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Leprosy Review

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

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LEPRA

Editorial Office: Lepra, Fairfax House, Causton Road, Colchester CO1 1PU, England
Assistant Editor: Jennet Batten, 94 Church Road, Wheatley, Oxon OX9 1LZ, England

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.

British Leprosy Relief Association
Registered Offices: 105–107 Farringdon Road, London EC1R 3BT

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Editorial

DISABILITY CONTROL IN A LEPROSY CONTROL PROGRAMME

Introduction

The Sixth Report of the WHO Expert Committee on Leprosy[1] recommends that 'prevention and management of impairments and disabilities, which have long been recognized as essential components of leprosy control programmes, should be implemented effectively'.

It is recognized that the best way to seek to prevent disabilities is to detect and treat patients at a very early stage in the disease.[2] It must, however, be emphasized that early detection and early treatment are no guarantee that nerve damage will not occur, though they minimize the risk. Sadly many patients still register for treatment with irreversible peripheral nerve dysfunction. The 1987 LEPRA Report[3] shows that 21·9% of new Malawian patients had disabilities (WHO disability grades 1 to 3) on diagnosis, and this occurred in a programme that delivers treatment to within 3 miles of patients' homes. The 1987 Tanzania National Leprosy and TB Programme Report[4] shows that 30% of the new patients had disabilities grades 1 to 3. Becx-Bleumink[5] reports that 28·3% of 853 new Ethiopian patients had loss of sole sensation on registration (19% bilaterally), and that 41·4% of a group of 1395 old patients had sole sensory loss (31·3% bilaterally).

Nerve function changes occur in some patients during treatment or surveillance, often 'silently' in the absence of any nerve pain. Indeed loss of sole sensation, which brings with it lifelong risk of sole wounds, almost always seems to occur silently and thus is not easily identified by field workers. In a group of 475 paucibacillary patients studied[5] on commencement and completion of their MDT course, 12·2% showed some recovery but also 8·2% suffered decrease in sole sensation whilst on MDT.

Once peripheral nerve impairment is established—that is, no longer amenable to reversal, with or without steroids—disability has a natural tendency to deteriorate; loss of protective sensation tends to result in unnoticed and uncared for wounds, paralysis in stiffness of joints, and dehydrated skin in cracks and callus. This tendency is unaffected by chemotherapy and special, specific measures have to be adopted to prevent it. Smith[6] in a follow-up of 118 disabled patients out of 175 detected in a survey in a well organized leprosy control programme in India, found that over a 4-year period (from 1979 to 1983) 71 (60·1%) showed no change in WHO disability grading (excluding grade 1), 19 (16·1%) showed improvement and 28 (23·72%) had deteriorated. The deterioration was more marked in the borderline lepromatous group, though all classification groups were affected. The mean grade for the 118 patients had increased from 1·58 to 1·70. The most striking differences in actual disabilities between the 175 (18·8%) disabled in 1979 and the 152 (14·6%) found disabled in 1983 were reductions in numbers with severe absorption from 9 to 1 and with plantar ulcers from 60 to 45. Dr Smith suggests that this decline is an effect of the disability control programme. There was little change in other disabilities.

In the absence of effective disability control, a patient who completes his course of

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chemotherapy having only 'invisible' sensory loss of the sole, may have lost half of his foot 10 years later. Such deterioration will not appear on present leprosy control records unless these include records of disability in all patients suffering peripheral nerve impairment, whether on or off chemotherapy. Recent reports from Nigeria[7] and China[8] evince concern over the significant numbers of patients (on and off chemotherapy) observed suffering severe deformities and handicaps. Thus the size and severity of the problem which disability and handicap pose to many present-day leprosy patients continues to give cause for concern, and will continue to do so for many years to come.

The purpose of this paper is to discuss ways in which the effectiveness of activities to control (prevent or limit) disability within a leprosy control programme can be improved. Much that is already known about action that can prevent disability is not being consistently applied. Thus it appears that improved management may be the key to improved efficiency and effectiveness. This paper does not attempt to deal with the valuable role of hospitals in the surgical and social rehabilitation of those already disabled.

Improving management of disability control activities

The WHO Expert Committee[1] recommends six specific managerial steps for the practical implementation of disability prevention and management at peripheral level.

The first recommendation states that 'the team leader, normally a physician, accepts responsibility for prevention of primary and secondary impairments and disability as part of his or her responsibility for patient care.' This is important. The team leader of a leprosy control programme needs to coordinate activities to control the bacilli with activities to control disability. All team leaders will be concerned over the problems that disability brings to their patients, and most arrange for health education talks to be given at treatment points on the subject of self-care. However if the effectiveness of activities to control disability is to be maximized, the team leader needs also to manage, supervise and evaluate such action. For example he needs to ask if existing resources of time and materials are targeted towards well thought out priorities, and are being used as productively as possible. He will ask whether community or rehabilitation workers outside the vertical leprosy programme could give more support to leprosy patients. When initiating a disability control programme, the team leader's first step may be to ask a physiotherapist or clinician having management skills to study disability problems, to measure the effect of present activities on the incidence of new disability, and to explore new possibilities for action and report back to him.

The second recommendation is that 'specific, limited, measurable objectives are set for preventing and limiting disability, and activity plans based on these objectives are formulated.'

The overall objective of disability control is:

THAT PATIENTS HAVE NO DISABILITY OTHER THAN
THAT WHICH WAS GENUINELY IRREVERSIBLE AT REGISTRATION

Thus if a new patient has no disability at diagnosis, the objective will be to prevent any from occurring. If a new patient already has disability on diagnosis, the objectives will be to prevent any worsening of that disability and to encourage recovery where possible. The overall objective can be subdivided into a number of specific, limited action objectives as shown on Figure 1. Staff need to recheck regularly (monthly if possible) for loss of sensation and strength not only in patients who are on treatment, but also during the period of surveillance. Activities to minimize risks of secondary skin cracks, joint stiffness, wound occurrence and wound neglect, need to be lifelong in patients with irreversible peripheral nerve damage. Therefore, when planning to control disability it is necessary to include all patients suffering peripheral nerve damage, whether or not they are on chemotherapy.

It will probably be necessary to implement and evaluate action to control disability in planned stages such as are indicated in the flow chart shown in Figure 2.

ACTION OBJECTIVES		**EVALUATION MEASUREMENT
1: PRESERVE NERVE FUNCTION Preserve nerve function where at risk	→	Scores from sensation maps & strength records
2: AVOID SECONDARY WOUNDS, CRACKS AND STIFFNESS		
2.1 Preserve vision in eyes with abnormal blink	→	Vision measurements
2.2 Keep insensitive hands free from wounds	→	Hand wound count
2.3 Keep insensitive feet free from wounds	→	Foot wound count
2.4 Keep non-sweating hands and feet free from callus and open cracks	→	Open crack count
2.5 Maintain or improve joint mobility in clawed digits and dropped feet	→	Joint angle measurements
3: AVOID COMPLICATIONS DUE TO WOUND NEGLECT Get wounds and cracks healed quickly, and without complications & bone loss	→ →	Wound measurements Bone loss score

**See fourth recommendation

Figure 1.

The third recommendation is that 'impairment and disability records are included in the clinical recording system'. The design of disability records is extremely important. Through them staff can identify:

(i) existing impairments and disabilities to which attention needs to be given;
(ii) improvements which indicate success in action to date and call for celebration; and
(iii) changes for the worse which signify failure to control disability and which indicate a need for prompt action.

It is the last-named information (iii) which is vital for programme evaluation.

The above information is required on the individual patient disability record to enable the clinician in charge of patient care to monitor progress in disability control. It is also needed for the team leader's regional or national statistics, to guide him as he plans for and evaluates action to control disability.

The Individual Patient Disability Record (see Figure 3).

Information required. The individual patient record should include the following information regarding eyes, hands and feet, together with keys to all tests and signs used:

- Serial sensation and strength records through which changes in nerve function can be monitored, plus a note as to the duration of any change.

Sensation maps need to show the area of sensory loss. Finger and toe drawings should be printed large enough to enable sensation and wounds to be clearly marked. Strength records need to indicate the movement tested and the degree of strength loss. These records can be used both to identify patients losing nerve function and needing neuritis chemotherapy, and to monitor and evaluate the effect of such treatment.

Stage 1* Study disability problems, available resources and obstacles that might impede activities to control disability

↓

Stage 2* Select specific, limited, measurable action objectives

↓

Stage 3* Make an implementation and evaluation plan

↓

Stage 4 Train staff in needed skills and implement the plan

↓

Stage 5 Monitor and evaluate the effectiveness and efficiency of the programme at regular intervals

↓

Stage 6 Modify the plan if and as indicated by stage 5 findings.
Select added objectives if and when resources allow

* See further notes below

Figure 2.

* Stage 1 includes gathering of information regarding disabilities, identifying important disability problems, and reviewing obstacles that may impede activities to control them. Information regarding numbers of patients with existing disabilities may be found in existing programme reports where the WHO disability grading has been used. More complete information may be gathered from disability records in existing Individual Patient Forms, or by conducting a disability survey in representative areas using the forms shown in Figures 3 and 4 as described below. Information can be obtained informally from patients and staff in regard to the impact of various types of disability on patients' lives, their beliefs as to their cause and 'cure' and any practical problems already encountered in implementing self-care. The data will indicate which are the more serious and widespread problems which need to be tackled first. The next step is to consider possible ways of dealing with these important problems. What resources are available, and what obstacles might hinder proposed action? Can the theoretical solutions be implemented in the given situation?

Stage 2. On the basis of the information collected in stage 1, action objectives can be selected. These should be feasible, observable and measureable.[9]

Stage 3. When making a plan to implement the selected objectives, it is necessary to outline the activities in detail. For example:
Which people will carry out what activities, and when? What skills do they need to acquire; who will teach them these skills? Where and when?
What materials will be needed, for example shoe materials, teaching pamphlets, record forms?
What funds are needed for the above activities, from where will these be obtained, by whom and when?
When, how and by whom will progress towards selected objectives be monitored and evaluated?

The sensory maps are also of value to staff training patients in wound avoidance, to remind them which particular areas are insensitive and thus at risk of injury and which areas are sensitive and thus 'safe'. Dropped feet, clawed digits and weak muscles need to be exercised.

- Secondary wounds, cracks and bone loss.

Wound sites, sizes, recurrence history and probable causes should be recorded, so that the feasibility of preventing recurrence can be assessed and the pattern of wound healing and recurrence monitored.

The level of bone shortening should be mapped so that any increase in shortening over the years can be monitored. In some situations wound recurrence may be unavoidable. If they are not to be continually disappointed patients and staff need to make sure that they have long term plans and expectations that are realistic. Open cracks should also be mapped and are an indicator of neglect of skin care. Although it is desirable to monitor changes in finger stiffness through finger angle drawings where possible, this is not feasible in most field programmes.

Methods of testing and recording. Basic methods are described in 'Preventing Disability in Leprosy Patients'.[10] Supervisory and teaching staff should seek to achieve reproducible test results

DISABILITY RECORD

PATIENT'S NAME Edet Eket 5031 CLASSIFICATION BT

RIGHT SIDE							STRENGTH SWP = Strong/Weak/Paralysed	LEFT SIDE						
							DATE	2/12/88	3/1/89					
mm	mm	mm	mm	mm	mm	mm	Light closure lid gap in mm	0 mm	0 mm	mm	mm	mm	mm	mm
Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Blink Normal	(Yes) / No	(Yes) / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No
							Little finger in	P	P					
							Thumb up (palm upwards)	S	S					
							Wrist up	S	S					
							Foot up	S	S					
							ASSESSOR	JW	JW					

KEY: Sensation tested by light skin denting with ball point pen at dot sites; √ = feels within 3 cm; X = does not feel; C = clawing; — = shortening level; ⊘ = wound or open crack

Worsening within past 6/12? Yes/No

PALMS RIGHT LEFT SOLES RIGHT LEFT DATE/ASSESSOR If answering "yes", detail below

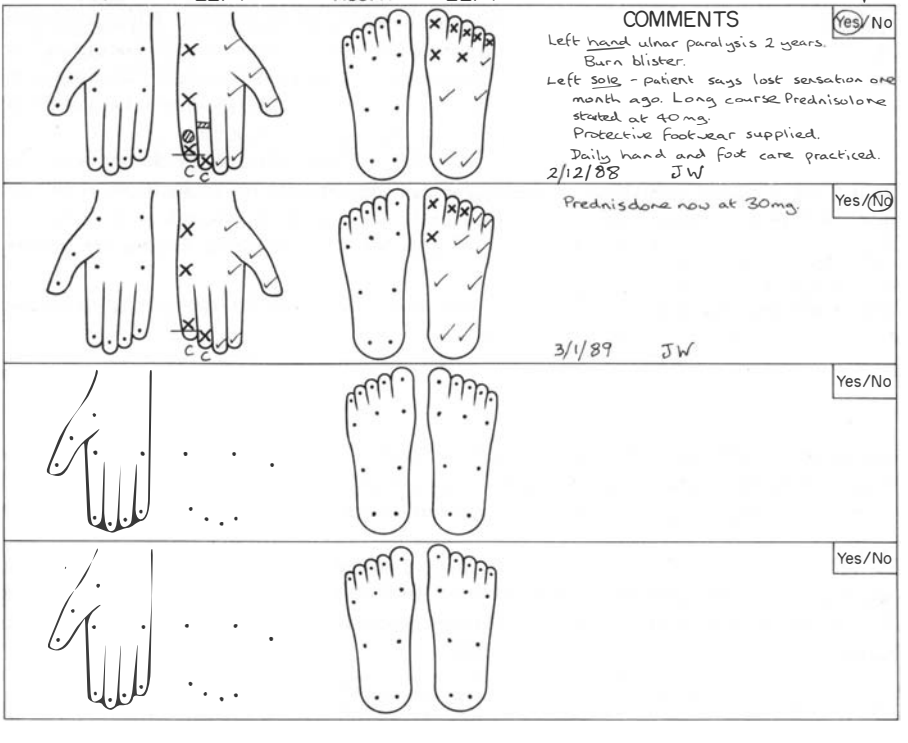

Figure 3. An example of a disability section of an Individual Patient Record

Note: More detailed strength key:
SRMP = Strong/Resistance reduced/Movement reduced/Paralysed

through careful training of staff and regular quality control checks. Periodically, for example, they should ask several staff members to each make a record on the same patient and then to compare results, with retests where findings differ.

Use. The baseline record is of great importance as it forms the basis for immediate action plans and for all later comparison. Thus it should be completed with the utmost care. New records should always be compared with previous records in order to check for change. Too often staff fail to make this comparison and thus lose the opportunity to take appropriate action when new problems arise[11] and to rejoice with the patient when improvements are achieved. Suspected changes should be confirmed by visual evidence or history.

The Team Leader's Regional or National Yearly Report

In order that he can give appropriate direction to the disability control programme, the team leader should aim to determine each year:

Numbers of patients affected by primary effects of nerve dysfunction (sensory and strength loss) and by secondary problems (wounds, cracks, bone loss).

Changes in type and in extent of disability occurring within the past year.

An example of a form on which such information is summarized is shown in Figure 4. Sensation, strength, vision, wounds plus open cracks and bone loss have all been scored. Changes in score since the previous year are shown in the final column. Sensory loss has been scored by counting 1 for each dot site on the hand or sole maps at which sensation (or bone) has been lost. Strength test results have been scored on the basis of 2 for paralysis, 1 for weakness and 0 for normal strength. Wounds plus open cracks have been counted. Bone loss has been scored by area.

Very significant changes can occur in the extent of disability without any change occurring in the WHO disability grade, and thus the grading is not appropriate for evaluation of the disability control programme.[12] The grading can however be used to gain a rough idea of the extent of disability in a group of patients, and as an indicator by which new case finding can be monitored from year to year.

The fourth recommendation is that 'arrangements are made for the provision of protective footwear and other aids.'

Protective footwear

Requirements of footwear for insensitive feet are that it should be as far as possible protective, accessible to field patients, locally repairable and acceptable to the patient in cost, function and style. Priority should be given to footwear for younger outpatients in whom the first ulcers can be prevented.

The team leader needs first to estimate numbers of patients with sole sensory loss, who thus need ongoing access to a source of protective footwear. In the absence of sole sensation records he may initially plan for footwear for 20% of accumulated patients. He then needs to acquire information regarding protective footwear currently available:

What sources of suitable, protective footwear currently exist?

How many pairs of protective footwear were made in programme workshops during the past year by each shoemaker, and in total? A full-time shoemaker, without any machinery to assist him, should be able to make 300 new pairs and also to repair 300 pairs in a year. Where production is below this target, this may be due to lack of orders for footwear, to lack of materials or to slow work habits.

How long does the average pair of sandals last? What are the weak points at which repairs are commonly needed? Can weak areas be strengthened?

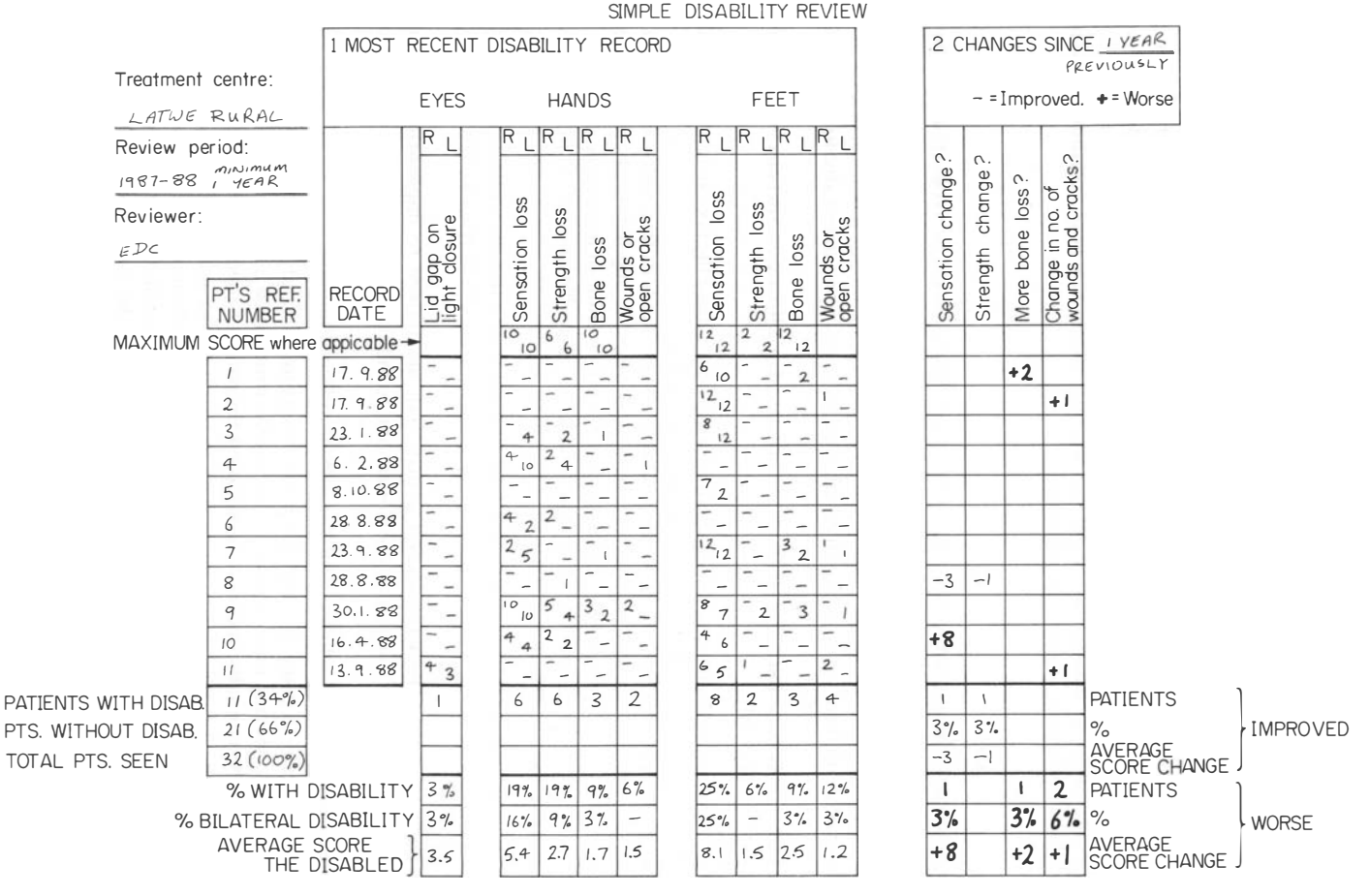
SIMPLE DISABILITY REVIEW
1 MOST RECENT DISABILITY RECORD
2 CHANGES SINCE 1 YEAR PREVIOUSLY
− = Improved. + = Worse
Treatment centre:
LATWE RURAL
Review period:
1987-88 minimum 1 YEAR
Reviewer:
EDC
EYES
HANDS
FEET
PT'S REF. NUMBER
RECORD DATE
Lid gap on light closure
Sensation loss
Strength loss
Bone loss
Wounds or open cracks
Sensation change?
Strength change?
More bone loss?
Change in no. of wounds and cracks?
MAXIMUM SCORE where appicable
PATIENTS WITH DISAB.
PTS. WITHOUT DISAB.
TOTAL PTS. SEEN
% WITH DISABILITY
% BILATERAL DISABILITY
AVERAGE SCORE THE DISABLED
PATIENTS
%
AVERAGE SCORE CHANGE
IMPROVED
WORSE

Figure 4.

Are patients making regular use of the footwear? If not, why not? Are they repairing the footwear safely?

On the basis of this information the team leader can plan to improve footwear design and supply. Programme shoe workshops may be asked to maintain a stock of standard-sized, protective footwear having adjustable straps. This can be distributed through programme supervisors to field patients with insensitive soles, but normally shaped feet. However, it is important that the team leader adopts a flexible approach when seeking possible sources of protective footwear and of footwear funding. It may well be that soft-insoled footwear which will afford protection can be bought in local shops or made or modified by local shoe-makers.[13] The cost of keeping all patients with sole sensory loss supplied with free footwear is likely to be prohibitive. However, many working outpatients are accustomed to buying their own market footwear, and thus should be able to contribute to the cost of protective footwear.

Other protective aids

Staff should learn through experience what other aids help patients to avoid injuries. The most generally useful are spectacles for eyes with inefficient blink, and thick, simply sewn towelling bags that can protect insensitive hands from cooking burns much more effectively than the pieces of cloth so often recommended to patients lifting hot pots. Field staff should try to carry two or three samples of aids with them for distribution as indicated, or to show to patients able to make or obtain their own.

The fifth recommendation is that 'patients are instructed in self-care and in behaviour designed to prevent further disability'.

All patients on chemotherapy or surveillance need to understand the need to report immediately any change in sensation or strength and any nerve discomfort.

Patients with peripheral nerve dysfunction affecting eyes, hands or feet, need to learn how they can gain access to replacement protective devices, and what lifelong habits of care they need to adopt in order to prevent secondary complications:[10] a daily routine of inspection, skin or eye care, and exercise; an all-day alertness to, and avoidance of, possible sources of injury; and early detection and effective care of wounds.

In particular patients with sole sensory loss need to learn from experience of sole injury just how much walking causes recurrence of their ulcers, so that they can keep their walking within safe limits if at all possible.

The sixth Committee recommendation is that 'staff are trained to implement the disability prevention programme, to teach patients self-care and to monitor and support the practice of self-care by patients.'

Three points regarding training methods deserve special emphasis:

- The need initially to make sure that the patient really understands his self-care, and that advice given is practical. Having once demonstrated needed routines to a patient and advised on their importance, it is best on subsequent occasions to ask the patient to demonstrate and discuss what he already does in the way of self-care rather than to repeat the advice. By observing as the patient demonstrates care, staff will be able to identify areas in which more teaching is indicated. For example the lady with cooking burns may be folding the cloth too thinly as she lifts hot pots, or may have failed to notice that her fingers are off the edge of the cloth. By listening carefully as the patient describes the practical problems he is encountering in following advice given, or his reasons for disbelieving this advice, staff will be better able to understand his problems, and to offer meaningful, practical support and ideas. For example the patient, whose wife carries the water for 5 km to the house, and who objects to his using it all for foot soaking, may learn either to soak in a water source

that he passes during his daily activities or to use only a cupful of water poured into a tilted bowl when cleaning his wound or soaking his callused heel skin.

- The need for staff to encourage patients to persevere in the self-care that they have learnt, and to demonstrate their concern and care by action rather than through words. Advice alone is not enough. Thus, for example, if field and ward staff see patients with neglected skin, they will enable the patient to carry out immediate skin care, and then express pleasure on seeing the improvements that result.

- The essential need for middle-level supervisors to maintain interest in disability control activities and standards.

Leprosy control consists of disability control as well as the control of bacilli. By improving management aspects of disability control it should be possible to increase its effectiveness, and thus to minimize the handicaps that can so seriously affect a patient's quality of life.

JEAN M WATSON

The Leprosy Mission International
80 Windmill Road
Brentford
Middlesex TW8 0QH
England

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Evaluation of *Mycobacterium leprae* antigens in the monitoring of a dapsone-based chemotherapy of previously untreated lepromatous patients in Cebu, Philippines

P R KLATSER,* M Y L DE WIT,* T T FAJARDO,† R V CELLONA,† R M ABALOS,† E C DE LA CRUZ,† M G MADARANG,†§ D S HIRSCH‡ & J T DOUGLAS‡

* *Royal Tropical Institute, N. H. Swellengrebel Laboratory of Tropical Hygiene, Meibergdreef 39, 1105-AZ Amsterdam, The Netherlands;* † *Leonard Wood Memorial Center for Leprosy Research, P.O. Box 727, Cebu City, Philippines; and* ‡ *University of Hawaii, Department of Microbiology, 2538 The Mall, Snyder Hall 111, Honolulu, Hawaii 96822, USA.*

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Summary Thirty-five previously untreated lepromatous patients receiving dapsone-based therapy were monitored throughout their 5-year period of treatment by serology and by pathology. Sequentially collected sera were used to evaluate the usefulness of four *Mycobacterium leprae* antigens as used in ELISA to monitor the progress of their therapy. ELISA results were compared with each other and with bacterial load over the treatment period and with duration of treatment. The ELISAs, based on the measurement of IgM antibody reactivity to the two neoglycoproteins (NDO and NTO) representing the phenolic glycolipid antigen of *M. leprae*, were found to be the most effective in monitoring treatment. A whole *M. leprae* based ELISA was less efficient in monitoring treatment because it failed to measure antibodies in 8 out of 35 patients and because it provided consistently lower values than either NTO or NDO. The ELISA-inhibition test based on the detection of antibodies to a species-specific epitope on the 36 K antigen of *M. leprae* was less suitable because of persistent reactivity during therapy, consequently resulting in no significant correlation with ELISA reactivities to NTO or NDO.

Introduction

Leprosy has been aptly described as a disease of 'a slow bacterium'.[1] In terms of treatment, successful progress is often first noted after a year or more of drug therapy. Apparent progress

§ Deceased 8 January 1988

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during the first two years of treatment in incident multibacillary patients is frequently marred by reactional states. One of the difficulties in treatment is unsatisfactory quantitative measurement of a patient's progress towards a successful outcome. Current measurement of a patient's response to drug therapy is subjective: clinical observation and bacterial index (BI). Additional quantitative tests would be useful in assisting the clinician in evaluating the result of the medication. The ELISA offers two types of measurements that may be suitable for this purpose: antigen and class-specific antibody detection. Currently, positive antigen detection is limited to those patients with well established disease and very high BI values. Others have reported the inability to detect phenolic glycolipid-I antigen later than 4–6 weeks after initiation of treatment in these patients.[2] Until better techniques become available for antigen detection, current methods will not serve to monitor therapy over the course of treatment. For this reason we have chosen to focus our efforts on evaluating antibody measurements over the course of therapy.

In this article we describe the results of 4 serological tests measuring antibody reactivity to 4 different *Mycobacterium leprae* antigens throughout the course of a dapsone-based treatment. The sera tested were collected during the course of a 5-year treatment protocol. Three tests measured IgM antibodies, two to neoglycoprotein antigens representing the phenolic glycolipid-I of *M. leprae*, one of which was a disaccharide antigen (NDO) and the other a trisaccharide antigen (NTO).[3–7] A third antigen tested was whole irradiated *M. leprae* (MLEP).[8] The fourth test (INH) was based on the inhibition of monoclonal antibody binding by human sera to a species-specific epitope on the 36 K protein antigen of *M. leprae*.[9–11]

Test results were correlated with duration of treatment and bacterial index. Furthermore, the usefulness of the antigens represented by the 4 tests as analysed in relation to each other and in monitoring therapy of lepromatous leprosy patients.

Methods

CASE DATA

Sera for this study were collected from patients who participated in the Joint Chemotherapy Trial (JCT) conducted by the Leonard Wood Memorial Center for Leprosy Research in Cebu, Philippines in collaboration with the Sasakawa Memorial Health Foundation Tokyo, Japan and the Department of Health, Philippines. Sera of patients from two chemotherapeutic protocols (1A and 1C) of the JCT were used. Patients in group 1A received dapsone 100 mg/day, 6 times per week for 5 years and rifampicin 1·2 g once on admission. Patients in group 1C received dapsone 100 mg/day, 6 times per week for 5 years, clofazimine 100 mg 3 times per week for the first 24 weeks and rifampicin 1·2 g once on admission. The patients were previously untreated incident lepromatous (LL) cases free of any serious intercurrent disease and screened by chest X-ray to be free of tuberculosis and of erythema nodosum leprosum (ENL) on admission to the trial. All were clinically lepromatous and histologically LL with an average BI of $4{\cdot}59 \pm 0{\cdot}4$.[12] A total of 38 patients were admitted over a 3-year period, sequentially and randomly allocated to either 1A or 1C. These patients were harbouring dapsone sensitive *M. leprae*, by mouse footpad inoculation.[13] There were 17 males, ages 12 to 56 years old (average age 25·47 years), on admission to group 1A. Seventeen males, 12–55 years old (average age 22·41 years), and 3 females, 16–22 years old (average age 18·33 years), were admitted into group 1C. Eight patients in 1A and 8 patients in 1C dropped out during the course of the drug trial. Preliminary evaluation did not show any significant differences between the two therapy regimens (1A versus 1C) in terms of clinical improvement, bacteriologic reduction and occurrence of reactional states. Because of the low number of patients in each treatment group, the varying length of patient participation within the trial, no statistically significant differences in ELISA or BI values, and the lack of observable clinical difference in patient recovery between the therapy regimens, the data from the two groups were combined unless otherwise stated.

SERA

Sera from each patient were collected on admission and sequentially every 12 months during the 5-year period of therapy. As previously stated, however, some patients have missed collections or dropped out during the therapy period.

INDIRECT ELISA

The ELISA used in this report was a n indirect assay using 0·05 ml antigen suspension dried onto 'U' bottom microtitre plates (Dynatech, Alexandria, Virginia, USA). Antigen-coated wells were blocked to prevent nonspecific antibody binding by adding 0·075 ml of 5·0% goat serum or 5·0% BSA (bovine serum albumin) in phosphate buffered saline (PBS), pH 7·2 and incubating overnight at 4°C or for 2 hr at 37°C. Serum was diluted 1 : 500. An antihuman IgM conjugate was used to detect specific IgM activity. The remainder of the assay was performed as previously described.[14–16]

INDIRECT ELISA ANTIGENS

Three antigens were tested: whole armadillo-derived irradiated *M. leprae* and two neoglycoprotein antigens, one of which mimicks the two terminal sugars and the other mimicking the three terminal sugars of the phenolic glycolipid-I (PG-I) of *M. leprae*.[7] These semisynthetic antigens are: ND-O-BSA (natural disaccharide) with octyl linkage to bovine serum albumin (BSA); and NT-O-BSA (natural trisaccharide) with an octyl linker arm attached to BSA.[17] The octyl-linked neoglycoprotein antigens ND-O-BSA and NT-O-BSA, and whole *M. leprae* were provided under NIH contract (NO1 AI-52582) by Dr P Brennan, Colorado State University. The ELISA in which ND-O-BSA was used as antigen is termed NDO-ELISA; the ELISA using NT-O-BSA is NTO-ELISA; and the ELISA using *M. leprae* is MLEP-ELISA.

INDIRECT ELISA ANTIGEN PREPARATION

Immunlon II plates (Dynatech Laboratories, Alexandria, Virginia 22314) were coated with antigen in a volatile coating buffer (0·01 M ammonium acetate/carbonate, pH 8·2). Whole *M. leprae* cells used as ELISA antigen were suspended in a volatile coating buffer at a concentration of 0·04 absorbance units at 420 nm. The ND-O-BSA and NT-O-BSA were diluted to 0·3 μg/ml from a stock solution of 100 μg/ml and mixed thoroughly. Each of the three antigens was coated on microtitre plates by adding 0·05 ml of antigen suspension to each well. The plates were incubated overnight at 37°C to dry the antigen onto the plate. Each well was examined for uniform coating and unevenly coated wells were eliminated from use. The antigen coated plates could then be stored for several months at room temperature.[14]

ELISA INHIBITION TEST

Polystyrene ELISA microtitre plates (Dynatech) were coated with 100 μl per well of a soluble *M. leprae* preparation (0·5 μg/ml) in 0·05 M sodium bicarbonate buffer, pH 9·6, for 18 hr at 37°C. The plates were washed three times with PBS containing 0·05% Tween 20 (PBS/Tween). Simultaneously, to each well was added 20 μl of serum and 80 μl of peroxidase-labelled monoclonal antibody F47-9 diluted 1 : 1000 in PBS containing 0·1% Tween 20 and 0·6% BSA and the plates were incubated for 3 hr at 37°C.[9,10] Sera were tested in duplicate. After washing with PBS/Tween, wells were incubated with 100 μl TMB-substrate solution (12 mg of 3,3′,5,5′-tetramethylbenzidine (TMB) in 5 ml of ethanol added to 15 ml of 0·1 M citrate/phosphate buffer, pH 5·0; H_2O_2 added to a final concentration of 0·015%). Reactions were stopped after 15 min by adding 50 μl 2 M H_2SO_4. Resulting absorbance values were measured at 450 nm. Each test plate contained negative (OD = 1·5) and three positive (75; 50; 15% inhibition) control sera. The percentage inhibition of the sera was calculated as $[(1\text{-}OD/OD_{neg}) \times 100\%]$.[10]

STATISTICAL ANALYSIS

Statistical analyses were conducted on two types of data, those on actual ELISA and BI values over time and the other on percentages of these initial values over time. The initial value at the start of therapy for each patient was scored as 100% and subsequent test values over the course of therapy were adjusted as a percentage of that initial value. The purpose for converting ELISA values to percentages of initial values was to allow comparisons of ELISA value declines, since each patient's pretreatment ELISA value would be different.

Wherever possible, indirect ELISA values for MLEP, NDO, and NTO were analysed using matched statistical analyses, i.e. repeated measures analysis of variance (ANOVA), paired *t* test, or Wilcoxon sign rank sum test. This method was used to evaluate the difference in IgM reactivities to the different antigens for each given therapy duration period sample. When evaluating results for each antigen over time, the number of samples that could be analysed in this manner usually was small because of missing data, i.e. one missing serum sample for an individual would affect matched analysis over all time periods. Then analyses for independent samples were used (ANOVA or unpaired *t* test), provided homogeneity of variance was fulfilled. If such was not fulfilled, then a nonparametric method was used, such as the Kruskal–Wallis ANOVA[18] or Wilcoxon rank sum analysis.[19] Both Pearson and Spearman correlation coefficients[20,21] were calculated between ELISA

Table 1. ELISA and BI values by treatment duration

	Months of therapy					
Test	0	12	24	36	48	60
NDO-ELISA	1·81*	1·25	0·79	0·63	0·42	0·35
	±·78	±·71	±·63	±·51	±·36	±·29
	(34)	(28)	(31)	(32)	(27)	(21)
NTO-ELISA	1·5	1·00	0·63	0·49	NT	NT
	±·78	±·71	±·57	±·46		
	(34)	(27)	(30)	(24)		
MLEP-ELISA	0·76	0·33	0·18	0·13	NT	NT
	±·7	±·52	±·25	±·13		
	(34)	(27)	(30)	(24)		
INH-ELISA	70·5	46·41	43·95	38·58	32·7	35·18
	±21·97	±30·0	±29·15	±28·7	±29·1	±26·4
	(34)	(28)	(31)	(32)	(27)	(21)
BI	4·71	3·89	3·35	2·5	1·56	1·38
	±·52	±1·1	±1·45	±1·44	±1·31	±1·02
	(34)	(28)	(31)	(32)	(27)	(21)

NT, not tested.

1 At any given therapy duration period, MLEP-ELISA values are significantly lower than either NTO-ELISA or NDO-ELISA values (repeated measures ANOVA, $p < 0{\cdot}001$).

2 NDO-ELISA values were significantly higher than NTO-ELISA values (repeated measures ANOVA, $p < 0{\cdot}001$), only for the initial samples, i.e. 0 months; at later treatment durations samples, ELISA values were not significantly different between NDO or NTO antigens.

3 For all test values, results from 12 months to the rest of therapy period are significantly lower than at 0 months.

* Results are expressed as the mean value ± standard deviation. The number of samples tested is given in parentheses.

results and in combination with BI or INH results. Coefficients of determination (i.e. r^2) were calculated as the ratio of regression sum of squares over the total sum of squares. Data that were converted to percentages of prior values were evaluated using similar methods. All probabilities presented are two-tailed.

Results

ELISA and BI values during therapy

When ELISA and BI values were compared between therapy groups 1A and 1C, no statistically significant differences were found between the values, nor were there observable clinical differences in bacteriologic reduction and occurrence of reactional states. Consequently, individuals from the two therapy groups were combined and analysed as one group.

The mean ELISA and BI values $\pm$ standard deviations during the course of treatment are presented in Table 1. For all treatment duration samples, ELISA values were significantly higher using NDO or NTO as antigens than using *M. leprae* as antigen ($p < 0{\cdot}001$ by repeated measures ANOVA). At the initial pretreatment sample, NDO values were significantly higher than NTO values (average difference of 0·316), $p < 0{\cdot}001$ by paired t test; however, for other treatment duration samples the NDO-ELISA and NTO-ELISA values were not significantly different.

After one year of therapy the mean values of all four ELISAs and the BIs were significantly lower ($p < 0{\cdot}01$) than the initial values at the beginning of therapy and stayed significantly lower throughout the therapy period. As the values begin to taper off between 24 and 60 months of therapy (Table 1), differences year-to-year may not be significantly different, but the values are nevertheless significantly lower than initial values. Eight patients who showed no reactivity in the MLEP-ELISA throughout the therapy period had high values in the other three tests.

No significant increases or decreases in any of the ELISA values were noticed during episodes of ENL, which occurred in half of the patients during the course of chemotherapy.

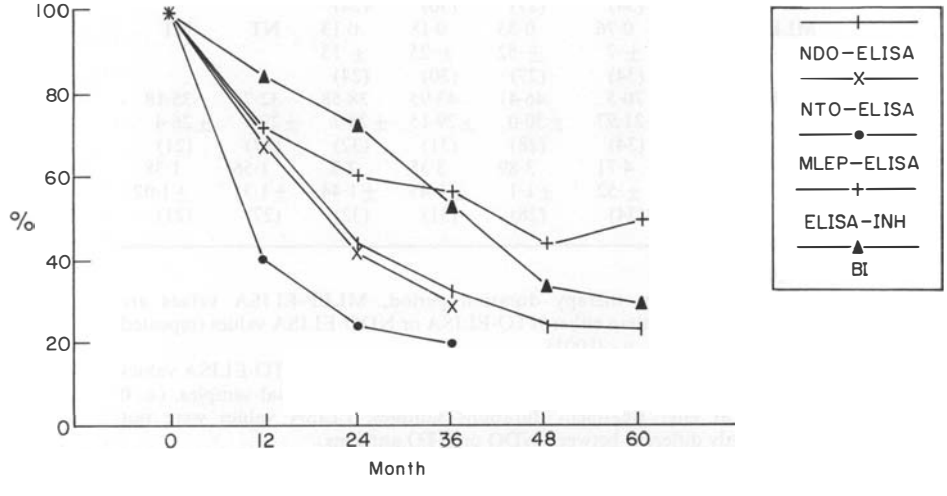

Figure 1. ELISA and BI declines over the course of dapsone treatment of lepromatous patients. Graphic representation of the mean values presented in Table 2.

Table 2. ELISA and BI percentages by treatment duration

	Months of therapy					
Test	0	12	24	36	48	60
NDO-ELISA	100[1]	70·1[2] ± 27·4	43·6 ± 26·0	31·9 ± 17·1	23·7 ± 14·7	22·9 ± 16·3
	(34)	(28)	(31)	(32)	(27)	(21)
NTO-ELISA	100	67·3 ± 26·8	41·1 ± 22·2	28·9 ± 15·4	NT	NT
	(34)	(27)	(30)	(24)		
MLEP-ELISA	100	39·8 ± 32·0	23·9 ± 17·0	19·3 ± 11·8	NT	NT
	(26)	(21)	(23)	(17)		
INH-ELISA	100	71·6 ± 44·3	59·8 ± 35·8	56·0 ± 43·7	43·5 ± 36·0	49·5 ± 31·9
	(34)	(28)	(31)	(32)	(27)	(21)
BI	100	84·2 ± 23·6	71·5 ± 29·6	52·6 ± 29·1	33·1 ± 27·3	28·8 ± 20·2
	(34)	(28)	(31)	(32)	(27)	(21)

1 The data from each assay were adjusted by assigning the initial value as 100% at the start of therapy for each patient. Subsequent values for each patient over the course of treatment were calculated as percentages of initial values.

2 Results are expressed as the mean value ± standard deviation. The number of samples tested is given in parentheses.

NT, not tested

For all test values, results from 12 months to the rest of therapy period are significantly lower than at 0 months ($p < 0{\cdot}01$ by ANOVA or Kruskal–Wallis test).

ELISA AND BI DECLINES BY PERCENTAGES OF PRIOR VALUES

The data from each assay were standardized by assigning the initial value at the start of therapy for each patient to be 100%. Over the course of treatment subsequent values for each patient were calculated as a percentage of the initial value. The average and standard deviations of these values are presented in Figure 1 and Table 2. There was no significant difference between NDO- and NTO-ELISA percentages, both with average declines to approximately 30% of the initial values after 3 years of treatment. Values for NDO-ELISA declined to an average 70% of initial ELISA values after 1 year of treatment, to 43·6% after 2 years, and to 22·9% after 5 years. Comparatively, MLEP-ELISA reflected a faster decline after the first year of treatment (to 39·8%, Table 2) and by 2 years of treatment average ELISA values were 23·9% of original values. ELISA-INH values reflected a slower decline, being 40–50% of initial values after 4–5 years of therapy. The BI values declined to 28·8% of initial values after 5 years of treatment.

CORRELATIONS BETWEEN ELISAS AND BI

Overall correlations (Pearson) between ELISA results and BIs for each treatment duration period and between the different tests are presented in Table 3. Spearman correlations also were calculated but conclusions and probabilities were similar to Pearson coefficients; the latter are presented in the results.

Table 3. Correlation coefficients between ELISAs and BI

	NDO-ELISA	NTO-ELISA	MLEP-ELISA	INH-ELISA	BI
NDO-ELISA	—	**0·817†**	**0·604†**	**0·329†**	**0·444†**
NTO-ELISA	0·866†	—	**0·682†**	**0·376†**	**0·570†**
MLEP-ELISA	0·354†	0·492†	—	**0·233***	**0·297***
INH-ELISA	0·369†	0·369†	0·366†	—	**0·095‡**
BI	0·399†	0·258†	0·285†	0·071‡	—

The bold printed figures represent correlation coefficients of percentages of initial values (see Table 2).

The normal printed figures represent correlation coefficients of test values (see Table 1).

* $p < 0{\cdot}05$

† $p < 0{\cdot}01$

‡ not significant

Percentages of ELISA and BI values were significantly correlated ($r = 0{\cdot}444$ for NDO-ELISA, $p < 0{\cdot}01$ at 172 df; $r = 0{\cdot}570$ for NTO-ELISA, $p < 0{\cdot}01$ at 123 df; and $r = 0{\cdot}297$ for MLEP-ELISA, $p < 0{\cdot}05$ at 123 df). Similarly, the OD values of the ELISAs showed significant correlations with BI values ($r = 0{\cdot}399$ for NDO-ELISA, $p < 0{\cdot}001$ at 172 df; $r = 0{\cdot}258$ for NTO-ELISA, $p < 0{\cdot}01$ at 123 df; and $r = 0{\cdot}285$ for MLEP-ELISA, $p < 0{\cdot}05$ at 123 df). It should be noted, however, that with coefficients of determination (i.e. r^2) of approximately 0·16, 0·07, and 0·08, respectively, the degree to which an ELISA value can be predicted by a BI value, or vice versa, is unreliable. INH-ELISA did not correlate with BI, either by test value or by percentages.

CORRELATIONS BETWEEN ELISAS

The correlation between NDO-ELISA and NTO-ELISA results is very high ($r = 0{\cdot}866$, $p < 0{\cdot}001$ at 123 df for ELISA values; $r = 0{\cdot}817$, $p < 0{\cdot}001$ at 123 df for percentages), indicating that both the ELISA values are similar and the rates of decline in those values are comparable. Please refer to Table 3. Correlations between either NDO-ELISA or NTO-ELISA with MLEP-ELISA are considerably lower, primarily since the values for MLEP-ELISA are significantly lower than either NDO-ELISA or NTO-ELISA. Correlations between any of the indirect ELISAs and INH-ELISA are similarly low, primarily due to the consistent reactivity over time with INH-ELISA. The coefficients of determination results (i.e. r^2) for MLEP-ELISA or INH-ELISA either with each other or compared to NDO-ELISA or NTO-ELISA are quite low (ranging from about 0·13 to about 0·24); whereas, the r^2 for NDO-ELISA compared with NTO-ELISA is quite high (about 0·75), indicating good agreement between both results.

Discussion

Our findings indicate a decline in ELISA reactivity and a decline in BI over the course of dapsone-based therapy. All patients were previously untreated lepromatous leprosy cases. During the course of treatment, these patients received two different dapsone-based chemotherapeutic protocols, differing only in the administration of clofazimine (for 24 weeks, group JCTI-C) at the beginning of the therapy period. Both groups received a single dose of rifampicin at the start of the therapy period and thereafter dapsone monotherapy for 5 years. Clinical and serological evaluation did not

indicate any significant difference between the two regimens (JCTI-A and JCTI-C), consequently, the data from the two treatment groups were combined for statistical analysis.

ELISAs measuring IgM antibodies to the NDO and NTO antigens showed a significant decline to approximately 30% of initial values after 3 years of therapy ($p < 0{\cdot}01$ by Kruskal–Wallis test) (Tables 1 and 2). Similar declines of antibody levels during therapy, using these and other antigens, have been previously described.[22–27] The overall NDO- and NTO-ELISAs showed comparable and statistically significant correlations with BI (Table 3), although variation was observed with individual patients. The coefficients of determination (i.e. r^2), however, are quite low, indicating that the degree to which an ELISA value can be predicted from a BI value likewise is low. As with BI, an ELISA measurement at a single point in time cannot be used to indicate effective treatment. Thus sequential sera taken during the course of treatment should be monitored and compared with the sample collected at initiation of treatment.

The overall NDO- and NTO-ELISAs were highly correlated with each other ($r = 0{\cdot}866$ for ELISA values and $r = 0{\cdot}817$ for ELISA percentages, $p < 0{\cdot}001$ for both, Table 3).

Although the MLEP-ELISA correlated significantly (Table 3) with the NDO- and NTO-ELISAs, several findings suggest that the MLEP-ELISA does not detect antibody reactivity to the sugar epitope of the phenolic glycolipid-I of *M. leprae*. At any given sampling time period, MLEP-ELISA values are significantly lower than either NTO-ELISA or NDO-ELISA values ($p < 0{\cdot}001$ by repeated measures ANOVA). The MLEP-ELISA showed a much faster decline during the first year of treatment than the other ELISAs. In addition, the sequential sera of 8 patients were negative from the beginning of therapy with the MLEP-ELISA, while being positive in the other ELISAs. This makes the MLEP-ELISA less efficient in monitoring patients on treatment.

The INH-ELISA showed a decline to approximately 50% after 5 years of treatment (Table 2). No significant correlation was found with the BI over the course of treatment (Table 3), which could be attributed to the persistance of activity during therapy. In 9 out of 35 patients no decline in their INH-ELISA activity was found throughout the treatment period. Similar findings have been reported with an ELISA based on the detection of antibodies to the lipoarabinomannan of *M. leprae*.[7,28]

In contrast to others[27] we found no relationship between the occurrence of ENL and changes in ELISA values.

Sequential monitoring with the ELISAs measuring IgM antibodies to the sugar epitope of the phenolic glycolipid-I of *M. leprae* were found to be the most suitable for monitoring lepromatous patients under chemotherapy. The NDO- and NTO-ELISA may be better quantitative measurements of progress during chemotherapy than the BI. The MLEP-ELISA is less suitable because it can fail to detect antibodies in some patients. The INH-ELISA is less suitable because of persistent reactivity during the course of therapy in some patients.

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Reliability of skin smear results: experiences with quality control of skin smears in different routine services in leprosy control programmes

L VETTOM & S PRITZE
Armauer Hansen Institute, Leprosy Reference Laboratory, Würzburg, Germany

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Summary The quality control of skin smears is an important tool in improving the diagnosis of leprosy. We evaluated the skin smears sent to us by 50 laboratory technicians of 29 projects in Asia, Africa and South America. The skin smears were judged according to taking, staining and reading. The correlation was altogether satisfactory. In reading, a low correlation was found in 11% (42 slides) and it was seen that the highest percentage of low correlations was found in the false negative smears. The evaluation of cases with a low correlation leads to the conclusion that using the new WHO classification of 1988 will not reduce the number of incorrectly classified cases. From 42 slides showing a low correlation of their BI results, 7% led to a different classification (paucibacillary instead of multibacillary or vice versa) according to the WHO definition given in 1982, but 8% according to the 1988 WHO definition.

Introduction

The examination of slit-skin smears—notably in the context of multiple drug therapy (MDT)—is an important tool in leprosy control programmes, namely for the diagnosis and classification of the disease, the assessment of progress, the duration of treatment in multibacillary cases and the diagnosis of relapses.[1]

Experiences with the standard of the bacteriological examination techniques are often disappointing. Georgiev & McDougall[1] recently stated that in a considerable number of countries in the main leprosy-endemic areas the standard of work regarding the taking, the fixing, the dispatching, the staining and the reporting of slit-skin smears was deplorably low.

Even though efforts for improvement have been undertaken in different countries, e.g. by intensifying the training of technicians, the overall situation was not suspected to have changed significantly.

In 1987, when we started quality control in our leprosy reference laboratory, the main objective was to get more detailed information on the actual standard of laboratory work in various leprosy control programmes.

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To date, little literature is available to describe a systematic approach to the quality control of slit-skin smears in leprosy. In 1985 de Rijk *et al.*[2] published their results on a periodical re-examination of samples of skin smears for leprosy taken in routine services. This quality control was based on the assessment of smearing and staining, as well as the assessment of the differences in BI results of slit-skin smears.

The quality control presented here was based on the criteria proposed by de Rijk *et al.* A detailed written evaluation was given to each participating technician in order to point out reasons which might have lead to a disagreement in the BI results.

Methods

Twenty-nine projects with 50 technicians working in different leprosy service laboratories world-wide were evaluated in this study. Table 1 gives a summary of continents and countries, number of projects and technicians participating in the quality control.

Information sheets and forms were sent to each project (Figure 1).

The comparison between the service laboratory and the leprosy reference laboratory was based on 8 slides with up to 6 smears each taken within the last 2 months. The results of all 8 slides read by one reader in the service laboratory, were reported in the corresponding circles on the form by someone responsible for the organization of the quality control in the respective laboratory.

The form was sent to our reference laboratory, where the smears were examined by a standardized procedure.

Smear taking was judged according to:

The amount of lymph (thin, thick);
Its quality (assessed by the presence of different cell types, e.g. lymphocytes, macrophages, erythrocytes and epithelial cells in the lymph);
Its distribution.

Smear staining technique was judged according to:

The demonstration of acid fastness of bacilli;
The contrast between bacilli and background;
The presence of artefacts.

Table 1.

Continents	Countries	No. of projects	Technicians
Asia	India	19	23
	Pakistan	1	2
	Korea	1	2
	Thailand	1	1
Africa	Ethiopia	1	10
	Nigeria	2	5
	Kenya	1	2
	Uganda	1	2
	Tanzania	1	1
S. America	Brazil	1	2

QUALITY CONTROL

Name and adress of Service Laboratory: ____________________

____

____

taken by: ____________________

____

Name and Position of Examiner: ____________________

____

____

Date of sample collection: ____________________

Samples chosen by: ____________________

Used staining technique:

a) Ziehl-Neelson (hot) ☐

b) Ziehl-Neelson (cold) ☐

c) others ☐

Short description of staining technique used: ____________________

____

Pat. Name	Slide-No.	Date	Results						Any specific comments
			BI	BI	BI	BI	BI	BI	
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:
			◯	◯	◯	◯	◯	◯	Service Lab:
			◯	◯	◯	◯	◯	◯	Reference Lab:

Comment Reference Laboratory:

____

____

(DAHW208/88)

Figure 1. Form used for quality control: circles under 'results' represent various smears with the number of bacilli found reported as bacteriological index (BI) according to Ridley's logarithmic scale.

BI accordance was determined according to the following scheme:

Very good, exact BI accordance is found in 6 out of 8 slides;
Good, half of the 8 slides show exact BI accordance and the rest slight deviations ('slight' deviation: BI difference of ± 1 in smears with BI > 2);
Satisfactory, 3 of 8 slides show exact BI accordance and the rest show slight deviations;
Unsatisfactory, less than 3 slides out of 8 show exact BI accordance.

One experienced person served as second reader. Through this procedure a relatively objective assessment was achieved. Double-blind conditions were not put into effect in order to analyse deviations in the results and to explain the reason for them to the technician whenever possible. Besides the evaluation of the reliability of the results an individual feedback was given to the technician from which we hoped to stimulate critical analysis and motivation.

A comment was written on the form, summarizing the assessment of the smears. Suggestions for improvement were given whenever necessary and participation in further quality control was proposed. The completed form was sent back to the service laboratory.

Results

The results of the quality control are summarized in Table 2. The quality of smear taking conducted by 13 technicians was unsatisfactory according to our assessment. In these slides only a small amount of lymph, irregularly distributed and containing lots of erythrocytes was found.

By 15 technicians the quality of taking was satisfactory if the smears showed a sufficient amount of lymph or regular distribution of material or scanty erythrocytes.

By 22 technicians the quality of taking was good, characterized by a sufficient amount of lymph, regularly distributed and with only scanty or no erythrocytes.

By 11 technicians the quality of staining was unsatisfactory under the following conditions: if the smears showed many artefacts predominantly due to unfiltered staining solutions, if an assessment of acid fastness ('pale' bacilli) was difficult and if there was a contrast, which rather impeded the correct judgment of acid fastness.

The quality of staining of 24 technicians was evaluated as satisfactory based on the absence of artefacts or the easy assessment of acid fastness or a good contrast.

The staining conducted by 15 technicians was considered to be good since it showed no artefacts and a good demonstration of acid fastness underlined by a good contrast.

Table 2. Number of technicians in different continents according to the quality of their performance in taking, staining and reading slit-skin smears

Continent	No. of technicians	Taking			Staining			Reading			
		+	±	−	+	±	−	++	+	±	−
Asia	28	14	4	10	7	13	7	1	12	6	9
Africa	20	8	9	3	8	9	4	0	9	2	9
A. America	2	0	2	0	0	2	0	0	2	0	0
Total	50	22	15	13	15	24	11	1	23	8	18

++ very good; + good; ± satisfactory; − unsatisfactory.

Table 3. Staining techniques used

1	Hot carbolfuchsin alk. methylene blue	(15 min); (10 min);	1% HCl in 70% ethanol (2–5 sec) (used by 13 technicians)
2	Hot carbolfuchsin alk. methylene blue	(10 min); (0·5 min);	3% HCl in 70% ethanol (5 min) (used by 4 technicians)
3	Hot carbolfuchsin alk. methylene blue	(15 min); (2 min);	5% H_2SO_4 (1 min) (used by 7 technicians)
4	Hot carbolfuchsin alk. methylene blue	(10 min); (5 min);	20% H_2SO_4 (2 min) (used by 1 technician)
5	Hot carbolfuchsin brilliant green	(10 min); (2 min);	20% H_2SO_4 (1 min); 1% HCl (used by 10 technicians)
6	Cold carbolfuchsin alk. methylene blue	(20 min); (10 min);	1% HCl in 70% ethanol (> 5 sec) (used by 6 technicians)
7	Cold carbolfuchsin methylene blue	(20 min); (2 min);	5% HCl in 70% ethanol (5 min) (used by 1 technician)
8	Cold carbolfuchsin methylene blue	(20 min); (2 min);	20% HCl in 70% ethanol (1 min) (used by 1 technician)
9	Cold carbolfuchsin methylene blue	(10 min); (2 min);	10% H_2SO_4 (20 min) (used by 5 technicians)
10	Cold carbolfuchsin methylene blue	(20 min); (2 min);	25% H_2SO_4 (10–20 min) (used by 2 technicians)

It is noteworthy that in the 29 participating laboratories 10 different staining methods were used, representing the routine stainings. These differences were mainly determined by the choice of hot or cold carbolfuchsin, the employed counterstaining with methylene blue or brilliant green and the agents, concentrations and times used for decoloration.

Summarizing Table 3, 35 technicians (70%) used the hot-staining method and 15 (30%) the cold-staining method.

According to the participating technicians the results of the readings (BI accordance) were satisfactory (Table 4).

When compared to the reference laboratory only one technician had very good results in the readings, 23 technicians had good results, 8 had satisfactory results and 18 had unsatisfactory results in their readings.

When the results of the readings were analysed in regard to the geographic distribution of the technicians, the folowing data were found (Table 5): In fact, the number of participating technicians is too small to draw an objective conclusion from Table 5. If only very good and good results in the readings are taken into account a very small difference in the BI accordance is found between Asian

Table 4. Assessment of reading according to 50 participating technicians

BI accordance	No. of technicians
+ +, very good accordance	1
+, good accordance	23
±, satisfactory	8
−, unsatisfactory	18

Table 5. Assessment of readings according to 50 participating technicians from 10 countries

Continents	Countries	No. of projects	Technicians	BI-accordance ++	+	±	−
Asia	India	19	23	1	9	5	8
	Pakistan	1	2		2		
	Korea	1	2				2
	Thailand	1	1		1		
Africa	Ethiopia	1	10		6	2	2
	Nigeria	2	5		1		4
	Kenya	1	2		2		
	Uganda	1	2			1	1
	Tanzania	1	1				1
S. America	Brasilien	1	2		2		

very + + good; + good; ± satisfactory; − unsatisfactory

(BI accordance + +/+ by 28 technicians (46%)) and African technicians (BI accordance + by 20 technicians (45%)).

The choice of regimen and the treatment duration in leprosy is determined by the number of bacilli found in the patient. In 1982 WHO recommended a classification of leprosy in paucibacillary (BI < 2 at any site) and multibacillary (BI ≥ 2 at any site) cases, implicating a 6-month treatment with two drugs in paucibacillary patients and a minimum 2-year treatment with three drugs in multibacillary patients (24).

When, independently of the results obtained by the individual technician, the quality of reading was analysed in all 390 slides examined, full correlation (reading 'same') of the BI was found in 173 slides (45%) (Table 6):

The highest percentage of full correlation was observed in the 106 negative slides (27·5%); in multibacillary slides a full correlation was found in 67 (17·5%). No full correlation was seen in paucibacillary smears. Acceptable correlation ('slight' deviation) was assessed in 343 (89%) of the 390 slides examined. Low correlation in the reading was found in 42 (11%) of the evaluated slides, listed in Table 7.

Table 6. Full correlation of BI results in the interobserver comparison

Service laboratory (BI)	Reference laboratory (BI)	No. of slides
Negative	Negative	106 (27·5%)
Paucibacillary	Paucibacillary	0
Multibacillary	Multibacillary	67 (17·5%)
		173 (45%)

Table 7. Low correlation in interobserver comparison of slit-skin smears according to negative, paucibacillary and multibacillary BIs.

Service laboratory	Reference laboratory	No. of slides
Negative	Paucibacillary	10 (2·6%)
	Multibacillary	12 (3·0%)
Paucibacillary	Negative	5 (1·3%)
	Multibacillary	8 (2%)
Multibacillary	Negative	4 (1%)
	Paucibacillary	3 (0·8%)
		42 (11%)

Discussion

The quality of slit-skin smears is one of the most important factors influencing the reliability of the bacteriological index (BI). The quality itself depends on different parameters. Some of these can easily be evaluated by quality controls, whereas analysing others is difficult or impossible. An unmistakable influence on the quality is evident in the taking and staining of skin smears, the quality of staining dyes and glassware, the fixing of smears and the dispatching of slides.

On the contrary, it is difficult if not impossible, to judge the technician's training, his reliability and his motivation, the correct selection of the sites chosen for taking the smears, the quality and maintenance of microscopes and the availability of good light sources.

Other hindrances encountered are due to the fact that the taking of skin smears and the staining/reading is often performed by different persons, so that the technician reading the smear is only partly or not at all responsible for its quality. Often the technicians do not get any clinical data, resulting in an isolated analysis without the corresponding context. If they were to have some clinical information they would probably be able to work more conscientiously. Finally, the results of the quality control are usually communicated only to the reader but not to those in charge of taking the smears. This lack of communication makes efficient improvement difficult.

As shown in Table 3, 10 different staining methods were used. There was no clear evidence that the quality of staining was significantly influenced by the method applied. It was not possible to determine the impact of the staining techniques on the number of bacilli found since only stained slides were available; however, in some slides the suspicion arose that the acid fastness of bacilli was not preserved or had disappeared.

Three slides were sent as negative to the reference laboratory, but were suspected to have been positive since very weakly stained bacilli were seen. Slides were restained and proved to be obviously positive. In these cases decoloration was probably inadequate but because of the small number of slides no definite conclusions in regard to the influence of the staining technique used can be drawn.

In 8 slides BI results of the service laboratory were significantly higher than those of the reference laboratory and fading of bacilli was suspected. After restaining the results showed a good correlation. Reasons for fading might be the continuing reaction of the acid if slides have not been washed carefully after decoloration with acid–alcohol, influence of immersion oil, xylene or sunlight, as discussed in the literature.[3–5]

In the sample of slides examined there was no tangible evidence that the quality of staining was significantly influenced by the method used. However, it is to be recommended that hydrochloride acid which is less aggressive to the decoloration of the bacilli than sulphuric acid should be used as the agent of choice.

The assessment of the BI accordance is a subjective method, and differences in the interobserver comparison have to be accepted to a certain extent.

Even under ideal conditions slight differences may be found mainly due to the irregular distribution of bacilli in the smear and the impossibility of accurately reading the same 100 oil immersion fields assessed by the first reader. On the other hand, especially if the bacteriological index is >2 the count of bacilli should result in the exact value within the logarithmic scale.

Assessing the BI accordance the single smear results of the service laboratory were compared to the corresponding results determined by the reference laboratory. Intentionally we did not use the average BI/slide in order to identify the slides where patients were incorrectly classified as paucibacillary and multibacillary according to the WHO definition.[6]

This definition describes those patients as paucibacillary where the BI is <2 at any site and as multibacillary those where the BI is ≥ 2 at any site. If the average BI is chosen as criterium, some multibacillary patients might be dismissed. In a patient with, e.g. a BI result of 1/1/1/1 per smear, the average BI will be one, which leads to the classification as paucibacillary. In a second patient the BI is 2/0/0/2 per smear leading to an average BI of 1, and suggesting a paucibacillary case whereas the patient is multibacillary.

As shown in Table 7 there were relatively few slides read as multibacillary by the service laboratory which were judged to be negative or paucibacillary by the reference laboratory (1·8%). Possible reasons for this might be artefacts which are sometimes difficult to distinguish from acid-fast bacilli (crystals, haemoglobin conglomerates, contaminants).

Two per cent of the slides were judged as paucibacillary by the service laboratory though these were multibacillary according to the reading of the reference laboratory. The most important reason for this was probably the fact that only a few oil immersion fields were counted, often in combination with an uneven distribution of the lymph on the slide. Some of these paucibacillary slides were judged to be negative by the reference laboratory (1·3%). Artefacts mistaken for bacilli were found to be the most common reason.

The highest percentage of low correlation was observed in the false negative smears (5·6%), probably due to the counting of only a small number of oil immersion fields (motivation, lack of time by the technician), bad microscopes and light sources as well as inadequate staining techniques. This is a very interesting finding, especially in the light of the WHO definition published in 1988 that paucibacillary cases are all those with a negative BI result, multibacillary all those with any positive BI result.[7] Based on our findings the careful conclusion can be drawn that if only the BI result is considered for classification, the number of incorrectly classified patients will not come down significantly. From 42 slides showing a low correlation of their BI results (Table 7), 27 (7%) led to a different classification (paucibacillary instead of multibacillary or vice versa) according to the WHO definition given in 1982, but 31 (8%) according to the 1988 WHO definition.

De Rijk *et al.*[2] already raised the question of the possibility of drawing a line between acceptable and unacceptable results. They proposed three criteria, namely the proportion of full correlation when the readings are the 'same' or the difference 0; acceptable correlation when the difference is 1 mark BI to either side; and the calculation of the variance as the sum (Σ) of the square values of the differences (D) divided by the number of observations (N). Based on these criteria the reliability of the BI results was then judged to be good according to the value of $\geq 50\%$ full correlation and/or 50–80% of acceptable correlation and/or a variance < 1 in all samples examined by a reference reader.

Relating to these values our reading showed full correlation in 45% of all smears examined, acceptable correlation in 89% and variance < 1 in 93·8%. Therefore, the conclusion can be drawn that our results are at least satisfactory.

The quality control was well accepted; up to now 50% of the projects which were asked to participate have sent slides and forms. This good response can partly be explained by the fact that in many leprosy control programmes the doctors are in charge of the supervision of the laboratory work, but do not feel able to do the assessment. Sending slides to a reference laboratory is therefore

a welcomed possibility to free themselves of this burden and at the same time give some feedback to the laboratory technician.

In due course we will know more details about the impact of the quality control on the work standard in the laboratory. The feedback we have got so far shows much interest and enthusiasm from the participants. In the future, experiences gained in quality control should stimulate further training, as well as influence the curricula of training and refresher courses.

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Bacillaemia in leprosy and effect of multidrug therapy

G CHATTERJEE,* S KAUR,‡ V K SHARMA,*
C VAISHNAVI† & N K GANGULY†
Departments of Dermatology and Experimental Medicine,† Post-graduate Institute of Medical Education and Research, Chandigarh-160 012, India*

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Summary Twenty-five patients of bacilliferous leprosy (17 LL, 8 BL) were studied by the modified haemolysis method for occurrence of bacillaemia and its clearance after two multidrug therapy regimens. Acid-fast bacilli were found in 76% of all patients and in 88·2% LL and 50% BL patients. Bacillaemia occurred with significantly reduced frequency in patients with type II reaction. Acid-fast bacilli were demonstrable in peripheral blood after 1 month in one patient on MDT of an Indian Working Group and 3 lepromatous patients on WHO multidrug therapy. However, bacillaemia could not be demonstrated in any patients after 2 and 3 months of treatment with both regimens.

Introduction

Bacillaemia, the finding of lepra bacilli in peripheral circulation, has been a topic of investigation since the turn of the century.[1] Initially bacillaemia was demonstrated in lepromatous leprosy,[2,3] recently, it has been documented even in tuberculoid leprosy.[4,5] The bacillaemia has been attributed to multisystem involvement in lepromatous leprosy.[4] It was planned to study the occurrence of bacillaemia in lepromatous patients and assess the efficacy of multidrug therapy regimens in the clearance of bacillaemia.

Materials and methods

Twenty-five untreated patients having bacilliferous leprosy (LL/BL) formed the study group. There were 22 males and 3 females, with an age range of 16–58 years (mean 37·5). Ridley–Jopling classification was followed.[6] A haemogram, urinalysis, chest skiagram, hepatic and renal function tests were carried out before starting therapy in all cases.

‡ Correspondence

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BACILLAEMIA STUDIES

Three samples of blood at 12-hr intervals were collected before starting the treatment. Repeat samples were taken at 1, 2 and 3 months in the first 10 patients and at 2 week intervals 1, 2 and 3 months after treatment in the remaining 15 patients. A total of 2 blood samples were collected at 12-hr intervals for the follow-up studies for bacillaemia, and a modified haemolysis method[7] was used for study. Briefly, 5 ml of blood was drawn from the antecubital vein and transferred to a heparanized vial (10 iu/ml). One millilitre of blood from the above was transferred to a half test-tube and the cells were disintegrated by ultrasonic vibrations (800 KHz) for 30 s. One millilitre of sterile distilled water was added and the sample was sonicated again for 30 s. This step was repeated to get a final volume of 4 ml. The same procedure was repeated with the remaining 4 ml of blood to make a final volume of 20 ml. It was centrifuged at 10,000 rpm for 30 min at 10°C in a propylene centrifuge tube. The supernatant was removed, and the deposit was washed and centrifuged again with 20 ml of sterile distilled water at the same speed for 20 min. The deposit was suspended in 1 ml of distilled water and a bacillary count done using the pinhead method.[8] The smears were made for Ziehl–Neelsen staining and studied under an oil-immersion microscope.

TREATMENT AND FOLLOW UP

Group I. The 10 consecutive patients (7 LL, 3 BL) were treated with WHO multibacillary regimen consisting of rifampicin 600 mg and clofazimine 300 mg once a month given under supervision, and dapsone 100 mg daily and clofazimine 100 mg on alternate days, self-administered.[9]

Group II. The 15 consecutive patients (10 LL, 5 BL) were treated with the India Working Group's multibacillary MDT consisting of intensive therapy with rifampicin 600 mg, clofazimine and dapsone 100 mg daily for 15 days and continued on the maintenance phase like the WHO multibacillary regimen.[10] The bacteriological and morphological indices (BI and MI) were repeated at 1, 2 and 3 months after therapy.

Results

The mean duration of the disease in 25 patients was 3·4 years. The average bacteriological (BI) and morphological (MI) indices were 3·9+/3·28% and 3·3/1·07% in LL and BL patients respectively. Seventeen patients of lepromatous leprosy (LL) included 12 polar lepromatous (LLp), 4 subpolar lepromatous leprosy (LLs), and 1 with histoid leprosy. Five LL patients had Type II reaction. The patients in group I and II were comparable in age, sex, duration, type of disease and average BI and MI. Bacillaemia was found in 19 (76%) out of 25 patients, 15 (88·2%) were LL out of 17 taken up and 4 (50·0%) were BL out of 8 patients taken up (Table 1). No statistically significant difference

Table 1. Bacillaemia in multibacillary leprosy

Type of leprosy	No. studied	No. (%) showing bacillaemia
LL	17	15 (88·2)
BL	8	4 (50·0)
Total	25	19 (76·0)

$\chi^2 = 2{\cdot}7$; $p > 0{\cdot}05$.

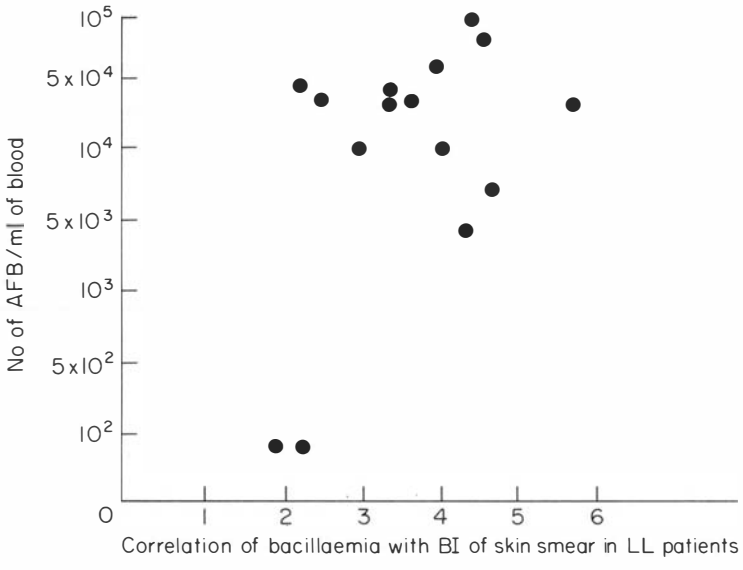

Figure 1.

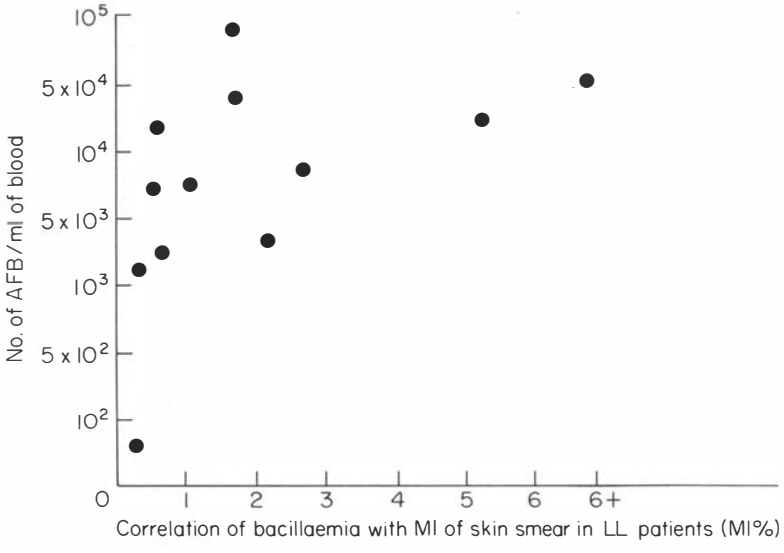

Figure 2.

was found in the frequency of bacillaemia in lepromatous and borderline lepromatous leprosy ($\chi^2 = 2{\cdot}24$; $p > 0{\cdot}05$). However, there was a statistically significant difference in the frequency of bacillaemia in patients with and without Type II reaction ($\chi^2 = 4{\cdot}48$; $p < 0{\cdot}05$), as only 3 out of 5 patients with Type II reaction showed bacillaemia. The correlation between bacillaemia and bacteriological index was good (Figure 1) and no correlation was demonstrated between bacillaemia and morphological index in slit-skin smears (Figure 2).

Table 2. Bacillaemia clearance after multidrug therapy

Type of MDT	Type of leprosy	No. studied	No. of patients showing bacillaemia after MDT			
			2 weeks	1 month	2 months	3 months
WHO (1982)	LL	7	ND	3	0	0
	BL	3	ND	0	0	0
Indian Working Group	LL	10	1	1	0	0
	BL	5	1	0	0	0
	Total	25	2	4	0	0

ND, not done.

The bacilli could not be demonstrated in peripheral blood 2 and 3 months after therapy in all the patients. However, bacilli were still demonstrable after 1 month in 3 out of 7 LL patients on WHO–MDT regimen (Group I) and in 1 out of 10 LL patients on the Indian Working Group regimen (Group II) (Table 2). The clearance of bacillaemia after 1 month of each of the two MDT regimens was not different ($\chi^2 = 2{\cdot}24$, $p > 0{\cdot}05$) though it seems that the Indian Working Group regimen resulted in earlier clearance. There was no significant reduction in BI, however MI was reduced to zero after 3 months of MDT.

Discussion

Bacillaemia occurs in 67–100% patients of bacilliferous leprosy.[2–4,11] The frequency of demonstration of bacillaemia has progressively increased with the modification of methodology.[4,7,12,13] Circulating bacilli were found in 92–100% patients with lepromatous leprosy (LL)[4,11] compared to our finding of 88·2%. However, in borderline lepromatous leprosy (BL) bacillaemia occurs less frequently[4] but there is apparently no direct correlation between frequency of bacillaemia and the bacteriological and morphological indices.[3,4] There was apparently good correlation between BI of slit-skin smear and bacillaemia in our patients. Sankara Manja *et al.*[13] also reported similar results.

Bacillaemia occurred with lower frequency in LL patients with Type II reaction compared to LL patients without reaction and the difference was statistically significant ($\chi^2 = 4{\cdot}48$; $p < 0{\cdot}05$). A similar finding has been reported earlier.[2,14,15] It may be due to stimulation of cell-mediated immunity in Type II reaction resulting in the increased clearance of bacilli.[16]

Drutz *et al.*[2] reported gradual clearance of bacillaemia over a 4-month period after dapsone monotherapy. The extracellular bacilli cleared first followed by intracellular bacilli. Subsequently, Ramu *et al.*[17,18] assessed bacteraemia in 36 LL patients at weekly intervals for 4 weeks after putting patients on 4 drug regimens, namely dapsone alone, dapsone and clofazimine, dapsone and isoniazide, and dapsone and rifampicin. They observed that bacillaemia disappeared after one week in the dapsone and rifampicin regimen, while it took 3 weeks with the other regimens. Bacillaemia cleared in all patients by 2 months with different multibacillary regimens in our study. The 15 days intensive multibacillary therapy did not show significant advantage in clearance of bacillaemia. The exact pathogenesis of clearance of bacilli from peripheral circulation in the presence of a heavy bacterial load in skin is not known. Probably the administration of drugs results in immediate bacteriostasis and thereby prevents the further multiplication and overspill from involved vasculature into the circulation. The immunostimulatory effect of antileprotics has been suggested as another possible factor.[17,19]

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Leprosy in children: correlation of clinical, histopathological, bacteriological and immunological parameters

V N SEHGAL* & JOGINDER
Department of Dermatology and Venereology, Maulana Azad Medical College and Associated LNJPN and GB Pant Hospitals, New Delhi, India

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Summary The study of leprosy in children has indicated an incidence of 10% amongst leprosy patients attending the clinic. The duration of the disease was usually less than 2 years. The expression of leprosy in this group was either a macule and/or a plaque. Classification was, therefore, different and conforms to indeterminate (I), borderline tuberculoid (BT) and borderline (BB) leprosy. Only occasionally were other clinical variants seen. The bacteriology was largely unproductive by slit-skin smears. The lepromin (Mitsuda) responses were positive in BT and unpredictable in BB patients. Epicutaneous responses to sensitization with dinitrochlorobenzene (DNCB) paralleled responses to lepromin. Microscopic pathology was of very little help. The correlation of these parameters was only 50–60% indicating that the diagnosis of leprosy should primarily be based on clinical features.

Introduction

Leprosy is a well-conceived entity in children.[1,3] The reports[3] of ever increasing numbers of children afflicted with the disease reflect that a sizeable population in certain vulnerable areas has an age at onset of leprosy between the ages 0–14 years. In India about 15% of cases belong to this age group.[4] It is generally believed that indeterminate, tuberculoid tuberculoid (TT), borderline tuberculoid (BT), and borderline borderline (BB) groups are frequently recorded amongst children,[5,7] whereas borderline lepromatous (BL) and lepromatous lepromatous (LL) are only occasionally encountered. This appears to be a paradoxical situation in children and runs counter to the concept that 'immune responses' are either negligible or poorly developed in young children.[8] Hence it is worthwhile to comprehend this phenomenon through clinical, bacteriological, histopathological and immunological parameters as prescribed by Ridley & Jopling.[9]

* Correspondence: A/6, Panchwati, Opposite Azadpur Subzimandi, Delhi-110 033, India.

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Patients and methods

Twenty-five children were amongst a total of 250 fresh leprosy patients attending the Urban Leprosy Centre of our Institution, during the National Leprosy Eradication Programme from August 1987 to July 1988. They were classified on the Ridley & Jopling scale[9] with some modifications.[10] They were subjected to skin biopsy for histopathological study. Slit-skin smear examination was done to determine bacteriological status.

Lepromin test was done using 0·1 ml of lepromin A containing 40 million bacilli per ml. The early (Fernandez) response was read after 48 hours and the late (Mitsuda) after 4 weeks. The Fernadez response was graded as negative, doubtful (±), 1+, 2+, 3+ depending upon reaction sizes of less than 5 mm, 5–10 mm, 10–15 mm, 15–20 mm or more than 20 mm respectively. The Mitsuda response was graded as negative, doubtful (±), 1+, 2+ or 3+ depending upon reaction sizes of 0, 1–3 mm, 4–6 mm, 7–10 mm, or more than 10 mm, respectively.

DNCB (Epicutaneous sensitization with dinitrochlorobenzene) testing was done according to WHO.[11] DNCB solution in acetone was used in 2 strengths—a sensitizer dose of 2000 μg and a challenge dose of 50 μg. Solutions were placed on the skin through firmly held steel rings above and below the cubital fossa. In the absence of a reaction at 15 days, a rechallenge with 50 μg was given in a similar way and test read after 48 hr. The response was graded as negative, 1+, 2+, 3+ or 4+. Twelve age- and sex-matched healthy children formed controls.

Observations

Children comprised about 10% of the leprosy cases diagnosed over a 12-month period in our Institute. Their distribution according to age and sex is shown in Table 1. The mean age was 10·6 years, while the duration of the disease varied from 2 months to 10 years, with a mean of 1·8 years. The majority (84%) of them had a disease duration of less than 2 years. Sixteen of them had borderline tuberculoid (BT) and 6 borderline borderline (BB) leprosy. The three other patients were classified as borderline lepromatous (BL), indeterminate (I) and polyneuritic (P) leprosy. Macules occurred in 14 children and plaques in 5 children. Both the lesions were present in the other 5 children. Well-formed granulomas in tissue sections were seen in 13 children, whereas a scattered infiltrate comprising lymphocytes and histiocytes was seen in the rest. In the single case of BL, acid-fast bacilli on slit-skin smear examination were demonstrated (Table 2).

Fernandez response was doubtful (±) in 3 borderline tuberculoid and 1 borderline borderline whereas it was negative in rest of them.

It is apparent from Table 2 that the late (Mitsuda) reaction depicted varying positivity from BT to BB leprosy. Moreover, there was no difference in sensitization with DNCB in the BT group and

Table 1. Age and sex distribution

	Males		Females	
Age group (Years)	No. of cases	%	No. of cases	%
0–5	1	6·25	1	11·11
6–10	5	31·25	3	33·33
11–14	10	62·25	5	55·55
	16	100·00	9	100·00

Table 2. Correlation of various parameters

No.	Clinical Diagnosis	Histopatho-logical	Bacterial index	Lepromin (Mitsuda)
5	BT	BT	0	1+
3	BT	BT	0	2+
1	BT	BT	0	3+
3	BT	NS	0	1+
2	BT	NS	0	2+
1	BT	NS	0	±
3	BB	BB	0	±
2	BB	NS	0	1+
1	BB	NS	0	±
1	BL	BL	5+	±

NS, non-specific

Table 3. Response to DNCB

Leprosy groups	No.	Grading of response				
		–	1+	2+	3+	4+
BT	16	1	3	5	2	5
BB	6	3	–	2	–	1
BL	1	1	–	–	–	–
I	1	–	–	1	–	–
P	1	–	–	1	–	–
Total	25	5	3	9	2	6
Controls	12	1	1	2	4	4

Table 4. Correlation of lepromin (Mitsuda) and DNCB response

Lepromin response	No.	DNCB response				
		–	1+	2+	3+	4+
–	0	–	–	–	–	–
±	6	4	–	2	–	–
1+	11	1	1	4	–	5
2+	7	–	1	3	2	1
3+	1	–	1	–	–	–

controls (Table 3). In the BB group, on the other hand, only three children could be sensitized—a response which is significantly poor when compared to BT and controls. ($p < 0{\cdot}05$). The correlation between lepromin (Mitsuda) and DNCB sensitization is shown in Table 4. The correlation of various parameters namely clinical, histopathological, bacteriological and lepromin (Mitsuda) is shown in Table 2. It is evident that a clinical–histopathological correlation was seen in 9 BT, 3 BB and 1 BL patient.

Discussion

It is well-established that children are more susceptible to acquiring leprosy than adults.[12] However, the spectrum of the disease among them is different. It is characterized by macules and/or plaques present more often on exposed areas.[7] Macule is a predominant lesion. Accordingly, the histopathology also reflects a non-specific picture in a large number of patients. This aspect has been well-documented in our study. As the formation of a granuloma is indicative of effective build up of immunity,[13] it follows that in children immunity was not as effective as in adults.

The Fernandez response to lepromin indicates a pre-existing hypersensitivity to either *M. leprae* or other cross-reacting Mycobacteria.[14] It appears that negative or doubtful responses in children could be due to inadequate pre-exposure to such organisms or to the inability of the immune system to respond to such exposure. The response pattern of the Mitsuda reaction was almost similar to that of adults in our study. A positive response in the indeterminate and the polyneuritic patients indicates their place nearer to the tuberculoid end of the spectrum. The impairment of DNCB responses in conformity with negative or doubtful Mitsuda reactions in BB and BL leprosy indicates the parallel impedement of specific and non-specific CMI.

A correlation of various parameters namely clinical, histopathological and lepromin (Mitsuda) responses was seen in only 56·7% of BT children. In the clinically BB group only 50% conformed to the histopathological picture of BB. Moreover, slit-skin smears failed to demonstrate acid-fast bacilli in any of them. Such discordance among various parameters has earlier been reported.[15 18] In one double-blind study,[15] such correlation was found to be only 44%. Our study, therefore, reiterates that clinical criteria should be the mainstay in the diagnosis of leprosy in children.

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Registration of the number of macules in paucibacillary leprosy for evaluation of early diagnosis and individual prognosis

M DEGUERRY*, E DECLERCQ*, C MISSON*, C VELLUT† & F BERTRAND*

**Department of Epidemiology, School of Public Health, Catholic University of Louvain, 1200 Brussels, Belgium; †Hemerijckx Government Leprosy Centre, Polambakkam 603309, Tamil Nadu, India*

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Summary The number of macules is usually registered at diagnosis in the first clinical examination of leprosy patients. The question studied here is whether this practice is of any interest as an indicator of the precocity of detection or the prognosis. The study is based on the 26,996 paucibacillary patients detected from 1957 to 1982 in Polambakkam Leprosy Centre (South India) for whom the number of macules and disability status are assessed and registered.

Several observations suggest that the proportion of single-macule patients among the newly detected cases is a more sensitive indicator than the proportion of new patients with disabilities for the evaluation of the delay between onset of the disease and detection. Its use could be especially helpful for programmes running for several years, when it becomes difficult to observe significant variations in the proportion of patients with disabilities.

Regarding the prognosis value of the number of macules, inactivation and relapse probabilities were calculated. Regularity of treatment is found to be a better predictor of early inactivation than the number of macules, while relapse probabilities are more affected by the number of macules.

Introduction

Evaluation should be an effective part of every leprosy control programme, and should be based on the collection and the analysis of appropriate and reliable data.

The OMSLEP information system is now used more and more for evaluation in the field.[1] It has been created at the request of the WHO in an attempt to standardize and make comparable the data collected, and to limit them to those really useful for decision-making. However, many health managers want to adapt it to the local situation and to collect some additional data. One of the variables often added to the individual patient form is the number of macules at detection for paucibacillary cases. Information concerning the number and evolution of macules should be collected in the patient clinical file at least annually to be useful for individual follow-up. The usefulness of this data as an epidemiological indicator, has never been properly evaluated. If limited

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to the number of macules at detection, this information could only be worth reporting if it can help to build either: a more sensitive indicator of early detection than the proportion of patients with disabilities among the newly detected cases; or an indicator of prognosis, either for the duration of treatment until inactivation of the lesions, or for the risk of relapse.

Thus this study has two objectives. First, to study whether the proportion of single-macule patients among newly detected cases is a more sensitive indicator of early diagnosis than the presence of disability. This objective is only verified if the several-macules stage is preceded by the single-macule stage and if the delay to go from one to several macules is shorter than the delay necessary to develop disabilities. The second objective is to evaluate the prognosis value of the number of macules at detection. It will be reached by comparing inactivation and relapse probabilities between single- and several-macule patients.

Material and methods

This study is based on the data routinely collected in the Polambakkam Leprosy Control Programme, in South India, where 47,068 patients were detected between 1955 and 1982. Among these patients eligible for the present study were those:

of the paucibacillary type of the disease (either clinical tuberculoid type or borderline type with negative bacteriological status);
detected from 1957 to 1982, as the first 2 years showed too many missing values regarding the number of macules at detection;
never treated before; and
with a number of macules and presence of disabilities both assessed at detection.

According to these criteria 26,996 patients were selected for the analysis. For the second objective, i.e. evaluation of the prognosis value of the number of macules, attendance to treatment had also to be known from detection to either inactivation or cure. This was the case for 26,106 patients.

Information on the number of macules and the presence of disabilities was only registered at detection, and not at the subsequent follow-ups. The term 'macule' was actually used for all kinds of patches, either flat or partly or wholly elevated, that are characteristic of leprosy. The number of macules at detection was recorded in only two categories: one macule, and more than one.

Disabilities included bone lesions, claw hands, drop feet, facial lesions and ulcers. Anaesthesia is not taken into account. Distinction was made between index and contacts patients. Patients living in the same household as an already registered case were considered as contacts. This distinction was necessary because:

mean age may be different for the contact and the noncontact populations;
the contact population is more likely to be infected; and
the contact population is more frequently and regularly examined, leading to a higher probability of early detection.

Contact status was unknown for 554 patients. Standard treatment was dapsone monotherapy, to be continued after inactivation for a consolidation period whose duration was based on the WHO recommendations.[6] Attendance for treatment is estimated as the number of attended sessions of treatment divided by the number of organized sessions and expressed in two groups ($\geq 75\%$ and $< 75\%$). Clinical status of the patients was recorded annually.

In the study area, inactivation was defined as 'complete subsidence of thickening and erythema in the patches resulting in the wrinkling and scanning of lesion with partial or complete return to sensation and complete subsidence of activity in the peripheral and trunk nerves'. Relapses concern patients who developed new signs and symptoms of the disease after stopping therapy.

To evaluate the validity of the number of macules at detection as an indicator of early diagnosis

and prognosis, a longitudinal study would be the appropriate methodology. Unfortunately, information concerning the number of macules and the disabilities was registered at detection only. Consequently, for the first objective (early diagnosis) we had to make do with a cross-sectional analysis to get hints on the evolution of the number of macules. For the second objective (prognosis), data concerning clinical status was collected at yearly follow-ups, enabling us to perform the appropriate longitudinal study. This was based on the actuarial or life-table method.[2]

Results

EARLY DIAGNOSIS

Distribution and mean age of the patients by number of macules and presence of disabilities at detection are shown in Table 1. The percentage of patients with disabilities is 3·7 times higher in the several-macule than in the single-macule patients. The difference of mean age observed between several and single-macule patients (1·8–3·9 years) is much smaller than the one observed between patients with and without disabilities (10·5–12·6 years). Mean age for each disability status, is lower for the single than for the several-macule patients. This observation is verified throughout the whole period for both index and contact groups, as shown in Figure 1. Due to small numbers, the distinction between index and contact was not possible for the patients with disabilities. Tables 2

Table 1. Distribution and mean age of the patients by the number of macules and presence of disabilities at detection

	Single-macule patients		Several-macule patients	
	Without disability	With disabilities	Without disability	With disabilities
No.	16,051	259	10,050	636
%	98·4	1·6	94·0	6·0
Mean age	23·1	35·7	27·0	37·5

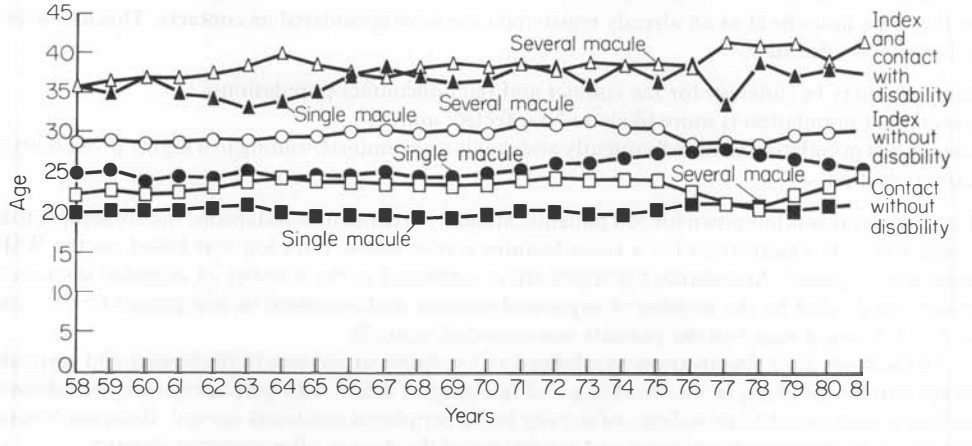

Figure 1. Three years moving average of the age of the patients according to the number of macules, the presence of disability and the contact status.

and 3 show the distribution of the patients by number of macules, presence of disabilities and contact status. The proportion of several-macule patients is similar for both index and contact groups, while the proportion of patients with disabilities in the index group is two times higher than in the contact group. Figure 2 describes the trends of proportions of single-macule and disabled patients among newly detected cases, from 1957 to 1982. The irregularities observed in 1960 in both curves reflect the extension of the leprosy control area, with a sudden detection of many old cases. For both curves, a significant slope could be demonstrated, using a logistic regression from 1961 onwards ($p < 0{\cdot}001$ for the disabilities and $p < 0{\cdot}001$ for the macules).

Table 2. Distribution of the patients by number of macules at detection and contact status*

	Single-macule		Several-macule		Total	
	Index	Contacts	Index	Contacts	Index	Contacts
No.	9,602	6,392	6,639	3,809	16,241	10,201
%	59·1	62·7	40·9	37·3	100	100

* Contact status was unknown for 554 patients.

Table 3. Distribution of the patients by presence of disabilities at detection and contact status*

	Without disability		With disabilities		Total	
	Index	Contacts	Index	Contacts	Index	Contacts
No.	15,572	9,997	669	204	16,241	10,201
%	95·9	98·0	4·1	2·0	100	100

* Contact status was unknown for 554 patients.

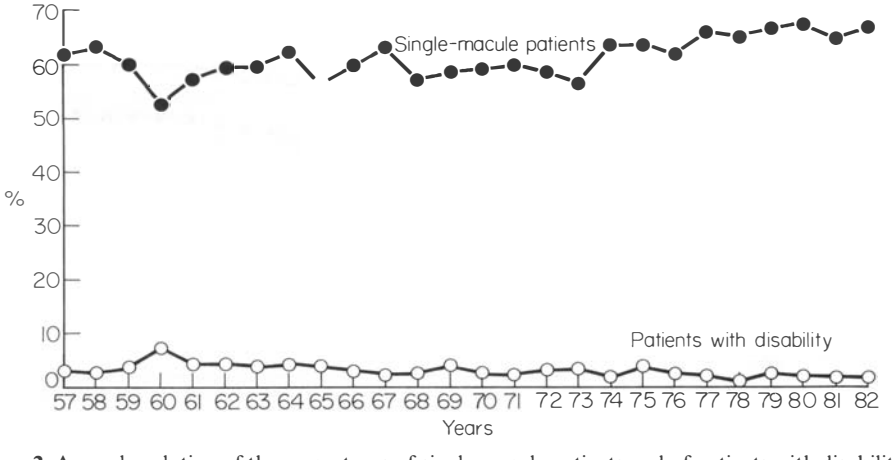

Figure 2. Annual evolution of the percentages of single-macule patients and of patients with disability.

PROGNOSIS

Whatever their number of macules, patients with good attendance to treatment inactivate sooner than patients with poor attendance (Figure 3). Within each group of attendance, single-macule patients inactivate sooner than several-macule patients. Figure 4 shows relapse probabilities after inactivation by number of macules at detection. These probabilities are lower for single-macule patients, even after a long observation period. This is still true when results are displayed by attendance to treatment (Figure 5).

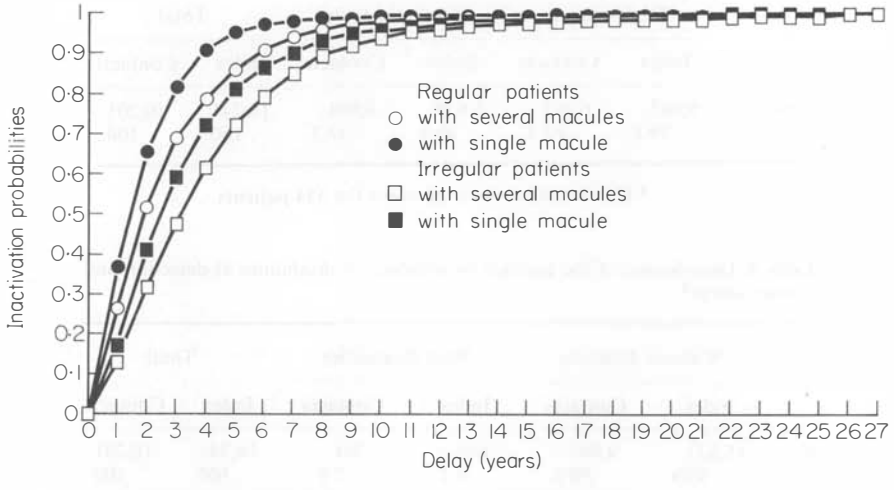

Figure 3. Cumulative inactivation probabilities from beginning of treatment, by number of macules at detection and attendance.

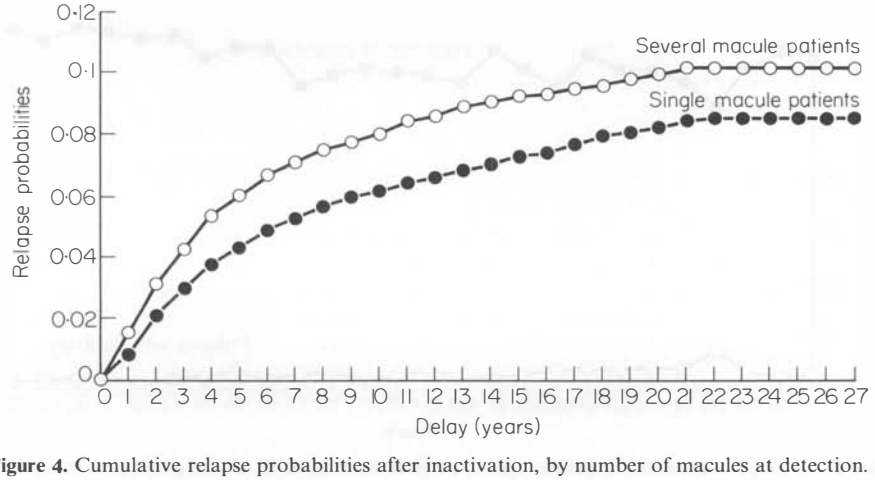

Figure 4. Cumulative relapse probabilities after inactivation, by number of macules at detection.

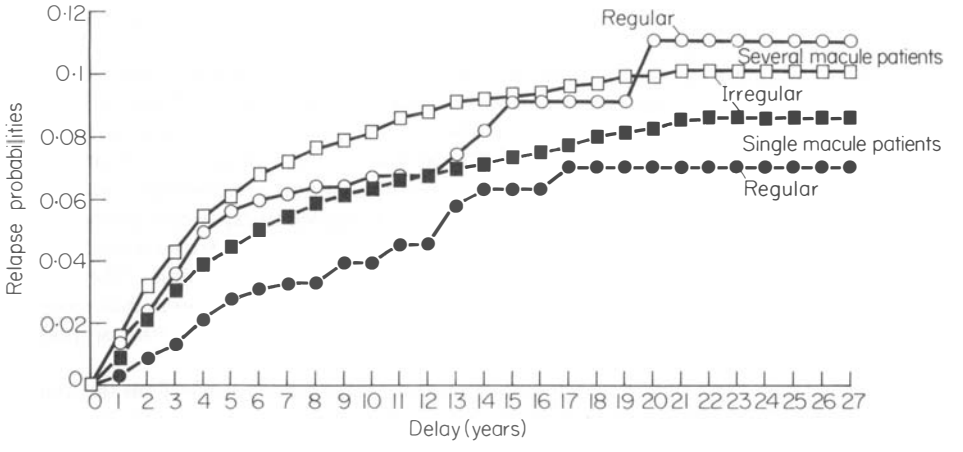

Figure 5. Cumulative relapse probabilities after inactivation, by number of macules at detection and attendance.

Discussion

EARLY DIAGNOSIS

The proportion of disabled among newly detected cases is widely accepted as an indicator of early diagnosis,[5] early detected patients having a lower probability of presenting disabilities. Repeated observations[3,4] showed that the proportion of disabled patients decreases with the improvement of detection activities. For the proportion of single-macule patients among newly detected cases to be also accepted as an indicator of early diagnosis, the several-macule stage should be preceded by a single-macule stage. With the limitations of a cross-sectional study, one would then expect to make the following observations:

a higher proportion of single-macule patients among the patients without disability than among those with disabilities;
an increasing proportion of single-macule patients when the proportion of disabled among newly detected cases decreases over time;
a lower mean age at detection for the single-macule than for the several-macule patients; and
a higher proportion of single-macule patients among the contacts than among the index, since the contact population is more frequently examined, and consequently detected earlier;

The actual observations reported in Tables 1 to 3 and Figures 1 and 2, are consistent with the expectations. One could object that the same observation could be made if the number of macules at detection was determined by the age at onset rather than by the delay between onset and detection, younger patients being more prone to develop only one macule. This can be refuted by the fact that the several-macule contacts are younger than the single-macule index patients. The significance of this observation is further enforced by its consistency throughout the study period. The proportion of single-macule among newly detected cases may thus be considered as an indicator of early diagnosis. Even if valid as an indicator, the proportion of single-macule patients is worth reporting only if it is more sensitive than the proportion of disabled patients.

Because disabilities take a long time to develop, the proportion of patients with disabilities can evidence changes in detection activities only after a long delay. Moreover, after many years, the

group of disabled patients is usually so small that minimal random variations in their number lead to great changes in the proportion.

In Table 1, we observe that the difference of mean age between several- and single-macule patients is much smaller than the difference observed between patients with and without disabilities. In Table 3, the proportion of disabled among contacts is two times less than among index cases, due to contacts being examined more frequently. On the contrary, the proportion of single-macule patients is almost similar for both groups. These two observations are consistent with a shorter delay for the development of several macules than the delay needed to experience disabilities. Thus it seems that the proportion of single-macule patients among newly detected cases is a more sensitive indicator of precocity of detection than the proportion of patients with disabilities. The proportion of single-macule patients would be an especially helpful indicator for programmes running for several years, when it becomes difficult to observe significant variations of the proportion of patients with disabilities.

There are however two difficulties attached to the use of an indicator based on the number of macules. First, a more careful clinical examination, and thus a more experienced staff, is needed to assess the number of macules than to detect disabilities. Second, it is based on paucibacillary patients only. However, if detection occurs progressively earlier for paucibacillary leprosy, it seems only logical to think that it evolves likewise for multibacillary leprosy.

PROGNOSIS

The second objective of the study was to evaluate the prognosis value of the number of macules at detection on inactivation and relapse probabilities.

Figure 3 shows that single-macule patients inactivate sooner than several-macule patients. The proportion of self-healing cases is probably higher in the first group, but that does not modify the prognosis value of the number of macules. It is however quite satisfactory to observe that regularity to treatment is a better predictor of early inactivation than the number of macules. However, one limitation of the study is the insufficient power of discrimination of the classification used for the macules—several macules just means 'more than one'. It is possible that a more detailed classification would give more gradual and convincing differences in inactivation probabilities. Figures 4 and 5 show that the number of macules is an important predictor of relapse probability, more so than the regularity to treatment. The number of macules at detection depends on, at least, two factors: the delay between onset of the disease and its detection; and the immune defences of the patients. While several-macule patients all have relatively poor immunity, the single-macule patients include those with poor immunity but early detected, together with patients who have good immunity. That could explain why, their immune defences on average being better, patients with single macule seem relatively protected against relapses. Regarding inactivation, though, the immune status has less influence on the necessary duration of treatment than the compliance to treatment.

The implications of these observations on multidrug therapy (MDT) are certainly worth studying. If the same results were observed after MDT, the selection of the MDT regimen and its duration should then be based not only on bacteriological, but also on clinical criteria.

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Report and evaluation of Brazilian experience in the rehabilitation of patients with leprosy

M VIRMOND*, F DUERKSEN† & A GONÇALVES‡
* *Health Department of RGS and Hospital 'Lauro de Souza Lima', Brazil; Health Science Centre, Manitoba University, Canada;* ‡ *Division of Dermatological Medicine, University of São Paulo, Brazil*

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Summary As part of an investigation of the rehabilitation of physically disabled leprosy patients, a report and evaluation of Brazilian experience in this area is given.

After describing leprosy as a genuine and relevant public health problem in Brazil because of the numbers involved, the suffering caused and the difficulties inherent in its control the authors emphasize the important role of physical disability in this context. The description of a project set up in 1975 shows a model based on a Reference Centre as an epicentre for irradiating triggering action in five Brazilian cities. The results obtained thus far consist of 32 courses given at the Reference Centre and approximately 449 surgical interventions performed by one of the authors, 93·10% of which were considered satisfactory.

The need to evaluate the clinical and therapeutic procedures involved from an epidemiological viewpoint is emphasized.

Introduction

The study by Gonçalves[1] of leprosy as a public health problem in Brazil reveals a serious and important endemic disease both in absolute and relative terms. For example, Central America as a whole has the same number of officially registered cases as only a single neighbourhood in the city of Saõ Paulo. Andean America (Bolivia, Chile, Columbia, Ecuador, Peru and Venezuela) has a number of registered patients only a little higher than the number affected in only one of the 23 Brazilian states. In fact approximately 80% of all cases occur in Brazil.

With respect to the difficulties inherent in the control of the disease, Sansarricq[2] has clearly stated that up to now the control of the disease has been directly related to individual care, while the impact of epidemiological measures depends primarily on the early diagnosis and adequate treatment of a large proportion of cases. However, the only detection method available is a clinical one and consequently it can only be applied by experienced professionals with specialized knowledge. Because of these difficulties, among many others, control programmes require complex and burdensome mechanisms involving organizational and logistic problems. These problems are

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further increased by the fact that regions where the disease is most prevalent are already burdened by other obvious and pressing health problems.

The suffering caused is related mainly to the deformities accompanying the evolution of the disease, which are variously identified as impairments, deficiencies and disabilities according to whether the viewpoint is that of the outside observer, the patient or society.[3] Some clinical epidemiological studies have revealed surprising data. One study[4] reported that the percentage of deformities is 35·85% in Argentina, 48·7% in Burma, 35·6% in the Cameroons, 23·4% in Nigeria, 32·22% in the Philippines and 41·46% in Thailand. In Brazil, one study[5] showed a 75·3% prevalence of grade 1 disabilities, 27·3% of grade 2 disabilities, and 4·8% of grade 3 at a health service in the State of São Paulo (the criteria of degrees of disability is adapted from the OMS, 1983[6]). In a study[7] of 2080 patients from the State of Rio Grande do Sul, 68·7% with some type of disability were detected, although the highest percentage (30·05%) corresponded to grade 1.

Materials and method

In view of the situation presented above, a project was started in 1975 for a more dynamic physical rehabilitation of leprosy patients. Joint efforts by the technical directorship of the 'Lauro de Souza Lima' Hospital of Bauru, SP, and by the president's office of the American Leprosy Missions, Inc., New Jersey, funded a visit to Brazil by one of the authors (FD), a surgeon specializing in the rehabilitation of leprosy patients. Starting from this visit and with the support of a Brazilian agency, the Evangelical Committee for the Rehabilitation of Patients with Hanseniasis (CERPHA), an ongoing programme of training and assistance for the rehabilitation of leprosy patients was instituted, with the 'Lauro de Souza Lima' Hospital serving as the central institution.

The main activities of the programme are concerned with the training of surgeons and technical medical personnel in rehabilitation procedures, so that these professionals will include patients with leprosy in their daily practice. Thus, we avoid the need to train someone to be a 'leprosy surgeon', i.e. a surgeon involved only with leprosy patients. In this way, plastic, orthopaedic and neurosurgeons (the main specialists involved with physical rehabilitation) will treat leprosy patients in their daily practice. The programme is also based on the local development of rehabilitation programmes using resources available in the community and integrated into the local leprosy control programme. For this purpose, once the location has been selected in terms of its epidemiological characteristics and by analysis of the technical staff available, the following procedures are implemented:

Training of staff at the National Reference Centre

In addition to being a Reference Centre for training, the 'Lauro de Souza Lima' Hospital acts as an integrated rehabilitation centre for the State of São Paulo, where all necessary facilities, surgery, physiotherapy, ortheses and prostheses, are available. The Hospital also co-operates with a nongovernmental agency, the Society for the Reintegration of the Disabled (SORRI), which acts mainly at the professional rehabilitation level. In view of the influence they exert on trainees, it should be emphasized that these two institutions are not limited to caring for leprosy patients, but also treat other types of disability.

Activities of programme implantation

These activities consist of on-site visits by specialists who select cases and operate in order to provide both patient care and teaching assistance to technical staff involved in the local programme as a continuation of the activities mentioned above.

The objectives of decentralization of patient care and removal of the stigma from the disease are

achieved by relying on local community resources. Thus, general hospitals are used for surgery, physiotherapy centres provided by the National Health Insurance System are utilized, and even the services of commercial shoe stores are sought for the preparation of special shoes or simple modifications. In this manner, an attempt is made to render the patients less dependent on the specialized leprosy control service by stimulating their integration into the general network of health care.

Activities of programme maintenance

These consist of periodical supervisory visits for motivation and programme regulation.

From a methodological point of view, in addition to current plastic surgery practice for facial lesions, the following techniques have been used in a systematic and standardized manner:

Lagophthalmos: temporal temporalis muscle transfer (Gillis,[8] and modified by Andersen[9]).
2 Claw hand: 'lasso' procedure of Zancolli[10] and four tailed transfer of the superficialis tendon (Stilles-Bunnell[11]).
3 Lack of thumb opposition: 'Y' technique of Bunnell–Brand[12] using the superficialis as motor.
4 *Drop foot*: transfer of the posterior tibial muscle with insertion into the tendons of the hallux extensor and into the common extensor of the toes.[13]
5 Clawed toes: transfer of the flexor to the extensor by the techniques of Girdlestone and Taylor.[14]

Results

TRAINING OF PERSONNEL

The continuity and impact of training activities at the Reference Centre may be appraised by considering that, with the completion of the latest course of rehabilitation (the 34th, given in October, 1988), a total of 420 professionals were trained over a period of 9 years.

IMPLEMENTATION OF LOCAL PROGRAMMES

The implementation of local programmes of rehabilitation was finalized in five Brazilian cities: Rio Branco AC, Manaus AM, Belem PA, Guarulhos SP and Porto Alegre RS.

The Rio Branco Programme is linked to the State Health Dermatology Service and involves the training of personnel for physiotherapy and surgery, and has generated a subprogramme in Cruzeiro do Sul. The surgical activities in Rio Branco are based on a general hospital of the Health Department and on a private general hospital (São Camilo Hospital). Modified shoes and prostheses are available from a workshop sponsored by a nongovernmental entity.

The Manaus Programme is based at the 'Alfredo da Mata' Outpatient Centre where prevention of incapacity and selection of cases are carried out. Surgery is performed at the 'Adriano Jorge' Hospital, linked to the Ministry of Health.

The Belem Program is located in the 'Demetrio Medrado' Centre for the Prevention and Treatment of Incapacities. The selection and preparation of cases is made in this Centre and surgery is performed in private general hospitals in the community.

The Guarulhos Program is located in the 'Padre Bento' Hospital of the State Health Department and receives professional rehabilitation support from a branch of SORRI in the same city.

The Porto Alegre Program is based at the Sanitary Dermatology Outpatient Centre of the State Health Department. Surgery is performed in general hospitals of the community and shoe modifications and prostheses are obtained from the National Health Insurance System.

Thus, the main programmes are located exactly where prevalence of the disease is most significant and the activities are performed by local trained personnel using the resources of the community in addition to those provided by official institutions.

Programme maintenance

Thirty-six programme maintenance visits had been made up to December 1987 with the main objective of encouraging expansion by including additional personnel in the programme.

Table 1. Distribution of operations performed by one of the physicians in charge of the programme from 1982 to 1987

Region	Surgery	Number	%
Upper limbs	Correction claw hand	51	11·35
	Neurolyses	30	6·68
	Correction of lack of opposition of the thumb	29	6·45
	Release of contractures	24	5·34
	Interphalangeal arthrodeses	16	3·56
	Others	13	2·89
	Prosthesis for the first web in the hand	07	1·55
	Nerve biopsies	03	0·66
	Skin biopsies	03	0·66
	Tumour excision	03	0·66
Subtotal		179	43·80
Lower limbs	Treatment of plantar ulcers	51	11·35
	Treatment of leg ulcers	35	7·79
	Correction of drop foot	32	7·12
	Correction of clawed toes	24	5·34
	Neurolyses	12	2·67
	Toe arthrodeses	10	2·22
	Nerve biopsies	03	0·66
	Skin biopsies	02	0·44
	Amputations	02	0·44
	Others	02	0·44
Subtotal		173	38·47
Face	Nasal reconstruction	22	4·89
	Correction of Lagophthalmus	22	4·89
	Blepharoplasty	15	3·34
	Correction of megalobule	11	2·44
	Correction of madarosis	08	1·78
	Excision of skin tumours	05	1·11
	Tarsorrhaphies	05	1·11
	Correction of ectropion	05	1·11
Subtotal		93	20·67
	Correction of gynaecomastia	04	0·89
Total		449	

Table 2. Frequency and distribution of complications recorded during the evaluation of patients after operation for correction of lack of thumb opposition due to paralysis of the median nerve

Complication	Number	Cases with complications (%)	Total number of cases (%)
Infection	1	11·11	3·44
Dehiscence of anastomosis	1	11·11	3·44
Migration of the tendon*	4	44·44	13·79
'Check-rein' deformity†	1	11·11	3·44
Loss of flexion strength in the forth finger	2	22·22	6·89

* This particular complication did not adversely affect the satisfactory results obtained for these patients.
† This is an adherence of the distal stump of the superficialis tendon which causes a flexion contraction of the proximal interphalangeal joint.

The surgical operations performed from 1982 to 1987 at the reference centre and at local programmes are listed in Table 1 (preliminary survey).

The evaluation of the specific results of surgery is beyond the scope of the present report. To illustrate, we will simply cite the evaluation of 29 cases of correction of loss of thumb opposition treated by the techniques of Bunnell–Brand.[14] Results were satisfactory in 93·10% of cases and unsatisfactory in 6·90%, as evaluated by the criteria established by Palande.[15] In general satisfactory results were those where the patients were able to abduct the thumb and make a pinch with the second finger in a manner adequate for routine activities. Results were considered unsatisfactory when one or more of the complications listed in Table 2 occurred.

Discussion

The data presented here led us to consider the priority that should be given to rehabilitation measures within a control programme. Indeed, several authors (e.g. Bechelli[16]) discuss the validity of rehabilitation of leprosy patients in countries with low budgets for control programmes. There is agreement that budget priorities should involve early diagnosis and adequate treatment, i.e. the measures that are the best to prevent deformities. However, there is sufficient evidence to show that physical rehabilitation should be included in the control of leprosy if we consider that:

1 The figures referring to deformities are highly significant. One study[4] reported the presence of deformities in 35·85% of patients in Central and South America. Dinis (cited by Mallac[17]) reported a 25% figure for Brazil. Enna[18] (1974) reported that 25% of registered cases required some type of surgical correction of deformity. Oberlin *et al.*[19] reported that 10–15% of patients in any treatment group could benefit from physical rehabilitation and finally Duerksen,[20] on the basis of data recently made available by the Ministry of Health of Paraguay, pointed out that 30–40% of patients with leprosy show deformities that could be corrected or relieved by physical rehabilitation.
2 For the patient, the major significance of the disease resides in the deformity. Specific medication obviously cannot achieve recuperation with respect to deformities already present and the meaning of 'cure' for the patient resides in the solution of his deformities and not in a negative reading of his smear. Thus, physical rehabilitation acts as a feedback element in the initial phases of the control programme, since many of the rehabilitation procedures require adequate clinical treatment and effective measures for prevention of disability.

3 In Brazil, the rehabilitation programmes functioning jointly with control programmes receive support mainly from alternative sources, which means that official budgets could be devoted to care during the initial stages of the control programmes.

Thus, considering that a concrete ideology and practice of surgical rehabilitation of patients with leprosy already exists in Brazil, the next essential step concerns clinical evaluation procedures, to be carried out in a rigorous manner according to epidemiological methodology with the objective of facilitating sectorial decisions. Indeed, a project has been designed for a multicentre exploratory study of the Brazilian experience in surgical rehabilitation of leprosy patients. The specific objectives are:

1 To evaluate the magnitude of the demand for physical rehabilitation within the context of: (a) the local epidemiological structure of leprosy; and (b) the local structure of the network of health services.
2 To evaluate the impact of the physical rehabilitation procedures on the basis of the following indicators: (a) clinical evolution; (b) functional evolution; (c) professional evolution; and (d) social evolution.
3 To evaluate the efficiency of the physical rehabilitation procedures on the basis of health administration indicators such as concentration and direct and indirect costs.

The importance of surgical procedures in physical rehabilitation could be determined by the case-control method as follows: after the information referring to item 1 is obtained, each surgical patient would be paired with a similar patient matched for nosographic and observed and recorded physical conditions who: (a) was submitted to any physical rehabilitation procedure; (b) was submitted to a clinical procedure only; and (c) was submitted to both clinical and surgical procedures.

This would involve the following groups:

Group 1: diagnosed patients who had not completed 12 months of clinical treatment.
Group 2: diagnosed patients with at least 12 months of continuous clinical treatment.
Group 3: diagnosed patients with at least 12 months of clinical treatment and submitted to care for the prevention of disability with simple techniques for at least 6 months.
Group 4: patients as defined in group 3 and submitted to rehabilitation surgical procedures at least 12 months before.

Conclusions and recommendations

1 In Brazil, the number of leprosy cases is significant from a public health point of view.
2 This is a disease with a high frequency of physical and social sequelae.
3 Studies have revealed that up to 30–40% of registered patients have functional sequelae involving disabilities that could be corrected or relieved by physical rehabilitation.
4 The social stigma attached to the disease and the relative lack of information about it among physicians represent an obstacle in the effective fight against leprosy.
5 Control programmes should include physical rehabilitation of the patient not only because this represents the final link in the chain of action, but also because it has a feedback effect in terms of target efficiency.
6 At a time when both theoretical and practical competence is available in Brazil, we believe that the next step should be an epidemiological evaluation of the clinical and therapeutic procedures involved in the fight against leprosy.

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SPECIAL ARTICLE

Educational material for the patient with leprosy

A C MCDOUGALL* & G D GEORGEIV†
87 Lower Radley, Near Abingdon, Oxfordshire OX14 3BA, England; †275 Turnpike Drive, Luton, Bedfordshire LU3 3RD, England

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Summary This paper addresses the need for suitably written and illustrated material for the patient with leprosy with emphasis on the effective administration of WHO recommended multiple drug therapy (MDT) and the prevention of deformities. The successful implementation of MDT strategy for leprosy control calls for attention to a 'package' of activities, amongst which the education of the patient regarding the disease and its modern treatment may be of crucial importance. Attention is drawn to the steady improvement in educational and literacy levels in many developing countries and to the potential of clearly written instructions for use by patients and staff. The importance of development of educational material in the context of the regional and local cultural milieu is stressed. Eight major 'messages' related to the causation of the disease, the importance of regular clinic attendance for monthly supervised drug administration, compliance to the daily domiciliary drug intake and action for prevention of disability, are proposed. These 'messages' are accompanied by outline drawings which can be used by staff for patient education both at the onset of chemotherapy and on the subsequent clinic attendances. The paper describes broad approaches but underlines the importance of local development of educational material for this purpose.

Not only for leprosy, but also for many other conditions in both developed and Third World countries, it has for long been recognized that the supply of educational material for patients, particularly with regard to compliance to prescribed medication, is either defective or non-existent. If one defines compliance as a combination of satisfactory intake of prescribed medication, regular attendance for supervised medication and/or clinical examination and adherence to any given regimen for an adequate period of time, the world problem of *non*-compliance in diseases such as high blood pressure, diabetes, glaucoma, schizophrenia, arthritis, epilepsy, leprosy, tuberculosis (and many more) is immense. Where early diagnosis and drug treatment are the basic means of control of diseases, as in leprosy and tuberculosis, patient compliance, using the above definition, is clearly of critical importance. The literature on this subject is enormous; since the early days of the

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production and clinical use of effective chemotherapeutic agents, the difficulties in persuading patients to follow prescribed courses of treatment (even for short courses) have been recognized and attempts made to analyse the causes and devise remedies. Many reviews of the subject have drawn attention to the fact that the overall rate or level of 'compliance' for a wide range of medication in different diseases, is deplorably low.[1–5] The losses in terms of benefit to patients and the national drug budget are self-evident.

The magnitude of this problem and the need to develop educational material for patients had been recognized by WHO and other international agencies over the years. In 1985, the WHO *Action Programme on Essential Drugs and Vaccines*[6] convened a meeting at which a working group examined the possibilities for the development of more effective written and illustrated material. They drew attention to 5 important steps to ensure the proper use of drugs, namely: accurate diagnosis, rational prescription, correct dispensing, suitable packaging and clear instructions to the patient. Two main approaches by way of strategy for improvement were identified: 1, the communication of 'general principle' messages through all appropriate institutions using a 'campaign' approach, and 2, communication of specific information for individual drugs through message communicators. The Report of this important workshop covers the production and use of both written and illustrated material, drawing attention to the numerous pitfalls, making it essential reading for anyone involved in health education for the proper use of essential drugs.

In the case of tuberculosis, the crucial importance of a regular and satisfactory drug intake in achieving clinical cure in individuals and breaking the chain of transmission has been well recognized since the early days of combined therapy for that disease. The problem of compliance with the self-administration of drugs in tuberculosis control has been reviewed in detail[7,8] and recently attention has been drawn to the continuing problems, even with short-course regimens.[9] In leprosy, numerous studies have been published through the years,[10–14] including the era of dapsone monotherapy, calling attention to the deficiencies of self-administered medication, regularity of attendance and adherence to the regimen for a sufficiently long period of time. Recently attention has been drawn to the need for the more effective application of available techniques in social and clinical psychology for the study of this problem.[15,16]

Much of what we have said so far refers only to the matter of drug treatment in leprosy, but we propose to expand the approach and to make outline proposals which cover: a, the supply of basic information on leprosy to the patient; b, the development of educational material to improve attendance and drug intake; and c, similar material to prevent, and perhaps also to treat disability and deformity, thus maintaining the principle of combined 'bacillus control' and 'disability control'[17] with emphasis on what can be achieved *in* the community.[18]

Basic information

The enormous variations in educational levels, cultural patterns and attitudes to disease which are likely to be encountered in leprosy programmes make it impossible to put forward, in any detail, a universally applicable set of statements. The general principles of communication with patients have been clearly spelled out and the importance of understanding local attitudes, beliefs and behaviour for the purpose of health education has been emphasized.[19] The basic information should be succinct and brief, unemotional, objective and realistic, focusing on the important facts and presented in correct order.[20] It is also vital to develop this information *through indigenous workers* with a knowledge of leprosy, who also have a good grasp of the cultural and socioeconomic conditions of their own people. 'Pre-testing' and testing of any package of information is essential before anything goes to printing and distribution. Teaching and learning materials for virtually all grades of worker in leprosy have been developed extremely well,[21] and on a scale which outclasses almost any other communicable disease, but very little has been developed for the patient. This may be significant; it is certainly not easy to do it effectively and mistakes can easily be made. But the

need, for the involvement of the patient (as also the family and the community) in case detection and the better use of multiple drug therapy (MDT), as recommended by WHO in 1982,[22] is outstanding—and needs attention. Patients are not fools; literacy rate in some leprosy endemic countries are surprisingly high[23] and we should pursue the possibility that patients, either by themselves or with the family, make good use of instructions leading to cure and the avoidance of deformity. The case for at least devising and trying out written and illustrated material for this purpose seems to us to be overdue.

Educational material to encourage the better use of drugs

In the WHO document referred to above,[6] attention was directed to the problems associated with correct use of drugs, assuming that diagnosis, prescription, dispensing and packaging were appropriate, and a variety of 'target groups' for such material were identified, including caretakers/parents of children, pregnant women, adults and the elderly. The working group further considered the framework (health infrastructure, non-governmental or voluntary organization, schools, etc.) through which educational material should be channelled, whilst emphasizing the importance of development of such material with (a) the active participation of the target audience, and (b) advice, where appropriate, from experienced prescribers, dispensers and pharmacists. They also listed the many ways in which the messages can be presented: written material in books, pamphlets, with or without simple illustrations, posters, slides/tapes; television/video, radio, cinema and live performances. These approaches are all potentially valuable but in the present communication we shall concentrate on the production of simple, written information, possibly supported by illustrations which may be useful for local development.

To develop relevant written materials for the effective education of the patient with the aim of improving participation in the treatment and cure process, the following questions need consideration:

What does the patient need to know about the disease and its treatment?
What is the level of ability of the health/leprosy worker in communication and the education of the patient?
What is the best and most practical means of educating the patient, including educational aids?

The educational process of the patient must begin at the time when the patient is told of the diagnosis and treatment is instituted. It is important to recognize the possibility of psychological trauma associated with a verdict which concerns not only health but also social status. Perhaps this is the most difficult time for the patient and the need for understanding and support by the health worker and the family is essential. This is the moment when confidence in the service and the treatment, including a close partnership between health worker and patient has to be established. The main content of this 'first encounter' has been clearly defined elsewhere.[24] Particularly in the context of the increasing use of MDT, we offer the following as a check-list to enlisting the cooperation of the leprosy patient as an active partner in the management of the disease and prevention of disability.

Causation of leprosy. Traditional beliefs about leprosy and its causation are often responsible for a lack of faith in modern treatment. It is therefore important for the patient to accept information about the 'germ' cause, the methods of transmission of the disease and the need to adhere to prescribed treatment for an adequate period of time. Knowledge of religion, regional attitudes, beliefs and behavioural patterns is essential. The possibility of illustrating the 'germ concept' will be discussed below.

Medication. The patient needs information about the treatment—when and how much to take, for how long and how it will help him. Warnings must also be given about likely side-effects (e.g. discolouration of urine and/or skin, gastrointestinal upset etc.) and their significance. In

monotherapy leprosy control, the name of dapsone was widely known to patients and families and the advice about its use was relatively easy. However, the administration of MDT is more complicated and this is particularly so for multibacillary cases, since besides the supervised monthly doses of rifampicin and clofazimine, the patient has to take two types of drugs at home (dapsone and clofazimine). The importance of regular monthly clinic attendance and strict adherence to the daily intake of domiciliary treatment needs persuasive explanation including the use of the 'double check' technique[25] to achieve maximum understanding by the patient. Field experience, at least at some areas, has shown that health workers encounter difficulties in instructing the patients on MDT.[26] In this context, the potential value of blister calendar packs should be kept in mind.[27]

Suggested *written materials* for WHO recommended MDT regimens for MB and PB leprosy are outlined in Tables 1 and 2 respectively. It bears repetition that these are intended as outline 'examples', *entirely open to discussion and development* by local advisers. We envisage these messages being printed on paper or card as a pamphlet or leaflet, easily folded or accommodated in a pocket and 'linked' to the drugs in their container or blister-calendar pack, notably by colour. Thus, in order to avoid confusion between PB and MB regimens, and perhaps also between child and adult regimens, the use of the same colour scheme for: 1, the container or blister-calendar pack; 2, the written instructions to the patient; and 3, the patient record card, would be an obvious additional advantage for all concerned—and almost certainly worth the small additional expenditure. We repeat that personal communication over and above any 'devices' which are provided for the better use of drugs by patients, is absolutely essential. The equation: good personal communication *plus*

Table 1. Educational material for the patient with *multi*bacillary leprosy

1 Your kind of leprosy disease is called 'MB'. It is caused by a tiny germ which hides in your body and causes the patches and lumps on your skin.

2 You can be cured by new, strong medicines. If you take them regularly, you should not develop any further trouble with your skin, eyes, hands or feet and your leprosy disease will be cured.

3 AT THE CLINIC (TREATMENT CENTRE), *every month*, you have to take:
3 egg-shaped brown capsules
2 long red capsules
1 white tablet
The doctor or health worker must see you swallow them.
After you swallow them, they join together to kill the germs in your body.

4 AT HOME, *every day*, you must take:
1 brown, round capsule (clofazimine)
1 white tablet (dapsone)
This daily treatment at home is important in order to stop any new germs growing in your body.

5 This treatment, at the CLINIC and AT HOME, must continue for at *least 2 years*.
Go *every month* to the clinic and take your medicine, every day, at home.
Some of the germs hide from the drugs and it takes a long time to kill them all.

6 If you take your treatment regularly, the patches and lumps will begin to go away after 4–6 months. But even when you can no longer see them, continue taking your medicines, until told to stop.

7 If you had deformity of eyes, hands or feet, perhaps with loss of feeling, *before* starting treatment, there may not be improvement in the deformity. But the treatment will kill the germs in your body and if it is taken regularly for at least 2 years the deformity is unlikely to get worse.

8 If you think that the treatment is not agreeing with you, report as soon as possible to the clinic (treatment centre) or a hospital. This refers especially to:
(a) pain, tingling or loss of sensation in the hands or feet;
(b) loss of strength (power) in the muscles of the arms or legs, or the face;
(c) unexplained fever;
(d) yellowness of skin and eyes (jaundice); and
(e) unexplained weakness.

Table 2. Educational material for the patient with *pauci*bacillary leprosy

1 Your kind of leprosy disease is called 'PB'. It is caused by a germ which hides in your body and causes patches or marks on your skin, perhaps with loss of feeling and weakness of muscle.

2 You can be cured by new, strong medicines. If you take them regularly, you should not develop any further trouble with your skin, eyes, feet or hands and your leprosy disease will be cured.

3 AT THE CLINIC (TREATMENT CENTRE), *every month*, you have to take:
2 long red capsules
1 white tablet
The doctor or health worker must see you swallow them.
After you swallow them, they work together to kill the germs in your body.

4 AT HOME, *every day*, you have to take:
1 white tablet (dapsone)
This daily treatment at home is important to stop any new germs growing in your body.

5 This daily treatment, at the CLINIC and AT HOME, must continue for 6 months.
Go *every month* to the CLINIC and take your tablet *every day* at home.
Some of the germs hide from the drugs. So it is important to continue for the full 6 months.

6 If you take your treatment regularly, the marks on your skin will usually disappear in about 6 months.
Do not be worried if your skin is not completely normal in colour after 6 months of treatment. It may take a little longer.
Be patient, and the colour will soon return to normal.

7 If you had deformity of eyes, hands or feet, perhaps with loss of feeling, *before* starting treatment, there may be no improvement in the deformity. But the treatment will kill the germs in your body and it is therefore important to take it for 6 months, as described above.

8 If you think that the treatment is not agreeing with you, report as soon as possible to the clinic (treatment centre) or a hospital. This refers especially to:
(a) pain, tingling or loss of sensation in the hands or feet;
(b) loss of strength (power) in the muscles of the arms or legs, or the face;
(c) unexplained fever;
(d) yellowness of skin and eyes (jaundice); and
(e) unexplained weakness.

appropriate, clearly written and illustrated instructions *plus* a suitable container for the drugs is likely, if only on common-sense grounds, to have a significant effect on many aspects of 'compliance', as defined above.

Finally, illustrated material, as shown in Figure 1 (a–d), and again entirely subject to local development and trial, may usefully reinforce written messages for patients on MDT. Those shown here are somewhat Africa-orientated and may be unacceptable elsewhere. But if suitably modified, they might be useful for patients and possibly also for health education by the staff. The 'devil' or 'monster' figure which may, in some cultures, identify with a disease-producing organism or germ, but if used at all as part of the basic information described above, pre-testing, preferably by a local sociologist or psychologist is essential.

Duration of treatment and expected results. The WHO recommended MDT regimens for both PB and MB forms of leprosy are significantly shorter in duration in comparison with monotherapy, and this seems to be an important factor in the impressive improvement in treatment compliance now seen with these regimens. It is of crucial importance that the patients understand the significance of the duration of treatment and its relation to the ultimate result of this treatment. The second question of importance is the patient's expectation of the prescribed medication. In the case of PB patients, treatment has, in some instances, to be terminated before the skin lesions have completely waned, giving the patient the impression that he is denied treatment when still needing it. Although sometimes resolved by continuing treatment with dapsone alone or by prescribing a placebo, this is not standard WHO advice; adherence to the recommended period, backed by

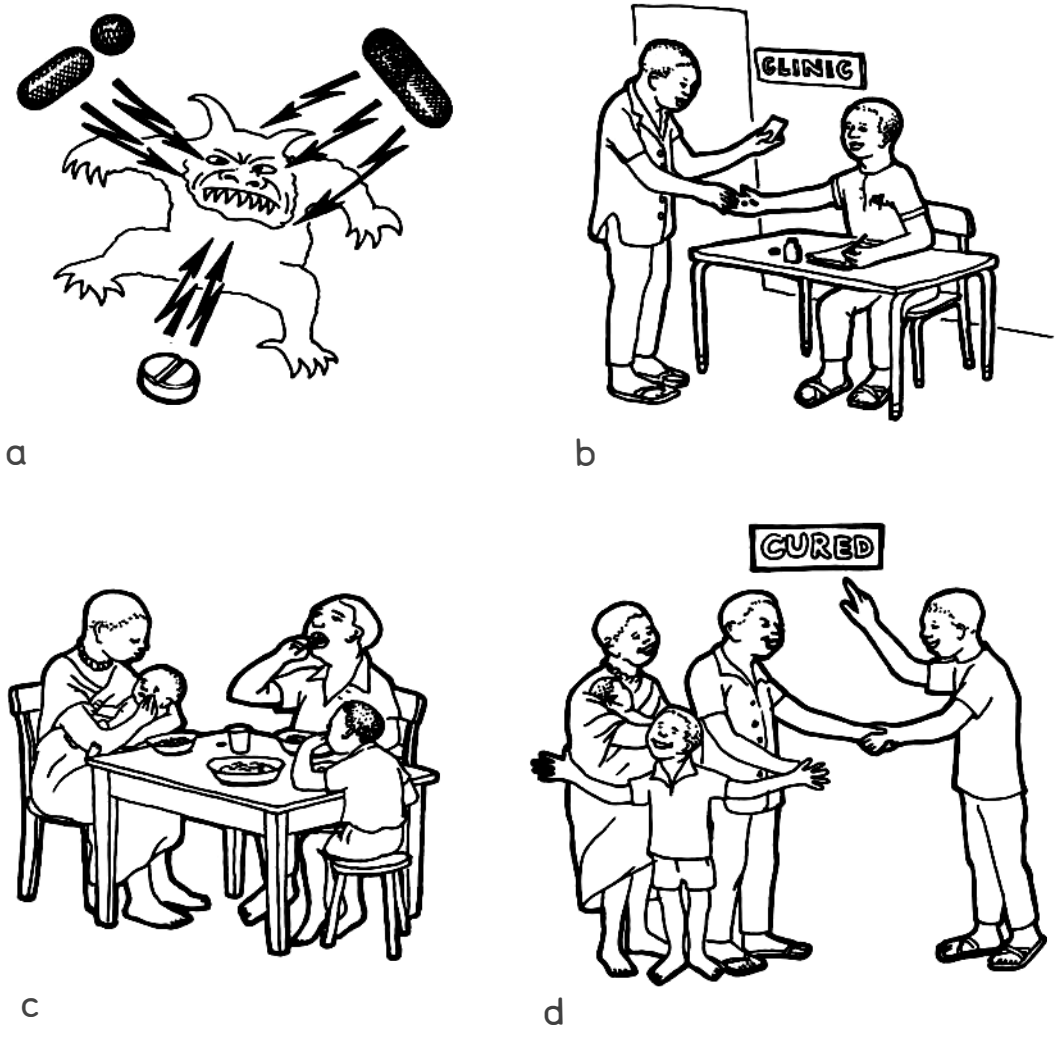

Figure 1. These four drawings are presented as a basis for local development or adaptation, to reinforce the eight messages in Tables 1 and 2. (a) Is intended as a 'devil' or 'monster' figure which may, in some cultures, convey the idea of a 'germ' causing leprosy (message 1) which can be killed by modern drugs (message 2). *Note*: three drugs are shown in this drawing (dapsone, clofazimine and rifampicin) and this refers to the treatment of *multi*bacillary leprosy. A modification showing only two drugs (dapsone and rifampicin) would be needed for *pauci*bacillarly leprosy. (b) Is related to the regular monthly clinic attendance for supervised medication, the supply of drugs for home treatment (message 3) and the reporting of any side-effects or early signs of reaction (message 8). (c) Emphasizes the importance of daily, unsupervised drug intake at home (message 4). (d) Illustrates the likelihood of cure if medication is taken regularly and for the prescribed period (messages 6 and 7).

careful clinical follow up and explanation to the patient of his status is preferable, even if more difficult.

With MB cases the situation might be quite the opposite—the clinical signs may completely resolve in 12–16 months and the patient then sees little reason to continue medication. In both cases, personal communication is the key to persuading the patient to respect the prescribed period of treatment. Another important but neglected aspect of the education of leprosy patients centres on the expectation of treatment with particular reference to deformity. Many patients, who had some deformity at the outset of treatment or who develop it during the course of treatment, may consider themselves as not cured, although they have 'completed' the treatment and became bacteriologically negative. The persistence of deformity despite regular treatment may be regarded by the patient, family and community as a failure of the drugs to cure the disease. It is thus essential that the expectations of chemotherapy, especially when deformity is established before MDT, are carefully explained to both patients and family.

The prevention of deformity and disability. The prevention of disability and deformity is an integral part of leprosy control; physical and social rehabilitation cannot be separated from the process of diagnosis, drug treatment and clinical management. Valuable teaching–learning materials on the prevention of disability in leprosy patients and the essential action which is needed to minimize disability are readily available.[28,29] Although written essentially for use by health staff, these documents are profusely illustrated with diagrams and line drawings and contain much information and advice which could be useful, almost without modification for patients. They also have great potential value for health education between staff and patients and as support material for the current strategy for the prevention of disability and the physical rehabilitation of leprosy patients.[30,31] The extent to which such information can be extended into the early recognition by the patient of symptoms which may herald the onset of adverse immunological reactions is beyond the scope of this communication, but calls for further study. If patient/staff ratios are favourable and educational levels high enough, there may well be scope for improvement in this area, as also the earlier recognition and treatment of 'silent' neuritis.[30]

Conclusion

We have recorded some ideas for the development of educational materials for patients with leprosy, whilst keeping in mind the pitfalls of any approach which is not locally orientated and tested out before being put into use. We are also conscious of the fact that good health education requires skills and ability and that the basic training of health workers in this important aspect of their work has been neglected. If our emphasis on attractive drug presentation, together with written and illustrated material, seems too strong, this is at least partly due to our concern about the increasing demands which are being made on the time of paramedical, nursing and community health workers. But the potential of MDT in the control of leprosy is now so great that it is no longer acceptable simply to diagnose this condition and send people away with handful of tablets and capsules. At the very least, each patient needs a few minutes of personal communication and it is beyond doubt that the effect of this will be reinforced by suitable, well thoughtout written and illustrated material. Many of us have textbooks, libraries, computerized information systems and journals. Peripheral health staff (whose actual needs are considerable) have very little, and patients even less. Perhaps we should put more money and effort into the identification and training of local people to develop educational material not only for leprosy but also for other diseases in relation to the WHO Essential Drugs Programme.

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SPECIAL ARTICLE

The cellular exudate–*Mycobacterium leprae* relationship and the critical reading of skin smears

MARIAN J RIDLEY
The Hospital for Tropical Diseases, London NW1 0PE

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Summary A careful reading of conventionally stained Ziehl–Neelsen skin smear preparations in leprosy provides a number of insights into the patient's situation, including his approximate position in the spectrum. This data serves as a cross-check on the primary results of the smear examination, and aids their interpretation for the purposes of diagnosis, assessment of the response to chemotherapy and the possible onset of relapse.

The use of the paucibacillary–multibacillary (PB–MB) classification of leprosy for the management of patients on multidrug therapy (MDT) relies heavily on the correct processing and interpretation of slit-skin smears. This, on the view of a recent WHO report,[1] is the weakest link in the whole control programme. Attention to technique will minimize, although it cannot eliminate, the problems inherent in this classification. For this reason the report recommends that all bacteriologically positive patients should be treated as if they were MB. But the determination of smear-positivity or smear-negativity still depends on technique. Error may arise at any stage of the taking, preparation, staining, counting and interpretation of smears, and some technical guidance has been well laid out by Leiker & McDougall[2] and Kim.[3]

In this paper we consider in detail some hitherto unreported data that can be gleaned from a thorough examination of a skin smear made under controlled laboratory conditions, taking account of cellular exudate as well as bacilli. Slit-skin smears are normally undertaken for the purpose of diagnosis, and to monitor the patient's response to treatment and the possible onset of relapse. The results also provide the definitive PB–MB classification (using the terms in their customary sense of scanty or many bacilli), and although they are not used directly in the Ridley–Jopling classification, the bacterial–cellular relationship as seen in smears, and the morphology and distribution of the bacilli, all provide some clues to the position in the spectrum. A proper understanding of the full data serves to cross-check the main results and gives a better insight into the patient's situation. It is necessary first to review the various modifications of acid-fast stain technique in relation to their effects on bacterial counts and morphology, and their appropriateness to skin smears as opposed to bacterial suspensions. We comment also on the measurement of leprosy bacilli.

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Methods

ACID-FAST STAINING

The smear is assumed to be well prepared, and composed of host tissue cells and bacilli spread evenly over an area about 5 mm in diameter on a clean glass slide. The modifications of technique that have been recommended have been numerous: fixation by mild heat or formalin vapour, the use of hot or cold staining solutions, the length of staining time, and differentiation by 1% acid–alcohol or 1–5% sulphuric acid, which may or may not be followed by a rinse in ethanol. The choice is determined partly by the composition of the smear: ideally, homogenates composed of a clean suspension of bacilli would not be treated in exactly the same way as an exudate containing proteinaceous, lipoidal or cellular elements that may interfere with the precise staining of bacilli.

Oxidation in 10% w/v periodic acid prior to staining in carbol-fuchsin[4] is not recommended for smears because of detachment of cells and bacilli. It has some advantages in histology but bacterial morphology is distorted.

Fixation by gentle heat on the under surface of the slide is the most effective, simple and quick to perform. Even under field conditions smears should be allowed to dry for a few seconds before fixation. Heat eliminates the precautions necessary in dealing with noxious formalin vapours, which may in any case cause detachment of bacilli from the slide or render staining more difficult. Phenol-gel protection before formalin fixation has some advantages,[5] but it is messy.

Stain temperature. The choice of hot or cold staining solutions usually depends on the facilities available, and on the relative importance attached to the numbers as opposed to the morphology of the bacilli. To ensure 100% detection of bacilli, and when diagnosis is the primary criterion, there is no better alternative to the use of hot solutions. Because the estimation of stain temperature is crude, it is better to err on the high side and aim for 60°C, the point at which steam begins to rise, but at this temperature, as well as during fixation by heat, there may well occur artifacts in bacterial morphology. Redistribution of cytoplasm may produce false solid staining, or globular condensation of cell wall and cytoplasm may produce a false granularity. In the latter situation bacilli may be lost through over-decolourization. At all stages excessive heat is to be avoided. The ideal temperature, satisfactory for both total count and bacterial morphology, is 45°C.[6] This is the point at which a change in surface tension leads to the formation of a metallic sheen on the surface of the stain.

Staining time is necessarily influenced by the method of fixation, the choice of hot or cold solutions, and the differentiating agent. But a standard time of 15 minutes is recommended, which is long enough to allow penetration of the dye when exudates are unavoidably thick or contaminated with protein or fat, and not so long that the stain precipitates.

Differentiation. Since *Mycobacterium leprae* is only weakly resistant to acid and very poorly resistant to alcohol, the use of either sulphuric acid or absolute ethanol is not to be recommended. Sulphuric acid has other disadvantages. It reacts with the peroxidase of macrophages and with haemoglobin to produce a brown or a prussian blue discolouration which impairs the recognition of bacilli, and attempts to reverse this reaction by washing are liable to cause detachment of some organisms. The differentiating agent of choice is 1% hydrochloric acid in 70% alcohol, the action of which is relatively mild. It is erroneous to think that prolonged staining will minimize the risk of losing the bacilli by overdifferentiation, rather the reverse. Overstaining of the cellular exudate impairs fine control of the differentiating process.

In general, in paucibacillary smears it is vital to stain every bacillus lest they fail to be detected. In multibacillary smears the loss of a few bacilli is less important, but in regressing patients, difficulties may be caused by the release of lipids from disrupted foam cells. The use of hot staining solutions overcomes this problem and aids penetration of the dye.

The following method is recommended as a routine procedure.

STAINING METHOD

1 Fix by gentle heat, using the flame of a spirit lamp or the pilot light of a bunsen burner on the under side of the slide until a ring of condensation forms around the flamed area (up to 6 sec).
2 Flood the slide with carbol-fuchsin to cover it completely, to allow for loss by evaporation. Heat gently until a metallic sheen appears on the surface of the stain, and stop just before steaming commences (45°C). Leave to stain for 15 min without further heat.
3 Wash the slide, directing the flow of water to one end and draining off at the other end. Tip off the water.
4 Differentiate in 1% acid–alcohol allowing the reagent to fall directly on the smear. When the excess dye flows from the smear, rinse in water. Repeat the differentiation and rinsing until a pink colouration in the thin parts of the smear, the end point, is obtained. A red colouration of any areas of thick exudate may be ignored. The time is variable.
5 Counterstain in 0·5% methylene blue in water.
6 Rinse in water.
7 Dry in air.
8 Examine under oil immersion.
The application of oil or mountant is irreversible, for attempts to remove it may cause the loss of large numbers of bacilli. Restaining entails exposure to oil and turpentine mixtures or prolonged immersion in xylene to detect all bacilli, but this distorts the cytology of the exudate. It is essential to stain correctly in the first instance.

MEASUREMENT OF BACILLI

Leprosy bacilli in fixed-stained smears were measured using a standard binocular microscope with × 100 oil immersion objective, and a × 10 eyepiece with graticule calibrated against a stage micrometer. The measurements obtained were further checked in a few instances by means of an image analyser (Mr C Souter, Histopathology Department, St Bartholomew's Hospital, London). The measurements obtained by the two methods were in close agreement with one another. It is of interest that the measurements of length are appreciably lower than those commonly quoted for *M. leprae*: in the slit-skin smears the length did not exceed 5 μm, although in the nude mouse longer forms of up to 7 μm might be seen. Very long forms may be the result not only of rapid unchecked growth but of an abnormality of internal filaments. The width of bacilli was too small for accurate measurement, but in LL it was of the order of 0·5 μm, in BT and BB about 0·2 μm.

In practice, the exact measurement of leprosy bacilli is not important for the examination of skin smears, and the measurements given are intended mainly as a guide to indicate the relative lengths of organisms observed in different types of case. The differences in length are easily perceptible without measurement. The figures are at a magnification that is close to that of the visual image under the microscope.

Cellular exudate

The cellular exudate in a skin smear usually includes keratinocytes and epithelial cells derived from the epidermis, in addition to the inflammatory cells, if there is a lesion, comprised of macrophages, monocytes, lymphocytes and perhaps polymorphonuclear neutrophils. When cells are disrupted in preparing the smear only the nuclei may be visible, but on searching around whole cells can be seen.

Epidermal cells. Keratinocytes and epithelial cells are recognized by their polygonal shape, rounded nuclei and copious pale cytoplasm (Figure 1). These cells are often clumped together and resemble endothelial cells, though the latter are much smaller. Keratin and eleidin granules are acid-fast. Rarely melanocytes with brown melanin pigment can be seen. These are not to be confused with granular bacilli in decrepit macrophages.

Table 1. To show a summary of the reading of smears

Classification	Acid-fast bacilli			Cellular exudate			Expected outcome after effective therapy
	Numbers	Morphology	Distribution	Macrophages	Lymphs	Pmns	
Untreated TT–BT	0 to 3+	Slender, solid 2 μm × <0·5 μm	Separate, ingested AFB are granular	Large, elongated nucleus, intact uniformly dense	Many or moderate	None	1 No AFB 2 Persisting cellular exudate
BB	0 to 3+ varies at each site	Slender, solid or fragmented. 2 μm × <0·5 μm	Separate, close proximity, often intracellular	Medium size, dark oval nucleus, intact	Moderate	None	1 No AFB, but increased lymphs, may suggest reversal reaction 2 Granular AFB with few lymphs may stabilize at BB 3 Previously negative sites may be positive
BT–BB–BL (downgrading)	3+ at every site	Majority slender few long forms, solid or fragmented 2 μm × <0·5 μm 3·5 μm × 0·5 μm	Single or small clumps, AFB arranged in parallel	As for BB, also some rounded nuclei of disrupted cells, intracellular solid AFB	Few	None	1 Granular AFB 2 Fall in BI As for BB
Smear negative Paucibacillary (PB, WHO) Idt, TT, BT	0			Large, intact, few monocytes	Few, none, many or moderate	None	1 Temporary rise in lymphs
BL	3+ to 4+	Slender, solid fragmented and granular, most are 2 μm long	Small clumps, AFB arranged in parallel or free, no globi	Medium size, round nucleus, dense, many intact, no foam cells	Numerous	None	1 Granular AFB spread over slide. No globi 2 Rapid fall in BI, may suggest reversal reaction 3 No foam cells
BL (continued)	4+ to 5+	Mixed slender and long thick AFB, solid fragmented, granular 1–2 μm or 3 μm rarely 4 μm long	No globi, small clumps of AFB in parallel, many free over slide	Medium size, round nucleus, pale nucleus and cytoplasm, often intracellular AFB, disrupted	Few	None	1 Fall in BI, granular AFB in small clumps, but more free, spread over slide indicates stability in BL and slow clearance 2 As above for BL

Table 1. (*continued*)

Classification	Acid-fast bacilli			Cellular exudate			Expected outcome after effective therapy
	Numbers	Morphology	Distribution	Macrophages	Lymphs	Pmns	
BL–LL (downgrading)	4+ to 5+ wide variation between sites	Mixed slender and long thick AFB, most solid 1–4 μm	Small or medium clumps, no globi	As for BL, also pale poorly formed foam cells, disrupted cells, round nuclei, monocytes	Few	None	1 Granular AFB with rise in lymphs may suggest reversal reaction. As for BL. 2 Poorly formed foam cells
LL	4+ to 6+	Solid or fragmented, majority 3 μm × 0·5 μm. But fragmented and granular AFB may predominate most being 3 μm. Or, mixed short and long solids 1–5 μm × 0·5 μm	Globi, round clumps and free AFB spread over slide	Very large pale vacuolated or foam cells, pale round nucleus, disrupted cells, free nuclei, fatty exudate, monocytes	None	None	1 Granular AFB 2 Slow fall in BI 3 Globi conspicuous 4 Intact foam cells at late end stage 5 Usually no lymphs except before reversal reaction and rapid fall in BI
ENL	2+ to 5+	Granular or debris	Globi with degraded AFB	Large foam cells often empty with shrivelled dark nuclei, fatty	None	Many	1 After subsidence of ENL there may be lymphs though no Pmns
LL (exacerbation and reaction	6+	Solid 3–5 μm × 0·5 μm	Globi, and clumps of AFB in parallel	As for LL, also large intact cells with solid AFB	None	Many	As for LL
LL (relapse in early stage)	0 to 6+ variable between sites	Few sites affected with solid AFB, most are 2 μm long, range = 1–5 μm × 0·5 μm other AFB may be granular	Globi and clumps of solid AFB in parallel at affected sites	Large pale, often intact with solid AFB, round nucleus, foam cells, and monocytes	None	None	1 Granular AFB As for LL 2 Not usually followed by reversal reaction 3 No lymphs
LL (resistance)	3+ to 6+ all sites similar	Solid at most sites, little variation in length, 3·5 μm–4–5 μm × 0·5 μm	Globi and clumps of solid AFB in parallel at most sites	Often intact, with pale round nucleus, ingested AFB, foam cells, monocytes	None	None	As for LL 1 No lymphs

AFB numbers, bacterial index;
lymphs, lymphocytes;
Pmns, polymorphonuclear cells;
LL relapse refers to relapse from causes other than primary drug resistance;
Morphology measurement is that of the majority of AFB.

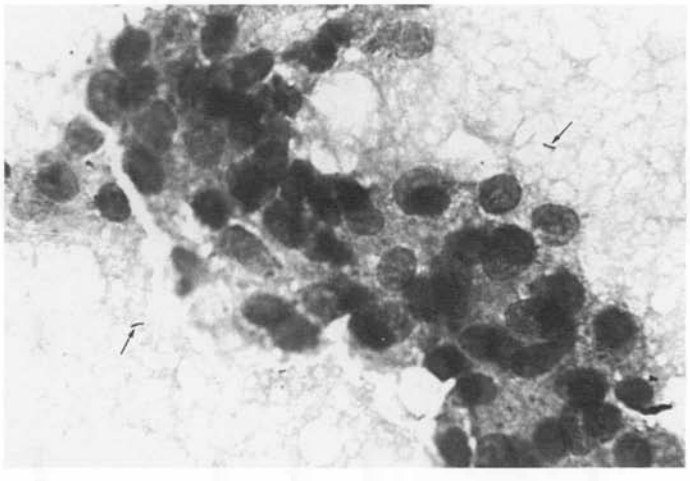

Figure 1. BB. Epidermal cells, and two solid-staining AFB 2 μm long (↑). Acid-fast stain × 1200.

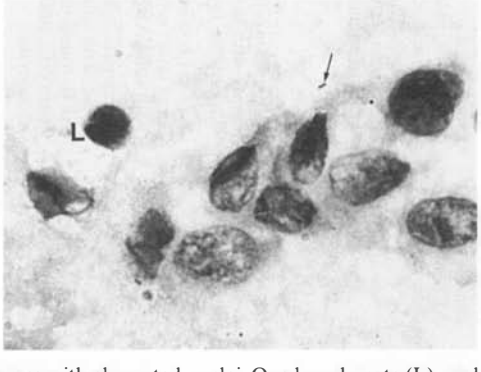

Figure 2. BT. Intact macrophages with elongated nuclei. One lymphocyte (L), and one ingested granular AFB 2 μm long (↑). Acid-fast stain × 1200.

Inflammatory cells. More important are the inflammatory cells in their various forms. Cellular identification is based on visual experience as in a blood film. Experience can be gained by studying the appearances of macrophages with ingested bacilli and similar cells without bacilli taken from patients with different forms of leprosy. Initially special stains like Giemsa, or better still immunohistological methods, help in identifying the inflammatory cells whose nature provides a useful check on diagnosis and the position in the spectrum (summarized in Table 1), which is of clinical and prognostic value.

Macrophages. In TT, BT and BB, the macrophages are large, fleshy, uniformly blue-stained cells with prominent elongated nuclei (Figure 2). Treatment may diminish their numbers but, especially when bacilli are present in the untreated smear, macrophages may persist after the bacilli have disappeared. In BL the macrophages have a dark rounded nucleus and dense blue-stained cytoplasm (Figure 3), and these are the cells that are associated with clumps of bacilli. In other cells poorly distinguishable phagosomes may be seen. After treatment only poorly delineated foam cells

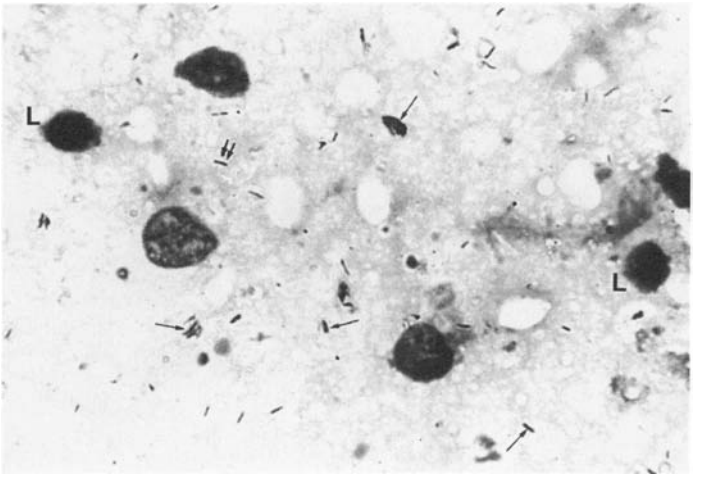

Figure 3. BL. Dark rounded macrophage nuclei and two lymphocytes (L). There are many solid-staining AFB 2–3 μm long (↑↑), and some in clumps arranged in parallel (↑). Note also one fragmented bacillus (top left), but no granular organisms. Acid-fast stain × 1200.

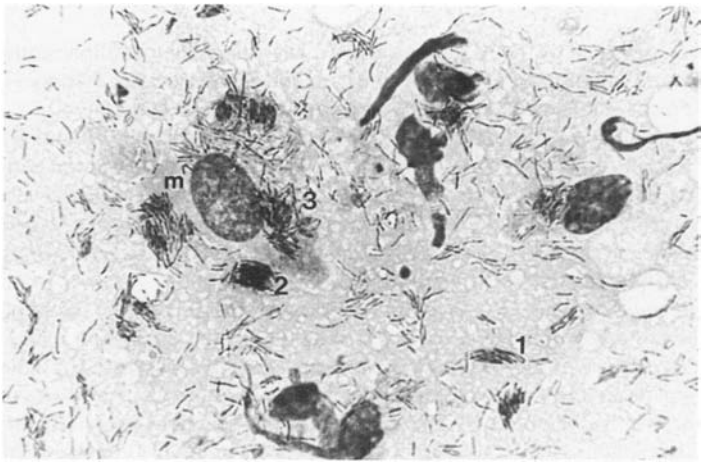

Figure 4. LL. Large vacuolated macrophages with pale round nuclei and ingested bacilli (M). There are several free nuclei. AFB are mostly 3·5–4 μm long with a range of 2–5 μm. Globi contain about 25 (1), 50 (2) or 100 organisms (3). Acid-fast stain × 1200.

may be present among larger numbers of empty, darkly stained macrophages. In LL the macrophages are pale, vacuolated, with characteristically large rounded nuclei, and sometimes contain ingested bacilli (Figure 4); often these cells are disrupted in the preparation of the smear. Bacilli, globi and nuclei are then dispersed over the slide. Foam cells are not inconsistent with active bacterial multiplication, but they are more prominent in the presence of non-solid organisms. Following treatment foam cells, sometimes with dark shrivelled nuclei, are the commonest cell type found in the smears of LL patients (Figure 5). In long treated LL patients, foam cells are not so fragile and remain intact in the smear.

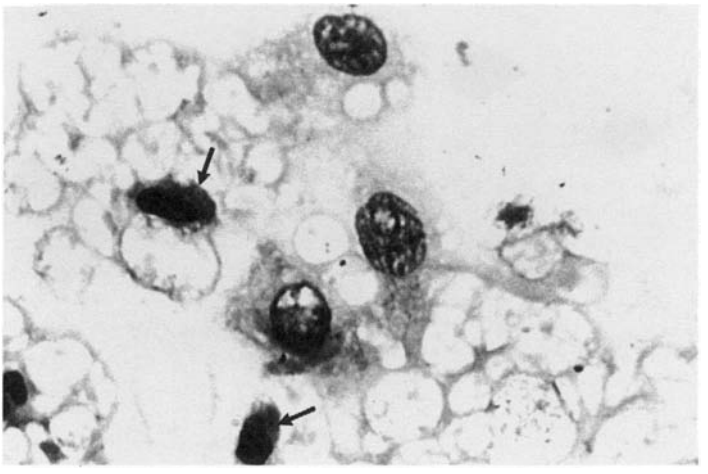

Figure 5. LL after 10 years treatment. Intact foam cells, two with dark shrivelled nuclei (↑), not to be confused with lymphocytes. Acid-fast stain × 1200.

Monocytes are identified by their kidney-shaped nuclei which almost fill the entire cell. They are plentiful in active untreated leprosy especially in LL and in drug resistance. Monocytes are also seen in relapsing lesions, together with a pleomorphic bacterial morphology.

Lymphocytes are moderately numerous in smears from tuberculoid TT and BT patients, and they may be very plentiful in BL (Figures 2 and 3), but they are not a feature of active or quiescent LL. Reacting LL patients who upgrade towards BT after treatment may show few lymphocytes, as do patients recovering from ENL after the disappearance of polymorphs. Lymphocytes never outnumber macrophages in any of the leprosy groups. When blood is present lymphocytes may be more conspicuous, but they are to be ignored.

Neutrophil polymorphs, seen in association with signs of highly active bacterial proliferation, with many solid-staining bacilli spread over the slide due to the disruption of macrophages, are usually a sign of an exacerbation reaction (or a reactional area in a histoid lesion); they are seldom if ever present in hyperactivity except as a result of such a reaction. In less active and more borderline patients, polymorphs may be present in the smears in type I reactions especially during upgrading from BL to BT. In many patients this occurs after commencing MDT. In regressing lepromatous patients with granular bacilli, many polymorphs signify ENL. Polymorphs present in smears from the ear lobes but not in those from other sites are of no significance.

Bacterial morphology

In acid-fast stained preparations *M. leprae* is a rod-shaped bacillus with parallel sides and rounded ends, and of variable size and characteristic mode of degeneration.[2] The disintegration of most bacilli, at least in LL, first affects the cytoplasm of the organism, and the fragmented and granular appearances are due to the irregular staining of cytoplasm within mainly intact cell walls.[7] This degenerative process is often related in part to the effects of chemotherapy, but it is also related to some extent to the patient's position in the spectrum. Bacterial morphology in the reading of smears is summarized in Table 1.

BEFORE TREATMENT

Bacilli, when detected in untreated patients in the TT to BB region of the spectrum, are typically solid-staining, and situated either singly or in a group of 2 or 3 in close proximity but separate. They are notably more slender, about 0·2 μm, than the organisms in LL and somewhat shorter, about 2 μm (Figure 1). Only rarely are granular bacilli detected, usually in macrophages and in patients who are immunologically unstable and liable to react, and especially in BB patients with a low BI.

In smears of BL and LL patients, solid-staining rods are usually conspicuous among a great variety of forms, although it is not uncommon to find a preponderance of fragmented and granular forms even before treatment.[8] In the latter case, smears from the ear lobes will almost certainly show solid bacilli, and numbers may be lower than at other sites.

BL and LL. The solid-staining bacilli of BL patients with a low BI are about 2 μm long, and characteristically slender like those of BB rather than LL patients (Figure 3). When large numbers are present some bacilli may be longer (3–4 μm) and thicker, like those in LL patients. In LL the bacilli are normally about 3 μm long and 0·5 μm wide, but the length may range from 1 to 5 μm (Figure 4). The longest bacilli are seen under conditions of unchecked growth. In BL the bacilli are often arranged in parallel in clumps, but the clumps are never large (Figure 3). Strictly speaking these clumps are not globi, which are more conspicuous, large and rounded in smears from LL patients, in which they tend to be spread over the slide. Bacterial degeneration is the same in BL as in LL. The distinction between these two groups is further aided by the nature of the cellular exudate (Table 1).

AFTER TREATMENT

In tuberculoid and borderline leprosy (TT to BB) bacilli should disappear relatively quickly, due to simultaneous degradation of cell wall and cytoplasm. Degenerate bacilli are fragmented rather than granular. Residual acid-fast debris is quickly cleared by immunocompetent cells.

In BL and LL fragmented and granular forms are predominant. In BL, if the initial BI was low it may quickly fall with treatment but if it was initially high the fall will often be slower. Globi are never found in BL, and the separate bacilli are spread over the slide. This contrasts with LL, in which most bacilli are found in globi. The elimination of organisms here proceeds very slowly, and even after years of monotherapy on DDS it is possible to find a few granular bacilli that still attain the full length of 4–5 μm. Under these conditions the finding of even a single such bacillus among highly granular organisms is a firm indication of the LL group. After MDT bacilli become more shrunken and darkly stained. MDT may be more damaging to the cell wall than DDS monotherapy.

In LL, bacilli with the same morphological characteristics (e.g. long solid forms, or fragmented and granular) tend to be concentrated around the disrupted macrophage from which they were released, so that the distribution of bacilli is not entirely uniform over the smear, at least as far as the morphological characteristics are concerned.

The number of lymphocytes present in smears with granular bacilli complement the fall in the BI as a monitor of the patient's response to treatment. Few lymphocytes, granular bacilli and a slow fall in the BI are the common findings in immunologically stable BL patients. Large numbers of lymphocytes and a rapidly falling BI are suggestive of upgrading.

SIGNIFICANCE OF BACTERIAL FORMS

Solid-stained bacilli are equated with viability. Nevertheless, recently dead bacilli which have not yet undergone morphological change will also appear solid, as will dormant but moribund bacilli. The circumstances under which such organisms might regain activity are unknown. In activity associated with drug resistance solid-staining bacilli are likely to be found at multiple sites, whereas

in relapse due to the recrudescence of 'persister' or dormant organisms fewer sites are likely to be involved.

Short solid bacilli, 1 μm $\times$ 0·5 μm, are common in new or relapsing LL lesions when bacterial proliferation is marked. Some of them are too short to qualify as solid under the definition of the solid ratio,[9,10] which is more strictly defined than the morphological index, yet they are not to be confused with non-solid forms, from which they are morphologically distinct. If all the bacilli present are short solids they are likely to be viable, and the same is true of course of short solids amongst long solid bacilli. Short solids amongst fragmented and granular organisms usually show, with careful scrutiny, some irregularity of staining, especially at one pole, so that they are most probably fragmented and non-viable. Short solid forms are frequently found in smears from the fingers, where they often appear to be viable but dormant.[11] They may be seen in the early stage of relapse.

Club-forms are bacilli characterized by metachromatic swellings that may be situated at any position within the rod. The bacillus is usually solid-staining, or the club may be isolated or in possession of a short acid-fast tail. The exact significance of club-forms is not clear. Our recent experience shows that in some patients on sulphone monotherapy they may be associated with bacterial proliferation; in other such patients, and those on MDT, the association is with past activity, recognizable bacilli being no longer present. This might suggest that club-forms are slow to decay, but that their future evolution is impossible to determine. It is suggested that until more evidence is available these organisms should be discounted from a morphological assessment.

The indices

BACTERIAL INDEX

The logarithmic index of Ridley is widely used for the enumeration of bacilli,[2,12] and because of the 10-fold differential between the steps of the index, agreement between observers should be good, given standardization of technique for the staining and preparation of the smear. Large discrepancies between observers, such as BIs of 1 and 5,[13] are due to serious technical shortcomings. This should not happen if due attention is paid to the cellular exudate as outlined above and in Table 1. An acceptable error would be one division on the log scale. It is possible for bacilli to be selectively concentrated at the periphery of smears of homogenates although there is no evidence that this occurs in skin smears.

The mean BI of all sites is the guide for monitoring the response to treatment, but in view of the variation between sites the individual indices must also be reported. The reason for differences in the rate of clearance of bacilli between different patients within the LL group is not known.

It is usual for patients in the TT–BT region of the spectrum to show no bacilli, or an index of up to 3+ at a few sites. A finding of 3+ at all sites including the ear lobes would suggest downgrading, perhaps associated with a larger bacterial deposit in peripheral nerve. In downgrading from BB to leproma the index is usually higher than 3+ at some sites.

On occasion one might find, say, 50 bacilli in a clump when there were no other organisms in 100 fields. The BI would be 2+, but the unusual distribution of the bacilli should be reported. If the organisms included solid-staining forms, more bacilli might be found in subsequent smears at the same site; and even in the first month of treatment the index might rise to, say, 3+ before falling to zero. This situation may be seen in relapse. If the bacilli were granular subsequent smears would probably be negative. The estimation of numbers of bacilli present in a clump or globus is somewhat arbitrary, being based on the size of the clump. A small clump is estimated to contain about 25 bacilli, a medium sized clump about 50 and a large one at least 100 (Figure 4).

MORPHOLOGICAL INDEX

The MI is the index of morphology in most general use,[2,12] its object being to indicate the percentage of viable forms of bacilli. However, it produces problems of standardization and reproducibility that are difficult to eliminate,[14] the chief difficulty being the determination of the bacilli to be considered as solid-staining.[2] When the total number of bacilli in the smear is less than 100 it is desirable to record the actual number of solid-staining or other organisms present.

SOLID-FRAGMENTED-GRANULAR (SFG) INDEX

The approximate ratio of each class of bacillus, solid, fragmented and granular, is estimated by assigning a value of 2 to the predominant class, 1 to any other class or classes present in significant numbers, and 0 to any class represented by very few or no bacilli. Permutations ranging from 2–0–0 (all solid) to 0–0–2 (all granular) correspond to SFG indices of 10 to 0. The SFG for each field of view is determined, and the mean score for several fields is taken.[2] The SFG ratio takes account of all bacilli (except those in globi which cannot be seen). It does not attempt to indicate the actual percentage of solid-staining organisms, but the results are usually more reproducible than those of the MI. An SFG of 3 (reading 1–1–2) is the lowest score to signify the presence of solid forms. LL patients on effective therapy would show readings of 0–1–2 (SFG = 1) or 0–2–2 (SFG = 2). An SFG of 3 after several years treatment could indicate failure of control or relapse, but not necessarily. The solid-staining organisms whose presence was indicated might be dormant or moribund and only potentially capable of regeneration.

MULTIPLE SITES

We support the recommendations of Leiker and McDougall[2] for the selection of sites for smears, which should number at least 4 and preferably 6.

Variation in the BI from multiple sites may be considerable in some untreated BL patients, but not usually in LL even after effective treatment. Large discrepancies in the BI usually arise as a result of relapse and enhanced activity at one or more sites, though not at others, and there are corresponding differences in bacterial morphology. Smaller variations in the indices can possibly be due to the position from which the smear was taken within the lesion. Smears from the active edge of the lesion are most likely to show solid-staining bacilli in LL patients; in TT, BT and BB they are the most likely to yield bacilli and large numbers of macrophages and lymphocytes. These cells are visible also in smear negative cases.

The ear lobes in tuberculoid patients may be negative, but they are positive in some BB cases in which bacilli are numerous, especially in those downgrading to BL. The ear is the first site to show large numbers of bacilli, and the first to be cleared of them in BL. The ear lobes remain positive for many years after effective therapy in LL.[15,16] In drug resistance solid bacilli quickly reappear at this site, more so than in relapse from other causes. Good vasculature and circulation no doubt explain the early appearance of bacilli in MB patients, and their clearance due to the circulation of drugs and immunocompetent cells in BL. Good circulation could also explain the lack of ear lobe involvement in tuberculoid patients, bearing in mind the high susceptibility of *M. leprae* to serous and other immunoreactive substances.

Nasal smears (or nose blows) are usually positive in LL patients, and to a less extent in BL or BB downgrading to BL, but not in BB or BT. The nasal site is quickly cleared following treatment. The morphology of the nasal bacilli is not a reliable guide to the general bacteriological status of the patient.

The fingers are to some extent a preferential site for bacilli on account of their low temperature and the superficial situation of the nerve supply.[11]

Acknowledgments

I am very grateful to Dr M Waters and Dr A Bryceson of the Hospital for Tropical Diseases for providing me with the material for this study over many years. Dr D Ridley has given critical judgement and close collaboration in all aspects of the work, for which I am thankful. The work was supported by the Special Trustees of University College Hospital.

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Letters to the Editor

TUBERCULOID (TT) LEPROSY; LOCALIZATION ON A TATTOO

Sir,

The precise mode of transmission of leprosy is still unknown. However, the skin, nasal mucosa and gastrointestinal tract have been favoured as the possible portal/s of entry of *Mycobacterium leprae*.[1] Prolonged and intimate skin-to-skin contact with infected individuals is universally accepted. Alternately the bacilli might enter the body through needle inoculation,[2] for example, tattooing.[3-6] Tattooing is common in Asian and African countries where leprosy is endemic. Leprosy occurring at a tattoo or scar, though infrequent, may be of epidemiological interest, concerning *M. leprae's* preference for settling in tattoos and scars. This is illustrated in the following recount:

Case report

V, a 35-year-old woman, was tattooed about 20 years ago. A year later she noticed a small erythematous patch on and around the tattoo mark over the back of her right wrist. The patch was asymptomatic for almost 15 years, after which she noticed an increase in its size which was primarily confined to the tattoo mark. She also experienced numbness and tingling in the right forearm and conspicuous impairment of sensation in the patch. Simultaneously she noticed a similar eruption over the index finger of the right hand. Here too, she had numbness and tingling along with impaired sensation.

On examination an erythematous and glazed plaque of 4 cm × 3 cm was seen. It was well defined, had regular borders, no atrophy was noticed and infiltration was marked at the periphery (Figure 1). Another plaque of similar morphology was seen on the dorsum of the index finger of the same hand. Sensations of temperature, touch and pain were impaired over the lesions and the right ulnar

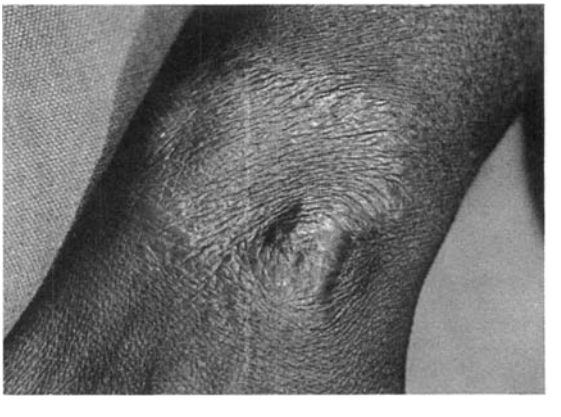

Figure 1. A well-defined plaque with regular outline. Centre is marked by tattoo.

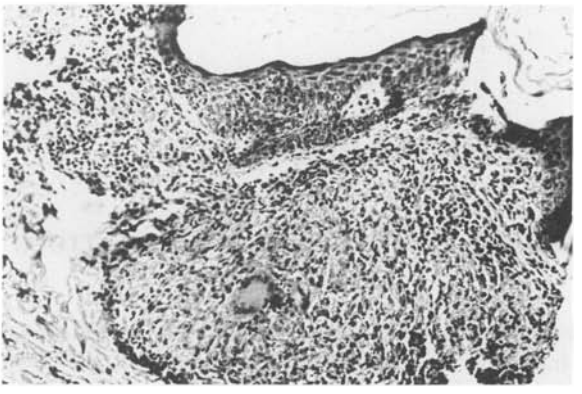

Figure 2. A well-formed granuloma comprising lymphocytes, epithelioid cells and giant cells located beneath the epidermis with the infiltration of cells in the epidermis (H&E × 100).

nerve was found to be thickened and tender. Haematoxylin and eosin stained sections revealed a granuloma formed by a large number of lymphocytes, epithelioid cells and giant cells. The granuloma was well formed and located just below the epidermis. Some of the cells were seen infiltrating the epidermis (exocytosis) (Figure 2). The nerve in the granuloma could not be identified and no acid-fast bacilli could be demonstrated in tissue sections and slit-skin smears. Lepromin (Mitsuda) was strongly positive. The diagnosis of tuberculoid tuberculoid (TT) was thus confirmed and the patient has been prescribed multidrug therapy comprising of 600 mg rifampicin once a month and 100 mg of diaminodiphenyl sulphone daily.

V N SEHGAL
& JOGINDER

Department of Dermatology and Venereology
Maulana Azad Medical College
New Delhi (India)

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LEPROSY SCORE CHART TO ASSIST CLASSIFICATION

Sir,

In Papua New Guinea (PNG) we have for some years used a clinical score sheet to assist in the diagnosis of tuberculosis in children.[1] The score sheet is easy to fill in and well used by a wide range of health workers, from medical officers in hospitals to rural health workers in health centres

throughout the country. Doubts have been raised[2,3] about the quality of leprosy smears and leprosy microscopy services in many countries and we have also experienced similar difficulties in our own Multiple Drug Therapy (MDT) programme in PNG.[4] Bearing in mind the above, we have developed a Leprosy Score Chart to assist in the classification of cases in our MDT programme, and to help minimize errors in classification. We have developed the following Leprosy Score Chart based on our TB score chart:

Circle box and write the score at the end of each line

Clinical finding	1	2	3	Score
Number of patches	0–5	6–20	20+	
Sensation	Absent	Reduced	Normal	
Edge of lesions	Obvious	Satellites	Unclear	
Loss of pigment	Yes	Some	Very little	
Surface raised	Edge only	Centre	Nodules	
Enlarged nerves	Less than 2		2 or more	
Muscle tests failed	Less than 2		2 or more	
Central healing	Yes	None		
			Total	

Patients with a score of 12 or more are classified as multibacillary (MB). All others are classified as paucibacillary (PB) unless smear result suggests MB, i.e. BI 2 or more. BILATERAL SYMMETRICAL EAR LOBE INFILTRATION IS AUTOMATICALLY MB.

We would appreciate comments from readers to assist us in further development of this concept. We are certain that there must be some clinical criteria available in a simple format to assist all health workers in classification of patients for MDT. We feel that we cannot afford to rely totally on laboratory services, which are often inaccessible or unreliable in developing countries.

J E NASH, B J HUDSON
& T PYAKALYIA

The Leprosy Mission
P.O. Box 447
Madang
Papua New Guinea

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REPLY: THE ROLE OF NERVE BIOPSIES IN THE DIAGNOSIS AND MANAGEMENT OF LEPROSY

Sir,

The paper by Dr R Nilsen *et al.* (*Lepr Rev*, 1989; **60:** 28–32) provides further evidence to substantiate the differences in bacterial load and histological response between nerve and skin lesions and the risk of relapse commencing in nerve. It is an important fact that skin lesions may not be representative of nerves, especially in paucibacillary patients. However, the authors go on to state, incorrectly, that their findings are at variance with our previous conclusion[1] that skin rather than nerve demonstrates the general tissue response to *Mycobacterium leprae*. Since they may not be alone in this view we should like to try to elucidate the position.

It is now 14 years since Pearson & Ross[2] and later Stoner[3] interpreted the predilection of *M. leprae* for nerve by reference to the immunological protection afforded to the bacillus by the Schwann cell basement membrane, the multilayering of the perineurium, the absence of lymphocyte recirculation within the fascicles and the blood–nerve barrier. This hypothesis, as far as we know, has not been contested and our own results[1,4] are strong evidence in support. Yet more often than not, attempts are made to interpret neural leprosy as the consequence of some uniqueness in the neural–bacillary relationship. It really does not make sense to say that 'an immunologically non-responsive form of leprosy can reside in nerve lesions and a responsive form in skin lesions'. A leprosy infection, like the patient, is one, even though the bacterial load and the response to it vary between sites some of which are immunologically protected and others exposed. For two reasons the general tissue response is the one seen in unprotected (or relatively unprotected) sites such as skin: 1, the majority of sites in the body are unprotected, the minority protected; and 2, it is only after exposure of antigen that the immunological response to it can be evaluated. Similarly the general bacterial level is the one which has developed at open sites, not behind immunological barriers. This in no way diminishes the importance of the vital events that do take place behind the barriers such as nerve. But to suggest that the classification of leprosy ought to be based on the status of nerve rather than skin lesions is not right. The events in a protected site are variable and unpredictable, and the findings in a nerve biopsy are valid only for that particular site.

The widely held view that there is an affinity between Schwann cell and leprosy bacillus is of course not incorrect, but the uniqueness of the affinity pertains to the bacillus, not the Schwann cell. There are a number of other human tissues besides nerve in which, perhaps uniquely, *M. leprae* is remarkably well tolerated. There are also a number of other protected sites, though none in which the bacilli multiply so freely as in nerve. In the context of leprosy, peripheral nerve is not unique, but it is pre-eminent among protected sites as the one with the best growth potential.[5]

D S RIDLEY

The Bland–Sutton Institute of Pathology
University College Middlesex School of Medicine
Riding House Street, London W1P 7PN

MARIAN J RIDLEY

The Hospital for Tropical Diseases
St Pancras Way, London NW1 0PE

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Book Reviews

The biology of the mycobacteria Volume 3. Clinical aspects of mycobacterial disease. **Editors: C Ratledge, J Stanford, J M Grange**

This is the third part of a four volume publication. This volume is devoted to the diseases that mycobacteria cause in man, whereas the first and second volumes dealt with mycobacterial physiology, identification and classification, and immunological and environmental aspects respectively. The arrival of a volume on the clinical aspects of mycobacterial disease is appropriate since this is, after all, the principal reason for the great and increasing interest in the mycobacteria, and is particularly timely since the current situation is such that in parts of the world where tuberculosis is declining, the relative frequency of clinical infections caused by other mycobacteria is rising—this is, therefore, the subject of much investigation and research. Of great importance, also, are the complications that may arise as a result of concomitant HIV infection, and the possible consequences of vaccination, for example with BCG, of individuals who are immunocompromised.

The book is a multiauthor publication which brings together a wealth of information on the study of mycobacterial disease. The authors provide extensive coverage of their particular area and a comprehensive list of references. In addition, it is illustrated throughout with a series of excellent photographs and diagrams.

The book commences with a thorough overview of the historical and current aspects of mycobacterial infection. The authors discuss man's ancient struggle to understand and conquer tuberculosis and leprosy, the extent of these problems in the world today, and how the study of the signs, symptoms and patterns of behaviour of these diseases, can be used to design and monitor control measures and to develop and deploy effective therapy. There is also an evaluation of the biochemical knowledge of mycobacterial metabolism and a review of the histopathology and morphology of many mycobacterial infections.

There are extensive reviews of both pulmonary and extrapulmonary tuberculosis including epidemiology, pathogenesis, diagnosis, prognosis and control, as well as a further chapter on the chemotherapy of tuberculosis. The section on leprosy gives detailed coverage of both the clinical aspects of this debilitating disease and the reactions which may occur. Histopathology, immunology and precipitating factors are discussed in addition to the possible mechanisms of the reactional state and the principles of management.

Many of the dozens of so-called 'environmental' mycobacteria such as *M. ulcerans*, *M. marinum*, *M. chelonei*, *M. fortuitum*, *M. avium-intracellulare*, *M. kansasii*, *M. xenopi* and *M. scrofulaceum* to name but a few are covered in two chapters on mycobacterial infections of the skin and of the deep tissues of man. Although uncommon relative to tuberculosis and leprosy, these organisms may cause devastating and most unpleasant disease in individual patients.

The final chapter looks to the future and at types of immunotherapy which may be employed to manipulate the immune response. Immunotherapy is currently seen as a potentially highly effective adjunct to conventional chemotherapeutic measures and aims to enhance the immune competence of the individual to enable the elimination of persistent bacilli following chemotherapy and the recognition of key bacillary antigens by the patient.

One of the main aims of the editors of this volume is to show that there is a continuous spectrum of knowledge from the fundamentals of basic research to the organization of a programme of eradication of mycobacterial disease. Thus, this book is likely to be of great benefit to both basic scientists and medical practitioners wishing to bridge the gap between the latest research data and the applicability of such information to clinical problems in the field.

A fourth volume in this series on the biology of mycobacteria is now being contemplated to deal with major recent advances in molecular biology, immunology and immunogenetics and the effect of the advent of the acquired immune deficiency syndrome (AIDS) on the epidemiology and control of the mycobacterioses.

Sue Sibley

Published by Academic Press, London, 1989.

***Leprosy: Basic information and management, 2nd edition.* A C McDougall and S J Yawalkar**

Leprosy is still a major health problem in many developing countries, with a WHO estimate of 10–12 million victims worldwide. This disease causes particularly deep suffering, as in addition to physical disfigurements and disabilities, patients have to bear the social stigma of their illness. However, the availability of multiple drug therapy (MDT) in recent years has enabled great progress to be made in the control of leprosy, contributing to a positive prognosis for many of these patients and reducing spread of the disease by lowering the infectivity of sufferers.

This booklet is the second edition of a publication providing a valuable source of basic and accurate information about leprosy and its management, which the authors hope will be of practical value in bringing successful therapy to all of those whom it would benefit. It is intended mainly for nonmedical readers such as community leaders, social workers, teachers, and patients and their families. Medical terminology is, therefore, kept to a minimum, or where used is fully explained, but this does not mean that it would not be useful background reading for paramedical workers in the field, or as an introduction to leprosy for medical students.

The booklet commences with an overview of the historical and global aspects of leprosy, and goes on to describe the causative organism, *Mycobacterium leprae*, and the possible routes of transmission. There are useful indications for health workers of the diverse clinical signs and symptoms over the broad spectrum of the disease to assist in diagnosis and differentiate from the many other skin disorders which may be prevalent in the area. Recommended regimens of treatment with dapsone, rifampicin and clofazimine, the principle antileprosy drugs of the MDT programme, are given, as well as advice for the management of complications such as 'reactions,' ulceration, paralysis, blindness, and chapped skin due to loss of sweating. Further sections describe the benefits of reconstructive surgery and 'grip-aids' to facilitate the use of tools and appliances by patients with crippled hands, and warn of the possible consequences of the advent of the AIDS virus in many of the countries where leprosy is endemic.

Health education, such as the need for complete compliance with treatment and early detection of infection before irreversible damage to nerves has occurred, is stressed throughout.

This publication is to be made available in Spanish and French in addition to English and should, therefore, attract a wide readership amongst people who are associated with leprosy in one way or another.

Sue Sibley

Published by Ciba-Geigy Ltd, Basle 1989.

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Leprosy Control and Field Work

Disabled Village Children. David Werner. Hesperian Foundation

'*Disabled Village Children* is a book of information and ideas for all who are concerned about the well-being of disabled children. It is especially for those who live in rural areas where resources are limited. But it is also for therapists and professionals who assist community-based programmes or who want to share knowledge and skills with families and concerned members of the community.

Written by David Werner with the help of disabled persons and pioneers in rehabilitation in many countries, this book has been prepared in a style and spirit similar to the author's earlier works, *Where There is No Doctor* and *Helping Health Workers Learn*. It gives a wealth of clear, simple, but detailed information concerning the most common disabilities of children: many different physical disabilities, blindness, deafness, fits, behaviour problems, and developmental delay. It gives suggestions for simplified rehabilitation, low-cost aids, and ways to help disabled children find a role and be accepted in the community.

Above all, the book helps us to realize that most of the answers for meeting these children's needs can be found within the community, the family, and in the children themselves. It discusses ways of starting small community rehabilitation centres and workshops run by disabled persons or the families of disabled children.

Over 4000 line drawings and 200 photos help to make the information clear even to those with little formal education.' (There is a full section on leprosy. This astonishingly comprehensive book of 654 pages is modestly sub-titled *A guide for community health workers, and families.* The illustrations and diagrams are superb. Every page of the book underlines the importance of what can be attempted and achieved in the community. Published by The Hesperian Foundation, P.O. Box 1693, Palo Alto, CA 94302, USA.)

Tropical Health Technology, Cambridgeshire, UK

Tropical Health Technology is a non-profit making organization, formed '. . . to assist developing countries by a sharing of resources.' The Directors are Monica and G E Cheesbrough, 14 Bevills Close, Doddington, March, Cambridgeshire, PE15 0TT (Telephone 0354-740825). The main objectives are the provision of low-priced training manuals, learning aids and appropriate equipment for use in district laboratories. Brochures available from the above address deal with: 1, Publications in tropical medicine, medical laboratory sciences, nursing and midwifery; and 2, laboratory equipment service to developing countries.

Of particular interest to those working in leprosy (and perhaps even more in tuberculosis), is the *Tropical Health Technology Microscope* of which the details are as follows:

A mains and battery operated high quality microscope, with special applications for tropical medicine work in developing countries is available from Tropical Health Technology and at a special low price to developing countries.

Specifications

Quadruple nosepiece with high quality 10 ×, 40 ×, 100 × objectives. High powers are spring-loaded. Tubelength 160 mm. Abbe condenser with iris and holder for dark-field stop and filters. Smooth-running mechanical stage fitted with coaxial controls and scales. Single easy to use focusing knob, incorporating coarse and fine movements. Trouble-free non-lubricating mechanism. In-built illumination with 6V 10 Watt quartz halogen lamp operating from mains electricity or from 12V battery (battery leads provided). Fitted with brilliance control knob and power indicator. Spare lamp is supplied. Rotatable mirror for use with daylight when mains or battery power is not available. Fully adjustable and rotatable binocular head with two wide-field 10 × eyepieces or monocular head with wide-field 10 × eyepiece. Dust cover and instruction booklet.

Model MIC.010 Monocular microscope with above specifications. A monocular viewing aid is available as an accessory.

Model MIC.020 Binocular microscope with above specifications.

A range of accessories is also available including dark-field stop, calibrated measuring graticule in 10 × eyepiece, 20 × objective, self-indicating silica gel. Wooden carrying case with lock, 12V sealed battery, solar panel.

For prices and further details, contact Tropical Health Technology at the above address.

Leprosy Hospital, Moniaya-Ogoja, Cross River State, Nigeria

The Medical Missionaries of Mary, a Congregation of sisters dedicated to medical work, was founded by Mother Mary Martin, in 1937—1987 was the Golden Jubilee year. The Medical Missionaries of Mary came to Ogoja at the invitation of Bishop McGettrick in 1946, to care for the leprosy patients in the area. Whilst other medical works have since been taken on by the sisters, the leprosy work continues to hold a place of great importance.

The Leprosy Hospital at Moniaya-Ogoja was, and still is, the Leprosy Referral Centre for the three Local Government Areas of Ogoja, Obudu and Ikom. In the 50-bedded hospital many patients are admitted for the treatment of ulcers and for skin grafting. Because of the good results nonleprosy patients also present themselves. Buruli ulcer appears to be endemic in this area. As the treatment is protracted, using antileprosy and antituberculosis drugs in combination, we have committed ourselves to the care of those patients, who, prior to coming to us will have made little progress after spending many months in various hospitals and clinics. In keeping with the World Health Organization's policy of integration of Leprosy and TB Control Services, we reopened the TB Service (closed for about 15 years). Some beds are given over to those who need hospitalization, whilst those admitted for supervised treatment are housed in the 'village' with the disabled and homeless leprosy patients.

The TB and Leprosy Unit in Obudu continues to give a good service to the patients in that area. In Ikom, the TB Unit is still separate from the Leprosy Unit but we are planning the integration of the two services.

The Multiple Drug Therapy Programme for the leprosy patients was pursued and by the end of 1987 almost all patients receiving chemotherapy in the Ogoja, Obudu and Ikom Local Government Areas, were receiving MDT.

Short course therapy for TB patients has been introduced in Obudu and Ogoja.

Signs of progress in the leprosy eradication campaign are:

1 A continuing fall in the numbers of patients needing chemotherapy.
2 Increasing numbers of patients released from treatment as cured.
3 Very few new cases found in school surveys, which is in contrast to the numbers admitted from school surveys in the past.

The monthly or bi-monthly staff meetings held in Obudu, Ogoja and Ikom continue to be the forum for the discussion of difficulties and problems related to the work, and for up-dating. Visual aids such as slides and flow charts, have been useful.

We welcome the opening of the Armauer Hansen Institute in Würzburg that will assist us through skin biopsies, with the quality control of the smears and in diagnosis, classification and response to treatment.

That we have been able to initiate and continue the MDT programme, is due largely to the long tradition of leprosy control (41 years) in this area. Dr Margaret Chambers was not only a great organizer, with vision, but a Trojan worker. Treatment centres were opened in all clan areas and staff were posted to these areas. Field work was well backed up by a laboratory service (smear examination) run by specially trained staff. School surveys were an important aspect of the work. Much of the treatment was actually taken to the patients in their homes so that contacts were seen and examined and so that the home situation was known to the staff.

In the late 1970s the new antileprosy drugs, first clofazamine and then rifampicin were appearing on the scene. These were utilized in the Moniaya Leprosy Control Services in various combinations. MDT was introduced on a regular basis in the referral hospital and therefore given only to those patients who had advanced disease or were suffering from reactions. This initiative introduced the staff to the concept of MDT. They had seen the obvious good effects and so welcomed the programme that embraced all their patients.

Even though the Moniaya Leprosy Control Services were without continuous medical supervision the staff were faithful to their duty of administering dapsone. The treatment centres were visited monthly, the work supervised, the staff encouraged and the needs of the disabled and abandoned patients were cared for. So it was that when it came to reviewing all patients prior to introducing MDT, many patients were considered ready to be released from treatment. During these 'reviews' it was also discovered that large numbers of patients were not attending even though their names were still on the register. Their records were scanned and it was obvious that many had received sufficient treatment, that their disease was inactive and that to attend clinics was an unnecessary burden. They were released from treatment 'in absentia'. The true defaulters were taken off the registers.

There was no elaborate retraining of staff or recruiting of staff for the MDT programme. The staff we worked with were those who had borne the heat of the day—the hours of trekking looking for patients, the large numbers presenting for surveys, the misunderstandings of a society that treated leprosy, its victims and those working against it, with fear and prejudice. Updating sessions in the form of seminars were held and all were trained to do the simple monthly review on every patient.

The main reason for the successful launching of the programme was the fact that we had at hand *a certain and adequate supply of drugs*, thanks to the generosity of our benefactors. Each supervisor collects a monthly supply for his patients from Moniaya. He must present a list of his patients and indicate the number of tablets and capsules needed for the month. Much is left to the supervisor. He keeps problems and discharges for the medical officer who might visit every 3–6 months. Any patient with a serious problem is referred to Moniaya.

Patients are taught to care for themselves. Much emphasis has been put on the prevention of ulcers and deformities, and the care of hands and feet. Foot wear for insensitive feet is provided by the Rehabitation Unit. At first patients received the 'release from treatment' pronouncement with mistrust and reluctance. All staff were taught to give a simple 'discharge talk' covering 5 points, to dispel anxiety:

1 It is explained to the patient that leprosy is a disease caused by a germ. It can be cured by regular attendance. He/she is told that the full examination has proved that the disease has been cured.
2 New hands and feet are not available. The patient is given full instruction on hand and foot care.
3 The patient is advised to report any problems or suspected recurrence of the disease.
4 The patient is asked to attend for review after 3 months, 6 months and then annually.
5 The patient is invited to share in the work by passing on his or her knowledge of the disease (the true facts) and encouraging those needing treatment to attend a clinic.

In the Annual Report for 1986, we outlined plans for the future. In administering MDT to all patients needing treatment, in giving time to teach patients to care for themselves, in being diligent about contact tracing and school surveys to find untreated patients, in availing of opportunities to enlighten the public about leprosy, in integrating tuberculosis control into the Leprosy Control Services, in improving mobility of staff, we have come a long way in fulfilling these plans.

Staff salaries are paid by Cross River State Government but without the continuous and generous support of our benefactors overseas and the support in goods and kind from our local friends and charitable organizations, we could have achieved very little. We are deeply grateful.

Cecily Bourdillon

Action Health 2000

The following is extracted from the latest *Bulletin*, March 1989:

'In 1988 Action Health successfully continued to run its elective programme, sending medical students to a variety of placements in developing countries. The value of spending an elective overseas is increasingly recognised by students, tutors and future employers. The experience exposes students to a wide range of health care systems, providing a valuable contrast to Western medicine. The elective scheme is instrumental in fostering a long term interest in health and development.

Action Health is able to offer a 'package' to medical students contemplating an elective abroad. This includes a placement which has been personally vetted, an orientation course to prepare them for their time abroad, and support overseas through project correspondents. Follow up on return is provided, to ensure that the experience is put to good use in this country.

We offer electives in a variety of health care settings from hospitals to rural primary health care projects. The focus of all of our placements however, is community orientated. Action Health has been organizing electives in China, India and Bangladesh for some time and has recently expanded into Africa. We now send students to Tanzania, Rwanda, Zaire, Zimbabwe and Uganda.

Action Health is hoping to expand this educational aspect of its work, and would like to encourage more students to apply for the scheme. We would be pleased to give an address about our programme to any interested medical schools, and to send details of placements and application procedure to individual students considering an elective abroad.'

Address: AH 2000, The Bath House, Gwydir Street, Cambridge, UK.

Mission Project Service

Sister Catherine Howard Executive Director of MPS, One Haven Plaza 25A, New York, NY 10009, USA has kindly sent the following information:

'The MPS offers a wide scope of services which include: consultative services for project organization, proposal review, planning for future support, and selecting suitable agencies for assistance. The staff will assist the project organizer in determining a project's suitability for international support, preparing a written proposal, and designing a plan for application to appropriate agencies. These services are provided free of charge by phone, mail, and office visit. In response to the needs of those seeking assistance from international agencies, the MPS has designed project education workshops and seminars. These programmes enable those seeking support to understand the world of international grant-seeking, to learn how to write proposals, to train others in proposal writing, and to select suitable agencies for support.'

A book entitled *Agencies for Project Assistance*, 3rd edition, 1988, profiles over 280 agencies that provide assistance in the developing world. Price US$50.00, handling and postage included, from the above address.

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Teaching Materials and Services

OXFAM: booklet on multiple drug therapy

The *OXFAM Practical Guide No. 3*, first published in 1984, with revisions in 1985 and 1987, as *Questions and Answers on the Implementation of Multiple Drug Therapy for Leprosy*. The new issue takes account of valuable comments received from various parts of the world and includes a short section on AIDS and appendices describing blister–calendar packs for paucibacillary and multibacillary leprosy. OXFAM, 274 Banbury Road, Oxford OX2 7DZ, England. A Portuguese version is available, and Spanish and French translations are under development.

WHO Publications

Tuberculosis control in primary health care

A recent publication from WHO entitled *Tuberculosis Control as an Integral Part of Primary Health Care* (Office of Publications, WHO, 1211 Geneva 27 Switzerland. Price: Sw. Fr. 9) carries the following summary on the back cover:

'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 treatment. After a succinct presentation of what programme managers need to know about sputum smear examination and the pros and cons of different chemotherapy regimens, the book explains how to plan and organize tuberculosis control at the all-important district level. The main managerial tasks are set out, including the proper attention to training and motivation of programme staff, many of whom may have to make the difficult transition from a specialized tuberculosis programme to primary care. Readers are alerted to the conceptual and practical problems likely to be encountered, and the usefulness of health systems research in solving these problems is stressed. The book concludes with a look at external collaboration. Bilateral and multilateral funding can do much to support tuberculosis control in the developing world, for example through an international pool of essential anti-tuberculosis drugs, provided that countries are careful not to allow external support to distort the development of their general health systems based on primary care.'

[This is an important publication, virtually essential reading for anyone engaged in tuberculosis, leprosy or combined tuberculosis/leprosy control programmes. Pages 30–3, dealing with tuberculosis control activities at district level are of particular interest; nearly all the problems listed (for which no specific answers are attempted) also apply to leprosy.]

A guide to leprosy control. Second edition

This is the second edition of a guide covering virtually every technical and managerial consideration involved in the planning and operation of a leprosy control programme. The book has been thoroughly revised in an effort to help managers and field workers meet the new challenges resulting from the use of multidrug therapy. Guidelines and advice, whether concerning the performance of a technical operation or the overall objectives of control, take their authority from the proven capacity of multidrug therapy to prevent or cure drug resistance in all patients.

With chapters on: magnitude of the problem and geographical distribution; epidemiology; limitations of the classical control strategy based on dapsone monotherapy; case-finding; diagnosis and classification; treatment and patient care; reorganization of services and operational strategies for leprosy control; health education; training; urban leprosy control; social aspects and rehabilitation; evaluation; and planning and programme management.

Price Sw. fr. 23/US $18.40. Pages, 122. Order No. 1152064.

Epidemiology of leprosy in relation to control
The above is a report of a WHO Study Group, Technical Report Series No. 716, and meets the need for practical guidance in monitoring the epidemiological impact of leprosy control procedures, particularly in light of the implementation of multidrug therapy. The opening sections review world data on both descriptive and analytical aspects of leprosy epidemiology in various contexts, including results from specific interventions such as chemotherapy and BCG immunization. The report also covers immunological methods useful in epidemiological studies, epidemiological indicators for measuring the impact of control methods and trends in disease dynamics, and operational indicators for monitoring control activities. A few simple essential measures for use as epidemiological and operational indicators are proposed as a minimum requirement for all leprosy control programmes based on multidrug therapy. The report also defines an additional set of indicators that should be used whenever possible.

Price: Sw. fr. 6/US $4.80. Pages, 60. Order No. 1100716.

Chemotherapy of leprosy for control programmes
The above is also a report of a WHO Study Group, Technical Report Series No. 675, which proposes globally applicable regimens to treat the different groups of multibacillary patients and a further combined regimen designed for the short-term chemotherapy of paucibacillary patients. The report also recommends ways of overcoming the operational problems created by the move from dapsone monotherapy to the complexities of multidrug therapy.

Price: Sw. fr. 4/US $3.20. Pages, 33. Order No. 1100675. The above three titles are available from: The Office of Publications, WHO, 1211 Geneva 27, Switzerland.

Combined seminars; London School of Hygiene and Tropical Medicine

Under the chairmanship of Professor K P W J McAdam, Head of Department of Clinical Sciences, an all-day seminar on leprosy was held on 13 April 1989 in the London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, for students in the MSc or DTM and H courses. The invited speakers (Colin McDougall, Sebastian Lucas, Keith McAdam, Michael Waters and Harold Wheate) covered the subjects of epidemiology, histopathology, immunology, vaccines, clinical features, therapy and leprosy control programmes in a series of short lectures. A written summary of each was distributed before the seminar, together with multiple choice questions suitable for inclusion in the examinations. The seminar was attended by over 100 students, as part of the core didactic teaching for MSc and DTM and H in London.

Diploma in Tuberculosis and Chest Diseases, Cardiff, UK

This diploma is offered by the University of Wales College of Medicine and the following is a synopsis of the course:

(*a*) In addition to the course of lectures covering the epidemiology of tuberculosis, bronchitis, pneumoconiosis and other chest conditions, particular attention is paid to the teaching of techniques for carrying out field surveys to measure the prevalence and attack-rate of such conditions. Detailed practical training is given in:

The technique of tuberculin testing and BCG vaccination.
The technique of doing simple pulmonary function tests suitable for field work.
The use of simple statistical techniques in planning surveys and evaluating their results.

(*b*) A course of lectures and demonstrations on the diagnosis and treatment of all chest diseases with particular reference to tuberculosis. This includes clinical instruction, radiology and physiological assessment, bacteriological and pathological diagnosis, medical and surgical treatment and rehabilitation. Facilities are given for the examination of patients in chest hospitals and clinics. There is also a short course of lectures on controlled therapeutic trials, and a series of lectures and demonstrations on radiography and nursing.
(*c*) A course of lecture-demonstrations on the pathology and bacteriology of chest diseases.
(*d*) A course of lectures and demonstrations on non-respiratory tuberculosis diseases.
(*e*) (1) Visits to industries to show the steps taken to reduce risks of pulmonary damage.
(2) Visits to rehabilitation centres.

Traditionally, one entire day (4 lectures) is devoted to the subject of leprosy. This is certainly the only course of its kind in the UK and one of the very few on tuberculosis available anywhere. Further information: The Departmental Secretary, Department of Tuberculosis and Chest Diseases, Llandough Hospital, Penarth, South Glamorgan, CF6 1XX, United Kingdom.

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News and Notes

IDRC Reports, Ottawa, Canada

The International Development Research Centre (IDRC) is a public corporation created by the Parliament of Canada in 1970 to support researchers in developing countries working in agriculture, health, earth sciences, engineering, information, communications and social sciences. The *IDRC Reports* is published quarterly and distributed free (on request) to a limited number of people world-wide. Its aim is to keep an international readership informed about the work IDRC supports in developing countries, as well as other development issues of interest. It is available in French as *Le CRDI Explore* and in Spanish as *El CIID Informa*. Address: IDRC, 250 Albert Street, P.O. Box 8500, Ottawa, Canada K1G 3H9

International Task Force on Rural Poor, India

Mr Mukat Singh, Director, Amarpurkashi Rural Polytechnic, via Bilari, District Moradabad, U.P.-202411, India has kindly supplied the following information about his centre:

From 20–24 December 1988 an international seminar on 'Working with the Rural Poor' was held in Amarpurkashi, N. India. It was attended predominantly by grass-root development workers. Historically, it was the first time that an international seminar to discuss rural poverty took place in a rural venue.

The discussion and the results both were exceptionally down to earth and consequently most useful and far reaching. The seminar issued twenty recommendations covering these topics—governmental initiatives for uplifting the poor, science and technology for the poor, exploitation and oppression of the rural poor and integrating education and development of the rural poor.

The last recommendation of the seminar stated that 'An international task force concerned with the rural poor must be set up, as a concrete and constructive outcome of the seminar'. The recommendation explained that: 'The aims of the Task Force will be to identify and publicise examples of integrating education and development for the rural poor. The International Task Force will strive to achieve recognition within the world community for the plight of the rural poor and will monitor the progress of the policies and programmes that benefit the rural poor most'.

The International Task Force has been set up following the decision of grass-root development workers. The idea has therefore come from 'below' and is not being imposed from 'above'. It is born out of the need and realization that the number of rural poor and the extent of their poverty are both on the increase. Even the many well intentioned policies of the governments to uplift the poor have either failed or become ineffective. This is largely due to the fact that the implementing agencies lack a genuine commitment to the rural poor. The growing view from the 'other side' is that the rich do not really want to share their bounty with the poor. Even the idea of a 'common interest' hammered by the Brandt Commission has so far failed to move the rich North to share 0·7% of their income with the poor of the South. The present average part that the EEC countries share with the Third World Countries is a trifling 0·34% of their total income.

The Task Force has been set up to fight this apathy and narrow self-interest. It is also intended to increase moral pressure on Third World governments and international aid agencies so that they do more for the cause of the rural poor. The following aims are in the constitution adopted on Feb. 18, 1989:

1 To identify policies, programmes and projects of integrated education and development or of any other innovative and pioneering nature that are contributing most to the all-round development of the rural poor.
2 To publicise the identified policies, programmes and projects and to help to make them as effective as possible.
3 To monitor the progress of the identified policies, programmes and projects and evaluate them.

Identification of good and effective policies, programmes and projects will involve collection of information from various sources, organising study visits and research programmes to selected projects and then identifying the most beneficial and effective projects and their workers. Providing moral support to identified projects and their workers will involve publication of reports and features about them with a view to according to them international recognition and publicity and providing them with support from various international pressure groups. Monitoring and evaluation of the policies and projects will involve action research by experienced and expert field staff.

Further information: Mr Mukat Singh at the above address. See also *The gentle revolution. The Guardian* newspaper, 17 February 1989.

Essays on leprosy: distribution to medical schools in India

A copy of *Essays on leprosy by Oxford Medical Students* (Editors: T J Ryan and A C McDougall, 1988) has been sent from the Department of Dermatology, The Slade Hospital, Headington, Oxford OX3 7JH, England, to the 106 medical schools of India, as listed in the *The World Directory of Medical Schools*, WHO, 1979. This collection of essays was originally published by the above Department for the St Francis Leprosy Guild as a tribute to the students who have contributed manuscripts of outstandingly high quality, either for the yearly LEPRA Prize Essay Competition or as dissertations for the Basic Physiological Science Degree in the University of Oxford. Further copies are available from Dr Ryan at the above address. Price: £10.00 including p. and p.

Handbook of Leprosy. Jopling and McDougall. Fourth edition. Translations

A translation into Portuguese is almost complete (Professor Lucio Bakos, Porto Alegre, Brasil) and it is hoped that it will be published by Livreria Atheneu, Rio de Janeiro, Brasil. Translation into French and Spanish are currently in production.

Action in International Medicine: AIM, London

The inaugural conference of Action in International Medicine (AIM) took place on 6–7 April in London. AIM is a unique body which brings together many colleges and academies of medicine and nursing around the world in a collaborative venture to improve health care in the Third World. Supporting institutions include:

Academie Nacional de Medicina, Venezuela; Académie Nationale de Médecine, France; Academy of Medicine of Malaysia; American College of Physicians; College of Physicians and Surgeons, Pakistan; Conférence des Facultés et écoles de médecine d'Afrique d'expression française; Hungarian Academy of Sciences (Medical Section); International Council of Nurses, Geneva; International Planned Parenthood Federation; Royal Australasian College of Physicians; Royal College of General Practitioners, London; Royal College of Physicians, Ireland; Royal Colleges of Physicians of London, and Edinburgh; and Royal College of Surgeons of England.

The conference was under the joint chairmanship of Sir John Reid, former chairman of the Executive Board of WHO and Chief Medical Officer for Scotland, and Sir Gordon Wolstenholme, former director of the Ciba Foundation and chairman of AIM. The 36 participants came from Australia, Brazil, Colombia, France, Ghana, Hungary, Ireland, Kenya, Pakistan, Venezuela, Switzerland, the UK and the USA, and included representatives of WHO, IPPF, the Commonwealth Secretariat, the Commonwealth Medical Association, the International Federation of Obstetricians and Gynaecologists, the International Foundation for Dermatology, and the American National Council for International Health. Dr Halfdan Mahler, until recently Director General of WHO, was a guest and speaker at the Conference dinner.

There was general agreement that AIM should act primarily in an advisory role to promote the development of district health systems. This organizational unit, akin to the health district in the NHS, is of fundamental importance to the development of comprehensive health systems. WHO has already given their development priority but because of insufficient resources is unable to carry forward the programme as strongly as it would wish. It therefore welcomes the participation of AIM. Two or three sites will be identified for initial projects in Latin America, Africa and S. or S.E. Asia. AIM will work closely with the local community and local health professionals to determine priorities. In many instances these are likely to be in health planning and epidemiology as well as training in specific clinical and nursing skills. Every effort will be made to achieve a 'multiplier effect', such that one site, by training professionals from other districts, will have an influence beyond its own confines. Each project will have an agreed duration, and selection of the sites will take into account the need to plan for sustainability of activities beyond the time of AIM's involvement.

The new organization founded by Sir Gordon Wolstenholme with the assistance of Professor Andrew Haines, is based at the Department of Primary Health Care at University College and Middlesex School of Medicine, Windeyer Building, Cleveland Street, London W1P 6DB.

Implementing Multiple Drug Therapy for Leprosy, OXFAM translations

A revised Portuguese translation has recently been completed (Jorge Macedo, CERPHA, Brasil). Translation into Spanish is far advanced (Professor Roberto Estrada, Centro de Investigacion de Enfermedades Tropicales, Acapulco, Guerrero, Mexico). OXFAM have recently given permission for translation into *French* to Dr Paul Ambassa, Organisation de Coordination pour la Lutte contre les Endemies en Afrique Centrale (OCEAC), Yau Yaounde, Cameroun.

International Foundation for Dermatology (IFD); site visit to Tanzania

The Board of Directors of the International Foundation for Dermatology (IFD) selected a Site-Visit Committee to travel on 4–8 April 1989 to Tanzania in order to determine the feasibility of aiding in the establishment of a *Regional Dermatology Training Center (RDTC)* in that country.

Through careful pre-site visit planning the Committee had the opportunity to meet with virtually all of the key individuals required for the approval and development of the RDTC. Among these were Minister of Health, Vice Chancellor of the University of Dar es Salaam, Director General of the Muhimbili Medical Center, Dean of the Medical School of Dar es Salaam, Professor and Chairman of the Department of Medicine at Muhimbili Medical Center, the Head of the Training and Health Manpower Division of the Ministry of Health, the Secretary of the Good Samaritan Foundation (GSF) at the Kilimanjaro Christian Medical Center (KCMC), representatives of WHO and UNICEF, and many others.

The Committee unanimously recommends that the International Foundation for Dermatology aid in the establishment of a Regional Dermatology Training Center at the KCMC in Moshi, Tanzania. The initial emphasis will be on a two-year training program at the Medical Assistant (MA) level. The program will emphasize clinical dermatology, sexually-transmitted diseases (including AIDS), leprosy, teaching/learning skills, and research. After the successful completion of this training, the trainee will receive the title of 'Dermatology Officer.' It is furthermore recommended by the Committee that this training program should meet the requirements of the University of Dar es Salaam Medical School and its parent University of Dar es Salaam leading to a Diploma for those who successfully complete the course.

Professor Aaron E J Masawe has been selected by the government to be the official Co-ordinator for Tanzania. Dr Masenga, Head of Dermatology at KCMC, has agreed to serve as the 'Principal' (i.e. Director) of the RDTC school.

The list of recommendations compiled for consideration by the Board of Directors of the IFD included the following:

to offer training in dermatology in the context of the Primary Health Care system of Tanzania;
to promulgate this training within the current Health Care System of Tanzania;
to extend this training to the health community of eastern, central and southern Africa;
to initially focus training on the Medical Assistant (MA)/Clinical Officer (CO) health cadre leading to a diploma in dermatology from the University of Dar Es Salaam. This training will serve as the qualification for the new position of Dermatology Officer (DO) allowing the delivery of dermatologic care at the appropriate level (i.e. Primary Health Care level—mainly at the District Hospital and lower levels);
to create an integrated curriculum embracing primarily the subjects of: (1) clinical dermatology; (2) sexually-transmitted diseases including AIDS; (3) leprosy; (4) health education; (5) teaching methodology; and (6) research techniques (e.g. data collection and retrieval).
to disseminate this knowledge via the DO to other health care workers;
to identify the length of the training period and the appropriateness of the program for the other countries in the Region (e.g., by promoting a Workshop on Regional Dermatologic Training Needs);
to disseminate this knowledge via the DO to other health care workers;
to identify the length of the training period and the appropriateness of the program for the other countries in the Region (e.g., by promoting a Workshop on Regional Dermatologic Training Needs);
to aid in the establishment of the RDTC at the Kilimanjaro Christian Medical Center (KCMC) in Moshi, Tanzania. This is a supraregional Consultant Hospital in the grounds of the Good Samaritan Foundation (GSF);
to construct two facilities in the grounds of KCMC, namely, (1) the RDTC, and (2) a hostel for 30 students; and
to create a Board of Management to govern the RDTC, to advise the Board of Trustees of the KCMC on all matters concerning the RDTC, and to assure that the RDTC will operate within the rules and regulations of GSF.

Global control of tuberculosis and vaccine development

In *Reviews of Infectious Diseases*,* Volume II, Supplement 2, March–April 1989 is an item entitled 'Research towards global control and prevention of tuberculosis with an emphasis on vaccine development'. It is in fact the report of a Fogarty International Center Workshop, held in Bethesda, Maryland, USA, 3–5 November 1987. The main headings are: Present approaches to tuberculosis control and prevention; Pathogenesis of tuberculosis and its implications for vaccine development; Molecular biology of mycobacteria; Immunology; Vaccine and new drug development; Future directions and priorities. The Introduction (Dixie E Snider, Division of Tuberculosis Control, Center for Prevention Sciences, Centers for Diseases Control, Atlanta, Georgia, USA) gives an extremely good summary of the current state of tuberculosis in the world (1 billion people infected; 16 million prevalent cases; 8 million new cases per year; 3 million deaths per year), together with a 'litany' of the inadequacies of current control methods.

* Available from the University of Chicago Press, Chicago Illinois 60637, USA

International Youth Workshop on Leprosy and Health, Munich, May 1989

A workshop with the above title was held in Munich, West Germany, 16–19 May 1989 organized by Aussätzigen-Hilfswerk Munchen e.V. in cooperation with the World Assembly of Youth (WAY; Ved Bellehoj 4, 2700 Bronshoj, Copenhagen, Denmark) and the World Health Organization (WHO). It was attended by representatives of youth organizations in India, Nepal, Pakistan, Bangladesh, Kenya, Ghana, Malaŵi, Tanzania, the Cameroons, Mexico and Peru. The main objectives were to review the outstanding problems in the control of leprosy and to discuss the practical ways in which youth organizations might actively participate. Mrs Mathilde Gruner, Managing Director of AHM (Zenettistrasse 45, D-8000 Munich 2, West Germany) welcomed delegates to the meeting, Dr Lois Philip (Health Education and Promotion, WHO) spoke on 'Communication and education for leprosy control' and Dr Colin McDougall (Oxford) spoke on 'Leprosy; the disease and its control', using panels of the exhibit on leprosy supplied by the Wellcome Tropical Institute in London. The country presentations revealed that very large numbers of young people, many of them registered as members of the boy scouts, girl guides or other youth organizations, are already involved in health care or community development. Given professional advice and logistic support, they would be more than interested to participate in national leprosy control programmes. Emphasis was given to activities which could be useful at district hospital level, preferably using the primary health care approach. Further enquiries to AHM at the above address in Munich.

DANIDA: Danish Department of International Cooperation

The following is extracted from an *Africa Health*, Denmark Supplement, April/May 1989, published by Africa Health Publications Ltd, 57–59 Whitechapel Road:

DANISH official aid to Tropical Disease Research is more than that given by the United States, Britain and France put together. This is a staggering statistic when one considers that the Danish population is only just over five million!

Most of the funding is channelled through the Danish Department of International Cooperation (DANIDA) which is a part of the Ministry of Foreign Affairs.

The UNFPA, WHO, and IPPF receive the bulk of support, and each in turn, dispenses large amounts of this to research institutions and individuals with whom they are cooperating. DANIDA's conviction that it is best to allow international organisations to coordinate the research effort, rather than fund a lot of projects independently, is not particularly popular amongst Danish researchers, but makes good logical sense in terms of allowing greater global coordination of work, thus preventing unnecessary repetition in different centres. In this respect DANIDA is going against the general trend, whereby aid agencies ensure the majority of their funds are 'tied' to initiatives emanating from within their countries.

Direct bilateral aid to Africa, concentrates strongly on developing primary health care programmes, with careful emphasis on infrastructural strengthening to support the health intervention. This so-called 'horizontal' aid support is well explained by the example of support for the essential drugs programme in Tanzania. In addition to the high profile work on developing distribution links, and the all important provision of drugs, the project also involves considerable general planning and administrative assistance at central and district level to ensure that the project does not operate in a vacuum, and thus has a much greater chance of succeeding in the long-term.

The basic philosophy can perhaps best be described as 'providing efficient, easily accessible and adequate health services, at low cost'. Assistance must be adjusted to the economic conditions of the recipient countries so as to make it possible to offer all groups of the community access to health facilities. Particular attention is given to providing paramedics (with relatively short-term training) with the knowledge and tools to make an impact in improving the health of their community.

Community participation is also a vital element to which DANIDA looks, before committing its support to a programme. People must accept responsibility for their own health rather than leaving it exclusively to doctors and health institutions.

Applications for assistance, should be for projects that provide input to one or several of the following parameters:

Development of infrastructure at the lowest level of the health care system, e.g. through construction and renovation of health services.

Education and training of community health workers and paramedic workers.

Improvement of planning, administration, and logistics—such as in connection with drug supply.

Provision of ante-natal, natal, and post-natal care to mothers, and child health care activities such as vaccination programmes for children under five years of age.

Strengthening of family planning programmes through information and education, easier access to appropriate family planning methods.

Programmes for the prevention of communicable diseases.

Prevention of diseases causing handicaps and rehabilitation of the physically or mentally handicapped.

Improvement of drinking water supply and sanitation conditions.

Dissemination of information on nutrition and appropriate diet and introduction of new ways of local food production.

Support to self-help projects.

Dissemination of information on dental care.

Research activities connected with assistance activities, particularly establishment and strengthening of the research capacity of local research institutions.

Further enquiries from DANIDA, Danish International Development Agency, 2 Asiatisk Plads, DK- 1448 Copenhagen K, Denmark

Second National Meeting of the Spanish Group on Mycobacteriology

This was organized by the Department of Microbiology of the Hospital of Santa Cruz and San Pablo, and the Faculty of Medicine of the Universidad Autonoma of Barcelona, 26–28 May 1989. The meeting began with a short symposium on leprosy (advances in immunology; technical aspects of diagnosis; a report on leprosy in Spain; multiple drug therapy for leprosy; vaccination). This was followed by sessions on serological and other tests for the rapid diagnosis of mycobacterial diseases; case reports of mycobacterial disease (clinical aspects); mycobacterial diseases and AIDS. The latter session was particularly interesting and important; numerous cases of tuberculosis in association with AIDS occurring in Spain were described and from the Leprosy Institute in Trillo, Guadalajara, one case of leprosy with possible AIDS was presented. Some delegates from this meeting attended a workshop held in Barcelona at the same time, organized by Ciba-Geigy, on the collection of data on leprosy cases from all parts of Spain, including computerization and the use of the OMSLEP system. Further enquiries about the Mycobacteriology Meeting can be obtained from: Professor Ausina, Facultad de Biologia, Universidad Autonoma de Barcelona, Barcelona, Spain.

Instructions to Authors

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

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

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

Proofs are submitted to authors for immediate return by air.

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