 5 years after the start of the programme, the registered prevalence had decreased from 4·4 per 1000 in 1986 to 1·6 per 1000; the coverage with MDT had increased from 6% in 1986 to 78%, and the case detection rate remained stable around 4 per 10,000 after an initial increase at the start of the programme.

The area

South Sulawesi is one of the 27 provinces of the Republic of Indonesia and is subdivided into 21 districts and municipalities. The total population in 1989 was 6,731,224, with 44% of the population under 15 years of age. The area on which this report is based consists of the 7 southern districts of South Sulawesi with a total population of 1,750,112 (Table 1).[1]

The province is mostly mountainous, with some low altitude plateaus in the centre, and a lowland area along the coast, where the majority of the population lives. Most of these coastal people belong to the Buginese or Makassarese tribes, which both have a long tradition of seafaring and trading within and beyond the whole Indonesian archipelago. The provincial capital is Ujung Pandang, Indonesia's fifth largest city, with a population of almost 1 million. The first line of the health services is formed by the Puskesmas or

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Table 1. Size and population of the 7 districts in South Sulawesi

District	Size (km sq)	Population 1989
Gowa	1,883·3	400,272
Takalar	566·5	195,176
Jeneponto	737·6	263,997
Bantaeng	395·8	140,037
Bulukumba	1,154·7	333,371
Sinjai	819·5	184,777
Maros	1,619·1	232,482
Total	7,176·6	1,750,112

Community Health Centre, usually staffed with at least 1 doctor and several paramedical and administrative staff. At present there are 254 Puskesmas in South Sulawesi. Leprosy control is integrated into the general health services, and controlled from the Puskesmas. Technical supervision and guidance is provided by specialized staff from the provincial and district levels. Referral is possible to the district hospitals, or to the specialized leprosy hospital in Ujung Pandang.

The leprosy problem

Random sample surveys conducted in collaboration with the WHO[2] between 1975 and 1979 indicated an estimated leprosy prevalence ranging from 4·2 ($\pm$3·5) to 15·3 ($\pm$2·4) (95% confidence limits) per 1000 inhabitants in the province.[3] This high estimated prevalence, combined with the fact that a considerable proportion of the population, including leprosy patients, travelled all over the Indonesian archipelago, thus spreading the infection to other provinces, made leprosy a public health priority in South Sulawesi. Although from 1982 onwards some MDT had been used in several districts, it was not until 1986 that a systematic approach to leprosy control was adopted using WHO-recommended treatment regimens.[2] Because of the expected size of the problem it was decided to start the programme in the southern part of the province in 7 districts (Gowa, Maros, Takalar, Jeneponto, Bantaeng, Bulukumba and Sinjai), and after the programme had been established apply the same system in the north of the province.

We describe the difficulties encountered, and the results achieved in the leprosy control programme in these 7 districts since its start in 1986.

The situation at the start of the programme and the re-registration

Before 1986 most leprosy-related activities consisted of random sample prevalence surveys, and the training of paramedical workers, both carried out by the National Leprosy Training Centre (NLTC) in Ujung Pandang. Leprosy control mainly consisted of providing DDS to leprosy patients or community leaders in their vicinity for further distribution.

Table 2. Registered leprosy patients, MDT coverage and new patients 1986–91

1 April	On register MB	PB	Total	Prevalence 1,000	MDT (%)	New patients MB	PB	Total	CDR per 10,000
1986	2,613	4,967	7,580	4·4	6	124	322	446	2·6
1987	2,289	3,570	5,859	3·4	13	221	444	665	3·9
1988	2,318	3,260	5,578	3·2	18	315	422	737	4·3
1989	2,714	2,726	5,440	3·1	32	368	394	762	4·4
1990	2,620	1,561	4,181	2·4	45	366	303	669	3·8
1991	2,107	807	2,914	1·6	78	406	315	721	4·0

Cumulative registers, which went back for 15 years or more, were kept in the Community Health Centres. In the beginning of 1986, there were more than 7500 patients on these registers (prevalence 4·4/1,000) (Table 2 and Figure 1).

Before the planned MDT implementation programme could be embarked upon, clearing the cumulative registers was a priority.

Paramedical workers from the health centres, in collaboration with the district and provincial supervisors collected information on all registered patients from the Health Centre, community leaders, and any other possible source.

Wherever possible patients were then visited at home to determine whether they still needed treatment, or could be removed from the registers.

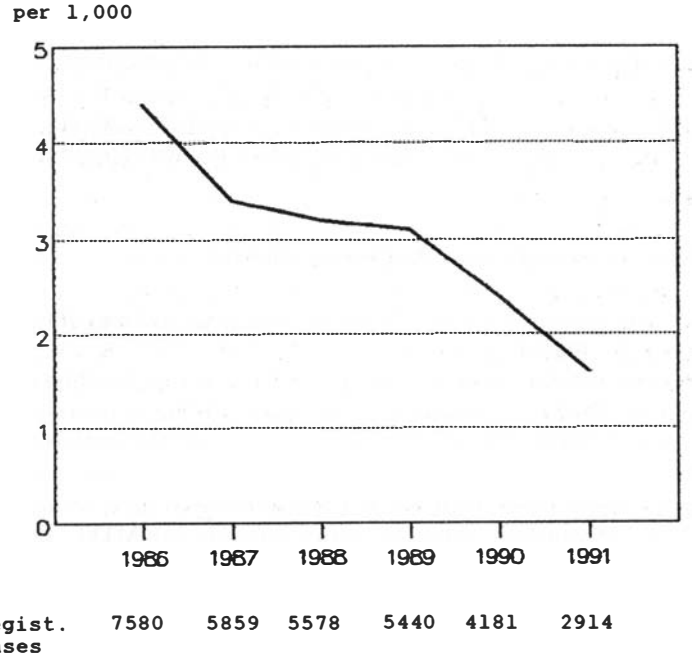

Figure 1. Registered prevalence rate per 1,000. 7 Districts of South Sulawesi, 1986–91.

Table 3. Results of re-registration

		%
RFC*	1,009	13
Died	1,319	17
Moved	441	6
OOC†	1,138	15
Other deductions‡	176	2
Still in need of treatment	3,497	46
Total	7,580	

* RFC, released from control, † OOC, out of control, ‡ other deductions includes wrong diagnosis and double registrations.

It appeared that more than 4000 patients could be struck off the registers for reasons shown in Table 3.

Criteria used to determine whether patients still needed treatment were as follows:

PB patients: all patients with active disease, and all patients who had been treated with DDS monotherapy for a period of less than $3\frac{1}{2}$ years were considered to be in need of treatment.

MB patients: all patients with active disease, all patients with positive skin smears at the time of the re-registration, and all patients who had been treated with DDS monotherapy for a period of less than 10 years were considered to be in need of treatment.

The patients who still needed treatment were started on the WHO recommended MDT, but only if they fulfilled strict conditions for admission to this treatment. These conditions made it essential that patients should come to the Health Centre once per month in order to receive the supervised dose of MDT. If a patient still needed treatment, but was not able to come to the clinic once per month, DDS monotherapy was continued.

The situation after the re-registration had been completed

The re-registration operation proved very time consuming, and was only fully completed in all 7 districts by the beginning of 1989.

However, it soon became clear that the health workers in the Puskesmas, and their supervisors from the district, focused their attention almost exclusively on the patients who were treated with MDT. The patients who did not fulfil the criteria for admission to MDT and had been left on DDS monotherapy were not expected to attend the monthly clinics, and DDS was often provided for several months at a time, as had been common practice before re-registration. Whereas many patients on MDT, due to the short duration of treatment (especially for PB patients), could soon be discharged from treatment, this was not the case for patients who had remained on DDS monotherapy.

As a result, during 1989, it was noticed that despite the fact that by then almost all new patients were started on MDT, the coverage with MDT, calculated as a point prevalence at the end of the year, did not increase much further. Some districts even started to show a

slight decline, when the number of MDT patients released from treatment became larger than the number of new patients started on MDT. The denominator in the equation,

$$\text{MDT coverage} = \frac{\text{Patients on MDT}}{\text{Patients on MDT} + \text{patients on DDS monotherapy}}$$

scarcely decreased, due to the large unchanging number of patients on DDS monotherapy.

If a higher MDT coverage was to be achieved, the treatment of the patients who were left on DDS monotherapy during the re-registration had to be re-assessed.

Much more flexible criteria for the admission to MDT were used this time: from now on disabled or elderly patients were to send a relative or neighbour to collect drugs, and where this was impossible blister–calendar packs were used for periods of unsupervised MDT of up to 3 months. By doing this it proved to be possible to increase the coverage of MDT dramatically from 45% as at 30 September 1990 to 78% just 6 months later, and further it should be noted, the regularity of treatment did not decrease, but remained around 90% (Table 2 and Figure 2.)

Discussion

When the programme started in 1986, it was not the continuation of a well-established DDS monotherapy programme, where merely the treatment schedule had to be changed.

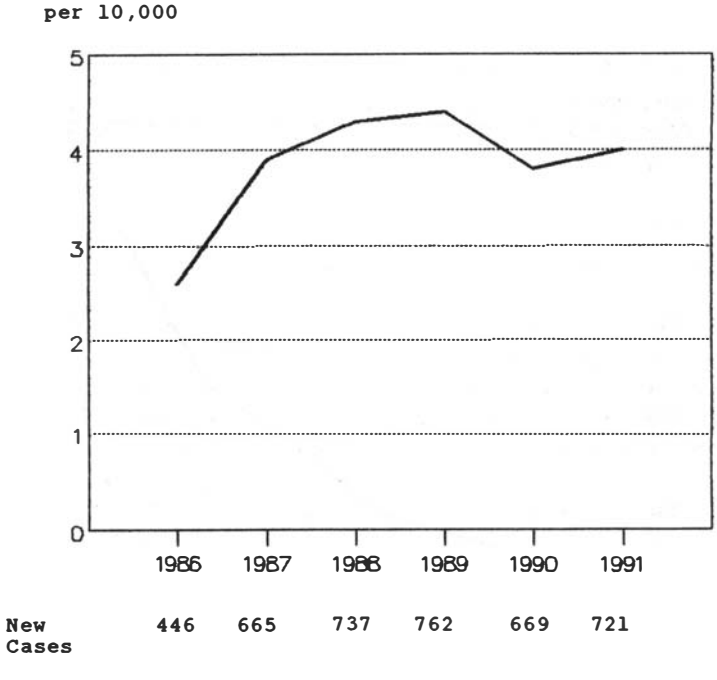

Figure 2. Case detection rate per 10,000. 7 Districts of South Sulawesi, 1986–91.

In fact it was necessary to build up a whole new programme, which may be best illustrated by the fact that more than 4000 patients could be struck off the registers during the re-registration.

It is well documented that the screening of patients before MDT is introduced in a programme leads to a reduction in patient load because many patients can usually be released from control.[4,5] However, in the case of South Sulawesi only 25% of the patients who were removed from the registers were released from control, and the others had already died or simply disappeared.

A welcome 'side-effect' of the operation was that during the re-registration a total of 1457 new patients were encountered. Some of them were household contacts of known patients, others came forward spontaneously, or were reported by fellow villagers.

In 1986, WHO-recommended MDT was still a relatively new treatment scheme, which is why strict criteria for eligibility for MDT treatment were rigidly adhered to. When patients could not come to the Puskesmas once per month they were not started on MDT, thus excluding many elderly and disabled patients, and patients living far away from the clinic. Later it became clear these criteria had been too strict. Re-assessment of patients not yet on MDT was started in 1990, with the aim of providing MDT to all patients still needing treatment. This re-assessment is far less time consuming than the original re-registration, and relatively few patients are being removed from the registers.

A relative disadvantage of changing the treatment scheme from DDS monotherapy to MDT is that a number of disabled patients who had been on DDS monotherapy for a long time, and had expected to continue this treatment for the rest of their lives, are discharged from treatment either during re-registration or after a period of 2 years of MDT. When

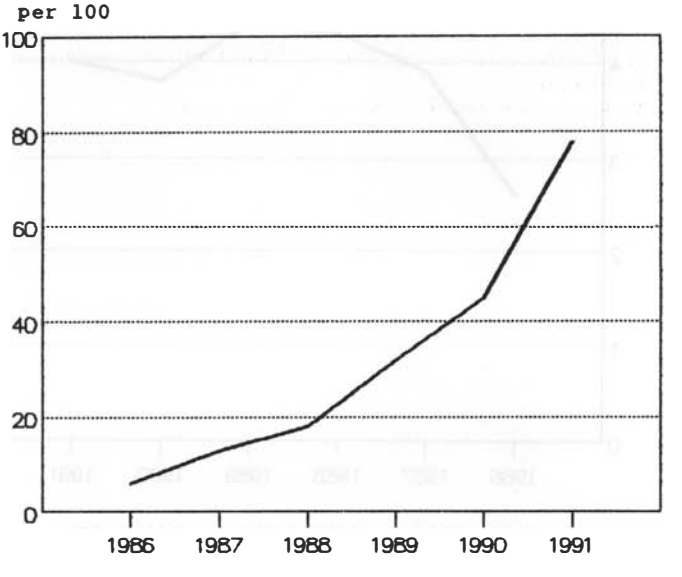

Figure 3. Implementation of MDT. Proportion of registered patients on MDT. 7 Districts of South Sulawesi, 1986–91.

either active surveillance or a 'care after cure' programme do not exist, these patients are at risk of losing whatever little contact with the health service they still had.

The first 5 years of the programme have seen a considerable decline in registered prevalence from 4·4/1,000 in 1986, to 1·6/1,000 in 1991 (Table 2 and Figure 1). The sharp decline in the first year is mainly caused by the re-registration activities, the decline from 1989 onwards can be attributed to the shortening of the duration of MDT treatment as is described for many MDT programmes.[6–8] The case detection rate shows an increase at the start of the programme in 1986, which should be attributed to the increased activities when the MDT programme started (backlog effect). After this initial increase, the case detection rate remains at the same level, and does not yet show a downward trend (Table 2 and Figure 3).

Acknowledgments

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Contrôle de la Lèpre dans sept districts de la province de south Sulawesi, Indonésie, 1986–1991

R Day, P Lever et M Asri

Résumé Cette communication décrit le programme de contrôle de la lèpre dans 7 districts de la Province de South Sulawesi en Indonésie. Cette province est connue comme celle où la fréquence de la lèpre est la plus haute de tout le pays. Le programme a débuté en 1986 avec la ré-inscription de tous les patients sur des registres cumulatifs. Des critères stricts étaient appliqués initialement pour l'admission des patients au MDT. En 1990, il est apparu que ces critères étaient trop stricts, ce qui a nécessité une seconde inscription des patients encore traités par la monothérapie DDS. Des critères plus flexibles pour l'admission à MDT ont abouti à une augmentation de la couverture par MDT de 45% à 78% en 6 mois.

Dès Avril 1991, 5 ans après le début du programme, la fréquence recensée avait diminué de 4,4 pour 1000 en 1986 à 1,6 pour 1000; la couverture par MDT avait augmenté de 6% en 1986 à 78%, et le taux de détection de cas nouveaux était resté stable autour de 4 pour 10,000 après une augmentation initiale au début du programme.

El control de la lepra en 7 distritos de Sulawesi del sur, Indonesia, 1986–1991

R Day, P Lever y M Asri

Resumen Este artículo describe el programa de control de la lepra en 7 distritos de la Provincia de Sulawesi del Sur en Indonesia. Se ha informado que esta provincia tiene el nivel más elevado del país. El programa comenzó en 1986 con la re-registración de todos los pacientes en registros cumulativos. Al comienzo, se aplicaron criterios estrictos antes de usar TMD. En 1990, se consideró que los criterios eran demasiados estrictos, haciendo necesario una segunda re-registración de los pacientes que continuaban con monoterapia DDS. Criterios más flexibles de admisión al TMD resultó en un aumento de aplicación de TMD, de 45% a 78%, en un período de 6 meses.

En abril 1991, 5 años después del comienzo del programa, la frecuencia de registración había bajado de 4,4 por mil en 1986 a 1,6 por mil; el alcance con TMD había aumentado de 6% en 1986 a 78%, y el nivel de detección de casos permaneció estable en un 4% por 10,000 después de un aumento inicial al comienzo del programa.

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Results of surgical procedures for the correction of foot-drop and of lagophthalmus due to leprosy

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Summary Leprosy mutilations of the muscles and skeleton can be relieved by reconstructive surgery, but evaluation of the results of these operations is seldom undertaken. Between 1975 and 1984, 59 leprosy patients were operated on at the Marie Adelaide Leprosy Centre, Karachi, Pakistan, for lagophthalmus with the transposition of the posterior tibial muscle.

We were able to re-examine 39 patients: tibialis posterior transposition was performed 25 times, and temporalis transposition was carried out 33 times; 18 of the 25 patients with the tibialis posterior transposition were pleased with the result, 7 were not: 21 patients could extend their feet above the neutral position; 24 of the patients with the temporalis transposition were satisfied, 9 were not: complete closure was demonstrated in 21 eyes; Persistent corneal damage was noted in 15 eyes; 12 of the 23 male patients cared for themselves, 16 lived with their families; 7 of the 8 female patients lived with their families.

The results of the rehabilitation, in relation to the degree of mutilation, are considered satisfactory for a developing country. These surgical procedures give a good result, provided they are followed by intensive physiotherapy.

Introduction

Since the beginning of the 1950s, the sequelae of leprosy involving the limbs and the face have been corrected by surgical intervention. After a time of euphoria, it was recognized that the permanent loss of sensation endangered the surgical result, or that other

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complications like infection or adhesions jeopardized the operative result.[1-3] Only a few follow-up studies were published.[1,4-6] This paper describes the results of two surgical procedures which were performed on patients with foot-drop and lagophthalmus. Both these complications are caused by the granulomatous damage of peripheral nerves (lateral popliteal and facial nerves) after infiltration by *Mycobacterium leprae* during the course of the disease.

Patients and methods

Every patient who received either a temporalis transposition or tibialis posterior transposition at the Marie Adelaide Leprosy Centre, Karachi, Pakistan between 1975 and 1984 has been included in the study. The principle of tendon transposition is to utilize the action of a muscle which is innervated by another nerve to replace effectively the defective function of another muscle. The procedures were performed in the following manner:

1 *Transposition of the tibialis posterior muscle in foot-drop (TPT)*[7]

Before surgery, the patient must learn to innervate the posterior tibial muscle selectively, i.e. to invert the foot. The ankle joint must be sufficiently mobile. During the operation, the tendon of the posterior tibial muscle is transected as far distally as possible. It is then re-routed above the medial malleolus and around the tibia ('circumtibial route'), or the interosseus membrane is incised and the tendon of the tibialis posterior is pulled anteriorly ('interosseous route'). The tendon is split into two slips and then sutured to the tendons of the anterior tibial muscle medially and the peroneus brevis or tertius laterally, while the foot is resting in a splint in dorsiflexion. Postoperatively, the foot remains in plaster for about 6 weeks.

2 *Transposition of the temporalis muscle in lagophthalmus (TMT), Johnson's method*[8]

The posterior part of the temporalis muscle is identified and the fibres are separated from the tendon. A strip of harvested fascia lata of 10-cm length is split into 2 slips and fixed to the separated part of the temporalis. The fascia slips are passed subcutaneously through both eyelids as close to the edge as possible. Both slips are sutured to the lacrimal ligament at the medial side of the eye. The patient will then close his eye through the action of the temporalis muscle when he is chewing.

In 1986, a clinical examination was done, and the patients were interviewed using the following questionnaire:

Occupation?
What do you live on (earning money, family support, public support)?
Married?
Type of accommodation and family support?
Were you satisfied with the operation? Why or why not?
Post-operative complaints?
Tibialis posterior transposition: ulcers?
Temporalis transposition: epiphora? pain?

In TPT-patients, the foot was inspected for mutilations, ulcers, and signs of regular care. Ulcerations at the tip and the lateral edge of the foot were especially sought for. The patient was asked to lift his foot as far as possible. The gait was observed. Finally, the range of mobility of the ankle joint was measured.

In TMT-patients, the visual acuity was estimated using Landolt's rings or counting fingers. The eyelids were inspected for entropion or ectropion, and the closure of the lids was checked. Corneal lesions were noted. The corneal reflex was checked with cottonwool to get an impression of the involvement of the trigeminal nerve. Epiphora was sought for and asked about.

Results

Out of 59 operated patients 39 were available for follow up. A total of 8 patients had died, and 12 had left the country or could not be located; 8 of them were women (average age 41 years) and 31 were men (average age 47·5 years); 12 of the patients were born within present-day Pakistan, 19 came from India or Bangladesh as refugees, 7 came from Afghanistan and 1 from Iran. In total 25 tibialis posterior transpositions and 33 temporalis transpositions were performed on these patients.

Tibilias posterior transposition

This operation was performed 25 times on 22 patients—21 patients could extend the tip of the foot above the neutral position, 3 could not; 1 foot had been amputated later on (Figure 1).

The gait of 14 patients was good in a normal heel-to-toe manner, 6 of the patients showed some degree of circumduction and 5 had greater difficulties in walking, or did not walk.

The physical findings of the patients who did not have a good result, or were not content with the operation for whatever reason, are given in Table 1.

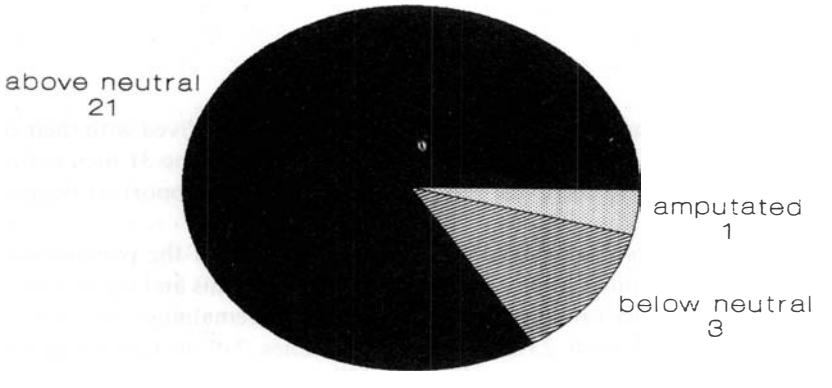

Figure 1. Tibialis posterior transposition—25 had the ability to lift the foot above the neutral position.

Table 1. Tibialis posterior transposition. The physical findings and patients' opinion in cases not classified as a 'good result'

Pathology of the foot	Gait*	ROM†	Patient's opinion	Comment
1 Pes cavus	Bad	30/25/0	Content	Could work No physiotherapy
2 Absorption of toes	Mod.	0/5/10	Content	Less ulcers
3 Absorption of toes	Mod.	0/0/20	Content	No ulcers since operation
4 Absorption of toes	Bad	0/5/25	Content	'Walking better'
5 Absorption of toes	Bad	5/0/15	Content	'Walking better'
6 None	Good	25/0/0	Discontent	'Ulcers healed by healer'
7 Neuropathic ankle	Mod.	15/5/0	Discontent	'Better before'
8 None	—	5/0/15	Discontent	Other foot amputated later
9 Ulcer MTH 1	Mod.	0/0/10	Discontent	Walking tiring
10 Metatarsal absorption	Mod.	0/0/10	Discontent	Recurrent ulcers
11 None	Mod.	0/10/25	Discontent	Worsened again
12 Amputated	—	—	Discontent	Postoperative gangrene

* Classified as good, moderate, bad.

† ROM: range of movement documented with neutral zero method (extension (dorsiflexion)—plantarflexion).

MTH 1: first metatarsal head.

Temporalis transposition

The operation was performed 33 times in 22 patients—21 eyes could be closed completely, 4 eyes showed a gap of 1 mm, when the patient attempted to close the eye. In 3 eyes, a gap of 2 resp. 3 mm remained, and in 2 eyes, a gap of 4 mm (Figure 2).

The vision of 12 eyes was good, 10 had a moderate loss of vision, 7 had severe loss, and 4 eyes were blind. Eyes had not usually been tested preoperation. In total, 19 eyes were anaesthetic, 3 of those showed keratitis, and 7 showed a corneal ulcer or opacity. Of the 14 eyes without corneal anaesthesia, 3 had keratitis and 2 showed a corneal ulcer or opacity.

The physical findings of the eyes of patients not considered to have a good result, or when the patient had any complaints about the success, are given in Table 2.

Social situation

Of the 8 women, 4 were married and lived with their husbands, 3 lived with their relatives or children, and 1 was a beggar living on public support; 13 of the 31 men earned their living, 4 were supported by relatives, and 14 lived on public support as beggars or in leprosy homes (Figure 3).

Excluding the patients from Afghanistan, the proportion of the patients caring for themselves rises from 13 out of 31 to 12 out of 23. The 7 Afghanis and the Iranian did not live with their families, only 1 earned his own living. Of the remaining 31 patients born in Pakistan, India and Bangladesh, 23 lived with their families, 2 of the remaining 8 were not married and without relatives, but earned their own living, 3 were living in a leprosy home, and 3 were beggars. The last mentioned 6 patients were all heavily mutilated.

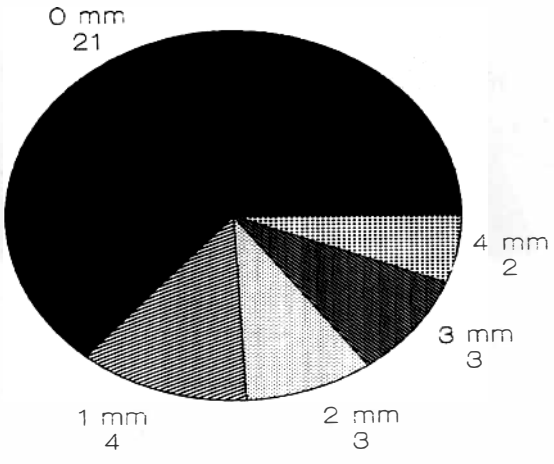

Figure 2. Temporalis transposition—33 had a gap remaining when the eyes are intended to close.

Discussion

TIBIALIS POSTERIOR TRANSPOSITION

Maximal dorsiflexion and the quality of the gait are considered to be the objective criteria for estimating the success of the operation. Selvapandian[9] stated that a degree of dorsiflexion of 15°–300° is desirable. This degree was rarely achieved by the patients in this study. In our opinion, a normal heel-toe-gait without lateral deviation of the foot is possible if the foot can be raised above neutral-zero in patients with a foot without further

Table 2. Temporalis transposition. The physical findings and patients' opinion in cases not classified as a 'good result'

Corneal path	Cornal anaesth.	Gap (mm)	Vision	Complaint	Comment
1 Ulcer	yes	2	0·5		Persisting ulcer
2 —	yes	0	0·5		UL does not open completely
3 —	yes	2	1		Ectropion LL
4 Opacity	yes	0	Blind		No epiphora
5 Keratitis	no	0	0·5		Closing slowly
6 —	yes	0	0·5		Closing slowly
7 Opacity	yes	0	Blind		Closing slowly
8 Ulcer	no	4	<0·05		Less epiphora, ectropion LL
9 —	yes	0	0·5	Epiphora	
10 —	no	0	1	Epiphora	
11 Keratitis	no	1	0·1	'No change'	Ectropion LL
12 Opacity	yes	0	0·05	'No change'	Closing slowly
13 Keratitis	yes	3	0·25	'No change'	Epiphora
14 Opacity	no	2	Blind	Epiphora	
15 Ulcer	yes	4	0·5	'No change'	
16 Ulcer	yes	3	Blind		
17 Ulcer	yes	3	0·05	'No change'	Epiphora

LL, lower lid; UL, upper lid

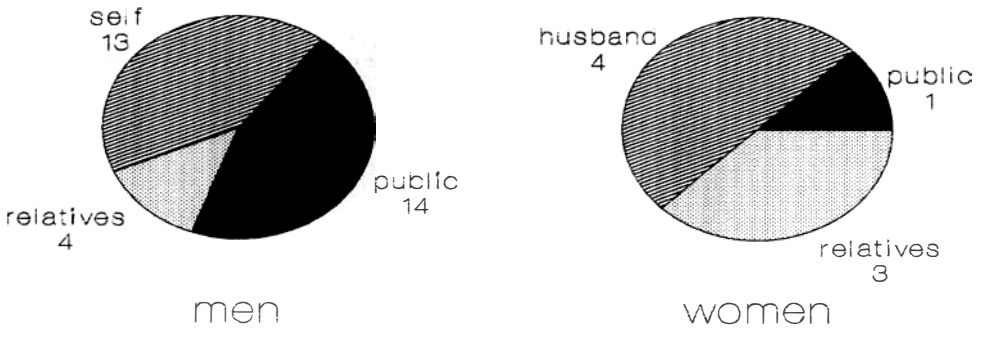

Figure 3. Social situation, the means of living are provided by men ($n=31$) and women ($n=8$).

mutilations. The higher the degree of absorption of the forefoot, the less lifting of the remaining tip is necessary.

The role of physiotherapy cannot be overemphasized. In patients who did not understand the necessity of exercise after surgery the operation proved to be useless. Ulcers will not heal without the correction of the foot-drop, but the operation alone is not sufficient to heal the ulcers themselves. Further education about correct care of anaesthetic feet is necessary.

A neuropathic joint cannot counteract the shortening muscle. An arthrodesis of the ankle joint might be more helpful to the patient.

TEMPORALIS TRANSPOSITION

From a functional point of view, we consider a remaining gap of 2 mm acceptable, as the cornea is moistened by Bell's phenomenon, if the patient closes his eyes frequently enough—28 of the patients achieved this, but 3 of the patients examined closed their eyes very slowly and did not seem to have enough training. Their eyes are certainly more endangered than the eyes with a small gap. Epiphora, which was a common complaint, might be due to infrequent closing of the eyes. Again, physiotherapy and education of the patient must be emphasized.

The amount of persisting damage to the cornea (15/33) is disturbingly high. In retrospect it is hard to decide whether surgery was performed too late, or if there is a need for additional eye protection.

RESULTS OF REHABILITATION

The WHO continues to demand the full professional and social integration of leprosy patients.[10] According to our results, this target would seem difficult to achieve in a developing country. In Pakistan, 31% of the population make up the work force as compared to 45% in Western countries.[11] With this high level of unemployment, chances for a disabled person are especially bad. In this instance, the number of 12 out of 23 male patients earning their own living represents almost the national level of employment. A

better level of employment can only be reached by special efforts and 'protected workshops'.

As some of the patients develop a fixed attitude towards their disability, which prevents them from seeking work, patients should only stay away from work or should be cared for in hospitals for as short a time as is possible ('preventive rehabilitation'[12]).

Due to the continuous education of the public, leprosy patients in Pakistan are no longer driven away by their families: 21 of the 31 patients lived with their families, or had married and started a family of their own.

For both operations, the motivation of the patient cannot be overestimated—4 of the patients with foot-drop and 2 of the patients with lagophthalmus did not perform any physiotherapy after discharge. Provided that exercises are performed both operations give a good result. The level of employment of leprosy patients receiving surgery in this limited study is similar to the national level, thus showing a positive effect on the prevention of dehabilitation or rehabilitation of the patients.

Acknowledgment

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Résultats des modes opératoires dans la correction chirurgicale du fléchissement du pied et de la lagophthalmie dues à la lèpre

M W Weber, A van Soest, G Neff, T Chiang et R Pfau

Résumé La chirurgie réparatrice peut remédier aux mutilations des muscles et due squelette dûes à la lèpre, mais l'évaluation des résultats de ces opérations est rarement entreprise. Entre 1975 et 1984, au Centre pour la Lèpre Marie Adélaide, Karachi, Pakistan, 59 lépreux ont été opérés de lagophthalmie par transposition du muscle temporal ou de fléchissement du pied par transposition du muscle jambier postérieur.

Nous avons pu ré-examiner 39 patients: la transposition du muscle jambier postérieur a été faite 25 fois, et celle du muscle temporal 33 fois. Parmi les 25 patients avec transposition du jambier postérieur, 18 étaient satisfaits du résultat, 7 ne l'étaient pas; l'extension du pied au-dessus de la position neutre était possible chez 21 patients. Parmi les patients avec transposition du temporal, 24 étaient satisfaits, 9 ne l'étaient pas; on a observé la fermeture complète sur 21 yeux et un dommage persistent de la cornée sur 15 yeux. 12 des 23 lépreux se soignaient eux-mêmes, 16 vivaient avec leur famille; 7 des 8 lépreuses vivaient avec leur famille.

Les résultats de la réhabilitation, par rapport au degré de mutilation, sont considérés satisfaisants pour un pays en voie de développement. Ces modes opératoires donnent de bons résultats à condition d'être suivis d'une physiothérapie intensive.

Resultados de intervenciones quirurgicas para la correccion de pie en extension y lagoftalmos debidos a la lepra

M W Weber, A van Soest, G Neff, T Chiang y R Pfau

Resumen Se puede aliviar mutilaciones causadas por lepra de los músculos y del esqueleto por medio de cirugia reconstructora, pero rara vez se efectúa una evaluación de los resultados de tales intervenciones.

Entre 1975 y 1984, 59 pacientes leprosos fueron operados en el Marie Adelaide Leprosy Centre, Karachi, Pakistán, para lagoftalmos, por medio de transposición del músculo temporal; o para pie en extensión, por medio de transposición del músculo tibial posterior.

Nos fue posible reexaminar 39 pacientes: se realizó la transposición tibial 25 veces y la transposición del músculo temporal 33 veces; 18 de los 25 pacientes estaban contentos con el resultado de la transposición del músculo tibial, 7 no estaban contentos: 21 pacientes podían extender los pies por encima de la posición neutra; 24 pacientes estaban satisfechos con la transposición del músculo temporal, 9 no estaban satisfechos. Se observó cierre total en 21 ojos, y daño persistente de la córnea en 15 ojos. 12 de los 23 hombres pacientes se cuidaban ellos mismos. 16 vivían con sus familias; 7 de las 8 mujeres pacientes vivían con sus familias.

Se consideraron satisfactorios los resultados de la rehabilitación en relación al nivel de mutilación, para un país en desarrollo. Estos procedimientos quirúrgicos tienen buenos resultados con tal de que se proporcione una fisioterapia intensa posterior.

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Neuritic leprosy: epidemiology and therapeutic responsiveness

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Summary We studied epidemiology, progression and therapeutic responsiveness in 62 cases of neuritic leprosy. Numbness was the main presenting symptom. Mononeuritis involving the ulnar nerve, followed by the common peroneal nerve was the commonest presentation. The lepromin test was positive in 34 cases while a slit-skin smear was negative in all cases. We treated 20 of these cases with dapsone monotherapy and 5 cases (25%) developed a skin lesion after an average duration of 3 months' treatment. We treated 42 cases with a combination of dapsone and rifampicin, and 3 cases (7%) developed a skin lesion after an average duration of 2–6 months. The subsequent diagnosis in cases developing skin lesions was borderline—lepromatous in 1 case, borderline–tuberculoid in 4 cases, tuberculoid in 2 cases and indeterminate in 1 case.

Introduction

Leprosy is regarded as the commonest cause of severe neuropathy in developing countries.[1] However, neuritic leprosy has always been a controversial subject. Wade[2] introduced a subgroup of polyneuritis in the classification of leprosy and this was accepted at the Madrid conference[3] and also included in the Indian leprologists' classification.[4] Cochrane[5] *et al*. and Noordeen[6] preferred the term neuritic to polyneuritic because many cases present with a mononeuritis. Further confusion arose with the use of the term primary neuritic for cases where nerve involvement was seen without a skin lesion and secondary neuritis for the cases where nerve trunk involvement was secondary to development of a skin lesion. Hansen and Looft[7] considered nerve involvement as secondary to the development of skin lesions while Desikan *et al*.[8] considered leprosy to be neutral in inception. However, such a distinction is no longer maintained and the term neuritic leprosy is used as synonymous with pure/ primary neuritic leprosy. The neuritic group has further been subdivided into tuberculoid, dimorphous and lepromatous subgroups on the basis of the histological findings.[9]

We have tried to evaluate the status of neuritic leprosy by studying the epidemiology, progression and therapeutic responsiveness.

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Materials and methods

In a retrospective study we analysed data of 42 cases of neuritic leprosy amongst male army personnel who had been treated with multidrug therapy—dapsone 100 mg per day and rifampicin 600 mg per month—between 1983 and 1990. For comparison 20 cases of neuritic leprosy treated before 1983 with dapsone monotherapy (100 mg per day) were also included.

Neuritic leprosy was diagnosed if there was anaesthetic skin area, weakness/wasting of muscles, or tingling sensation/neuralgic pain accompanied by nerve trunk thickening. Routinely, a skin biopsy was done before treatment from a maximal anaesthetic area and if histopathological evidence of leprosy was found the case was excluded from the study. Slit-skin smears (SSS) were performed from both ears, buttocks and an anaesthetic area in all cases. A lepromin test (Dharmendra antigen) was also carried out. However, a nerve biopsy was not performed in any of the cases. All these cases were offered institutional antileprosy treatment for 6–12 months. Following treatment patients were observed for 1 to 5 years. A skin biopsy was performed in those cases that developed skin lesions during institutional therapy or thereafter, and these were subsequently classified by the Ridley–Jopling method.

Results

ON MULTIDRUG THERAPY (42 CASES)

A total of 392 paucibacillary cases of leprosy were given institutional treatment at our centre between 1983 and 1990. (Our centre offers institutional treatment to paucibacillary cases only.) These cases were classified as indeterminate—113, tuberculoid—99, borderline–tuberculoid—138, neuritic—42, and the proportion of neuritic cases was 10·7%. The details of complaints at onset in 42 neuritic cases are given in Table 1 and the commonest is numbness. The average delay before seeking medical advice was 3 months after detection by the patient and the average age was 32 years. None of these patients had any family history of leprosy and no regional predeliction was noted. The details of nerve involvement are given in Table 2 (a). SSS for AFB was negative in all cases. The lepromin test was positive in 26 cases and negative in 16. All 42 cases were put on multidrug therapy, and 3 developed skin lesions after an average period of 2·6 months following therapy. The

Table 1. Presenting symptoms in cases of neuritic leprosy treated with multidrug therapy

Initial complaint	No. of cases
Numbness	27
Weakness	22
Wasting	7
Deformity	7
Tingling/Pain	5

Table 2. Details of nerve involvement in cases treated with (a) multidrug therapy, and (b) dapsone monotherapy

Nerves involved	(a) No. of cases treated with MDT	(b) No. of cases treated with dapsone monotherapy
Ulnar	17	9
Radial	2	2
Lateral popliteal	8	6
Medial cutaneous nerves of forearm	2	—
Multiple nerves	13	3

subsequent diagnosis in these 3 cases was 2 cases of borderline–tuberculoid and 1 case of tuberculoid.

ON DAPSONE MONOTHERAPY (20 CASES)

The majority (16) of these cases presented with numbness as the initial complaint. Weakness of hands/feet was noted in 13 cases, muscle wasting in 12 and deformity in 3. The details of nerve involvement are given in Table 2(b). SSS for AFB was negative in all cases. The lepromin test was negative in 8 cases and positive in 12. During surveillance after starting treatment 5 of these 20 cases developed skin lesions which were clinically and histopathologically suggestive of leprosy; the average interval between initiation of therapy and development of skin lesion was 3 months. The subsequent diagnosis in these 5 cases was 1 case of borderline–lepromatous, 2 of borderline–tuberculoid, 1 of tuberculoid, and 1 of indeterminate.

Discussion

Neuritic leprosy, which has been reported in India to be between 5·5%[10] and 17·7%[6] of all leprosy cases, accounted for 10·7% of all paucibacillary cases in the present series. This high incidence justifies its inclusion under a separate independent subgroup in the Indian classification. Although Ridley–Jopling did not include neuritic leprosy as a separate subgroup in their classification they clearly stated that neural leprosy can occur in any kind of spectrum leprosy apart from LL.[11] Mononeuritis is the commonest presentation, and was seen in 74% of the patients. This was also observed by Noordeen[6] and Uplekar & Antia[12] and lends support to the shift of terminology from polyneuritis to neuritis. Like Uplekar & Antia[12] we also found the ulnar nerve to be the commonest involved nerve, followed by the lateral popliteal, while Noordeen[6] observed the lateral popliteal to be commonly involved. Median nerve thickness as mononeuritis was not observed by us while in polyneuritic leprosy it was observed in 3 cases. Radial nerve thickness was generally noted at the wrist, and 25% of our patients on dapsone monotherapy developed skin lesions. This relatively high incidence observed, compared with other reports, may be because in the army the strict periodic medical examination of soldiers facilitates early case detection. Many of these cases would have reported with skin lesions at onset had their disease not been detected at an earlier stage. A case of polyneuritic leprosy who

developed multiple skin lesions after 3 months of monotherapy was diagnosed as borderline–lepromatous leprosy. SSS which were negative earlier subsequently became positive. However, he subsequently showed a good response to therapy. The lepromin test remained negative throughout. Waters *et al.*[13] reported a case with radial nerve thickness, histologically diagnosed on nerve biopsy as borderline–lepromatous leprosy. However, they feel that the skin lesion in this case was missed because of hysterical anaesthesia.

Experimental evidence has suggested the skin[14] as well as the upper respiratory tract[15] to be the routes of entry for *M. leprae*. We feel that entry through the skin produces the mononeuritic type of disease while the respiratory route may be responsible for the polyneuritic type of disease. It has been postulated that after entering through the skin *M. leprae* invades axonoplasmic filaments and only after rupture of the Schwann sheath can the organism burst into the corium of the skin.[3] Therefore the bacillary load in nerves is found to be higher than that observed in the associated skin lesion. However only 3 patients out of 42 (7%) on multidrug therapy subsequently developed skin lesions. This suggests that prompt and better killing of the organism by MDT arrests the spread of the disease from the nerves to the skin. This also supports the suggestion of Desikan[8] that leprosy is neural in inception. Other workers[6,16] have also reported the development of skin lesions in neuritic leprosy when treatment is irregular. This indicates the efficacy of the early introduction of therapy in neuritic leprosy for the prevention of the development of skin lesions, this being more beneficial with MDT compared to monotherapy. The possibility of developing new skin lesions while on treatment as part of a reversal reaction has been mentioned earlier.[17] Can appearance of skin lesions in neuritic leprosy be a part of reversal reaction and monotherapy/multidrug therapy have a role in modifying its incidence? The importance of a biopsy from normal looking anaesthetic skin is to exclude a cutaneous leprosy lesion which may not be clinically apparent but histopathological evidence may be convincing, as has been reported earlier.[10,18,19] The possibility of different strains of *M. leprae* to explain the various combinations of skin and nerve involvement has already been ruled out by Rees.[20]

Noordeen[6] observed that there is a tendency for spontaneous regression of a thickened nerve even without treatment. However, we observed that cases with a relatively longer duration of illness reported with weakness and deformity. In general, it is our observation that nerve thickness takes longer to regress compared to the associated skin lesion, also confirmed by Srinivasan *et al.*[21] in histological studies.

Meralagia paraesthetica is the important clinical differential diagnosis in neuritic leprosy. These cases do not improve on antileprosy treatment and local infiltration of lignocaine and steroids medial to the anterior superior iliac spine has been reported to improve this condition in some patients.

Sometimes compression of the lateral popliteal nerve due to prolonged working in a squatting posture leads to weakness/anaesthesia of the foot. However, this is transitory and should be carefully excluded.

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Lèpre névritique: épidémiologie et sensibilité à la thérapeutique

S Talwar, P K Jha et V D Tiwari

Résumé Nous avons étudié l'épidémiologie, l'évolution et la réponse au traitement dans 62 cas de lèpre névritique. L' hypoesthésie était le principal symptôme observé. L'observation la plus fréquente était celle d'une mononévrite intéressant le nerf cubital, puis le nerf sciatique poplité externe. Le test à la lépromine était positif dans 34 cas tandis que le frottis de peau fendue était toujours négatif. Nous avons traité 20 de ces cas par la dapsone seule; 5 d'entre eux (25%) ont présenté des lésions cutanées après 3 mois de traitement en moyenne. Nous avons traité 42 cas par une association de dapsone et rifampicine; 3 d'entre eux ont présenté une lésion cutanée après 2 à 6 mois de traitement en moyenne. Les diagnostics suivants ont par la suite été établis dans les cas présentant des liaisons cutanées: lépromateux borderline—un cas; tuberculoide borderline—4 cas; tuberculoide—2 cas; indéterminé—un cas.

La lepra neuritica: las reacciones epidemiologicas y terapeuticas

S Talwar, P K Jha y V D Tiwari

Resumen Hemos estudiado la epidemiología, progreso y respuesta terapéutica en 62 casos de lepra neurítica. El síntoma principal que se presentó fue adormecimiento. La presentación más común fue mononeuritis implicando el nervio ulnar, seguido por el nervio peroneal. La prueba de lepromina fue positiva en 34 casos y, al mismo tiempo, un "smear" de incisión de piel fue negativo en todos los casos. Tratamos 20 de estos casos por monoterapia con dapsona, y 5 casos (25%) desarrollaron una lesión cutánea después de una duración media de tratamiento de 3 meses. Tratamos 42 casos con una combinación de dapsona y rifampicina, y 3 casos (7%) desarrollaron una lesión cutánea después de una duración media de 2 a 6 meses. El diagnóstico posterior en los casos que desarrollaron lesiones cutáneas fue lepromatoso incierto en 1 caso, tuberculoide incierto en 4 casos, tuberculoide en 2 casos e incierta en 1 caso.

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Neurological examination of patients suffering from leprosy: is it worthwhile?

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Summary We examined 28 male leprosy patients to discover if a more extensive neurological investigation than usual would be worthwhile in diagnosis and/or management. Our findings were fully compatible with what might be expected from a mononeuritis multiplex, either due to leprosy or other causes. The following observations are noteworthy. Changes of position sense and a decrease of some tendon reflexes were present in a minority of the patients. In soles of the feet, considered to be an- or hypaesthetic, some residual pain sensation could occasionally be detected. Functional testing of at least one muscle group (m. triceps surae) appeared to be more reliable than manual testing according to MRC criteria. We concluded that an extensive neurological examination is probably not required for diagnosis. It does provide, however, more accurate information on the extent of damage to the peripheral nervous system, which may be important for management and for assessment of treatment effects. The use of a myometer is advocated.

Introduction

Leprosy is predominantly, though not exclusively, a disease of nerves and skin, and therefore it would seem logical to submit patients (suspected of) suffering from leprosy to a full neurological examination. In current practice, however, examination is restricted to selected aspects of neurological functioning, as is clear from handbook literature[1–3] and as we observed during a visit to the two main leprosy hospitals of Nepal in May 1991. In these hospitals, pressure sensation was carefully tested during so-called body charting, either using the ballpoint method or Semmes–Weinstein filaments,[4] and weakness of skeletal muscles was examined either by simple functional tests or manually. Peripheral nerves were palpated to assess whether they were enlarged, and the skin was examined for dryness and fissuring as indicators of loss of sweating. Pain sensation was examined when indicated. Other parts of the neurological examination for peripheral neuropathies were, however, disregarded. Tendon reflexes were not elicited, and vibration sense, position sense and co-ordination were not examined.

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It is not clear why the most common neurological methods of examination are not employed, as these are neither difficult nor time consuming. With a little training, they could easily be applied by both doctors and paramedical workers, even under the most primitive conditions. The scarcity of neurologists among those caring for leprosy patients may have prevented the introduction of some useful methods, but maybe the omitted neurological techniques are believed to contribute so little to diagnosis and to assessment of treatment effects that they are considered to be not worth the trouble. In support of this assumption Sabin and Swift state—but do not document—in their chapter on leprosy, which appears in one of the most authoritative handbooks on peripheral neuropathies,[5] that vibration sense and position sense are usually spared and that stretch reflexes are preserved.

We had the opportunity to perform an explorative neurological examination of 28 male leprosy patients, admitted to the Anandaban and Green Pastures Hospitals in Nepal. The aim of our investigation was to discover if a slightly more extended neurological examination would be of value in the care and treatment of leprosy patients.

Patients and methods

The patients were male and between 20 and 50 years old. They suffered from advanced forms of leprosy and had been admitted to hospital for neuritis or ulcer treatment, or for surgical reconstruction. They had undergone a standard examination programme which included 'body charting' to detect skin lesions and anaesthesia, skeletal muscle tests and palpation of peripheral nerves. Standard testing involved manual examination and the assessment of power of a large number of limb muscles according to MRC criteria, and functional tests of facial and hand muscles. Slit-skin smears, lepromin tests and other relevant laboratory tests had been performed in all cases. In these patients we tested: (i) gait; (ii) toe- and heel-walking; (iii) Romberg sign; (iv) tendon reflexes; (v) positional sense; and (vi) pin-prick sensation. Vibration sense was not included because an adequate tuning fork was not available! Examination of gait involved walking to and fro for 5–10 m. When toe- and heel-walking, the patients were encouraged to lift their heels and toes as high as possible. For the Romberg sign, patients were asked to stand with their feet together and their eyes closed for 20–30 s. The examined reflexes were the biceps and triceps reflexes in the upper limbs and the knee and Achilles tendon reflexes in the lower limbs. The ulnar and radius reflexes were not included as these are often not present in otherwise normal subjects.[6] The position sense of 1–5 digits per limb was examined. Examination of pin-prick sensation was performed with a wooden toothpick to preclude the risk of bleeding. Examination of this sensory modality was restricted to the plantar side of the toes and the volar and/or dorsal sides of the index or middle finger, the little finger and the ulnar sides of the hands and lower arms.

Results

GAIT, TOE- AND HEEL-WALKING AND THE ROMBERG SIGN

Recent lower limb surgery or ulcer treatment prevented gait examination in 10 cases. Gait was never broad-based and no clear-cut evidence of ataxia was seen; three patients were

found to have (not or not yet operated) unilateral or bilateral asymmetrical foot drop, confirming the results of previous muscle testing. Toe-walking demonstrated in 1 of these patients a unilateral mild weakness of plantar flexors of the foot which had not previously been discovered, and in another a slight instability of gait and abnormal toe-walking was shown, but the reason for this could not be established with certainty because he had toe deformities as well as a marked disorder of position sense. In this latter case, the Romberg sign (swaying or loss of equilibrium whilst standing with eyes closed) was positive. In 3 other cases, testing of the Romberg sign revealed swaying. In the remaining 14 cases the Romberg sign provoked no swaying.

TENDON REFLEXES (Table 1)

The tendon reflexes were mostly preserved, both in BT and in BL/LL patients. The Achilles tendon reflex in BT patients was to some extent an exception as it could not be elicited in 40–50% of the cases. It is remarkable that in 3 cases (2 BT and 1 BL) tendon reflexes could not be elicited at all. This is compatible with a generalized disorder of the peripheral nerves but is occasionally seen in otherwise normal individuals.

POSITION SENSE (Table 2)

Position sense of 1 or more digits in 1 or more limbs was abnormal in up to 33% of the cases. With few exceptions, loss of position sense was asymmetrical and not found simultaneously in toes and fingers. If position sense was affected in 1 digit, other digits of the same limb were often not affected to the same degree or not at all. Loss of position

Table 1. Presence of tendon reflexes in BT, BL/LL, BB and PN patients

Reflex	BT ($N=17$) n (%)	BL/LL ($N=9$) n (%)	BB ($N=1$) n	PN ($N=1$) n
Biceps				
right	12 (71)	8 (89)	1	1
left	13 (76)	8 (89)	1	1
Triceps				
right	11 (65)	7 (88)*	1	1
left	14 (82)	6 (75)*	1	1
Knee				
right	12 (71)	7 (78)	1	1
left	15 (88)	7 (78)	1	—
Achilles				
right	7 (50)†	6 (67)	—	1
left	9 (56)‡	7 (78)	—	—

N, number of patients per leprosy type; n, number of patients with tendon reflexes; number of patients in whom reflex could be examined: *, 8; †, 14; ‡, 16.

Table 2. Intact position sense in BT, BL/LL, BB and PN patients

Location	BT ($N=17$) *n* (%)	BL/LL ($N=9$) *n* (%)	BB ($N=1$) *n*	PN ($N=1$) *n*
Fingers				
right	10 (67)*	8 (89)	0	1
left	12 (71)	9 (100)	0	1
Toes				
right	8 (67)†	7 (78)	0	1
left	14 (88)‡	6 (67)	0	—

N, number of patients per leprosy type; *n*, number of patients with intact position sense; number of patients in whom position sense could be examined: *, 15; †, 12; ‡, 16.

sense reflects dysfunction of thick sensory nerve fibres innervating muscle spindles (A α fibres, 13–30 μm in diameter) and Golgi tendon organs located in muscle tendons (A β fibres, 6–12 μm).[7] As Romberg sign[7] and tendon reflexes[8] are equally dependent on functioning of thick sensory nerve fibres (innervating muscle spindles), it was considered interesting to compare the results of these examinations with those of position sense (Table 3). Approximately 50% of the patients in whom evidence of a disorder of thick sensory nerve fibres was found on examination of (Achilles) tendon reflexes and position sense showed an abnormality of the Romberg sign. When the Romberg sign was considered to be abnormal, tendon reflexes (1 case) or tendon reflexes and position sense (3 cases) were also abnormal.

PIN-PRICK SENSATION

Pin-prick sensation was not abnormal in the examined digits of four cases (3 LL, 1 BT) and could not fully be examined in 2 (BT) cases. In all other cases pin-prick sensation was abnormal in 1 or more digits of 1 or more limbs. This result confirms that of the previously performed standard examination of pressure sensation, but it should especially be noted that in patients who are used to walking barefoot, callous formation is often heavy, and in such cases, pressure examination of the soles of the feet may erroneously lead to a

Table 3. Relationship between Romberg sign and position sense/tendon reflexes of the lower limbs

Position sense/reflexes	Romberg sign: Normal	Romberg sign: Abnormal
Normal	11	0
Abnormal	3	4

conclusion of anaesthesia instead of hypaesthesia. We saw patients who were considered to have anaesthetic soles, but who still felt some pain.

Discussion

The neurological manifestations of leprosy are highly characteristic. Hypaesthetic, hypopigmented skin lesions are not likely to be seen in other diseases and in leprosy the decrease in cutaneous sensation related to skin temperature is unique.[5] Facial muscle weakness usually presents as lagophthalmus, whereas in most other facial nerve disorders, the weakness of peri-oral muscles predominates or is at least not less pronounced than the weakness of peri-orbital muscles. *Palpable* thickening of peripheral nerves is common in leprosy. It may be found, locally, in some cases of entrapment neuropathy,[9] but is otherwise rarely seen. It occurs in a minority of the patients with hereditary (autosomal dominant) motor and sensory neuropathy type I (HMSN type I or Charcot Marie Tooth disease) and in cases of (autosomal recessive) HMSN type III (Déjerine Sottas disease) which is a very rare disorder.[10] Refsum disease, which is even more rare, is reported to lead in some cases to palpable peripheral nerve thickening,[11] but this is not confirmed by other authors.[12] Polyneuropathy with palpable thickening of peripheral nerves and foot ulceration has been described as an exceedingly rare manifestation of neurofibromatosus.[13] Plexiform neurofibromas in patients suffering from neurofibromatosus are usually associated with typical skin lesions, which allows easy differentiation from leprosy.[14] In amyloid neuropathy, nerves may be thickened, but the suggestion in some textbooks on leprosy[1,2] that palpable nerve thickening is a clinical feature of familial or primary amyloid neuropathy is erroneous.[15,16] This all supports the view that the differentiation of leprosy neuropathy from other neuropathies will usually be quite straightforward. It may only prove problematic in some pure neuritic cases without peripheral nerve thickening.

The findings of this study suggest that: (i) position sense may be affected asymmetrically in 1 or more digits of 1 or more limbs, compatible with local pathology in 1 or several peripheral nerves, as in mononeuritis multiplex; (ii) changes in cutaneous sensibility are commonly well covered by current methods for investigation of pressure sensation; (iii) tendon reflexes are usually but not always preserved; and (iv) evidence for diffuse changes of thick sensory nerve fibres in the lower limbs leading to sensory ataxia is slight and usually lacking. These results fit nicely with the concept of leprosy neuropathy being a mononeuritis multiplex—with the exception of far-advanced cases of LL leprosy. On their own, they do not allow the distinction of leprosy neuropathy from other causes of mononeuritis multiplex and therefore are not helpful in the differential diagnosis of pure neuritic cases. They do demonstrate, however, that changes of position sense and of Achilles tendon reflexes are not exceptional.

The value of grading muscle strength according to the MRC scale is currently under discussion.[17] We agree with Fritschi that functional tests are easy to perform and highly informative.[18] They are therefore particularly useful in field conditions. For assessment of the effects of therapy, as for example by corticosteroids in neuritic patients, a myometer is to be preferred to manual testing as it is more accurate.[19–22] The present investigation included 2 simple functional tests: toe- and heel-walking. Heel-walking confirmed what was already known from manual investigation. Toe-walking requires lifting the weight of the whole body against gravity and is therefore a much more sensitive test for triceps surae

muscle weakness than manual testing. Weakness of the m. triceps surae reduces stability when standing and leads to a flat-foot gait. In this investigation, toe-walking revealed mild weakness of the triceps surae muscle in 1 limb of 1 case. Weakness of the triceps surae muscle is not generally considered to be a feature of leprosy, but has previously been reported in 7 of 25 LL patients.[23]

Loss of position sense of the fingers reflects a severe impairment of the distal, thick sensory nerves. It has an adverse effect on manual dexterity and hinders rehabilitation. This study shows that loss of position sense of the fingers occurs frequently in advanced forms of leprosy. Proper case management should therefore include prevention and/or improvement of this defect.

We could not investigate if the examination of pain sensation might facilitate the early diagnosis of leprosy. Our results indicated, however, that for proper case management, it may be useful to examine the pain sense in areas where patients are liable to develop ulcers. Loss of pain sensation and unperceived traumata are generally held to be responsible for the occurrence of ulcers.[9] Examination by pin-prick revealed residual pain sensation in some of the feet that were considered to be anaesthetic. It is our experience in patients with hereditary sensory neuropathy that prognosis, when foot ulcers recur, is better when slight pain sensation is preserved than when it is totally absent.

In conclusion: (a) in diagnosis, no grounds were found to advocate a more extensive neurological examination than is customary; and (b) a full neurological examination may, however, be relevant for case management as it assesses in greater detail the extent of damage to the peripheral nervous system. It is suggested that quantification of muscle strength by means of a myometer may be of value for the assessment of effects of therapy.

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Examen neurologique des patients souffrant de la lèpre: est-il justifié

F G I Jennekens et A Jennekens-Schinkel

Résumé Nous avons examiné 28 lépreux males pour découvrir si un examen neurologique plus extensif que l'habituel serait justifié pour le diagnostic de la maladie et sa direction. Nos résultats sont tout à fait compatibles avec ceux que l'on attendrait d'une mononévrite multiple, due soit à la lèpre soit à d'autres causes. Les observations suivantes méritent d'être notées: Des changements de la sensation de la position et une diminution de certains reflexes tendineux étaient présents chez une minorité des patients. Sur les plantes des pieds considérées comme anaesthésique ou hypoesthésiques, on pouvait parfois déceler un reste de sensation de douleur. Le test du fonctionnement d'au moins un groupe de muscles (muscle triceps sural) s'est révélé plus fiable que le test manuel selon les critères MRC. Nous avons conclu qu'un examen neurologique extensif n'est probablement pas necessaire pour le diagnostic. Il fournit, pourtant, une information plus précise sur l'éstendue de l'atteinte du système nerveux périphérique, ce qui peut être important pour la conduite et l'évaluation des effets du traitement. L'utilisation d'un myomètre est recommandé.

El estudio neurologico de los pacientes leprosos; ¿vale la pena?

F G I Jennekens y A Jennekens-Schinkel

Resumen Hemos examinado 28 hombres pacientes leprosos para establecer si valdría la pena hacer una investigación neurológica más extensa que la normal, para el diagnóstico y/o el tratamiento. Los resultados que obtuvimos eran totalmente compatibles con lo que se anticiparía de una mononeuritis multiplex, debida a la lepra u otras causas. Se destacan las siguientes observaciones. Se presentaron cambios del sentido posicional y una reduccíon de algunos de los reflejos de los tend ones en una minoría de los pacientes. En las plantas de los pies que se consideraban an- o hipo-anestéiscos, se podía detectar ocasionalmente una sensación de dolor residual. Pruebas funcionales de la menos un grupo de músculos (m. triceps suræ) parecían ser más fiables que las pruebas manuales, según los criterios MRC. Hemos concluido que probablemente no es necesario un extenso estudio neurológico para el diagnóstico. Sin embargo, éste proporciona información más precisa sobre el alcance del daño al sistema nervioso periférico que puede ser importante desde el punto de vista del tratamiento y de la evaluación de los efectos que ha tenido. Se favorece el uso de un miómetro.

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Primary neuritic leprosy in a black South African

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Summary A case of primary neuritic leprosy in a black South African is described, in which the multiple peripheral nerves were affected. The clinical picture and electrophysiological studies are in keeping with a picture of mononeuritis multiplex. Selective involvement of the facial nerve branches with normal blink reflex latencies was observed. The biopsy of the sural nerve disclosed features most consistent with borderline leprosy.

Introduction

Cases of primary neuritic leprosy in which no skin lesions of leprosy develop are not infrequent on the Indian subcontinent. In reports from other parts of the world patients with this form of leprosy were either Indians or Pakistanis.[1–6] Hargrave & Marion[7] described primary polyneuritic leprosy in an Australian aboriginal. Here we describe a black South African male with polyneuritic leprosy.

Case report

A 37-year-old black male was admitted to Kalafong Hospital in November 1989. He gave an 18-month history of pain in both hands followed by weakness and loss of sensation. He had no relevant past medical history. He denied ever having skin lesions. He seemed familiar with cutaneous manifestations of leprosy because his sister and father suffered from leprosy.

The significant physical findings were:

a. Bilateral fusiform thickening of the following nerves: the posterior auricular nerves, the ulnar nerves, the radial cutaneous nerves with the left much thicker than the right,

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the common peroneal nerves and the sural nerves. All thickened nerves were firm and nontender.

b. Bilateral lower motor neurone facial paresis of moderate severity affecting mainly the temporal and zygomatic branches which resulted in the inability to close his eyes.
c. Both his hands showed atrophy of the thenar and hypothenar muscles, the interosseous muscles and claw hand deformities. All hand muscles were weak bilaterally.
d. He had a glove and stocking distribution of spinothalamic loss but normal position and vibration sense. He had loss of the distal phalanx of his right big toe and he walked with bilateral footdrop. The clinical picture in the lower limbs was consistent with damage to the common peroneal nerves and posterior tibial nerves bilaterally.

The rest of his neurological system and the systemic examination were normal. There were no skin lesions of leprosy and there was no loss of eyebrows and eyelashes. The results of specal investigations were as follows:

1. NEUROPHYSIOLOGICAL TESTS

Nerve conduction. Both median nerves showed abnormally slow motor conduction velocities and low compound motor action potentials. No response was elicited on stimulation of the left ulnar nerve (motor), left posterior tibial nerve (motor) and the right radial nerve (sensory).

Blink reflexes were obtained stimulating the supraorbital nerves and recording from the orbicularis oculi muscles. The right and left blink reflexes were normal.

Needle examination. Needle examination of the right vastus lateralis, right pronator teres and right paraspinal muscles was normal. Needle examination of the following muscles showed signs of denervation (fibrillation potentials and/or long duration motor unit potentials): right tibialis anterior, right gastrocnemius, right abductor hallucis, right first dorsal interosseus and right abductor pollicis brevis.

These neurophysiological tests implied total axonal degeneration in those nerves from which no response could be elicited and a combination of demyelination and axonal damage in the extremity nerves from which response could be obtained.

2. SKIN-SPLIT SMEARS

Smears taken from 6 standard sites were all negative.

3. NERVE BIOPSY (left sural nerve) (Figures 1 and 2).

There was a chronic granulomatous infiltrate in the nerve bundles and perineurium as well as extensive destruction of nerves and fibrosis. The infiltrate consisted of epithelioid cell, lymphocytes and scanty giant cells, more of foreign body than Langhans type. A few broken acid- and alcohol-fast organisms were seen on special stain.

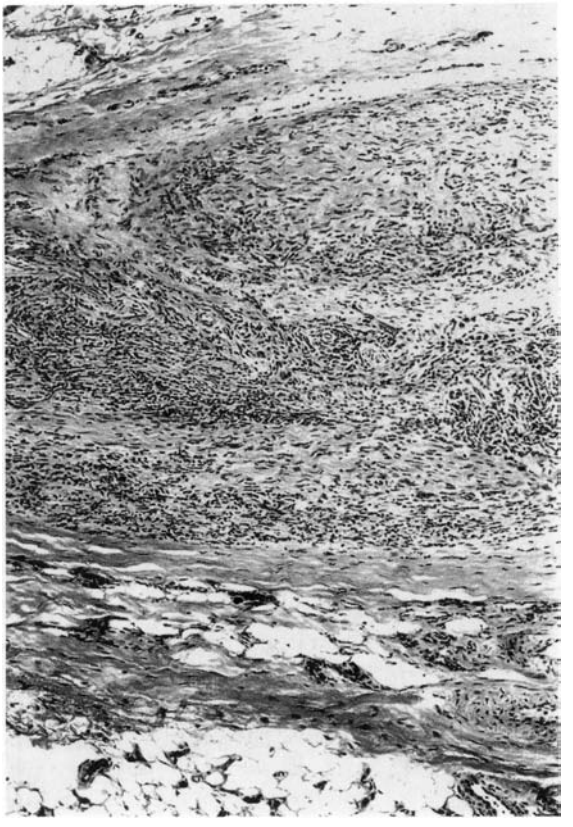

Figure 1. Granulomatous infiltrate in peripheral nerve bundles. H & E × 80.

4. OTHER TESTS

The following tests were normal or negative:

Full blood count, tests for syphilis in serum and cerebrospinal fluid, serum glucose, SMA II, lumbar puncture including pressure and chemistry, chest x-rays and the electrocardiogram.

Discussion

An epidemiological study conducted by Noordeen[8] showed the neuritic form to constitute 17·7% of all types of leprosy seen in Chingleput District, Tamil Nadu State, India. In Africa a neuritic form of leprosy seems to occur much less frequently. To our knowledge primary neuritic leprosy has not been so far reported in a black African. According to R E Pfalzgraff (personal communication) neuritic leprosy occurs in Africa but it constitutes less than 1% of cases. The extent of nerve damage in our patient with involvement of all 4 limbs and 14 nerves affected is very unusual, as most patients with a neuritic form show

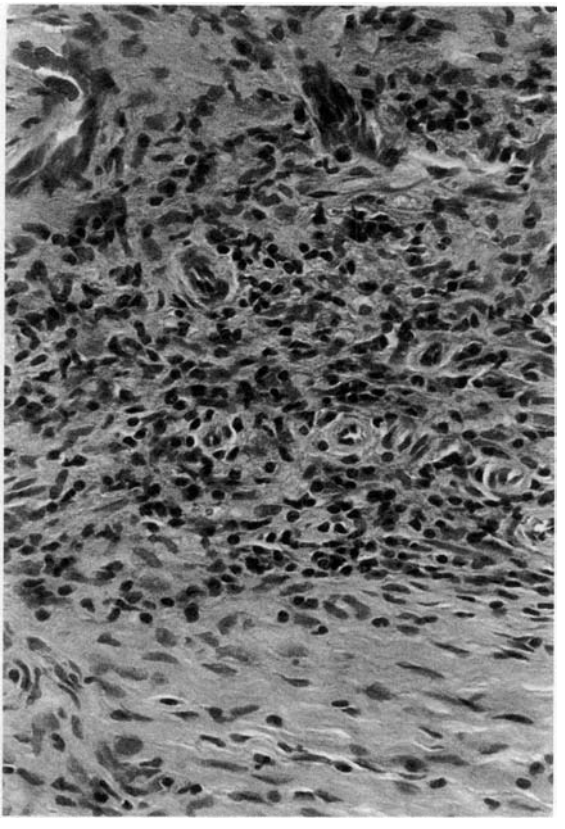

Figure 2. A detail of the granuloma showing central epithelioid cells with peripheral lymphocytes and fibrosis. H & E × 160.

rather mild symptoms. Histological classification of the case appears difficult. Granulomatous changes with numerous epithelioid cells and a mixture of lymphocytes would suggest a BT type, whereas partial preservation of peripheral nerves, the foamy nature of some macrophages and the presence of acid-fast debris are in favour of him being a BB or BL type. The large number of involved nerves would also point toward borderline–lepromatous type.

Kaur *et al.*[9] have demonstrated, however, that in neuritic leprosy the number of affected nerves, the nerve pathology and immune response are not interrelated.

Hereditary motor sensory neuropathy type I and III are diseases that most closely resemble primary neuritic leprosy. The age and mode of onset, the preservation of vibration and positional sense and the normal cerebrospinal fluid proteins are factors against the diagnosis of hereditary neuropathies. The normal blink reflexes were surprising in view of the clinical evidence of peripheral facial nerve involvement. This would imply that the process was mainly axonal and/or that the facial nerve involvement in neuritic leprosy can be highly focal and that specific peripheral branches of the facial nerve can be affected in isolation.

Acknowledgments

We wish to thank Dr L S de Haas for help in assessment of the histopathology of the nerve biopsy.

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Lepr Rev (1992) **63,** 277–281

Lèpre névritique primaire chez un Noir d'Afrique du Sud

N A Mafoyane, W K Jacyk et B P Lotz

Resumé Nous décrivons un cas de lèpre névritique primaire chez un noir d'Afrique du Sud, où plusieurs nerfs périphériques étaient atteints. Le tableau clinique et les observations électrophysiologiques évoquent la mononévrite multiple. Nous avons observé l'implication sélective des branches du nerf facial avec latences normales du reflexe de clignement des paupières. La biopsie du nerf saphène a présenté des signes très compatibles avec une lèpre borderline.

La Lepra Neurítica Primaria en un Sudafricano Negro

N A Mafoyane, W K Jacyk y B P Lotz

Resumen Se describe un caso de lepra neurítica primaria (un sudafricano negro) en que estaban afectados nervios periféricos múltiples. El cuadro clínico y los estudios electro-fisiológicos son consistentes con un caso de mononeuritis multiplex. Se observó una implicación selectiva de las ramas de los nervios faciales con latencias del reflejo de parpadeo normales. La biopsia del nervio sural reveló características que eran principalmente consistentes con una lepra incierta.

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SPECIAL ARTICLE

Estimated number of leprosy cases in the world*

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Planning for leprosy control requires estimates of the number of leprosy patients at different levels. During the period between the mid-1960s and the mid-1980s, global estimates had remained constant at between 10 and 12 million. The introduction of multidrug therapy (MDT) in many countries and the consequent reduction of the disease's prevalence has necessitated a reassessment of this. Based on available information and its interpretation, the number of leprosy cases in the world for 1991 has been estimated at 5·5 million. The number of individuals deformed by leprosy, including those cured of the disease, has been estimated at between 2 and 3 million.

Introduction

Leprosy continues to be an important public health problem in most parts of Asia, Africa and Latin America. The magnitude of the problem is often expressed by the number of cases registered by the leprosy programmes, although it is recognized that registered cases do not reflect all the cases existing in any given area. Therefore, from time to time, attempts have been made to estimate the prevalent number of cases at national, regional and global levels. More recently, and particularly since 1985, the leprosy situation in many parts of the world has undergone major changes, following the widespread introduction of multidrug therapy (MDT) as recommended by the WHO Study Group on Chemotherapy of Leprosy for Control Programmes in 1981.[1] This has necessitated updating the current global estimate of leprosy cases so that future strategies and planning are based on more updated information.

Problems in estimating leprosy

Estimates on disease prevalence are generally based on well-planned, sample surveys. In fact this had been attempted in limited situations[2] for estimating leprosy prevalence and

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detailed methods have also been outlined.[3] However, in terms of obtaining prevalence information for large areas or countries as a whole, sample surveys are neither practicable nor cost-effective. The main reasons for this are the very low frequency of occurrence of leprosy and its uneven distribution which demand huge sample sizes in order to attain reasonable levels of precision. Even more, non-sampling errors, including inadequate coverage for examination of individuals, observer variations, and varying and imprecise case definitions, introduce gross inaccuracies which make even total population surveys difficult to interpret. In spite of the above problems, estimates on leprosy prevalence are required at different levels and therefore attempts have been made to make estimates by applying indirect methods, involving extrapolations through application of correction factors to already available information, for instance on the number of registered cases. Such correction factors have been derived from apparently reliable information available from limited areas. Extrapolations have also been attempted from information on prevalence among children,[4] prevalence of deformities, and even from rapid village surveys. Sometimes a combination of more than one method has been suggested.[5] It should be recognized that, although from the purely statistical point of view the precision of many of the estimates can be questioned, the estimates in general have been found to be reasonably adequate for planning purposes.

Previous estimates on the global problem of leprosy

The magnitude of the global problem of leprosy has been expressed by the WHO, through estimates on the number of prevalent cases in the world at any one time. Such estimates have been found to be valuable for planning and priority setting. In 1966, based on a country by country analysis, it was estimated that the total number of cases in the world was 10,786,000[6]. The figure was updated in 1972[7] giving estimates of 10,407,200 cases. The WHO Expert Committee in its fifth report estimated a figure of over 12 million cases.[8] The WHO Study Group on Epidemiology of Leprosy in Relation to Control in 1983[9] referred to an estimate of 11,525,000 cases. Since then, an estimated figure of 10–12 million has been frequently mentioned in several documents. All the above attempts at making estimates have assumed that the leprosy situation, in different countries and globally, has been rather static in terms of numbers, that elimination of the disease through cure and death has been compensated for in full by the occurrence of new disease, and that case definitions had remained unchanged.

Methods applied for making current estimates

It is well known that leprosy is very unevenly distributed at the global, national and even at the sub-national levels. Information on registered cases clearly indicates that the top 25 countries contribute nearly 95% of all registered cases in the world, of which the top 5 contribute 82%.[10] Therefore, in order to make a reasonably reliable global estimate of the prevalence of the disease, greater attention was given to making estimates for the top 25

countries, and estimates were made on a detailed review of information on registered cases. In the case of the top 5 countries, estimates were arrived at following more intensive reviews of all the available information and discussion with relevant programme managers. In general, estimates for the 25 countries were arrived at by applying correction factors to registered cases, in addition to extrapolating from other related information as well as reviewing information provided by WHO consultants and programme managers. For leprosy-reporting countries/territories other than the top 25, numbering some 127, estimates were made by developing and applying appropriate correction factors for each WHO Region, unless more reliable information was available for any country, including some that had been collected earlier through a questionnaire. The correction factor for each Region was calculated as the ratio between the registered cases in those countries of the Region included in the top 25 and estimates made earlier for them. Although admittedly this is a crude method, it was found to be reasonably satisfactory for making global estimates.

Estimated number of cases in the world

Based on the methodology indicated earlier, the global number of leprosy cases, as of 1991, has been estimated at about 5·5 million. This figure is about half the 10–12 million estimated during the 1960s, 1970s and 1980s. This large reduction is a result of (a) the large number of patients cured through MDT which has a finite period of treatment; (b) eliminating from existing registers those individuals who do not qualify as 'cases', as defined by the WHO Expert Committee on Leprosy in its sixth report,[11] which recommended that for the purpose of prevalence only a patient requiring or receiving chemotherapy should be recognized as 'a case of leprosy'; (c) possible late effects of intensive dapsone-based control activities in some areas; (d) strengthening leprosy control activities in many countries whilst introducing MDT; and (e) natural declining trends as observed in some parts of Africa. Table 1 provides information on the estimated cases according to WHO Regions and by countries grouped according to number of cases.

Table 1. Number (× 1000) estimated cases in countries by WHO Region (1991) (figures in parenthesis refer to number of countries involved)

Estimated Cases in Countries	WHO Regions[a]						
	AFR	AMR	EMR	EUR	SEAR	WPR	TOTAL
200 or more	360 (1)	270 (1)	0 (0)	0 (0)	3440 (3)	0 (0)	4070 (5)
100–199	0 (0)	0 (0)	0 (0)	0 (0)	250 (2)	120 (1)	370 (3)
20–99	375 (9)	57 (2)	152 (3)	0 (0)	54 (1)	87 (2)	725 (17)
1–19	178 (21)	60 (10)	52 (8)	7 (2)	5 (2)	28 (7)	330 (50)
less than 1	3 (15)	4 (27)	3 (10)	2 (12)	1 (1)	3 (12)	16 (77)
Total	916 (46)	391 (40)	207 (21)	9 (14)	3750 (9)	238 (22)	5511 (152)

[a] AFR = Africa; AMR = Americas; EMR = Eastern Mediterranean; EUR = Europe; SEAR = South-East Asia; and WPR = Western Pacific

Estimated number of leprosy patients and former patients having deformities

While the estimate of 5·5 million relates to cases requiring or receiving chemotherapy, there are a large number of patients who have been cured and discharged from registers but still have residual deformities of WHO grade 2[12] resulting from past leprosy. These individuals constitute a substantial burden to the community from the rehabilitation point of view. Currently, as most leprosy programmes are not involved in rehabilitation activities they do not possess or maintain information on such patients, although there is some information available on patients under treatment who have deformities. With the increasing application of MDT and the large number of patients being discharged from registers, some programmes are increasing their focus on deformed patients, whether under treatment or cured. It, therefore, becomes important to make estimates for such individuals. It is possible to attempt to estimate the number of deformed patients by making reasonable assumptions on (a) the estimated number of new cases in the past, going back at least 50 years; (b) the proportion of such cases ultimately developing deformities; (c) the survival rate of deformed patients; and (d) the intensity and efficacy of leprosy control activities. In order to make an estimate for the number of persons in the world deformed by leprosy and surviving through 1991, assumptions were made on the above factors and different figures covering different periods were assumed for the estimated new cases, the proportion who became deformed, and the survival rates. Depending upon the assumptions made, the estimates arrived at varied between 2 and 3 million deformed individuals, irrespective of whether or not they had active disease. Thus, it is reasonable to conclude that by 1991 there were an estimated 2–3 million individuals in the world who had deformities (WHO Grade 2) caused by leprosy.

Estimated number of cases in the top 25 countries

Table 2 gives information on the estimated number of cases for the top 25 countries and also the number of registered cases in each country by WHO Region. They also happen to be countries with more than 20,000 cases each.

The 25 countries having the largest number of estimated leprosy cases and contributing 93·7% of the total estimated cases in the world are discussed here purely from the point of view of their contribution to the total global case-load. They are not necessarily the top 25 countries from the point of view of estimated rate of prevalence. Thus, their ranking for the estimated number of cases and the estimated prevalence rate would vary considerably. However the top 25, from the point of view of total estimated cases generally, coincides with the top 25 from the point of view of total registered cases (except for 3 countries) although the individual rankings within the 25 vary.

Discussion and conclusions

It is clear that, for planning purposes, there is a need to have estimates of leprosy patients at different levels irrespective of the limitations and imperfections with regard to available information or methodologies. At the global level, there is an urgent need to update the figures particularly in view of the major changes that have taken place over the past 7–8

Table 2 Number (× 1000) of estimated and registered cases in the top 25 countries by WHO Region (1991)

Region	Estimated	Registered
Africa		
Nigeria	360	156
Mozambique	65	24
Ethopia	60	16
Zaïre	58	9
Madagascar	50	19
Côte d'Ivoire	40	14
Uganda	30	8
Mali	28	13
Cameroon	22	10
Chad	22	11
Sub total	735	280
South-east Asia		
India	3000	1996
Myanmar	240	112
Indonesia	200	102
Bangladesh	150	25
Nepal	100	25
Thailand	54	13
Sub total	3744	2273
Americas		
Brazil	270	260
Colombia	31	19
Argentina	26	16
Sub total	327	295
Eastern Mediterranean		
Sudan	52	36
Egypt	50	7
Iran	50	14
Sub total	152	57
Western Pacific		
Viet Nam	120	20
Philippines	47	39
China	40	30
Sub total	207	89
Total 25 countries	5165	2994
Total all countries in the world	5511	3162

years as a result of the implementation of MDT and related activities. It is also important to recognize that a proportion of cured patients have residual deformities requiring rehabilitative support, and it is therefore necessary to estimate the deformity load in the community in addition to estimating the magnitude of the problem from the disease and chemotherapy perspective.

The current estimate of 5·5 million cases may be considered by some as an underestimate, particularly in relation to previous estimates. On the other hand, the

current estimates, as derived from information on registered cases, may be considered as an overestimate by some, particularly in relation to the situation in some countries where the registered cases include a substantial proportion of inactive cases. In relation to possible underestimation, it should be recognized that the previous estimates of 10–12 million were made several years ago and since then drastic changes have occurred in the leprosy situation. It should, therefore, be recognized that the reduced estimate reflects the outcome of successful leprosy control activities in recent years. It is also clear that the opportunity to further reduce prevalence through intensified control using MDT is very considerable, and the estimate may fall further in the future if the anticipated intensification of leprosy control materializes. In addition, there is a need to address the rehabilitative needs of the estimated 2–3 million deformed individuals by implementing existing technologies and developing better technologies and strategies and applying them widely.

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SPECIAL ARTICLE

Modified multiple drug therapy in the National Leprosy Eradication Programme, India

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The National Leprosy Control Programme (NLCP) started in India in 1955, using dapsone monotherapy, with emphasis on health education, survey, case detection and rehabilitation. The Central Government changed its strategy and name to the National Leprosy Eradication Programme (NLEP) in 1982–83, following the recommendations of the Swaminathan Committee.[1] Since 1983 multiple drug therapy (MDT), essentially as recommended by the World Health Organization (WHO) in 1982,[2] but with an intensive phase of daily medication for 2 weeks for multibacillary cases, has been implemented in a phased manner, with emphasis on high endemic districts. By 1990, it was possible to report that 1·6 million out of the 2·4 million registered patients were under MDT and that the number of cases discharged from treatment was exceeding the number of new cases detected each year.[3] About 4·5 million cases have been taken off the leprosy registers in India during the past 10 years.

Despite this evidence of progress, an appraisal of the situation in India in early 1990 indicated that the pace and extent of the implementation of MDT was unsatisfactory. From the previously identified total of 196 districts with a prevalence of 5 or more per 1000 of the population, 66 had been unable to implement MDT, mainly because of an inadequate NLEP infrastructure, coupled with poor prospects for the recruitment and training of staff in the foreseeable future. Professor G K Vishwakarma, Director of Health Services, undertook a critical review of the situation (which was likely, if not tackled, to undermine the objective of eradication of leprosy in India by the year 2000), and this led the formulation of a 'modified' MDT approach, later published as *Guidelines for Modified MDT Scheme in Selected Districts* by the Leprosy Division of the Ministry of Health and Family Welfare, New Delhi.[4] The Foreword draws attention to the main concern of bringing the remaining 66 districts under MDT as soon as reasonably possible, using the primary health care (PHC) infrastructure (as opposed to the vertical, specialized structure of the NLEP), and to the main objective of the 66-page booklet in providing guidelines to all categories of health staff for the extension of MDT through, '. . . an economically feasible system of service delivery'.

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The methodology of modified MDT (MMDT) is described in considerable detail; there are 18 main sections, 6 annexures and 17 appendices. The salient features are described under two headings—administrative and technical. The former includes instructions for the setting up of a District Leprosy Society, under the chairmanship of the District Collector, which is to take overall responsibility for the operation of the programme. The District or Zonal Officer of the District will act as secretary and the Chief Medical Officer of the District as vice-chairman. A system of awards or incentives is described for: a, PHC functionaries, based on performance, together with the sum of 3 rupees for each new case detected; and b, patients, who will receive 10 rupees for each supervised monthly dose and 100 rupees if and when they complete the prescribed course of MMDT for either pauci- or multibacillary leprosy. The technical directions are 4 in number: 1, the period of initial, intensive chemotherapy, as currently used in the NLEP,[5] giving dapsone 100 mg, clofazimine 100 mg and rifampicin 600 mg daily for the first 14 days, followed by the standard WHO regimen, will not be used; 2, fixed duration chemotherapy (2 years for multi- and 6 months for paucibacillary cases) will be the rule. Thus multibacillary cases no longer need to continue treatment '. . . for a period of 2 years (24 months) or until achievement of smear negativity, whichever is later'.[5] However the Guidelines include provision for the continuation of treatment in certain paucibacillary cases, beyond 6 months, especially in cases with multiple lesions. This step is to be taken only after careful review by a medical officer, including detailed clinical and bacteriological examination for errors in classification; 3, the rapid survey approach described in existing NLEP guidelines will be replaced by intensification of health education activities to encourage voluntary reporting; and 4, the bacteriological examination of skin smears in MMDT programmes will be confined to multibacillary cases and suspected multibacillary cases. However, MMDT is to be started on the basis of clinical examination.

The annexures deal with administrative, technical and financial components in detail and there are clear instructions on the registers, records and reports needed. Furthermore, 2 training manuals, 1 for medical officers and health supervisors and the other for health workers, have recently been published by the Leprosy Division, specifically for the implementation of MMDT through existing health care services.[6]

MMDT is reported to have been started already, on a limited scale, in a few districts in India and a conference was held in January 1992 in Puri, Orissa, to discuss the steps needed for the implementation of MMDT in the 2 districts of Keonjhar and Kalahandi. This brought together representatives from the Directorate of Health Services for Orissa, the Gandhi Memorial Leprosy Foundation, DANLEP, The Damien Institute (Bhubaneswar), Cuttack Medical College and The Damien Foundation (Belgium). Solutions were sought to questions concerning the re-deployment of staff and their training in leprosy control, the working relationship between NLEP and PHC staff, the change from dapsone monotherapy (used for the better part of 20 years), to the effective use of MMDT, through the PHC system, the provision of transport specifically for leprosy work and the constant availability of adequate stocks of dapsone, clofazimine and rifampicin at all times. The meeting in Puri (possibly one of the first to systematically plan for the use of MMDT) emphasized the importance of preliminary screening of all registered 'cases' in order to clearly identify those in need of chemotherapy—a procedure which invariably results in marked reduction in the true prevalence figures.

Greatly inspired by Mrs Indira Gandhi's personal interest and support for leprosy

work in the early 1980s, it is the stated intention of the Government of India to eradicate leprosy by the year 2000. Whether this may need revision to 'elimination'[7] or to 'the provision of MDT for all by the year 2000' has yet to be seen, but meanwhile there is no doubt that the guidelines described above are evidence of the determination of the health authorities in India to radically improve the present situation without delay. They could well be studied by those responsible for programmes in other parts of the world (Brazil, Myanmar, Indonesia, Nigeria and several other African countries come to mind) where the benefits of MDT have as yet been made available to only a small percentage of those in need. Furthermore, in view of the many thousands of patients, in 66 districts of India, for whom MMDT has been designed, careful monitoring of this initiative may provide valuable information on the feasibility and effectiveness of using the PHC system, with main responsibility at district level.

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Lepr Rev (1992) **63,** 291–295

Letters to the Editor

MINOCYCLINE CURES TUBERCULOID LEPROSY

Sir,

A 21-year-old woman was seen in March 1991 to investigate an asymptomatic plaque on the right forearm. Examination revealed a well-defined, slightly erythematous, raised, dry, anaesthetic and analgesic oval plaque of 3×2 cm on the volar aspect of the right forearm. There was no thickening of the cutaneous or peripheral nerves. She also had numerous acne—papules, comedones and nodules on the face and chest. A clinical diagnosis of tuberculoid leprosy with acne vulgaris was made and she was investigated further.

Routine laboratory blood tests that included total and differential leucocyte counts, haemoglobin level, and ESR were within normal limits. Serum bilirubin and SGPT were normal. Urinalysis was normal. Slit-skin smears from the plaque and earlobes did not show any acid-fast bacillus. A skin biopsy from the plaque was done and she was asked to return after 3 weeks for the biopsy result and treatment for leprosy. For the acne vulgaris she was prescribed oral minocycline 50 mg bd for 6 weeks. Meanwhile we received the biopsy result which revealed tuberculoid granuloma in the dermis and these features were consistent with the diagnosis of tuberculoid (TT) leprosy. Because she moved some distance away she was only able to come for the biopsy result in August 1991, that is, 5 months after her initial visit to our clinic. She had not received any routine antileprosy drug, but only minocycline prescribed for acne vulgaris. During this visit, when examined, to our surprise her leprotic skin lesion was found to have completely regressed leaving an atrophic, hypoalgesic, ill-defined macule. The histopathological study of the biopsy specimen from this atrophic macule revealed only sparse collections of lymphocytes around the neurovascular bundles. There were no tubercles or epithelioid cells. No antileprosy drug was given and she was further followed up in December 1991 when there was no evidence of activity of the leprosy lesion.

Recently many new drugs have been reported to be effective against *Mycobacterium leprae*, including derivatives of fluoroquinolones, macrolids, rifamycin, phenazine and betalactam antibiotics.[1] Minocycline, an alkylated aminotetracycline, has also been reported to be effective against *M. leprae* in experimental animals.[2] It is an established antimicrobial and it seems to be safe in the long-term therapy of acne.[3] The drug is highly lipophilic, facilitating good tissue penetration.[4] This same lipophilic property probably allows it to penetrate the cell walls of *M. leprae* more effectively. In higher concentration it is bactericidal and its minimum inhibitory concentration (MIC) against *M. leprae* has been estimated to be about 0·2 mg/l.[2] The leprosy lesion in our patient was accidentally cured following 6 weeks' minocycline, the drug being prescribed for the treatment of her associated acne. It is well known that a majority of tuberculoid lesions may regress spontaneously, because of the high cell-mediated immunity the affected persons possess against *M. leprae*. But this spontaneous cure occurs only after prolonged periods, which may take a few years. The rapid regression of the leprosy lesion within 5 months of the initiation of minocycline therapy in this patient suggests that it resulted from the antimycobacterial and anti-inflammatory effect of

minocycline, rather than the spontaneous cure achieved by the high CMI she possessed. The safety in the prolonged treatment of acne with minocycline is well established. The adverse effects that may rarely occur during minocycline therapy include gastrointestinal discomfort like nausea and vomiting, benign intracranial hypertension manifesting as vertigo, dizziness and visual disturbance, and blue-grey to brown pigmentation of the skin.[4] The safety of this drug in pregnancy has not been established. In leprosy more clinical trials, especially in bacilliferous types, are indicated to confirm its antileprosy effects, but a pilot study in 8 LL and BL patients has already shown the drug to be highly effective.[5]

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THE TEACHING OF LEPROSY IN THE MEDICAL COLLEGES OF ORISSA, INDIA

Sir,

The State of Orissa has a very considerable leprosy problem. Out of a population of over 26 million, the estimated number of cases is about 320,000, giving a prevalence rate of 12·14 cases per thousand, which is fourth highest for the number of cases in the 25 States and Union Territories of India.[1] The overall deformity rate is 30% and the child rate 28%. The percentage of people of tribal origin varies between 30 and 40% in different parts of the State and the overall literacy rate is 48%. Leprosy control activities started with the National Leprosy Control Programme in 1955, changing to the National Leprosy Eradication Programme in 1982–83. Multiple drug therapy (MDT) was introduced in Ganjam District in 1982 and has now been extended to all 13 districts, using the modified MDT scheme advised by the Leprosy Division of the Directorate of Health Services, Government of India, in 1990,[2] for the last 2 districts, Keonjhar and Kalahandi.

As part of a programme of health education in leprosy, the Health Education Unit at Jatni, Puri District, supported by the Gandhi Memorial Leprosy Foundation (GMLF) in Wardha, Maharashtra, has, over a period of years, attempted to involve the 3 medical colleges of the State at both undergraduate and teaching staff level. The colleges are situated at Sambalpur in the western part of Orissa, Berhampur in the south and Cuttack, about 30 km from the capital, Bubaneswar. Our approach has been mainly based on the recommendations of a symposium held in MKCG Medical College, Berhampur, published by the GMLF in December, 1983.[3] It was recommended that the teaching of leprosy should not be separated from the mainstream syllabus, with the need for extra time, but that it should be part of the routine teaching process in various disciplines. Thus, recommendations were made for leprosy to be included and used as a 'model' wherever possible in the teaching of anatomy (dissection), histology, physiology, biochemistry, immunology, pathology, microbiology, clinical medicine, surgery, ophthalmology, ear, nose and throat diseases, and social and preventive medicine. Our first contacts have been with the principals and heads of departments of the colleges, with emphasis on an interdisciplinary approach. A series of meetings or seminars,

usually on selected aspects of leprosy, have been held in all 3 colleges since 1980, with invited experts from Bombay, Delhi, Madras, Calcutta, Bangalore, Pune and other parts of India. Extensive use has also been made of a wide range of teaching and learning materials, including: 1, items from the TALMILEP (1990) Booklist, Teaching and Learning Materials in Leprosy;[4] 2, posters provided by the Wellcome Tropical Institute, London, UK; 3, colour transparency teaching sets from the Indian Registry of Pathology ICMR, New Delhi, and the Medical Education Department of Glaxo Laboratories, Bombay; and 4, videos on leprosy from Wardha and Karigiri, South India. In addition, GMLF and other voluntary agencies have supplied 21 books on various aspects of leprosy for the 3 medical college libraries. Translation of several items from the above TALMILEP list into Oriya has already been carried out and others are projected for 1992.

The above meetings have been well attended, with many questions from undergraduates and college staff, and we have been extremely fortunate in the consistently high level of cooperation and interest shown by deans and heads of departments. Although it has not yet been possible to carry out an objective assessment of improvement in terms of attitude, knowledge and clinical performance, our impression, on talking to students, graduates and staff members, is that these have improved significantly within the past 10 years. Questions on leprosy now appear in the MBBS, MD and MS (Ophthalmology) examination papers. Basically our approach does not differ from that reviewed in an editorial in a previous issue of this Journal[5] and which has been used successfully in other parts of India, notably Bombay.[6] However, the constant presence of a GMLF Health Education Unit in this State over a period of 12 years, with opportunity for repeated contact with medical colleges, backed by the provision of teaching and learning materials for students and medical staff, may well account for the progress which has been made. The recommendations on the teaching of leprosy to medical undergraduates referred to above are to be completely revised and reprinted this year, in collaboration with the medical colleges, giving more emphasis to the activities and achievements of the National Leprosy Eradication Programme, in association with a number of voluntary agencies. It is our intention to continue this work and to intensify our contacts with medical colleges so that medical students in this State graduate with a basic knowledge of leprosy, coupled with a compassionate attitude to patients and an appreciation of the potential of multiple drug therapy in the control and eventual eradication of this disease.

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Acknowledgment

I am indebted to Dr A Colin McDougall, Department of Dermatology, Slade Hospital, Oxford, UK, for his encouragement to submit this letter for publication.

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THERMAL SENSIBILITY TESTER. CAN IT BE USED TO FIND EARLY NERVE DAMAGE IN LEPROSY?

Sir,

The newly-developed 'Thermal Sensibility Tester',[1,2] has been used for several studies in the diagnosis of leprosy with interesting results.

We discovered that it has not been clarified whether this Thermal Sensibility Tester was also designed for testing for early peripheral nerve damage (hand and foot) in leprosy patients. Some believe that this tester could be used in the follow-up of nerve damage.

In peripheral nerves unmyelinated C-fibres are supposedly also the earliest involved and therefore this belief would be an attractive concept.

We have recently performed a study concerning the sensory thresholds in the hand in leprosy patients and have tested a control group of 50 normal people with the Thermal Sensibility Tester.[3]

We used 2 testers and before testing made sure that the tester was working. We tested 5 points on each hand 3 times and gave a positive score if 2 out of 3 were felt.

This group was divided into 3 according to their profession; heavy, mixed and light work. Our findings are in Table 1.

Table 1. Thermal Sensibility Tester in 3 groups

Type of work	Positive score
Heavy work (farmers)	51·5
Mixed work	62·1
Light work (office, teachers)	76

The Thermal Sensibility Tester was not felt by almost half of the persons tested in the heavy work group (farmers). Even 24% of persons in light work were unable to feel the difference between the hot tip and the ambient temperature tip. All groups joined together indicate that one-third was unable to feel the difference between the 2 ends.

From these test results we can conclude that The Thermal Sensibility Tester can be used in the *diagnosis of early leprosy*, but does not seem to be appropriate for tests to find *early nerve damage* in leprosy.

We hope to submit the results of the other data of this study for publication soon.

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COMMENT: NASAL MYIASIS IN LEPROSY

Sir,

'Nasal myiasis in leprosy' by Hussain *et al.* (*Lepr Rev*, 1991; **62:** 389–94) makes interesting reading.

It is of clinical interest (and surprise as well) that after nearly 50 years of dapsone therapy and over 8 years of multidrug therapy (MDT), nasal myiasis in leprosy is still 'on the prowl' in the part of India where the authors are working. Perhaps this condition still occurs in other parts of the country but is not documented. It is no wonder that the presentation at a clinical meeting of cases with nasal fistulae arising in the wake of neglected nasal myiasis in leprosy cases caused considerable surprise among the participants. With the advent of chemotherapy in leprosy (be it dapsone monotherapy or MDT), which confers considerable benefit on the nasal lesions and symptoms in the multibacillary cases quite early in the course of treatment, and also better patient care, infestation of the nose with maggots has become a rarity, like leprous laryngitis and the relentlessly progressive destruction of the elements in the anterior segment of the eye. This presentation is most welcome because it serves to bring this now rare, painful and distressing condition to the knowledge of the younger generation of leprosy workers and which incidentally has not attracted much attention in many of the textbooks on leprosy.

Nasal myiasis occurs in lepromatous and borderline–lepromatous cases coming from the lower economic strata of society, who are in a very poor state of health, almost moribund, and who do not have the energy to brush aside the flies. In the 1940s I saw a few leprosy cases with nasal myiasis. I remember distinctly one of these cases for two reasons: 1, It was the lone case from whose nasal cavity I pulled out an incredible number of maggots after the application of turpentine nasal swabs; and 2, This patient, whose nasal problem had become intolerable on a Sunday morning when our Clinic remained closed, sought help from the Government General Dispensary located in the same compound. He told the Medical Officer that 'poochis' (worms) were coming out of his nose and mouth. Without a second look, he was promptly prescribed 'Santonin' and 'Calomel' in divided doses (the then prevailing treatment for ascariasis) on the presumption that the patient was passing round worms from his nasal and buccal cavity. Not an unusual mode of exit for the worms in children carrying belly loads of the parasite.

An interesting observation that has emerged out of this presentation is that, 'occasionally the larvae burrow deep into the floor of the nasal cavity and eat away the bony palate to produce a palatal fistula'. This opens up another concept in the pathogenesis of the perforation of the hard palate in bacilliferous cases. It is indeed amazing that these slender, supple maggots which generally fluorish on dead and decaying soft tissue can nibble away apparently normal bone!

Other sites for the occurrence of myiasis in leprosy in the past were the neglected trophic ulcers over the planter surface and the lateral malleoli and suppurating lesions in the hands and feet. It is of interest to record here, that although the presence of maggots 'jam-packed' under the edges of the ulcers or wriggling about on the surface of the ulcers was frightening and repulsive, their presence was a blessing since they made a 'clean sweep' of the dead and decaying tissue, thereby making the ulcer more presentable.

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Lepr Rev (1992) **63,** 296–298

Teaching Materials and Services

Tropical Diseases 'Electronic museum'; Wellcome Trust, London

Based on the Wellcome Museum of Medical Science, we are creating a sophisticated teaching archive in the area of tropical medicine. Our 3-part 'electronic museum' will consist of an archive, interactive learning material and software tools.

The Archive contains the basic units of information—pictures and text. It takes the form of a videodisc and database containing up to 30,000 video stills as well as a limited amount of moving material. **Interactive Learning Material** is currently being created by teachers using the archive with a computer program called an authoring system. This structured material will be accessible via menus leading to *diseases* (e.g. malaria), *topics* (e.g. malnutrition), *countries* (e.g. Ghana), and *clinical features* (e.g. jaundice). The system will also contain a 'Challenge Option', which will provide the user with the opportunity to diagnose and treat simulated cases of tropical disease. Easy to use look-up facilities will enable users to browse any part of the archive. We also hope to provide access within the system to CD-ROM based texts such as the Oxford Textbook of Medicine.

The Software Tools going out with a delivery workstation will include authoring facilities which will enable the creation of further interactive learning modules as a continuous process. Other facilities will enable the editing of existing learning material to suit local needs. The tutorials produced with the archive are not intended to provide a full coverage of the field of tropical medicine. They will, however, serve examples of the ways in which learning material can be produced from the archive, as well as provide a reasonable volume of instantly usable material.

The first part of the Project has necessarily been concerned with the building of computer structures, the acquisition of staff and the gaining control of a very large visual database.

We are now able to begin to switch the focus of activity to the production of the interactive learning modules which will make the videodisc into a powerful learning tool.

Dr Marshall, in consultation with Professor Harold Lambert and other members of the Advisory Group, has restructured the disease and clinical feature lists into a series of 'units' of information. These units may take the form of diseases, clinical features or countries, or a fourth option we have added, that of topics. Examples of topics are blindness, malnutrition and child mortality. This will enable us to tackle a number of diseases in natural groupings and cover other important issues.

We are now developing strategies for the future. These are intended to achieve the following:

The evaluation and dissemination of this archive in ways which will maximize its use to the tropical community.

2 Mechanisms to receive and referee interactive learning material produced using the archive at institutional level worldwide.

3 Mechanisms to collect new pictures and other images and to use them to produce further editions of the videodisc.

4 Development of academic and technical support networks which will include the supranational agencies. These will facilitate the use of the archive worldwide for learning as well as for the production of further learning material.

5 Research and development into cheaper hardware platforms to deliver the material. These will include methods of image storage that avoid the use and therefore the cost of a videodisc player.
6 Development of software that will enable the printing of the computer based learning material in the form of booklets which will increase its availability in areas unable to afford or support the delivery hardware.
7 Translation of the material into other languages.

For further details write to: The Wellcome Trust Tropical Diseases Videodisc Project, 183 Euston Road, London NW1 2BN.

INFOLEP: Leprosy Information Services

INFOLEP Leprosy Information Services is a project of the Netherlands Leprosy Relief Association (NSL) in Amsterdam, The Netherlands.

INFOLEP's services are to a great extent, aimed at the leprosy field projects in countries supported by the NSL.

INFOLEP also functions as a library and documentation centre offering its services to all those who need information on leprosy, in all its various aspects.

The objective of INFOLEP is to set up and maintain a vivid information network in the field of leprosy primarily for the NSL-supported leprosy projects and for those studying or preparing to work in this field.

On a pro-active basis, INFOLEP supplies information to all the NSL-supported leprosy field projects. This occurs through regular mailings, consisting of publications, articles, journals and other materials deemed relevant.

Local initiatives, in endemic countries, to produce teaching and learning materials in leprosy control can receive technical and financial support through INFOLEP.

INFOLEP has an extensive collection of materials on leprosy and leprosy control, consisting of books, journals, brochures, articles, reports, slides, (video) films and others, which can be consulted and/or borrowed. The greater part of the collection deals with scientific medical aspects, whereas the smaller, but steadily increasing part, focuses on teaching and learning materials on leprosy.

The collection is accessible through different catalogues. Since January 1990, retrospective storage and retrieval takes place by a computerized system (CDS/ISIS). This offers the possibility of free text searching, which enables you to find your information on title, author, subject or keyword.

INFOLEP is subscribed to two CD-ROM databases, i.e. MEDLINE from 1985 and HealthPLAN fromm 1981 onwards.

Both databases are frequently updated and complement each other. MEDLINE covers the biomedical, clinical aspects of medicine, whereas HealthPLAN gives information on the non-clinical aspects of health care, like health education, management, administration, social aspects etc. Both are bibliographic files with informative abstracts giving you an idea of the contents of an article.

Other services include:

* photocopy service (for a fee)
* inter-library loans, including photocopy service (for a fee)
* international bibliography on teaching and learning materials on leprosy
* audiovisual equipment for the use of video-films and slides.

For further information please write to: INFOLEP: Leprosy Information Services, Netherlands Leprosy Relief Association (NSL), Wibautstraat 135 II, NL-1097 DN Amsterdam, The Netherlands.

Tuberculosis control as an integral part of primary health care; WHO

The summary of this 48-page booklet begins:

'The era of specialized health programmes, each aimed at a specific disease, is over. But while countries acknowledge the need to integrate various disease control activities into their general health services, the integration process is fraught with difficulty. The aim of this book is to help the managers of primary health care programmes and of tuberculosis control programmes to achieve step-by-step integration, giving priority to case-finding and management.'
Available from: WHO, 1211 Geneva 27, Switzerland. Price: Sw.Fr. 9.

Workbook on Community-based rehabilitation services

This 136-page book, written by S P Murthy and Lyn Gopalan, has been sent in by Dr Maya Thomas, Field Director, Disability Projects, Action Aid, P.B. 5406, Rest House Road, Bangalore 560 001, India. It is a joint publication of 'Vikasa' Community-based Rehabilitation Project of Karnataka Welfare Association for the Blind and the Disability Division of Action Aid. The subject matter is detailed and wide-ranging and includes procedures for evaluation and assessment in order to analyse the difficulties which have been encountered by many CBR programmes in the past 10 or more years.

Leprosy in Haiti (La maladie de Hansen en Haiti)

This is a well produced 48-page book by Dr Claude Péan and published by the Institut Cardinal Leger contre la lèpre, 130 avenue d l'Épée, Outremont, Québec, H2V 3T2, Canada. There are very good colour pictures of the clinical aspects of leprosy, including reactions and differential diagnosis. This book deserves wide circulation in French-speaking countries where leprosy is endemic.

The Heiser Program for Research in Leprosy and Tuberculosis

The Heiser Program, well known for many years in the field of leprosy research, now includes tuberculosis. Awards are available under the heading of post-doctoral research fellowships and research grants. All enquiries to: Mrs Barbara Hugonnet, Director, Heiser Program for Research in Leprosy and Tuberculosis, 450 East 63rd Street, New York New York 10021, USA.

Questions and Answers on the Implementation of MDT for leprosy (in Portuguese)

This booklet on multidrug therapy and originally published by OXFAM, England, is now available in Portuguese under the title *Perguntas e Respostas sobre a Implementacao da Multidrogaterapia (MDT) em Hanseniase.* Over 2000 copies have been distributed and used by the National Leprosy Programme in Brasil. It is available from CERPHA, Rua Guapeni 54/101 CEP 20.520, Caixa Postal 24046, Rio de Janeiro, Brasil

Teaching and learning materials on leprosy (in French)

Lèpre: Matériel Didiactique en Langue Française, 1990 is available from L'Association Française Raoul Follereau, 31 rue de Dantzig, BP 79, 75722 Paris Cedex 15, France. This is a comprehensive account of what is available in French under the main headings: Ouvrages fondamentaux; Généralités sur la lèpre; épidémiologie-enrigistrement; clinique dermatologique; laboratoire; traitement (PCT); chirurgie-réhabilitation; éducation sanitaire; thèses et mémoires.

Lepr Rev (1992) **63,** 299–304

News and Notes

New leprosy treatment, *TDR News*

The following article appeared in No. 38 of *TDR News*:

Large-scale trials began in February 1992 of a new, rapid drug treatment that could help to wipe out leprosy, which today still affects an estimated 5–6 million people worldwide, including 2–3 million people who have deformities as a result of the disease.

The treatment, which is given orally, combines a new antibiotic, ofloxacin, with rifampicin, an antibiotic discovered in the 1960s and the mainstay of standard leprosy (and tuberculosis) therapy. Scientists believe the combination of the two drugs will be the most powerful treatment yet discovered for leprosy.

The combination promises to shorten duration of therapy to only 1 month, as against the 6 months to 4 years required by the standard multidrug therapy. 'This should make leprosy treatment far more acceptable to the many patients who balk at taking drugs for months or years and brings the possibility of wiping out the disease much closer, 'says Hiroshi Nakajima, the WHO Director-General.

Multidrug therapy was introduced by WHO 10 years ago and involves the administration of 2 drugs (dapsone and rifampicin) for patients with mild (paucibacillary) leprosy and of 3 drugs (dapsone, clofazimine and rifampicin) for those with severe (lepromatous) leprosy. Over the past 5 years it has cured over 2 million of the world's known leprosy patients in 91 countries where leprosy is a public health problem.

'Such rapid and effective use of drugs is certainly a remarkable achievement,' says Dr Nakajima. 'Its only a first step though. There are still about 40 to 50% of leprosy patients who are not receiving drug treatment. Our task now is to ensure that *all* leprosy patients across the globe have access to multidrug therapy.'

The trials of the new ofloxacin-rifampicin treatment, which are being organized by TDR and the WHO's Leprosy Unit, will take place in 7 countries—Brazil, Kenya, Mali, Myanmar, Pakistan, the Philippines and Viet Nam. They will compare the new regimen with the standard multidrug therapy. Results of the trials, which will involve about 4000 patients, should be available in 4 or 5 years.

'If successful, this ofloxacin-rifampicin regimen would represent a major advance in the treatment of leprosy,' says TDR director Tore Godal. 'The first drug used against the leprosy bacillus was dapsone and for many patients it had to be taken every day for life. Then came multidrug therapy, which brought treatment time down to 4 years at most. And now we're talking about 4 weeks' treatment.'

Ofloxacin was launched in 1985 by the Japanese pharmaceutical firm Daiichi Seiyaku for the treatment of infections, particularly of the urinary and respiratory tracts: it has cured between 70 and 98% of the 1·5 million patients who have already received the drug, producing mostly mild side-effects in only a few patients.

Ofloxacin kills the leprosy bacillus by inhibiting an enzyme that controls the way DNA coils itself inside the bacillus. In 1986, French researcher Jacques Grosset of the Pitié-Salpétrière

Hospital Medical School in Paris found ofloxacin to be second only to rifampicin in the speed and efficacy with which it killed leprosy bacilli in laboratory animals.

The present trials were set up on the assumption that ofloxacin should be able to kill any mutant bacilli resistant to rifampicin much more quickly than do the other components of multidrug therapy. Shaik K Noordeen, chief of the WHO Leprosy Unit believes that if the new treatment is shown to work, it could be extremely useful for patients living in outlying communities for whom compliance with months or years of multidrug therapy is a problem. Initially, the rifampicin-ofloxacin 4-week treatment would be administered under medical supervision in clinics or health centres. But as experience with this treatment grows, community-based or even home treatment could be envisaged.

Ofloxacin and rifampicin are much more expensive than dapsone and clofazimine, making the new 4-week treatment about the same price as the standard 2-year or 6-month multidrug therapy. But again, with increased use, the price, particularly of ofloxacin, could be expected to fall.

Selected annotated bibliography on essential drugs: WHO

This publication (WHO/DAP/90.3) comes from the WHO Action Programme on Essential Drugs and Vaccines, WHO, 1211 Geneva 27, Switzerland. It has 214 pages and includes author, country and subject indexes. The introduction reads as follows:

The literature on the rational use of drugs has become more complex since the early 1970s. Within the last decade, interest has increased in developing a conceptual framework for the rational use of drugs. Governments, international and non-governmental organizations, universities and individuals have been actively involved in the many different aspects, including the formulation of the concept of essential drugs and the development of mechanisms to increase the availability of appropriate drugs at different levels of health care. National policies and programmes have been developed which determine the type and quantity of drugs needed, their rational use and the means to procure and distribute them effectively, taking into account local economic, social and political environments.

This second edition of the annotated bibliography builds on the publication issued in May 1988 and contains 173 additional references. It provides an entry point to the literature on these diverse activities. It directs the reader to key reports, articles and books related to essential drugs. The bibliography is not exhaustive. Some publications were excluded because of space and time constraints, and because of their limited circulation and accessibility. In addition, most of the material is from English language sources only.

The publications are organized in alphabetical order by author/corporate author and each is placed, according to its main focus, into one of 13 sections: assurance of quality; audiovisuals; drug information; economics and finance; health aspects; human resources and training; monitoring and evaluation; periodicals; pharmaceutical industry; policy and regulation; selection; supply; use. Keywords highlight specific subject areas and countries that are covered in each publication. A list of keywords pertaining to each section follows this introduction. The material is indexed by author, corporate author, subject area and country.

Most of the WHO publications should be available in national libraries. In case of difficulty it is suggested that the libraries of the WHO Regional Offices be approached for assistance.

WHO depository and reference libraries in each country (addresses available from WHO Headquarters) hold copies of all WHO publications. WHO publications may also be purchased from the WHO sales agents or the Distribution and Sales Office in WHO Headquarters. Please note that WHO documents are not for sale and may only be requested from the headquarters programme or regional office indicated in each bibliographic reference.

Blister–calendar packs for leprosy and tuberculosis in the Philippines

Dr A Galvez, Consultant in Chronic Diseases, WHO, Regional Office for the Western Pacific, United Nations Avenue, PO Box 2932, Manila, the Philippines, has written with details of multidrug therapy experience using blister–calendar packs (BCPs) for leprosy and tuberculosis. BCPs were originally introduced in 2 provinces of the Leprosy Control Programme, and after evaluation they were adopted nationwide for all patients. Procurement is at national level and allocation is based on registered patients and expected new patients in each province, per year. Distribution is through existing field health units at regional, provincial, municipal and barangay (village midwife) levels. Patients collect their antileprosy drugs in BCPs on a monthly basis, with supervision of the monthly medication. Empty packs are returned on each occasion, in return for a new supply. Patients are questioned at the time of collection about drug intake and visits are made to the patients' homes during each monthly period. Following this experience in leprosy, the Philippine Tuberculosis Control Programme adopted the use of BCPs for their drugs, using short course regimens of rifampicin, isoniazid and pyrazinamide (first 2 months), followed by rifampicin and isoniazid (4 months). These packs, issued at weekly intervals, and with appropriate monitoring by health staff for any adverse reactions, are available in all field health units and hospitals, nationwide.

Treatment of severe colitis in Behçet's syndrome with thalidomide

This case report was reported in the *Journal of Internal Medicine*, 1990, **228,** 405–7. Written by H Larsson of Lund University, Sweden it describes the use of thalidomide in a 35-year-old male patient suffering from severe Behçet's syndrome since 1979, as 'a final pharmacological measure to avoid colectomy during a severe attack of Behçet colitis.' The effect was dramatic and the patient was discharged from hospital 3 weeks after starting the treatment; at 5 months, the patient's condition was still satisfactory. The discussion includes the proposal that this drug should be considered as a first-line treatment in colitis associated with Behçet's syndrome.

Global evaluation of the introduction of multidrug therapy

This 58-page document, published jointly by the WHO and the Department of Epidemiology, Catholic University of Louvain, Brussels, Belgium and in consultation with ILEP 'presents information on MDT from 173 countries and territories worldwide . . . and is intended to be a stimulus for all those in charge of leprosy control programmes to implement MDT in the field and to collect the necessary information to monitor the process.'

The report is divided into 5 parts: summary of statistics by WHO regions; detailed statistics by WHO regions; annual trends by WHO regions; summary of statistics by country; and detailed statistics by country.

World leprosy atlas

This 200-page annual publication is a very useful reference document. It includes data on leprosy patients from 173 endemic countries and territories. 'Information about the last available statistics on population, registered leprosy cases and newly detected cases at national level and by administrative division was requested from the Ministries of Health of all these countries during 1991. A total of 79 answers were obtained by early December. As far as possible, figures presented in the Atlas only concern patients registered for, or still requiring, treatment. Patients under surveillance after treatment, or registered for care, are thus not taken into account.' For further details write to: EPID 30/34, Ecole de Santé Publique, Clos Chapelle-aux-Champs 30, 1200 Bruxelles, Belgique.

St Francis Leprosy Guild, London

The St Francis Leprosy Guild (founded 1895) exists to help missionaries, doctors, nurses and other workers care for the victims of leprosy. The 1992 Report records financial support for 92 different centres in Angola, Bangladesh, Bolivia, Brasil, Cameroon, Egypt, Ethiopia, India, Indonesia, Jamaica, Kenya, Korea, Madagascar, Mauritius, Myanmar (Burma), Nigeria, Pakistan, Papua New Guinea, the Philippines, Sri Lanka, Sudan, Tanzania, Thailand, Uganda, Vietnam, Zaire and Zambia. Including certain special grants and educational grants (the latter include support for medial medical student electives). The total dispensed in 1991 was £396, 231.

National Leprosy Organization Workshop of Voluntary Leprosy Institutions of Andhra Pradesh, India, 1991

The Meeting was opened by Dr K V Desikan, describing 'the present national scenario'. Shri S P Tare delivered the keynote address which covered all the session topics: Care after cure; rehabilitation; problems of voluntary organizations; and people's participation. Some very interesting points are made in this short 6-page report, e.g. 'The rigorous MDT schedule of drug delivery has also affected attention to individual patients.' Shri A Parathasarathy expressed the view, 'that the function of a physiotherapist is not to dress ulcers, but to prevent deformities'.

Copies are available from: Gandhi Memorial Leprosy Foundation, Hindinagar, Wardha 442103, India.

Bombay Leprosy Project celebrates 15 years

At the above celebration the Bombay Leprosy Project was congratulated on its work of the past 15 years. A brochure distributed at the Meeting contains contributions from the fields of surgery, rehabilitation and medicine which show among other achievements 'how the services of BLP have helped in increasing the acceptance of leprosy patients in their institutions'.

National Leprosy Organization Diary

This diary has now been published for 11 years. It includes many facts on leprosy including: definition, signs of the disease, classification, prevalence in India and further reading.

Copies may be purchased from: National Leprosy Organization, Hindinagar, Wardha 442103, India.

Disability in the developing world, IDEA

This is a multidisclipinary, 5-day course to share information and experience and to extend the debate on disability and development issues. It is an opportunity to discuss and learn more about the challenges facing disabled people and service providers in developing countries. The Course is relevant to people from all professional backgrounds who are concerned with disability, and will take place between 7 and 11 December 1992 in London (accessible venue).

Application forms and further information on this and other courses from: M. Greenhalgh, IDEA, William House, 101 Eden Vale Road, Westbury, Wilts BA13 3QF, UK. Tel: 0373 827635.

14th International Leprosy Congress, Florida, USA, 1993

There is great hope that the WHO resolution to eliminate leprosy as a public health problem by the year 2000 can be achieved. The questions remain: Is present technology sufficient? Are social, economic, and political conditions of endemic countries adequate? What will happen to patients with social and physical disabilities? The 14th Congress will address these issues and formulate plans of action.

For further details of this Congress, to be held between 29 August and 4 September 1993 in Orlando, Florida, USA write to: ILA Congress, c/o ALM International, 1 ALM Way, Greenville, South Carolina 29601, USA.

Leprosy Courses, Fontilles, Spain, Autumn 1992

Sanatorio de Fontilles are running 2 courses which are to be held in Fontilles, Alicante, Spain: (1) for auxiliary staff between 13 and 24 October 1992; and (2) for paramedical workers between 2 and 7 November 1992.

For further details write to: Dr J Terencio de las Aguas, Sanatorio San Fco, de Borja, 03791 Fontilles, Alicante, Spain.

WHO model prescribing information: drugs used in mycobacterial diseases, 1991

This is the third in the WHO's series of model prescribing information, which is produced to assist national authorities, particularly in developing countries, when preparing drug formularies, data sheets, and teaching materials. This volume covers some 13 essential drugs used for the prevention and treatment of tuberculosis, for the treatment of leprosy, and for the treatment of diseases caused by nontuberculous mycobacteria, including localized cutaneous lesions, pulmonary disease, lymphadenitis and disseminated disease.

Model prescribing information is presented in 3 main chapters. The first, devoted to tuberculosis, opens with a detailed overview of the disease, its clinical features, and the main principles of prevention, tuberculin testing, and chemotherapy. The special problems of diagnosis and treatment of HIV-infected patients are briefly discussed. Readers are also given detailed information on the properties of antituberculosis drugs, preferred treatment regimens, monitoring of patient compliance and therapeutic response, and the treatment of relapsing and unresponsive disease.

Against this background, model prescribing information is presented for 10 drugs used in vaccination, chemoprophylaxis, and chemotherapy. Each drug is profiled in terms of its clinical uses, dosage and mode of administration, contraindications and precautions, use in pregnancy, adverse effects, and possible interactions with other drugs.

Drugs used in the treatment of leprosy are covered in Chapter 2, which also features background information on the disease and the main principles of multidrug therapy. The final chapter provides prescribing information for drugs used to treat nonspecific mycobacterial infections.

Available in English (French and Spanish editions in preparation) from: World Health Organization, Distribution and Sales, 1211 Geneva 27, Switzerland. Price: Sw. fr. 9./US$8.10, and in developing countries Sw. fr. 6.30.

Breakthrough in leprosy surgery

Research funded by LEPRA has produced an exciting breakthrough in rehabilitative surgery for leprosy patients, according to an article published in *The Lancet* at the end of last year.

Success in dramatically restoring lost sensation to nerves paralysed by leprosy provides new hope for many thousands of people disabled by this ancient disease.

This new surgical technique has been applied to disabled leprosy patients for the first time in a co-operative project involving the Royal College of Surgeons in London, a southern India leprosy centre and LEPRA. Using muscle grafts to replace damaged nerves, early results show a 70% success rate in restoring sense of touch and temperature to damaged feet and hands.

While strong antibiotic drugs now provide an effective cure for leprosy—and the search for a preventive vaccine continues—millions of patients have been permanently disabled through infection, and tens of thousands are added to this total each year because damage to their nerves prior to drug treatment leaves them prone to continued injury and disability.

In addition to the purely practical disadvantages faced by disabled leprosy patients, they also have to cope with deep-rooted prejudice which can lead to loss of families, homes and jobs. This new technique offers the hope of preventing injuries which specifically identify leprosy sufferers and therefore could contribute to a reduction in the age-old stigma attached to the disease.

The paper published in *The Lancet*, written by 3 doctors based at the Royal College of Surgeons and 3 working at the Sacred Heart Leprosy Centre in Tamil Nadu, describes the successes achieved in operations on 10 leprosy patients in India. This follows extensive initial research in London at the Royal College.

Sections of nerve up to 6 cm long have been replaced by tubular muscle fibre, which provides a route encouraging the regenerating nerve to grow and bind, restoring lost sensation. The technique was developed from surgery originally carried out in the U.K. to repair nerve damage suffered by accident victims.

'For the first time we have a technique to restore protective sensation in selected leprosy patients with severe nerve damage' said one of the paper's authors, Dr Jerome Pereira.

'For individual patients, regaining the protective sensation which allows them to feel stones and thorns underfoot will mean the difference between dependence and independence. We are very hopeful that this relatively simple technique will eventually be widely available in the areas where it is most needed.'

The encouraging results achieved in India will now be tested further in multicentre trials in Ethiopia, Brazil and again in India to determine the effectiveness of the technique in all types of leprosy.

Handbook of leprosy, W. H. Jopling and A. C. McDougall (in Portuguese)

This title is once again available in Portuguese from Livraria Atheneu, Rua Bambina 74, Rio de Janeiro, RJ, Brazil. Price: US$22 approx. Of the 1200 copies printed over 500 have already been sold, almost entirely in Brazil. The English edition is available from the publisher, Butterworth–Heinemann, Halley Court, Jordan Hill, Oxford OX2 8EJ, U.K.

Ofloxacin for the treatment of leprosy

The following is the summary of a publication on the above subject by B Ji and J Grosset in *Acta Leprologica* (1991) **7**, 321–6:

Among the major commercially available fluoroquinolones, ciprofloxacin was inactive against *M. lepr*ae in mice; pefloxacin was active, 50 mg/kg daily showed bacteriostatic activity but 150 mg/kg daily displayed bactericidal activity; ofloxacin was more active than pefloxacin, 50 mg/kg daily exerted the same level of bactericidal effect as pefloxacin 150 mg/kg daily, and ofloxacin 150 mg/kg displayed profound killing activity. Two clinical trails with 6 months of pefloxacin and/or ofloxacin in 31 previously untreated lepromatous patients have been completed. Pefloxacin 400 mg twice daily or 800 mg once daily or ofloxacin 400 mg once daily were equally effective; definite clinical improvement with drastic decrease of morphological index to the baseline were observed in all patients at 2 months after beginning of treatment; about 99·99%, or 4 'logs', of organisms viable on Day 0 were killed by 22 doses of either pefloxacin or ofloxacin. The side effects from the 2 trials were rare and mild, and the patients tolerated extremely well the combinations of pefloxacin/ofloxacin plus multidrug therapy (MDT) regimen for multibacillary leprosy recommended by WHO. The amount of rifampicin-resistant mutants in lepromatous patients before treatment are no more than 4 'logs', thus, all rifampicin-resistant mutants may be eliminated by 22 doses of either pefloxacin or ofloxacin. It is, therefore, possible that the combination of ofloxacin and rifampicin may considerably shorten the required duration of MDT.

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.

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