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Leprosy Review

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

LEPRA

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Editorial Office: LEPRA, Fairfax House, Causton Road, Colchester CO1 1PU, England
Assistant Editor: Susan Boobis, 118 Malvern Avenue, South Harrow, Middlesex HA2 9EY, England. e-mail: sboobis@aol.com

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Editor's Choice

This issue has a very clear theme of nerve damage and many different ways the ways it can be studied, prevented and hopefully ameliorated. The issue was not specifically planned this way and I think it reflects the determination of the leprosy community to find solutions for the problem of nerve damage.

There are three large epidemiological studies, two from Bangladesh (Croft *et al.*, pp. 140–159; Richardus *et al.*, pp. 160-173) and one from Ethiopia (Meima *et al.*, pp. 189–203). All look at different aspects of nerve damage in new leprosy patients. In both Bangladeshi studies, intensive case finding has resulted in an increased number of female cases being detected. Another positive finding was that the proportion of grade two disability was lower in women than men at the time of diagnosis. The finding that there is a lower case detection rate in women ages 18–30 may reflect socio-cultural rather than biological factors. Multibacillary patients continue to present with high levels of disability, with rates of grade two disability at 18% in Bangladesh and 23% in Ethiopia, respectively. The Ethiopian study looked at risk factors for disability and found that delay in presentation and age were the main risk factors with nearly half the patients having a delay of more that 2 years from symptom onset to registration. The problems of case finding in women and encouraging early registration will clearly be important issues for future leprosy control planning.

The study by Croft *et al.* found that the posterior tibial nerve was the nerve most commonly affected. This finding would not surprise surgeons who see a large burden of morbidity from posterior tibial nerve damage. In our surgical series, ulcer surgery for non-specialist surgeons outlines basic principles to improve foot quality and prevent ulcer recurrence. The poster accompanying this issue, 'Foot Care', is planned as a tie-in with the surgery articles and focuses on ulcer prevention. It is a striking poster and I hope will be used widely in clinics for teaching self care.

Science Commentary is a new section which I hope will attract many readers. In this section, scientists will be writing about new findings and explaining their relevance and excitement for other leprosy workers. Gilla Kaplan and her colleagues have given this section an excellent start with a very clear explanation of the mechanism by which *M. leprae* binds to Schwann cells.

We have had many positive response to our proposed special issue on LECS but many people are asking for more time to prepare articles. So we have decided to postpone the LEC issue until December and will continue to accept articles until Sept 1. I'm sorry that I gave readers such short notice for the LEC issue

The Editorial has been prepared by Irene Allen, the editorial assistant in the Lepra offices. We thought that readers might appreciate a glimpse inside the editorial office.

Diana N.J. Lockwood (Editor)

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Editorial

LEPROSY REVIEW: ORIGIN, POLICY, CONTENT, CIRCULATION, FINANCES AND THE FUTURE

Origin and purpose

The Journal began life in 1928 as *Leprosy Notes*, a quarterly distillation of the findings of leprosy workers around the world, which was distributed to others in need of up-to-date information. Although less publicised as a contribution to the well-being of those with leprosy, *Leprosy Notes* and what was made of the publication is incalculable, and may still be fairly regarded as one of LEPRA's major steps towards the achievements of its aims. In 1930, under the Editorship of Dr. Robert Cochrane, an eminent leprologist who was LEPRA's (then called BELRA) first Medical and General Secretary, *Leprosy Notes* was re-named *Leprosy Review* and transformed into a high-quality medical Journal.

Leprosy Review is now a leading journal in its field, and is catalogued in several places including *Index Medicus*, *Current Contents* and the *Science Citation Index* to name but three. *Leprosy Review* had impact factors of 0·447 in 1996 and 0·607 in 1997 (data from the Journal Citation Reports database).

Editorial policy and content

The Journal has an average of 96 pages per issue. As well as original and special articles, the Journal contains The Editor's Choice, at least one Editorial, and one or more Review Articles. Letters to the Editor, Case Reports, Book Reviews and Obituaries of those concerned with leprosy are also included. *Leprosy Review* also prides itself on providing information to its readers on Teaching Materials and Services to which they might otherwise not have access, and also for its wide-ranging *News and Notes* section which enables readers to catch up on what else is going on in and around the world of leprosy. An index is included as an integral part of Issue 4 each year.

The Journal is published with the main objective of contributing towards the better understanding of leprosy and its control, and therefore is open to any manuscript dealing with leprosy or related subjects. Papers are submitted from all over the world and cover every aspect of leprosy, including research. In addition, considerable emphasis is given to material of education value which is of direct benefit and relevance to the practical aspects of the

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control of leprosy under field conditions, and therefore to the individual patient. Naturally the subject matter of any individual issue is dependent on the manuscripts accepted for publication at that time.

Leprosy Review has, since 1996, provided a free poster on an aspect of leprosy of interest to many people. Those published so far have been on Reversal (Type I) Reactions, ENL (Type II) Reactions, Immunology, Prevention of Disability, Making Slit Skin Smears, Examining Slit Skin Smears, Eye Examination, and Care of Microscopes. An evaluation of these posters was undertaken by way of a questionnaire after the first four had been distributed. An overwhelming majority of subscribers responded and judged them to be an excellent aid to their work, although of course there were minor quibbles where an African audience didn't like Asian photographs (and *vice versa*) but on the whole they have been a great success. So much so in fact, that over 10,000 additional posters were sent out on request, and following the ILA Congress in Beijing a further 13,800 copies of the posters have been ordered.

The Editorial Board invite special articles or editorials from expert authors from time to time, and supplements or special editions on a particular subject or theme of major importance are published when appropriate (such issues have included coverage of items at the ILA Congress and special issues to honour a particular person or event).

Peer review

The name(s) of the author(s) and the place where the work was done has to be indicated clearly below the title of the manuscript, all of which are submitted for peer review by at least two referees with a specialisation in the field of the paper. Opportunity is also given for readership feedback on printed manuscripts via the *Letters to the Editor* pages and all authors are given a chance to respond to any such comment. Proofs are submitted to authors for immediate return by air.

Circulation

Leprosy Review is despatched to 1687 subscribers in 110 countries from all continents throughout the world and is published quarterly in March, June, September and December of each year. 931 issues are sent out free of charge to centres unable to provide the foreign currency to pay for it, 756 are paid for either by individuals, institutions or covered by ILEP grants. The majority of issues go to India (358), Brazil (58) and Nigeria (54) and the cost has remained at £30 since 1990, heavily subsidized by LEPRA to ensure that this vital information reaches those least able to pay for it. Circulation reached a low of 1480 in 1994 but rallied well after that and since the new Editor has been in place has increased by over 200.

Finances

The total cost of production and distribution of the Journal in 1997 was £32,097 ($51,355 by

the exchange rate on 30.11.98)* This can be broken down:

Printing	£16,976	($27,162)
Despatch	£9,767	($15,627)
Editorial Office	£5,353	($8,566)

* IJL costs are given as $126,706 = £79,191

Printing and postage costs are subject to variations due to price increases in paper and services, although the best possible rates are worked out with the printers and despatch house. Despite the increased circulation and quality of the Journal there are still only three people involved in its production and distribution. The Editor is unpaid, the Assistant Editor receives an hourly rate for work done on the Journal, and the Editorial Assistant is an employee of LEPRA.

Future developments

Following the great success of the first two series of posters, another set will be published, and further topics will be considered in the future.

Summaries of original papers, Contents, Editor's Choice, the Editorial and summaries of original articles from each issue are available on LEPRA's website (http://www.lepra.org.uk)

In a climate where one of the first things to go in an Institution's cash-strapped budget is a Journal, LEPRA is striving to ensure that all those who wish to have the Journal should have it without being penalized for lack of funds. Therefore it will continue its stated policy of providing '*. . . free copies to doctors working with leprosy who are unable to afford the above subscription, and to selected libraries covering tropical medicine*'.

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REVIEW

Leprosy: applying qualitative techniques to research and intervention

JESSICA A. OGDEN, AND JOHN D. H. PORTER
Departments of Infectious and Tropical Diseases and Public Health and Policy, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK

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> 'Leprosy is, after all, far more than a biomedical phenomenon. It maintains its grip on those human populations already suffering from poverty, inadequate housing, and nutritional deprivation.... Society contributes to the suffering caused by this disease, and society must use every means at its disposal to mitigate that suffering.'[1]

Introduction

Leprosy is far more than a biomedical phenomenon. Although biomedicine has assisted in reducing leprosy prevalence in recent years, one team of researchers note that:

> 'reduction in prevalence alone is not sufficient as the social consequences of the disease on the life of the patient are often severe and persist even after its cure. The social aspects associated with this disease are therefore as important, if not more important than the biological ones'.[2]

It is these long-term effects of leprosy on patients, families and communities that have to be addressed, even if the public health goal of eradication is reached.

Leprosy control permits workers in infectious disease control to address health in its broadest sense. Because leprosy patients require long-term rehabilitation, it is important to understand the dynamics of care and support for patients in communities. To address 'health' rather than disease, and to place leprosy within this context of health, requires biomedical workers to consider different perspectives for finding solutions to the care of leprosy patients. If research on leprosy addresses the social, economic and environmental factors that influence people's lives then it can help us develop health systems which more effectively meet communities' health needs.

Correspondence to J.A. Ogden

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A *qualitative approach* to leprosy treatment and control provides an opportunity for changing prevailing biomedical perspectives through the creation and development of research. This research will need to include disciplines outside of biomedicine. Through developing the research tools and conducting the research, investigators have the opportunity to hear the narratives of leprosy patients and to experience different ways of seeing a health problem. The qualitative approach also questions whether it is possible or even appropriate to change patient behaviour or whether as health care professionals we should provide a service that suits their needs.

It should be stressed here that while social scientists and biological/medical scientists share an understanding of the word and concept of *quantitative* research, they tend to mean different things when they speak of *qualitative* research. For those in the medical tradition 'qualitative' tends to refer to data, which are measured on categorical scales—more than/less than, yes/no—and the values on these scales are represented by numbers. Social scientists, on the other hand, will refer to any research which does not use numbers to represent values as qualitative, 'presumably because the data, by their nature unenumeratable (*sic*), *should not* be counted'[3]. In this paper, we discuss a *qualitative* approach, which draws upon the principle that the kinds of information sought are not amenable to 'measurement' but can none the less be made intelligible.

In this paper, we explore some principles of qualitative research which address the social and economic consequences of leprosy and leprosy-related disability. We note some pitfalls to be wary of, and the opportunities using these methods and perspectives in programme-related operations research.

Background to qualitative methods

Qualitative approaches to research and intervention are well suited to explorations of the social and economic impact of disease and disability on individuals and communities. Qualitative approaches can also help in the development of appropriate and effective interventions to support programme activities of case detection, case holding and social and economic rehabilitation.

As efforts at active case finding and effective treatment of existing cases with multi-drug therapy continue apace and the overall numbers of active leprosy cases continue to fall, locating adequate numbers of patients to yield meaningful or 'significant' statistics will become more difficult. In matters concerning human wellbeing, the variables of importance are often poignantly identified through listening to people's stories. These variables are not always amenable to 'measurement'. In studies of *social impact*, one needs to know not only the extent and nature of the suffering of individual patients, but to have a comprehensive understanding of the broader social context in which that suffering occurs. Important lessons can be extrapolated from the stories of a carefully selected and relatively small number of informants, and data gleaned from rigorous and systematic qualitative research can provide a sound basis for planning and implementing effective and appropriate treatment and patient support.

Past uses of qualitative approaches in leprosy control

Qualitative research is not new to leprosy control. Past studies have included work on knowledge and attitudes, treatment-seeking and treatment compliance;[1,4–8] gender;[2,9,10]

beliefs and practices of leprosy patients;[11] socio-cultural responses to leprosy; stigma issues;[4,12–14] issues in social and economic rehabilitation[1,15] and the integration of leprosy control and primary health care.

Although intrinsically interesting, this type of research often looks primarily or exclusively at so-called 'traditional customs' or beliefs, leaves out rigorous investigation of important social structural factors and is not always useful or easily applied to policy and programmes. It can also lead researchers to make 'immodest claims of causality'[16] by masking the importance of structural inequalities. Rao *et al.*,[2] for example, note that among Indian women, 'lack of time, money and mobility are more often causes for poor treatment compliance among female (leprosy) patients' than are 'traditional customs'. The better sociological research articles are those which clearly and rigorously address the *cultural* dimensions of relevance, while placing these within their broader social-*structural* and/or political-economic context (for leprosy[1,2,17]). This orientation is discussed in detail below. Useful guidelines exist for assessing qualitative health research papers.[18–21]

A word (and a warning) about 'qualitative methods'

It may seem obvious that qualitative research methods are only as good as the scientists using them. An important weaknesses of much qualitative research has been the use of the *tools* without an understanding of the theoretical *principles* underlying and underpinning them.

A problem of this 'tool-orientation' relates to the recent proliferation of Rapid Assessment Procedures (RAPs). Known by their supporters as 'practical anthropology', RAPs have been used to gain community and target-group views about the causes of and cures for ill health. They are also used to assess people's reactions to specific interventions. A specific package of techniques has been designed, with the non-specialist in mind, to gain information about health-related beliefs and behaviours. As Scrimshaw and Hurtado[22] note, obstacles to the use of anthropological approaches and data within the health field have included the long periods normally spent in the field by anthropologists, and the collection of a large amount of theoretical material required within the discipline.

> 'Another', they write, 'has been that the theoretical concerns of anthropology have not been those of applied health or nutrition programmes. Although the ideal ethnography may be built from both of these elements, a great deal of practical, diagnostic, and applied work can be accomplished in a shorter time and by using a simpler approach.'

'Thus a built-in assumption of these methods is that they *leave the theory out*, relying instead on a user-friendly toolbox approach to rapidly investigating the sociological dimensions of illness and healing. As Manderson and Aaby[23] put it:

> '...It would be unrealistic to expect theoretically informed anthropological interpretations of social life or cultural issues when the data are collected by researchers without a background in the discipline, notwithstanding the technical skills that may be relatively readily acquired'.

A related problem arises when quantitative researchers employ qualitative tools *as if they were the same as quantitative tools*. Lacking knowledge about the principles of qualitative

research, these researchers subsequently get nervous with the small numbers required for conducting qualitative work, and the lack of 'measurement' employed. Thus the counter-productive attempt to *measure the unmeasurable* begins, producing data of questionable utility.

It is important that qualitative research carried out for leprosy is facilitated and analysed by those with social science training. There are key foundational principles that can be used by health professionals when conceiving a research project in relation to leprosy.

Some basic principles

From our perspective, the first of the 'basic orientations of qualitative methods' spelled out by Green and Britten[24] is the most important. They note that qualitative research is based on a commitment to 'naturalism': 'health behaviour' is understood in the context of everyday life. Illness and health are understood and approached differently by lay people than by practitioners. Lay people experience and react to illness in the context of their whole life, while the perspective of the epidemiologist, doctor or pubic health professional is narrowed by the requirements of scientific enquiry or clinical practice.[25] Health professionals see patients in terms of their illness, whereas the patient is managing the illness within a range of competing needs, priorities, expectations and social roles. Thus our research needs to look beyond the leprosy patient and his experience of illness to see how this experience is influenced by the household and community of that individual. His choices will be crucially framed and constrained by broader social and cultural structures.

Thus, it is important to enquire beyond the experiences of individual patients to address issues in the household and community. It is equally important to look at provision of care and support within the health and social services: what services are available, how they are used and why. Widening the scope still further, these services are themselves resourced and constrained by features in the national and international policy landscape, which may also need to be addressed.

A qualitative approach, therefore, understands the patient and their experience, choices and needs as being nested within many layers of context. The impact of disease and disability, the ability of the patient to adhere to therapy and the choices they makes in relation to advice given, will all be influenced by each layer that surrounds them. The simplest and most straightforward analogy would be of an onion: the innermost portion being the patient herself, each subsequent layer representing a dimension of context for the patient. Research can and should be conducted at each level to develop an understanding that is both comprehensive and useful for policy.

Methods: getting the whole picture

Throughout this paper we have used the term *qualitative approach* rather than *qualitative methods* for two reasons. Firstly we want to stress the importance of conceptual understanding in employing the tools. Secondly, is the point that within a qualitative approach it may be useful and appropriate to use *quantitative tools*. Rigorous and systematic research on health behaviour should employ a range of methods, held together within an overall framework that takes an essentially qualitative orientation (as described above and in Green and Britten[24]).

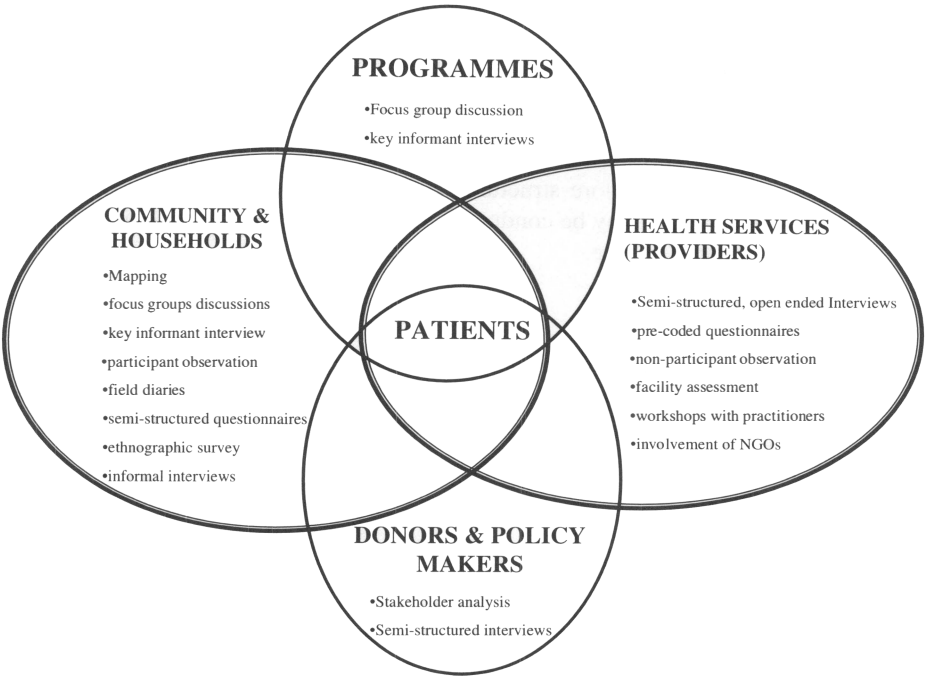

Figure 1. Structure of a qualitative approach

The key domains and methods, which can be employed in this research, are outlined below. While not intended as a *formula*, this outline can provide a guide to the approach advocated.

IN THE COMMUNITY

To understand the main resources and constraints to health in the community, mapping, focus group discussions (FGD) and key informant interviews can be undertaken.[24,26–28] Research teams need to ask: what are the aspects of this community that may influence the wellbeing of leprosy patients? Key questions in addition to mapping may include: *what are the main health problems in this area; what are the main sources of care; how do people normally seek treatment; what are the main constraints to health?* Participant observations may also be carried out through field diaries recording daily general information.

IN THE HOUSEHOLD

Household data may be useful: 1) to get more detail on socio-economic and demographic features of the community; 2) to understand approaches to treatment-seeking; and 3) to get further details on specific patient households. For the first and second domains, a semi-structured questionnaire may be appropriate (e.g. an ethnographic survey.[29] Informal interviews with members of specific patient households can also be carried out (see below).

AMONG PROVIDERS

Interviews can be carried out among the local providers. The aim is to learn who is treating leprosy patients, how these providers understand, diagnose and treat people with leprosy, the extent to which they refer patients on and what they charge for treatment. Normally a semi-structured, open-ended interview schedule is appropriate, although if there are many providers in the area a more structured pre-coded questionnaire may be employed. Non-participant observations may be conducted to get a further perspective on the treatment process at the key sources of care.

WITHIN THE PROGRAMME

If the research is to feed into programme operations, it is important to involve the programme at an early stage and to maintain their involvement. FGDs and/or key informant interviews with various cadres of programme staff may help researchers to identify problems and potential within the programme.

AMONG PATIENTS

Again, it is appropriate to combine methods. It may be useful to conduct some general interviews and observations at drug delivery points and take a sub-sample of those patients for further study. Gathering illness narratives through open-ended, in-depth interviews will be essential and it may be useful to obtain these narratives from a range of patients: those currently on treatment (with various levels of disability), those released from treatment, and those who have left treatment. Case studies can be conducted of a sub-sample of patients, ideally from each of the three categories above.[30]

AMONG POLICY MAKERS AND DONORS

While this level of analysis may seem abstract, in fact it is quite specific to the problems at hand. A policy or stakeholders analysis may enable the research team to identify potential barriers to uptake of recommendations and also the support for taking forward the changes or projects suggested.

Situating the central research questions about the impact of illness and disability on leprosy patients in their broader social context enables key nodes for intervention to be identified. Programmes based on research of this kind will not focus on changing patient behaviour, but will address specific changes within the health and social services which can be made to better support patients and communities in dealing with this disease and its repercussions.

Conclusions

The *qualitative approach* described provides an opportunity to ensure that the broader social, economic and environmental factors affecting people with leprosy are addressed in the provision of appropriate care. The approach also encourages research across disciplines and the inclusion of other important sectors like housing and education. This multi-disciplinarity and cross sectoral approach to infectious disease programmes is being increasingly encouraged to provide innovative means to addressing the control of infectious diseases like leprosy and tuberculosis.[31]

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Science Commentary

How *Mycobacterium leprae* infects peripheral nerves

VICTORIA H. FREEDMAN*, DAVID E. WEINSTEIN** & GILLA KAPLAN*

**Laboratory of Cellular Physiology and Immunology, The Rockefeller University, 1230 York Avenue, New York, NY 10021, USA*

***Departments of Neuroscience, Pathology and the Comprehensive Cancer Center, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, USA*

It has long been known that leprosy is an infection of the peripheral nerves. Even when only limited numbers of skin lesions are present and only small numbers of *Mycobacterium leprae* are found in the skin, the organisms preferentially localize to the peripheral nerves. Histologically, bacilli are seen in intracellular vacuoles of either myelinating Schwann cells[1] or in macrophages which have migrated from the blood into the perineural space. Infection of the nerves can result in chronic demyelination/remyelination, often leading to calcification and permanent loss of neural function.[2] Because of this, leprosy is the leading cause of non-traumatic peripheral neuropathy.[3] Although it is clear that the Schwann cells are the main targets of *M. leprae* infection, the molecular basis of this tropism, and how the organism gains entry into the nerve and then into the Schwann cells, was not known.

The field of leprosy research has now been excited by two recent papers by Rambukkana *et al.*[4,5] in which the investigators describe a molecular mechanism for the selective affinity of *M. leprae* for Schwann cells. The studies have identified a glycoprotein which binds to ('opsonizes') the surface of *M. leprae* which is in turn bound by a molecule on the Schwann cell surface (a 'receptor'), thereby providing a potential mechanism for internalization of the bacilli by Schwann cells.

The Schwann cell/axon unit of peripheral nerves is covered by a basal lamina (Figure 1) which consists of a number of extracellular matrix molecules, including laminins, type IV collagen, entactin/nidogen, and heparin-sulphate proteoglycans.[6,7] The laminins are glycoproteins composed of three chains, α, β, and γ. There are 11 distinct isoforms depending on the configuration of the chains. In the Schwann cell basal lamina of the peripheral nerve, the predominant form is laminin-2, which is composed of the $\alpha 2$, $\beta 1$, and $\gamma 1$ chains.[8] This configuration is not found in the central nervous system. In their first paper, Rambukkana *et al.*[4] showed that *M. leprae* binds specifically to the G-domain, which is located at the C-terminal end of the $\alpha 2$ chain of laminin-2.

Correspondence to: G. Kaplan

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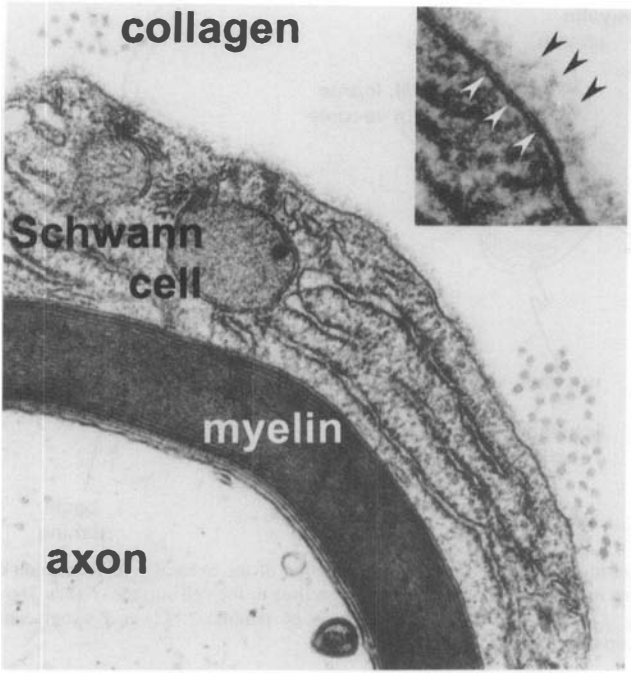

Figure 1. Electron micrograph of a myelinating Schwann cell/axon unit of a peripheral nerve. The axon surrounded by a myelin sheath of the Schwann cell is shown. On the surface of the cell the basal lamina can be seen. Collagen fibres (in cross section) are present in the extracellular space. The insert shows a higher magnification of the cell membrane (white arrowheads) covered by the basal lamina (dark arrowheads). Magnification × 36,400; insert, × 180,000.

Schwann cells express on their surface proteins which can mediate binding to components of the extracellular matrix of the basal lamina. α-Dystroglycan is one such protein.[9] The dystroglycans of Schwann cells are encoded in one transcript and then cleaved resulting in an extracellular portion, α-dystroglycan, and a transmembrane portion, β-dystroglycan. In the second paper, Rambukkana *et al.*[5] showed that *M. leprae* bound to the G domain of laminin-2, is in turn bound to α-dystroglycan on the Schwann cell surface. α-Dystroglycan bound to laminin-2/*M. leprae* is associated with the transmembrane molecule β-dystroglycan. At an intracellular binding site, β-dystroglycan binds to dystrophin, an intracellular protein which in turn binds to actin.[10] These four proteins (laminin-2, α-dystroglycan, β-dystroglycan, dystrophin) thus provide a bridge between *M. leprae* and the internal environment (the cytoskeleton) of the Schwann cell (Figure 2). Subsequent to binding on the cell surface of the Schwann cell, Rambukkana *et al.*[5] observed clustering of the α-dystroglycan/*M. leprae* complexes, which presumably leads to internalization of the bacilli into a cytoplasmic vacuole and establishment of Schwann cell infection.

This raises the question as to how *M. leprae* gains access to the peripheral nerve. It is likely that infected blood monocytes from broken skin or mucous membranes transport the bacilli into the naive nerve during the normal trafficking of macrophages through the peripheral nervous system. This type of trafficking occurs in all individuals, as a low, steady state monocyte exchange between nerves and blood.[11] However, in an *M. leprae* infected individual, it is possible that an infected macrophage might enter a nerve and be trapped

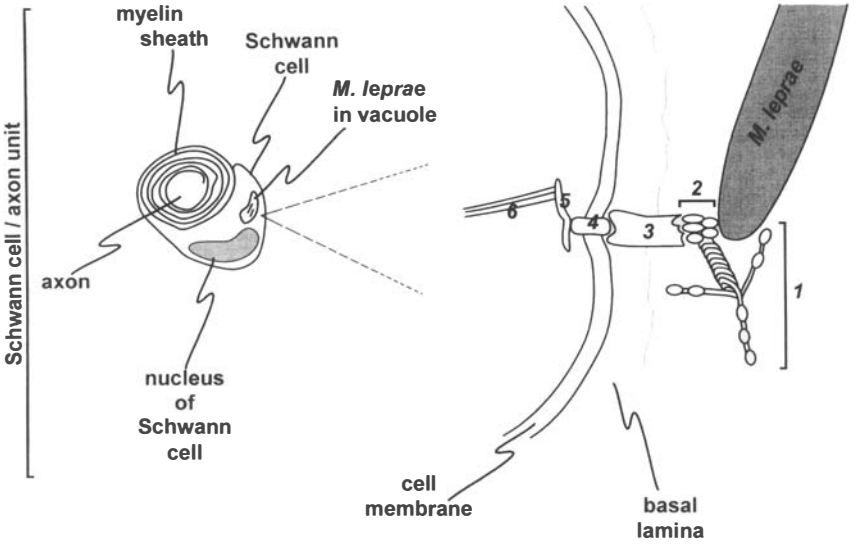

Figure 2. A schematic representation of *M. leprae* infection of the Schwann cell/axon unit (left) and an enlarged diagram of the proteins involved in the binding of the bacillus to the cell surface (right). The numbers in the figure denote the following: *(1)* laminin-2; *(2)* α-2G domain of laminin-2; *(3)* α-dystroglycan; *(4)* β-dystroglycan; *(5)* dystrophin; *(6)* actin cytoskeleton.

there. When the load of replicating organisms ultimately leads to destruction of the cell, the bacilli would be released into the endoneureal space. The mycobacteria would then be bound by laminin α-2, which would tether them to the α-dystroglycan on the surface of myelinating Schwann cells. Internalization would then occur. Infected Schwann cells would degenerate, increasing recruitment of macrophages into the nerve.[12] Because α-2 laminin and the α-dystroglycan are restricted to peripheral nerves, *M. leprae* infection would not occur in the central nervous system.

Leprosy has long-term sequelae, which persist despite successful antibiotic treatment and microbiological cure of the infection. In millions of individuals, intractable peripheral neuropathies ensue.[13] These complications are difficult to manage clinically, at least in part because we do not understand the underlying mechanisms of pathogenesis. Such understanding requires more research. Studies such as those reported by Rambukkana *et al.*[4,5] illuminate a mechanism of leprosy pathogenesis and may result in new interventions to treat and/or prevent nerve damage. Unfortunately, the perception that leprosy is no longer a significant disease has resulted in a virtual elimination of funding for leprosy research. The investigations described here, elucidating the molecular events of leprosy infection of peripheral nerves, illustrate the potential usefulness and importance of continuing research in leprosy.

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Nerve function impairment in leprosy: design, methodology, and intake status of a prospective cohort study of 2664 new leprosy cases in Bangladesh (The Bangladesh Acute Nerve Damage Study)

RICHARD P. CROFT*, JAN H. RICHARDUS**, PETER G. NICHOLLS+ & W. CAIRNS S. SMITH+
**The Leprosy Mission, Danish Bangladesh Leprosy Mission, Nilphamari, Bangladesh*
***Departments of Public Health, Erasmus University Rotterdam, The Netherlands*
+Department of Public Health, University of Aberdeen, Scotland, UK

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Summary The Bangladesh Acute Nerve Damage Study (BANDS) is a prospective cohort study designed to investigate epidemiological, diagnostic, therapeutic and operational aspects of acute nerve function impairment in leprosy. The study is based at a single centre in Bangladesh, in an area with a high prevalence of leprosy. The centre, Danish Bangladesh Leprosy Mission, has a well-established vertical leprosy control programme. In this paper, the study design and methodology are described, together with definitions of nerve function impairment (NFI) used in this and subsequent papers. The study recruited 2664 new leprosy cases in a 12-month period. The male:female ratio is 1·25:1, and 17·61% of the cohort are under 15 years of age. In all, 83·33% of the cohort are paucibacillary (PB), and 16·67% multibacillary (MB). However, the MB rate amongst males is 19·72%, and amongst females is 12·85%, despite an equal period of delay to diagnosis. 55% of patients presented for treatment within 12 months of developing symptoms. 6·12% of the total number of cases were smear positive, and 36·71% of the MB cases were smear positive. 9·61% of the total number of cases were graded as having World Health Organisation (WHO) disability grade 1, and 5·97% had grade 2. Amongst MB cases, 27·48% had WHO grade 1 disability present, and 18·24% had grade 2 present, compared with 6·04% and 3·51%, respectively, amongst PB cases. A total of 11·90% of the cohort had sensory NFI of any kind, and 7·39% had motor NFI. Ninety patients presented with NFI needing treatment (3·38%), and of these, 61 (67·78%) had silent NFI. MB patients had a prevalence of reaction/NFI needing treatment nearly 7 times higher than PB cases (15·32% amongst MB; 2·30% amongst PB), and males nearly double that of females (5·67% amongst males, 2·96% amongst females). The most

Correspondence to: R. P. Croft, 70 Culver Lane, Reading, RG6 1DY, UK. e-mail: richard@rcroft.demon.co.uk

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commonly affected nerve by function impairment was the posterior tibial (sensory) with 6·46% of nerves affected (9·38% of patients), followed by the ulnar nerve with 3·23% of nerves impaired (5·56% of patients). Future research and publications, building on this foundation, will focus on the following areas: the incidence of NFI and reactive events, the risk factors for developing NFI, and the response to treatment of patients developing acute NFI.

Introduction

Although leprosy is known primarily as a skin disease, it is nerve damage and the resulting disabilities that set the disease apart in people's minds. It is accepted that leprosy control programmes should include both the provision of chemotherapy as well as activities to actively prevent the occurrence of impairments. Understanding of the process and epidemiological patterns of nerve function impairment (NFI) in leprosy is essential for the development of methods to predict, detect and manage this problem.

There are still many difficulties and unsolved problems concerning nerve function impairment.[1] In the first place, definitions and diagnosis of NFI in leprosy have not been consistent. Early detection is essential for the successful treatment of NFI and more understanding is needed of risk factors and the reasons for diagnostic delay. In addition, applicable methods for early detection under field conditions are limited and are often not properly validated.

Epidemiological investigations have usually been limited to certain causes of NFI (e.g. type I and type II reaction), and are often retrospective and hospital based,[2–6] with some exceptions.[7,8] Van Brakel[2] has drawn attention to the absence of any prospective studies designed to establish the incidence rates of the various leprosy reactions.

Since knowledge of NFI is so fragmented, a systematic research programme was initiated in a well-established leprosy control programme in a highly endemic area of Bangladesh.[9] The programme is called the Bangladesh Acute Nerve Damage Study (BANDS), and its objective is to study the epidemiological, diagnostic, therapeutic and operational aspects of (acute) NFI in detail by means of a prospective cohort study of newly diagnosed leprosy patients. This paper explains the objectives, study design, research questions, definitions, and data procedures of BANDS, and describes the cohort of leprosy patients at the time of recruitment into the cohort.

Definition and concept of NFI

Although this study received the acronym BANDS, with 'ND' standing for nerve damage, the more correct nomenclature is nerve function impairment, or NFI. This follows the International Classification of Impairments, Disabilities and Handicap (ICIDH) as recommended by the WHO.[10] In ICIDH 'impairment' is defined as 'any loss or abnormality of psychological, physiological, or anatomical structure or function'. 'Nerve function' in this study refers to the sensory, motor and autonomic function of peripheral nerve trunks. In BANDS, nerve function is assessed by testing the functioning of innervated organs such as muscles and sensory mechanoreceptors, rather than the nerve fibres themselves. NFI is thus

defined as 'clinically detectable impairment of motor, sensory or autonomic nerve function'. The level of impairment that is clinically detectable depends on the sensitivity of the instrument or method of testing used. It does not include impairment of nerve conduction that is only detectable by electrophysiological means. Finally, 'acute' (or recent) NFI is defined as NFI of up to and including 6 months duration. Autonomic function is not easily tested by clinical means alone, and therefore plays no practical role in the detection of NFI in this study.

Various underlying aetiological processes lead to nerve function NFI in leprosy patients. These are recognized as separate clinical entities, including reversal (or type 1) reaction and erythema nodosum leprosum (ENL or type 2 reaction). However, even in the absence of signs and symptoms of leprosy reactions, NFI can develop within a relatively short time span. This is usually referred to as 'silent neuropathy'[4] or 'silent neuritis'[11] or 'quiet nerve paralysis.[12] A problem sometimes encountered in leprosy control is that the indication to treat NFI with corticosteroids is based on the clinical picture of leprosy reactions, and that this treatment is restricted to severe cases that are admitted to hospital. The intention of treatment is sometimes to reduce symptoms such as fever, pain, and oedema, and not necessarily to prevent permanent NFI. This is perhaps less the case nowadays, since the publication of several papers in the 1990s that highlighted the need for field-based corticosteroid treatment to be available for patients, not necessarily prescribed by a doctor, and more focused on NFI.[6,13,14] However, the message that the focus of managing leprosy patients should be on the condition of their peripheral nerves remains one of central importance. Nerve function needs to be assessed regularly to detect (often insidious) changes accurately from month to month and respond with appropriate therapy. Both diagnosis and treatment of NFI need to be simple and feasible at field level.

From this operational perspective, NFI has been taken as the outcome indicator for the prospective cohort study introduced in this paper. The focus is thus primarily on the *nerve*.

Study design

BANDS is a prospective cohort study. It is based within the routine activities of a well-developed vertical leprosy control programme. New leprosy cases were enrolled continuously over a 12-month period. The patients were treated with multidrug therapy (MDT) as recommended by WHO, and are being followed up for a period of 3 years in the case of paucibacillary (PB) patients and 5 years for multibacillary (MB) patients from the date of registration. During the follow-up period, patients are being assessed regularly for the presence of specific risk factors and monitored for any development of signs and symptoms of acute NFI during and after leprosy treatment. The treatment of acute NFI is according to fixed regimens in the field, with severe and complicated cases referred to hospital.

Cohort size

It was estimated that a total sample of 2000–3000 new leprosy patients would enable the detection of significant associations between acute NFI and the most important risk factors.

Risk factors under study

- Leprosy grouping (paucibacillary, multibacillary)
- Leprosy classification (Ridley–Jopling)
- Skin smear result
- Skin lesion count
- Anti-leprosy treatment
- Age
- Sex
- Duration of symptoms before diagnosis
- Existence of nerve function impairment at time of diagnosis
- Nerve enlargement
- Leprosy reaction
- Mode of detection
- Distance to clinic
- Chronic disease status (e.g. diabetes, TB)
- Physical trauma/surgical operation

Description of the control programme

The study is based at the Danish Bangladesh Leprosy Mission (DBLM) in Nilphamari, north-west Bangladesh. The project, which started in 1977, is presently administered by The Leprosy Mission (TLM). The area has the highest prevalence of leprosy in the country[9] with a case detection rate in 1996 of 5·7 per 10,000 population. DBLM is responsible to the Government of Bangladesh for administering a leprosy control programme covering the four northern districts of Nilphamari, Rangpur, Thakurgaon and Panchagar. The population according to the 1991 Census is 5,529,600 and the area covered is 7163 square kilometres.

Bangladesh is a flat, riverine delta with a monsoon climate. The population is primarily rural (> 80%). Communications are good, with roads of reasonable standard reaching remote areas. This ease of communication makes it relatively uncomplicated for patients to attend clinics and for field staff to trace defaulters. The leprosy control activities in the four districts are administered by four Leprosy Control Officers (LCOs) who relate to a medically qualified Field Director. Leprosy Control Supervisors (LCSs) supervise activities at sub-district or 'thana' level, with Leprosy Control Assistants (LCAs) at grassroots level. Fifty to 60 clinics operate in the project area, at least monthly but often more frequently. There are over 100 field staff at different levels. Each clinic is attended by a LCS, LCAs, a Physio-technician and a Footwear Technician. Day to day management of leprosy patients is largely the responsibility of the LCS who confirms diagnosis, starts MDT, and in collaboration with the Physio-technician, may start prednisolone in the field for patients with reactions or acute NFI.

Recruitment and admission procedures

SELECTION OF THE PATIENT

Inclusion criteria

- All newly diagnosed and previously untreated leprosy patients living in the leprosy control area, with or without acute nerve damage.

- Newly diagnosed but previously treated leprosy patients living in the leprosy control area with a past history of incomplete DDS monotherapy or WHO-MDT.

Exclusion criteria

- Leprosy patients living outside the leprosy control area.
- Relapse cases.

INITIAL ASSESSMENT OF PATIENT

History

- Previous personal history and past treatment of leprosy.
- Duration of leprosy symptoms.
- Risk factors for acute NFI.
- Detailed clinical examination.

Skin

- Number and location of lesions.
- Type of lesion.
- Anaesthesia in lesions.
- Signs of inflammation in lesions (heat, erythema, swelling, pain).
- Oedema of hands/feet.

Nerves

- Systematic palpation of the following nerves: facial, radial, ulnar, median, lateral popliteal, posterior tibial. The degree (and score) of enlargement is recorded as follows: no enlargement (0); slightly enlarged (1); moderately enlarged (2) and very enlarged (3). Other cutaneous nerves (e.g. radial cutaneous, supraorbital, sural) are also palpated and the presence of enlargement recorded on the body chart. This is helpful in the diagnosis of leprosy, but in BANDS only the enlargement of the six main truncal nerves was recorded for analysis.
- Check for pain, tenderness and enlargement. The recording and scoring system is given in Table 1.

Table 1. Nerve pain recording and scoring system

Definition	Score
No pain or tenderness	0
Slight pain complaint only/tender on pressure	1
Painful at work, sleep not disturbed	2
Pain disturbs sleep	3

Nerve function tests

Sensory testing (ST)

- Sensory testing of the palms of the hands and soles of the feet is routinely carried out at every clinic visit by LCAs. Any abnormality is referred to the Physio-technician and LCS. Testing is carried out using a ball-point pen, as described by Jean Watson[15] at 12 standard points on each palm, and on 11 points on the soles. On the palm, five points are taken as supplied by the ulnar nerve and seven for the median (see Appendix 1).

Corneal sensory testing

- Each patient is observed whilst being examined to see whether blinking is normal. If so, no further testing is done. If blinking is less than 5 per minute, sensation is directly tested by applying a thin twist of clean cotton wool to the cornea whilst the patient looks up. Absence of involuntary blink response (in addition to the low blink rate already observed) is taken to be indicative of corneal anaesthesia.

Motor testing

- Motor testing is also carried out by trained Physio-technicians on every patient at every clinic visit, using a modified 5-point MRC scale (Table 2).[16] Muscle movements that are routinely tested for by means of a 'quick muscle test' (QMT) are shown in Table 3. Patients with abnormalities undergo a more detailed assessment by a Physio-technician, but the decision to treat is usually based on the QMT.

Wounds and deformities

- Presence of ulcers on palms or soles; size; presence of infection.
- Presence of visible deformities e.g. claw hand, drop foot, etc.

Skin smears

Skin smears are normally taken from one ear lobe and the edges of two active lesions (or both sides of one lesion if only one is present). In cases where skin lesion edges cannot be clearly discerned (i.e. LL, PN cases) smears are taken from both ear lobes and the forehead. Reading takes place at one of the two laboratories, in Nilphamari or Thakurgaon.

Table 2. Modified 5-point MRC scale for muscle strength scoring

Hands and feet	MRC grade	Eyes
Full ROM[1], full resistance	5	Normal muscle strength
Full ROM[1], reduced resistance	4	Closes, stays closed against some resistance
Full ROM[1], no resistance	3	Closes fully on strong closure, no resistance (may be gap on gentle closure)[2]
Reduced ROM[1], some joint movement	2	Gap on strong closure[2]
Flicker only	1	Flicker only
Full paralysis	0	Complete paralysis

[1]ROM: range of movement.
[2]In addition, lid gap in mm is measured and recorded.

Table 3. Movements/muscles tested (quick muscle test, QMT)

Nerve	Movement	Muscle/muscle group
Ulnar	Little finger abduction	Abductor digiti minimi
Median	Thumb abduction	Abductor pollicis brevis
Radial	Wrist extension	Wrist extensors
Lateral popliteal	Foot dorsiflexion	Foot dorsiflexors
Facial	Closes eyes (strong and gentle closure tested)	Orbicularis oculi

Diagnosis of leprosy

Leprosy was diagnosed when at least one of the following criteria was present:

- Hypopigmented or erythematous skin lesions with reduced or absent sensation.
- Enlarged nerves with or without NFI.
- Acid fast bacilli of characteristic appearance in skin smears.

Classification of leprosy

Patients were classified for treatment purposes as MB or PB according to the national guidelines used in Bangladesh.[17] These guidelines classify as MB those cases where the total number of skin patches and palpably enlarged nerves ('nerve lesions') is 10 or more and/or the skin smear is positive; and they classify as PB those cases where the total number of skin patches and nerve lesions is less than 10 and which are smear negative. An analysis of the BANDS database has shown that this system of classification produces results very similar to the more conventional 'WHO system' which uses a skin lesion count only to classify into PB and MB (<6 skin patches PB; ≥ 6 patches MB.[18] In addition, leprosy cases are routinely classified clinically according to the scale described by Ridley and Jopling,[19] adding the indeterminate (I) and pure neural (PN) groups included by some other classification systems such as the Indian.[20]

Treatment

All patients have been treated according to WHO guidelines for MDT current at the time of the study: PB cases: rifampicin 600 mg supervised dose, DDS 100 mg daily, total 6 months treatment; MB cases: rifampicin 600 mg and clofazimine 300 mg supervised dose, DDS 100 mg daily and clofazimine 50 mg daily, total 24 monthly doses. This dose regimen is used for all normal-sized adults; lower doses for small adults and children are given as described in the Bangladesh national treatment guidelines.[17]

FOLLOW-UP

The follow-up period starts at registration and continues for 3 years in PB cases and 5 years in MB cases. The frequency of assessment varies according to the patient's treatment status, 'released from treatment' (RFT) patients being followed up less frequently. Each assessment includes the following: (1) examination of skin and nerves; (2) nerve function tests

(ST/QMT); (3) identification of specific risk factors; and (4) appropriate health education advice for regularity of MDT, complications of leprosy, side effects of treatment and self care for prevention of disability. All tests and assessments are carried out blind of previous tests and field staff actively follow up defaulting cases as a normal part of their work.

ACUTE NERVE FUNCTION IMPAIRMENT/REACTION

All patients are instructed to report to the clinic (in addition to routine follow-up visits) if they develop any signs and symptoms of reaction/NFI such as:

- Change in appearance of skin lesions
- New skin lesions
- Pain
- Weakness
- Paraesthesia/anaesthesia

They will be examined by an LCS and a Physio-technician who will diagnose any reactive phenomena and give treatment according to the DBLM treatment guidelines.[21] This will usually be given in the field, but serious cases are referred to hospital for more intensive management.

Follow-up of acute nerve function impairment

Patients receiving prednisolone in the field according to the DBLM treatment guidelines are assessed weekly at home or in the clinic by field staff for the first month, and fortnightly thereafter. Assessment includes sensory and motor testing, and checking for drug compliance and side effects. Any complications are immediately referred to the supervisor, who may decide to admit the patient to hospital.

Definitions of acute nerve function impairment and reactive treatment events

At the time of the study start-up, the criteria used to define acute NFI and reactive events was that used in the DBLM treatment guidelines.[21] In summary, this system defined a 'reactive event' (i.e. NFI/reaction requiring treatment using prednisolone in therapeutic doses) as follows: a patient in whom the *sum* of sensory, motor, nerve pain and skin scores was ≥ 2, and where the duration of the score was 6 months or less. The scores could be generated from *any* nerves, and could be added between nerves and modalities (e.g. left ulnar sensory score + right facial motor score). However, as the study progressed, the study group decided that this system was over-sensitive. Further, it was felt that it was not logical to add scores between different nerves and modalities to arrive at a composite score. As a result, the group adopted the criteria given in Tables 4(a) and (b) to define NFI/reactive events requiring treatment. Importantly, NFI is defined as a reduction by ≥ 2 in the motor or sensory score of *any one nerve only*, with no summation of scores between nerves or modalities. These definitions were developed from another major study, the Trials in Prevention of Disability currently running in Bangladesh and Nepal.

Since all nerve test scores are stored in the database, prevalences of NFI can be generated

Table 4. (a) Definitions of NFI and reactions used in analysis

Term used	Definition
Nerve function impairment (NFI)	*Sensory:* Reduction by ≥ 2 points in the sensory distribution of any one nerve *Motor:* Reduction by ≥ 2 in the MRC grade of the movement tested of any one nerve
Partial nerve function impairment (partial NFI)	*Sensory:* Reduction by 1 point in the sensory distribution of any one nerve *Motor:* Reduction by 1 in the MRC grade of the movement tested of any one nerve
Severe nerve pain	Score of ≥ 2 in the pain score of any one nerve
Mild nerve pain	Score of 1 in the pain score of any one nerve
Type 1 reaction	Inflammation of skin lesions characterized by swelling, erythema, local heat and tingling or pain. It may be accompanied by nerve function impairment
Type 2 reaction	Reaction occurring in lepromatous cases only characterized by painful skin nodules (erythema nodosum leprosum, ENL), fever, and sometimes other organ involvement: lymphadenitis, orchitis, iridocyclitis. In addition, nerves may be involved with nerve pain/tenderness or nerve function impairment

(b) Criteria for defining a treatment event

- Sensory NFI in any one nerve
- Motor NFI in any one nerve
- Nerve pain (severe) in any one nerve
- Type 1 or 2 reaction
- Composite score of partial sensory or motor NFI + mild nerve pain in the same nerve

In this system, scores cannot be added between different nerves or different modalities except in the single case of partial NFI and mild pain in the same nerve.

using any criteria, and the revised definitions are used in all analysis. However, patient management was affected by this change. In subsequent papers describing the incidence of NFI and response to treatment, this will be examined more closely.

Data collection and analysis

Data relating to patients has been collected in a routine way using standard DBLM registration cards, treatment sheets and nerve function testing sheets. In addition, a special BANDS data form has been introduced to enable monthly follow-up data and questions relating to risk factors to be recorded.

A special relational database computer program was written using Microsoft FoxPro 2.6 for Windows. The process of data audit began early on during patient enrolment. Simple quality check programmes were developed using Epi Info software. Besides this, a full clinical audit was undertaken of the records of all patients considered to be at risk of developing a leprosy reaction (MB patients, any patient who had a reactional episode, and any patient with nerve function impairment at registration).

Description of the cohort at intake

Recruitment for the BANDS cohort was started in April 1995 and completed after 12 months of intake. The number of patients in the BANDS cohort is 2664. Figure 1 shows the distribution of patients according to 5-year age bands, and sex. There are a total of 1481 males and 1183 females included (M:F ratio 1·25). Of all patients, 469 (17·61%) are children (age < 15 years).

Table 5 summarizes the number of patients according to the PB/MB and Ridley–Jopling classifications, and according to bacteriological index (BI). 83·33% are classified as PB, and 16·67% as MB leprosy. Of the MB cases, 36·71% are skin smear positive. Table 6 shows the breakdown by sex and leprosy group. The proportion of males with MB leprosy (19·71%) is 53% higher than that amongst females (12·85%).

Figure 2 shows the duration of symptoms before diagnosis, registration and treatment with MDT among patients in the cohort. Just over half of all patients (55%) reported having noticed symptoms up to 1 year before registration. The remaining patients reported having symptoms for more than a year, with 18% having symptoms for over 3 years.

Table 7 summarizes the number of patients with WHO disability grading 0, 1 and 2, broken down by sex and leprosy group. A total of 2249 (84·42%) had no disability at intake. 9·61% had disability grade 1, and 5·97% had grade 2. Both grade 1 and 2 disability prevalences in males are almost double those in females. Disability rates are 4–5 times higher amongst MB cases compared with PB.

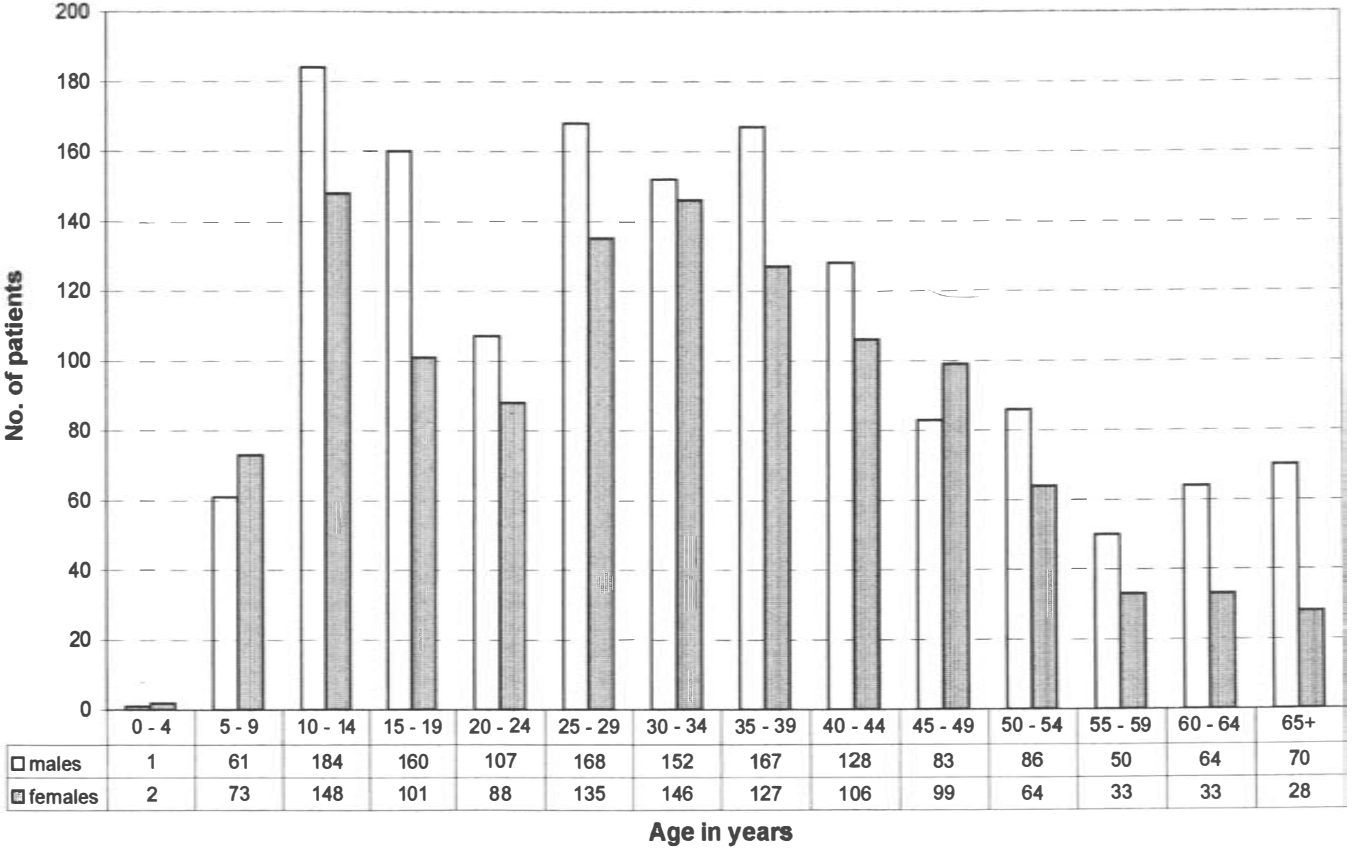
Table 8 and Figure 3 show the number of nerves with sensory and motor NFI at registration. This includes nerves with both acute and longstanding NFI. The posterior tibial is the most frequently affected nerve with 6·46% affected (9·38% of patients), followed by the ulnar with 3·23% of nerves affected by either sensory or motor NFI (5·56% of patients).

Table 9 shows the presence of acute NFI/reactive events at the time of registration. The definitions used are strictly those presented in Table 4. Ninety patients (3·38%) had acute NFI at registration, of whom 61 (67·78%) were patients with no other signs (i.e. silent neuritis).

Three hundred and sixteen patients had sensory NFI present at registration (11·90%). Amongst MB patients 166 (37·39%) were sensory impaired, but only 150 (6·76%) of PB patients were sensory impaired. One hundred and ninety-seven patients had motor NFI present at registration (7·39%). Amongst MB patients, 92 (20·72%) were motor function impaired, and 105 PB patients had motor NFI present (4·73%). A total of 381 patients had sensory and/or motor NFI present (14·30%), 181 amongst MB patients (40·77%) and 200 amongst PB patients (9·01%).

Discussion

Since it is nerve damage which is the cause of most deformity and consequent disability, handicap and stigmatization, NFI is the principal outcome measure of the study. The objective of the study is to describe accurately the associations of NFI with the risk factors under observation so that patients at risk of developing NFI can be identified. The study is field-based and all the techniques used for measuring NFI were already being used in the control programme, and in the routine work carried out for all leprosy patients at every



	0 - 4	5 - 9	10 - 14	15 - 19	20 - 24	25 - 29	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	65+
□ males	1	61	184	160	107	168	152	167	128	83	86	50	64	70
▨ females	2	73	148	101	88	135	146	127	106	99	64	33	33	28

Figure 1. BANDS intake cohort-age/sex distribution.

Table 5. Leprosy group, Ridley–Jopling classification and bacteriological index of BANDS cohort

	Classification				Bacteriological Index					
Ridley–Jopling	PB	MB	Total		Unknown	0	≤3+	≥4+	Total BI + ve	
I	49	0	49	1·84%	1	48	0	0	0	0·00%
TT	263	0	263	9·87%	4	259	0	0	0	0·00%
BT	1801	286	2087	78·34%	21	2040	26	0	26	1·25%
BB	1	17	18	0·68%	1	13	3	1	4	22·22%
BL	0	84	84	3·15%	0	0	30	54	84	100·00%
LL	0	51	51	1·91%	0	2	6	43	49	96·07%
PN	106	6	112	4·10%	1	111	0	0	0	0·00%
Total	2220	444	2664		28	2473	65	98	163	
	83·33%	16·67%	100·00%	100·0%	1·05%	92·83%	2·45%	3·68%	6·12%	

clinic attendance. Thus, it is hoped that the results will be applicable to leprosy control programmes.

DBLM has been using the ballpoint pen test (BPT)[15] for sensory function testing for many years before starting the study, and this method of testing was continued for BANDS. The BPT is advocated on the grounds that is cheap and readily available, and criticized on the grounds that the force applied may vary considerably and therefore the results are likely to be unreliable.[22] Also, since it is a threshold (yes/no only) test it relies on a count of the number of sites at which gross sensation is lost to provide an indication of the level of sensory loss. On the other hand, graded monofilament testing (as described by Bell-Krotoski[23]) is advocated on the grounds that the results are reliable, since the force required to bend the accurately manufactured monofilaments is relatively constant and repeatable,[24] and since they are a graded test they provide a quasi-quantitative estimate of sensory loss. The monofilament test is sometimes criticized on the grounds that the monofilaments used are less easily available, and too 'technical' and time-consuming for widespread use. Lienhardt, Currie and Wheeler carried out inter-observer testing using BPT, monofilament and voluntary muscle testing (VMT) in Ethiopia.[25] They found a 32–58% agreement using monofilaments with a weighted kappa (κ_w) statistic of 0·736–0·814, indicating good agreement ($\kappa_w \geq 0{\cdot}60$ indicates good agreement) and an agreement of 71–84%, κ_w 0·604–0·793 with the BPT. In an inter-observer reliability test recently carried out at DBLM, the κ_w for BPT was 0·86, and for monofilaments was 0·92.[26] Both these studies confirm that BPT can be adequate for study purposes. However, since the test is less sensitive than monofilament testing, the prevalence of SNFI detected by BPT will be an comparative underestimate. A cohort of sufficient size

Table 6. Sex and leprosy group

Sex	PB		MB		Total	
Male	1189	80·28%	292	19·72%	1481	55·59%
Female	1031	87·15%	152	12·85%	1183	44·41%
Total	2220	83·33%	444	16·67%	2664	100·00%

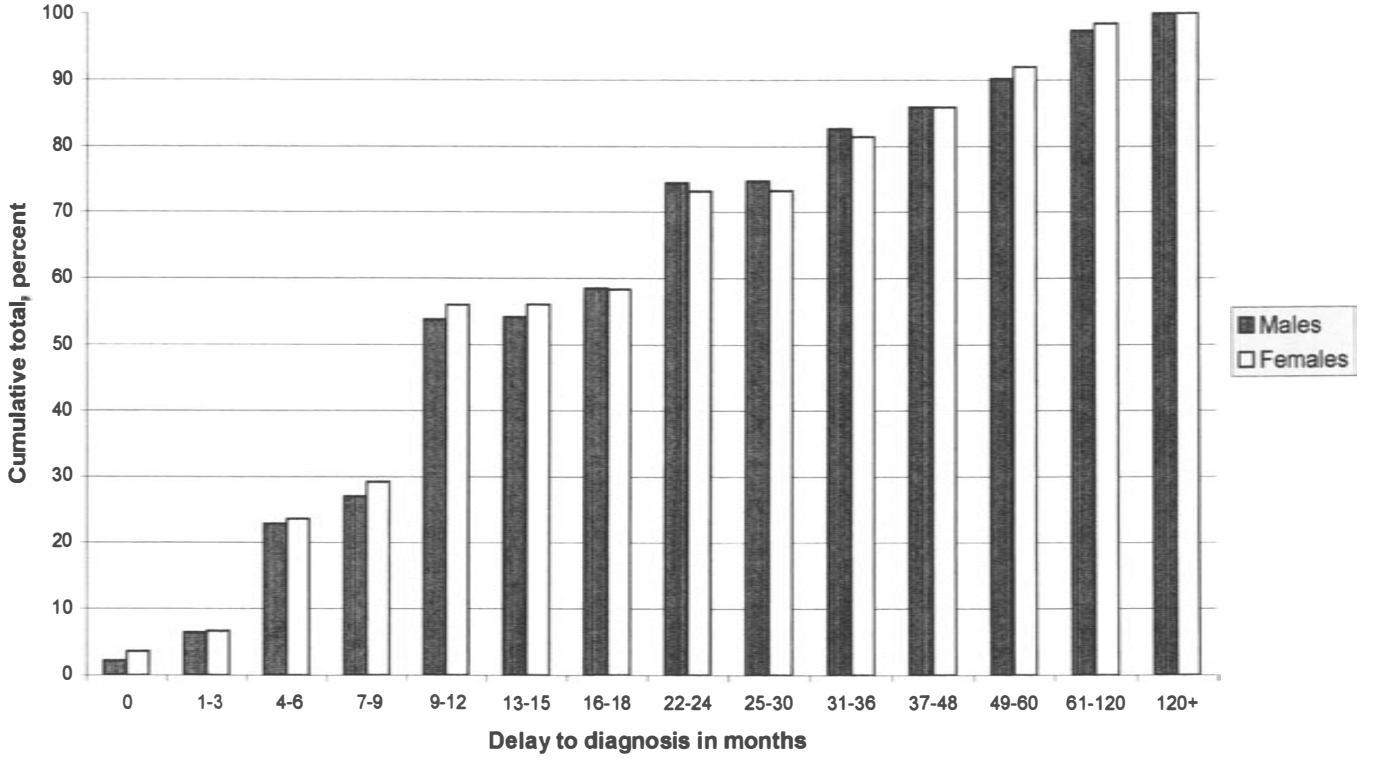


Figure 2. Bar graph showing delay to diagnosis by sex amongst patients in the BANDS cohort.

Table 7. WHO disability grades by sex and leprosy group

Disability grade	Males		Females		MB		PB		Total	
0	1196	80·76%	1053	89·01%	241	54·28%	2008	90·45%	2249	84·42%
1	174	11·75%	82	6·93%	122	27·48%	134	6·04%	256	9·61%
2	111	7·49%	48	4·06%	81	18·24%	78	3·51%	159	5·97%
Total	1481	100·00%	1183	100·0%	444	100·00%	2220	100·00%	2664	100·00%

(2664) was recruited to achieve the aims of the study. The male:female ratio is 1·25, while the true sex ratio in the community is 1·05:1. The relatively high child rate (17·61%) is similar to rates obtained in other parts of Bangladesh, and reflects in part a continuing high level of transmission of *M. leprae*, and in part the operational emphasis on school health education programmes and surveys carried out by the field staff.

Table 8. Nerve function impairment at intake by nerve (5328 of each nerve)

		Sensory NFI		Motor NFI		Sensory or motor NFI	
Nerve	Side	Nerves involved	% nerves involved	Nerves involved	% nerves involved	Nerves involved	% nerves involved
Facial	R			22	0·83	22	0·83
	L			20	0·75	20	0·75
	R + L			42	0·79	42	0·79
	R or L			32	1·20	32	1·20
Ulnar	R	65	2·44	77	2·89	92	3·45
	L	59	2·21	61	2·29	80	3·00
	R + L	124	2·33	138	2·59	172	3·23
	R or L	106	3·98	123	4·62	148	5·56
Median	R	51	1·91	21	0·79	56	2·10
	L	54	2·03	22	0·83	61	2·29
	R + L	105	1·97	43	0·81	117	2·20
	R or L	86	3·23	38	1·43	97	3·64
Radial	R			2	0·08	2	0·08
	L			3	0·11	3	0·11
	R + L			5	0·09	5	0·09
	R or L			4	0·15	4	0·15
Lateral popliteal	R			27	1·01	27	1·01
	L			36	1·35	36	1·35
	R + L			63	1·18	63	1·18
	R or L			58	2·18	58	2·18
Posterior tibial	R	168	6·31			168	6·31
	L	176	6·61			176	6·61
	R + L	344	6·46			344	6·46
	R or L	250	9·38			250	9·38
Any	R	213	8·00	120	4·50	255	9·57
	L	214	8·03	108	4·05	255	9·57
	R + L	427	8·01	228	4·28	510	9·57
	R or L	316	11·90	197	7·39	381	14·30

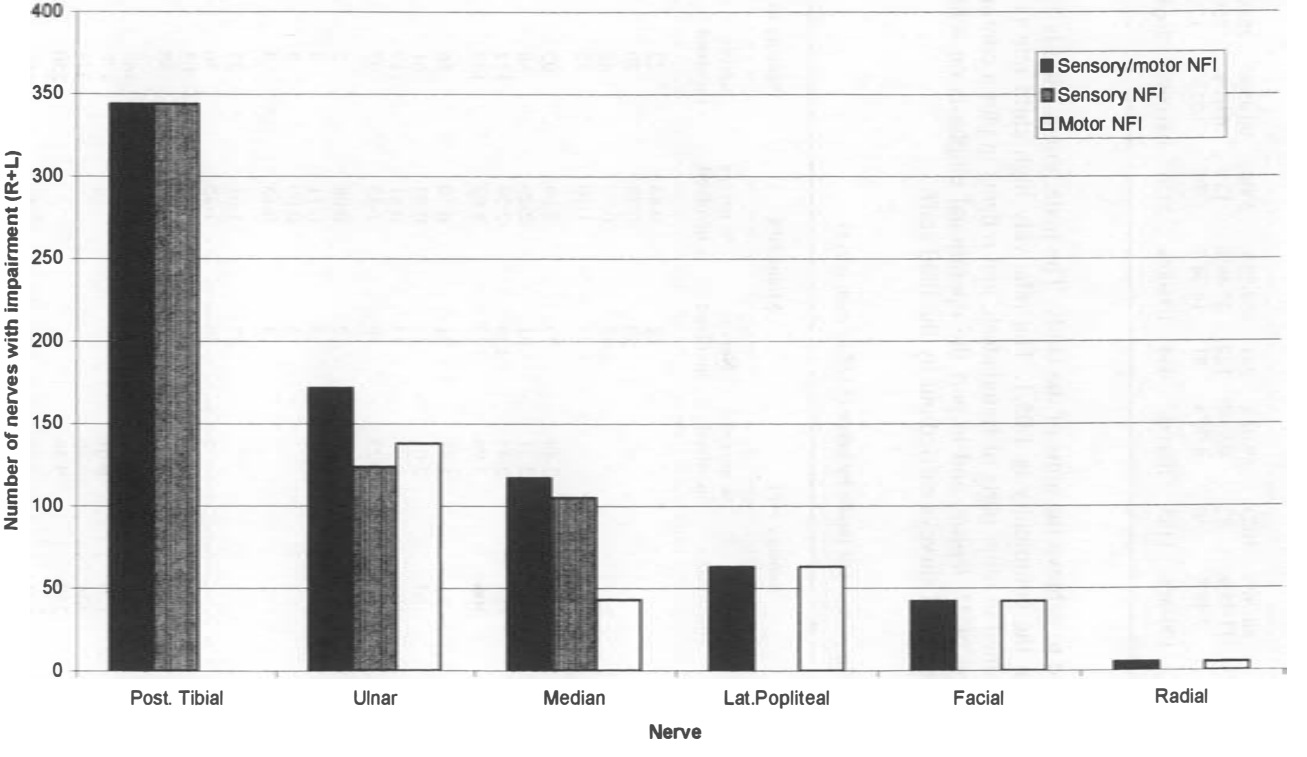


Figure 3. Graph showing number of nerves with impairment of function amongst cohort, by nerve.

Table 9. Acute reactive/NFI events at intake amongst BANDS cohort patients

Non-specific terminology of NFI/reaction	Specific terminology of NFI/reactions	Male	Female	MB	PB	Total (specific terminology)	Total (non-specific terminology)
Neuritis	NFI only (silent neuritis)	45	16	25	36	61	64
	NFI + nerve pain	0	1	1	0	1	
	Nerve pain only	0	0	0	0	0	
	Partial NFI + mild nerve pain	0	2	1	1	2	
Type 1 reaction	Type 1 + NFI	15	7	16	6	22	52
	Type 1 + NFI + nerve pain	4	1	3	2	5	
	Type 1 + nerve pain	2	0	1	1	2	
	Type 1 + partial NFI + mild nerve pain	0	0	0	1	0	
	Type 1 only	15	8	18	4	23	
Type 2 reaction	Type 2 + NFI	1	0	1	0	1	3
	Type 2 + nerve pain	0	0	0	0	0	
	Type 2 only	2	0	2	0	2	
Total cases with any reaction or NFI		84	35	68	51	119	119
Total		1481	1183	444	2220	2664	
Any reaction/NFI prevalence		5·67%	2·96%	15·32%	2·30%	4·20%	
95% confidence intervals		(4·57–7·01)	(2·10–4·14)	(12·16–19·08)	(1·73–3·03)	(3·73–5·34)	
Total cases with NFI		65	25	46	44	90	
NFI prevalence		4·39%	2·11%	10·36%	1·98%	3·38%	
95% confidence intervals		(3·43–5·52)	(1·40–3·15)	(7·76–13·67)	(1·46–2·68)	(2·74–4·16)	

The high proportion of PB cases (83·33%) probably reflects the success of the programme at early case finding, a notion supported by the finding that the majority of cases (73·8%) report duration of symptoms as no longer than 24 months at the time of diagnosis. It is interesting that the MB proportion amongst males (19·71%) is 53% higher than that amongst females (12·85%). This does not represent a greater delay to diagnosis amongst men, since Figure 2 shows that the delay to diagnosis amongst males is almost the same as that amongst females; maybe the disease develops more rapidly in males.

The classification by Ridley–Jopling shows another weakly bimodal distribution with very high numbers of BT/TT patients, and another much smaller peak of BL patients. A similar kind of distribution was also found in other cohorts in Nepal and India.[2,4,27,28] The proportion of pure neural leprosy (4·20%) is significant, although it is much less than the 18% described by Noordeen from India.[29] Overall, the smear positive rate amongst the cohort is low (6·12%), but it is still a considerable rate amongst MB cases (36·71%). Out of all the 163 smear positive cases, the majority (98/163, 60·12%) had a high BI of >3+.

The WHO grade 2 disability (visible deformity, lagophthalmos with diminished visual acuity) prevalence among new cases is low at 5·97%, indicating again that the programme is successful at early detection of cases. There is a greater number with grade 1 disability (anaesthesia, lagophthalmos with normal vision) who are at potential risk of secondary damage. (It should be noted that the most recent definition of grade 2 disability in eyes includes all lagophthalmos under grade 1[30]). MB cases show a markedly higher disability rate, 45·72% having either grade 1 or 2 compared to 9·55% amongst PB cases. Males show a WHO disability rate almost double that of females (grade 1, females – 6·93%; males – 11·75%; grade 2, females – 4·06%; males – 7·49%). This is in line with the higher proportion of MB cases amongst men and the higher prevalence of nerve damage amongst MB cases.

A total of 11·90% of the patients had sensory NFI of any kind, and 7·39% had motor NFI of any kind. This was rather less than van Brakel's findings with a cohort of new patients registering at a hospital in Nepal (29% sensory impaired, 24% motor impaired).[4] Analysis by nerves affected shows an interesting ranking order, with the posterior tibial clearly the most commonly affected (6·46% of nerves), followed by the ulnar with 3·23% of all nerves affected. Other nerves followed in this order: median (2·20%), lateral popliteal (1·18%), facial (0·79%) and radial (0·09%). This was very similar to the ranking found by Richardus and others in a retrospective cohort study carried out at DBLM,[6] although palmar sensory loss was not divided into ulnar and median nerve distributions, and numbers presented were of patients affected, and not nerves.

The proportion of patients presenting in reaction or neuritis requiring treatment with prednisolone was 4·20% of the intake. The proportion of MB patients with a reaction or NFI (15·32%) is nearly 7 times higher than that for PB (2·30%), which is in line with others' findings that MB patients are at higher risk of developing reactions and neuritis.[2] These findings agree with other studies conducted amongst field patients including a study by Boerrigter,[31] who found a reversal reaction (RR) rate of 2·2% among TT and BT patients at registration; and Becx-Bleumink who found the rate of RR to be 3·4% amongst BT patients and 4·9% amongst BLs.[8] These rates are much lower than van Brakel's cohort of new hospital outpatients, with 30% of BT patients and 31% of BL patients presenting in RR.[2] This may reflect later case presentation in Nepal, as others have noted;[32] in addition, there was a higher proportion of MB patients amongst the Nepali group. Van Brakel's study was based at a referral centre, and the self-referred patients presenting are often those with a higher proportion of complications. Males appear to be at nearly double the risk of having a

reaction or NFI needing treatment at diagnosis (5·67%; females 2·96%), a fact partly explained by the higher MB rate amongst men.

Of the 90 patients who presented with NFI needing treatment at diagnosis, 61 (67·78%) were silent, that is, there were no other signs including nerve pain or skin reactions to call attention to the neuropathy. They represented 2·29% of the total intake. Van Brakel found that almost 7% of his retrospective cohort of 536 patients had silent neuritis at first examination.[4] Bernink and Voskens found 28 out of 856 patients (3·3%) in Indonesia who had silent neuritis.[33] Both papers underline the need for routine sensory and motor testing of leprosy cases in order to identify such patients, and the BANDS study emphasizes this need if the prevention of disability is to be taken seriously.

Future research

This paper describes the design and methodology of the Bangladesh Acute Nerve Damage Study and the intake status of the cohort of 2664 patients. Future research and publications, building on this foundation, will focus on the following areas: the incidence of NFI and reactive events, the risk factors for developing NFI, and the response to treatment of patients developing acute NFI.

Acknowledgements

The authors are grateful for the enthusiasm and commitment of the staff at DBLM in carrying out this study in the field. Mr Pjotr Prins gave invaluable help in writing the computer database programme used for BANDS. Dr Alison M. Anderson gave generously of her time and expertise to help in advice and audit. Ms Hanna Møller wrote the manual for the computer programme. Dr Rosemary Croft made many helpful suggestions. I am indebted to Mrs Jane Denny for conscientiously editing the manuscript. BANDS is financially supported by The Leprosy Mission International.

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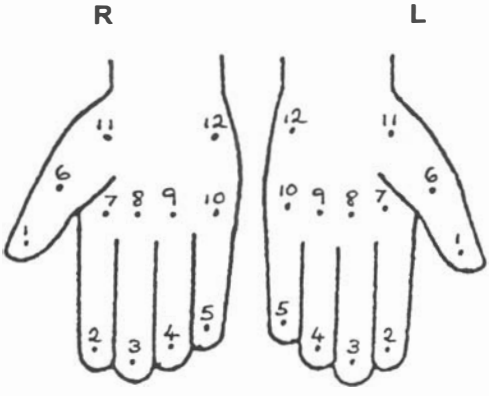
Appendix 1

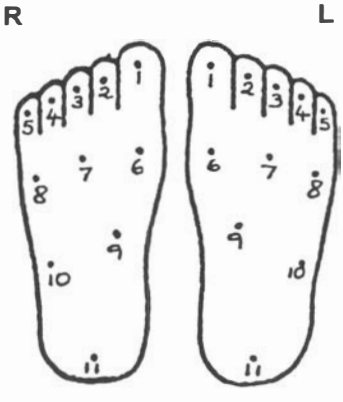
Diagram showing sensory function testing points used on soles and palms

a Palms

Points 1, 2, 3, 6, 7, 8 and 11 are taken as median nerve distribution
Points 4, 5, 9, 10 and 12 are taken as ulnar nerve distribution



b Soles



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Case detection, gender and disability in leprosy in Bangladesh: a trend analysis

J. H. RICHARDUS*, A. MEIMA*, R. P. CROFT** & J. D. F. HABBEMA*

**Department of Public Health, Erasmus University Rotterdam, The Netherlands*

***The Danish-Bangladesh Leprosy Mission, Nilphamari, Bangladesh*

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Summary A trend analysis is presented of all newly detected leprosy cases over an 18-year period (1979–1996) in a highly leprosy endemic area of Bangladesh. A total of 23,678 new cases were registered, with an average of 860 new cases per year in the first 12 years, and increasing to around 3000 in 1996. The male : female (M : F) ratio decreased from 2·3 to 1·4. The proportions of newly detected cases with MB leprosy and of newly detected cases with any disability decreased over time. These reductions were more marked in the higher age groups of both sexes. The reduction in disability was primarily attributable to a decline in grade 2 disability. New case detection rates (NCDR) of all leprosy patients per 10,000 general population increased for males from 3 to 6; and for females from 1 to 4, while the NCDR of MB leprosy decreased in males from 1·4 to 0·6, and in females fluctuated around 0·45. The NCDRs of leprosy patients with disabilities showed an initial decrease in the first period, especially in males, but later showed an increase. The NCDR of males with disability was about twice as high as that of females. Finally, female NCDRs in the ages between 15 and 30 were low by comparison with the male NCDRs at the same time. This may be due to the sociocultural characteristics of the Bangladeshi society, with gender differences in exposure, health seeking behaviour and opportunities for case detection. Operational changes in the control programme have contributed to the changed profile of newly detected cases. This study shows that the application of general population statistics is essential for understanding the dynamics in leprosy control programmes under changing operational conditions. Combining case detection figures with such statistics helps to identify population groups that are possibly not benefiting sufficiently from the services provided, and to clarify the dynamics in control programmes and the future trends and programme requirements.

Correspondence to: Jan Hendrik Richardus, Department of Public Health, Erasmus University Rotterdam, PO Box 1738, 3000 DR Rotterdam, The Netherlands. Tel: +31 10 4088285, Fax: +31 10 4089449, e-mail: richardus@mgz.fgg.eur.nl

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Introduction

Interest in gender inequality is increasing in public health research. Many health status indices show females to be disadvantaged. Males and females have different health risks due to differences in biology, but also due to differences in their social roles and expectations. Women may have different exposure to disease and infection, and diseases may have different effects on women, not only medically, but also in sociocultural and economical aspects. This is particularly marked in the developing world where women may also have less access to health services than men. In a disease with a strong social stigma, such as leprosy, the impact of gender inequality may be considerable. A recent review on women and leprosy[1] concluded that sex differences in case detection of leprosy exist, but information varies considerably between country. The relative importance of biological, health services-related and community-related factors is also unclear and differs between region or country. More information is needed on gender issues, both for understanding the epidemiology of leprosy and for taking operational measures in leprosy control programmes to reduce gender inequalities in health.

This study presents a trend analysis of newly detected leprosy patients over an 18-year period (1979–1996) in a moderate to high leprosy endemic area in North West Bangladesh. The objective was to investigate the relative contribution of females to newly detected cases in relationship to age, leprosy classification and disability, in varying operational circumstances. The time period under study includes three relatively distinct operational situations: the pre-multidrug therapy (MDT) era; a transition phase with the introduction of MDT; and the present era where the introduction of MDT has been completed and full coverage of the geographical area with leprosy control services has been achieved. A study of gender differences in new case detection rates in these distinct time periods may reveal the extent to which males and females are affected by leprosy, the effect of leprosy control services, and possibly illustrate reasons for gender inequalities.

Materials and methods

PROJECT DESCRIPTION

The study is based on data from the Danish Bangladesh Leprosy Mission (DBLM) in Nilphamari, Northwest Bangladesh. DBLM has conducted a vertical leprosy programme in a moderate to high endemic area (estimated prevalence in 1993: approximately 5 per 1000) since 1977.[2] The DBLM leprosy control programme covers the districts of Nilphamari, Rangpur, Thakurgaon and Panchagar. The population (1991 census) was 5,529,600 and the area covered is 7163 km^2, giving a population density of 772 persons per km^2. Since 1994, the DBLM has been responsible for leprosy control in the four districts of the Rajshahi Division. Soon after DBLM was established, the programme was treating more than 95% of registered leprosy patients in these districts.

TIME FRAME

An 18-year period (1979–1996) is included in this analysis. During this time frame, three distinct 6-year periods with different operational characteristics can be distinguished. In the first period (1979–1984), the project had started on a small scale, with a limited number of

staff and clinics. Treatment was with dapsone monotherapy and case finding primarily passive. The second period (1985–1990) was a transition period. MDT was introduced for all new cases, the geographical coverage with clinics expanded within the four districts, and the programme became better known and accepted by the population. By 1991, MDT had been introduced completely in the programme. In the last period (1991–1996), major financial impetus was given to the programme and complete coverage of all districts with a network of easily accessible clinics was established, with more than 50 clinics and 110 paramedical workers involved. This period saw expansion into a comprehensive and accepted leprosy control project with health education programmes, rapid village surveys, regular follow-up of all patients, field treatment of reactions and nerve function impairment, hospital services for reconstructive surgery, and rehabilitation programmes. General health services (provided by the government) developed less rapidly, and BCG coverage remained low during this period.

INCLUSION CRITERIA

All cases diagnosed with leprosy for the first time and registered in the DBLM programme during the time period 1979–1996 are included in this study. They are presented in the age categories: 0–14 years, 15–39 years and ≥40 years. It is estimated that 5% of patients come from outside the DBLM project area. They were not excluded because the home village of DBLM patients could not always be established accurately.

LEPROSY CLASSIFICATION

From the beginning of the DBLM programme the Ridley–Jopling classification was recorded for the type of leprosy of a new patient and skin smears were taken from most new patients.[3–5] To prevent inconsistencies in trend descriptions caused by changing definitions over time, the following criteria were applied for data analysis: cases with Ridley–Jopling classification BB, BL and LL and all cases with positive skin smears (BI > 0) are defined as MB, and all other cases are defined as PB.

DISABILITY GRADING

Disability is graded according to the WHO leprosy disability grading system.[4] For hands and feet, grade 0 is defined as no anaesthesia, visible deformity or damage; grade 1 as anaesthesia present, but no visible deformity or damage; and grade 2 as visible deformity or damage. The WHO has defined a comparable system for grading disabilities of the eyes, also on a scale from 0 to 2.

POPULATION STATISTICS

Detailed population statistics including sex and age distributions are available at district level in the Bangladesh census data of 1981 and 1991, allowing the calculation of population based case detection rates.[6–8]

NEW CASE DETECTION NUMBERS AND RATES

The newly detected leprosy cases in the 18-year period of this study are analysed at two

levels. The first level only includes the newly detected cases (or numerator), and studies their distribution patterns over time according to sex, age, leprosy classification and disability. In the second level, the denominator (population from which the cases originate) is taken into account to calculate new case detection rates (NCDR).

STATISTICAL ANALYSIS AND ILLUSTRATION OF TRENDS

For comparison of proportions and case detection rates, the Chi-square test was used. Logistic regression was performed for testing the statistical significance of trends. Statistical analysis was carried out in SPSS. To illustrate trends over the study period, curves (smoothing splines) were fitted to several graphs with the statistical package S-Plus 4.

Results

Figure 1 shows the new cases detected over the 18-year period in absolute numbers according to sex, and gives male : female (M : F) ratios. Graphs are given for all ages combined and for the age groups 0–14 years, 15–39 years, and 40 years and above, separately. The total number of new leprosy patients registered over the whole period is 23,678 with an average of 860 new cases per year in the first 12 years, and increasing in the last 6-year period to around 3000 new patients in 1996. The M : F ratio decreased from approximately 2·3 in the first 6-year period to around 1·4 for 1994–1996. The age groups 15–39 and 40 + years are responsible for this decrease; in the children's age group (0–14 years) the M : F ratio fluctuated between 1·1 and 2·0 without showing a clear trend.

Figure 2 gives the MB proportion, according to sex and presented in three age groups. The initial proportion of MB leprosy in 1979 in all age groups together was 58% for males and 45% for females. This proportion reduced over time to 10% for males and 4% for females in 1996. The reduction was most marked in the two higher age groups. In the child group, the proportion MB cases in boys fluctuated around 20%, but fell in girls to less than 5% in 1996. The declines took place mostly in the last 6-year period, as shown by the flow of the spline functions. The largest reduction in proportion of smear positives among newly detected cases took place in the last 6-year period (proportion smear positive among those with smear taken for the three subsequent 6-year periods: 29%, 23% and 9%, smears were taken from at least 93% of new cases).

Figures 3 and 4 show the proportion of new cases presenting with disabilities. Figure 3 shows the proportion with any disability (WHO grading 1 plus 2), according to sex and presented in the three age groups. There is a nearly parallel decline in proportion with disability in males and females. In males the overall decline is from 65% in 1979 to 20% in 1996; in females the decline is from 55% to 10%. The decline is observed in all three age groups and is steeper for the two higher age groups, with an acceleration in the last 6-year period (as is illustrated by the flow of the spline functions). Figure 4 includes the proportion of new patients presenting with disability according to WHO grade 1, 2, and 1 plus 2, categorized by sex. It can be seen that the decline in grade 2 disability contributed most to the decline in total disability.

Figures 5–8 present new case detection rates per 10,000 population per year (NCDRs) for the DBLM project area. Total sex-wise NCDRs are given in Figure 5. The male NCDR increases from 2·5 per 10,000 in 1979 to nearly 6 per 10,000 in 1996, a more than two-fold

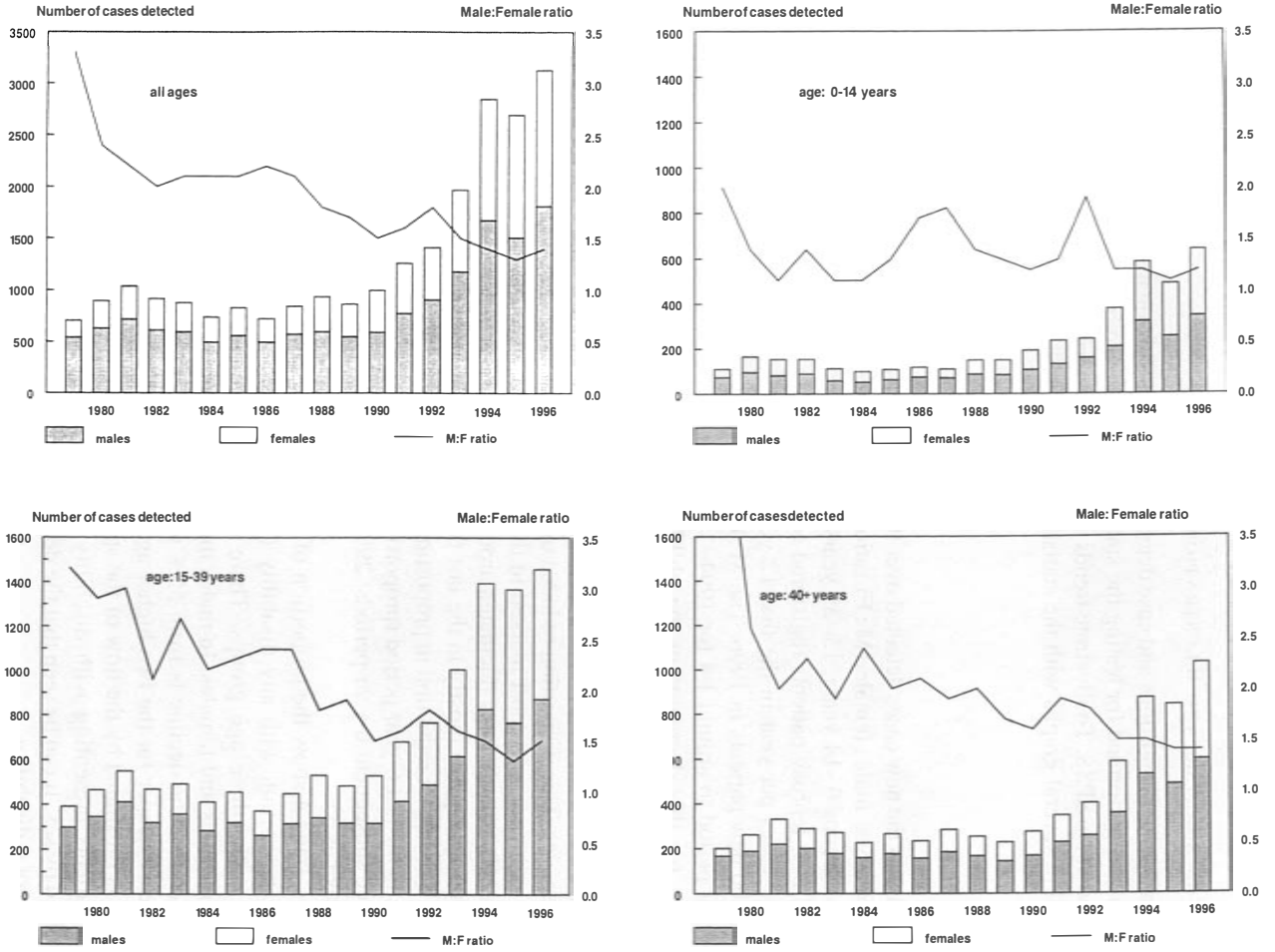


Figure 1. Number of newly detected leprosy cases from 1979 to 1996, according to sex and including male : female ratios, and presented in the following age groups: all ages; 0–14 years; 15–39 years; and 40 years and above.

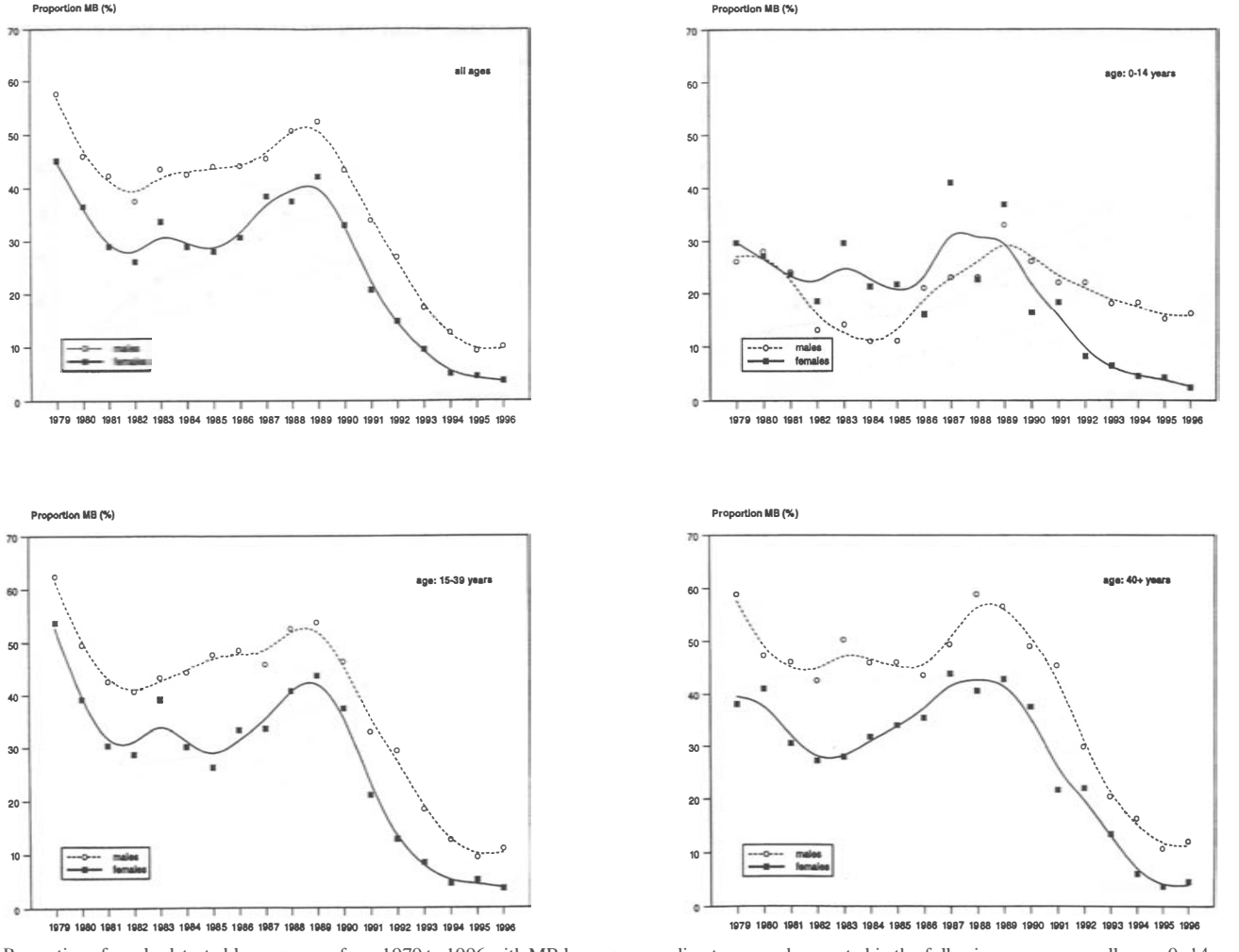


Figure 2. Proportion of newly detected leprosy cases from 1979 to 1996 with MB leprosy, according to sex and presented in the following age groups: all ages; 0–14 years; 15–39 years; and 40 years and above.

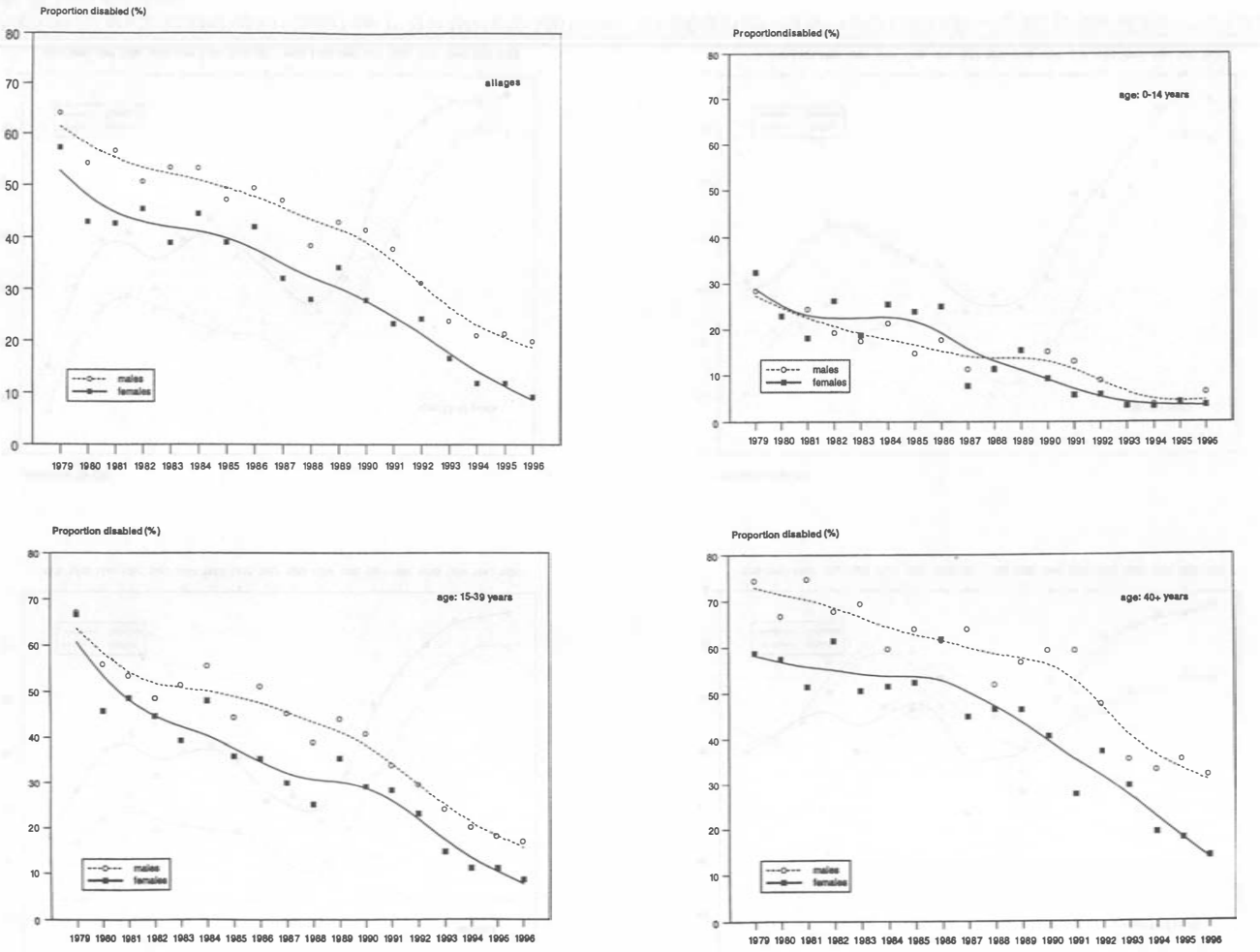
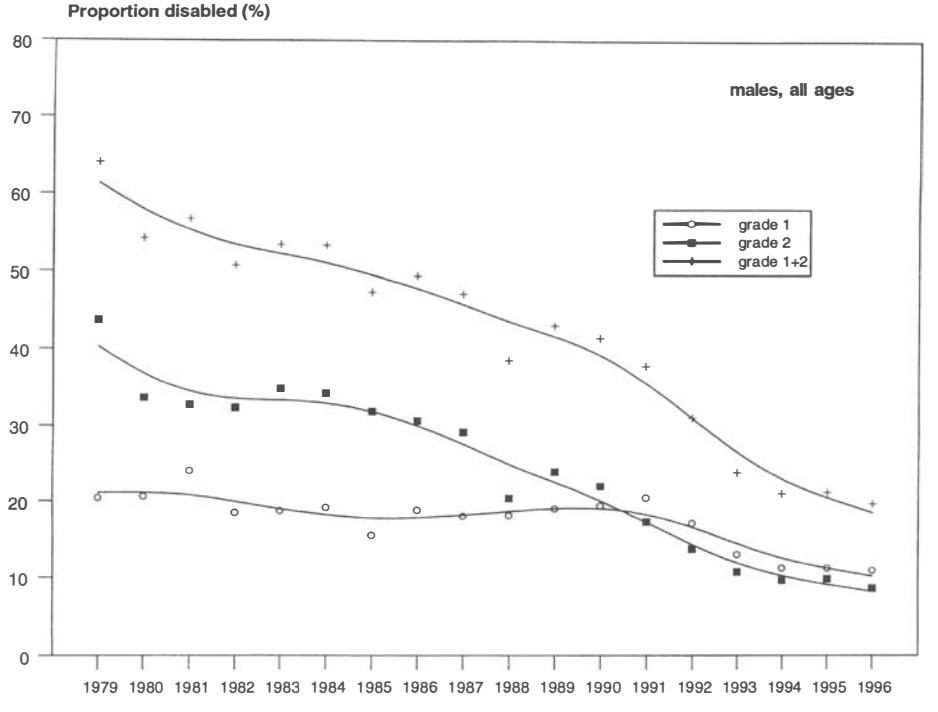
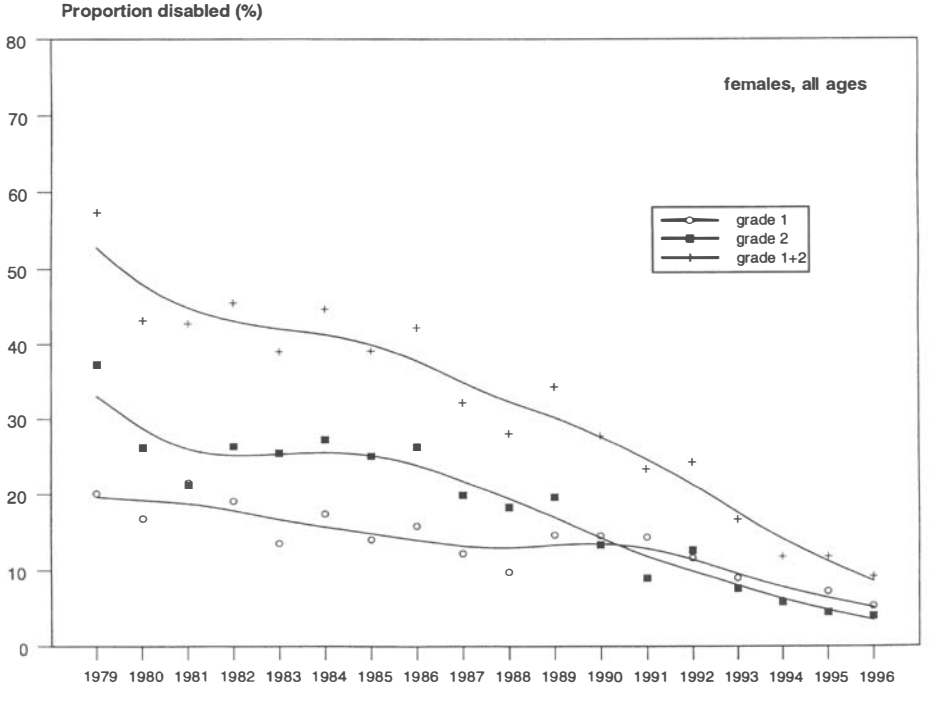


Figure 3. Proportion of newly detected leprosy cases from 1979 to 1996 with disability grade 1 or grade 2, according to sex and presented in the following age groups: all ages; 0–14 years; 15–39 years; and 40 years and above.


Proportion disabled (%)
80
70
60
50
40
30
20
10
0
males, all ages
grade 1
grade 2
grade 1+2
1979 1980 1981 1982 1983 1984 1985 1986 1987 1988 1989 1990 1991 1992 1993 1994 1995 1996


Proportion disabled (%)
80
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females, all ages
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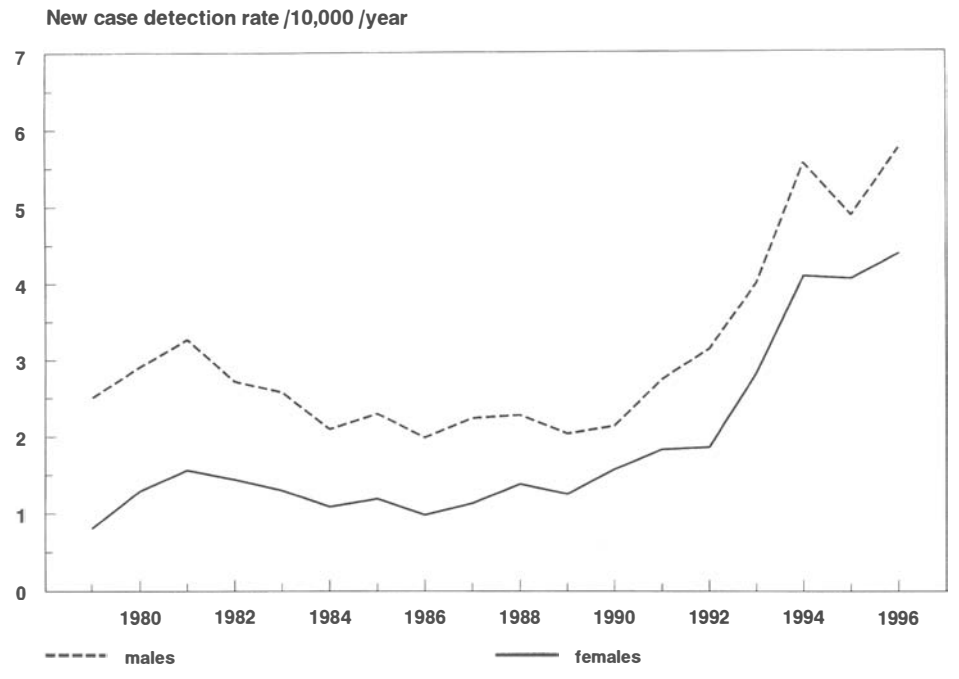

Figure 5. New case detection rate of leprosy patients in the DBLM project area per 10,000 general population per year from 1979 to 1996, according to sex.

increase. A four-fold increase from approximately 1 to 4 per 10,000 is observed for females. In Figure 6, the age specific NCDRs are shown separately for males and females for each of the three 6-year periods. The shapes of the age specific NCDR curves for males and females are quite distinct at young adult ages. After an initial increase, the NCDR in females shows a marked decrease at age 15, only to increase again after age 24. In males the increase in NCDR continues into adulthood, with stabilisation setting in around age 30. This pattern is most marked in the last 6-year period. The NCDR increased considerably in all age groups for both males and females in the third 6-year period (1991–1996). Although the increase in NCDR varied with age, shifts in case detection towards young or old age from one period to the next, indicating changes in the age distribution of underlying incidence, could not be shown.

Figure 7 gives the NCDR for new patients with MB leprosy. The male NCDR per 10,000 decreased from around 1·4 in 1979 to 0·6 in 1996. The female NCDR for MB leprosy fluctuated between 0·3 and 0·5 per 10,000 in the first two periods, and started to decline in the third 6-year period, attaining a level of 0·16 per 10,000 in 1996. Finally, NCDRs of new patients with disability (grade 1 only, and grade 1 plus 2) are given in Figure 8. By comparison with females, NCDRs for males with disability are more than twice as high for both grade 1 disability and any disability (grade 1 plus 2). After decreasing or stable initial trends, the NCDRs for both males and females showed an increase after 1988 for all disability grades.

Figure 4. Proportion of newly detected leprosy cases (all ages) from 1979 to 1996 with disability grade 1; grade 2; and grade 1 + 2, according to sex.

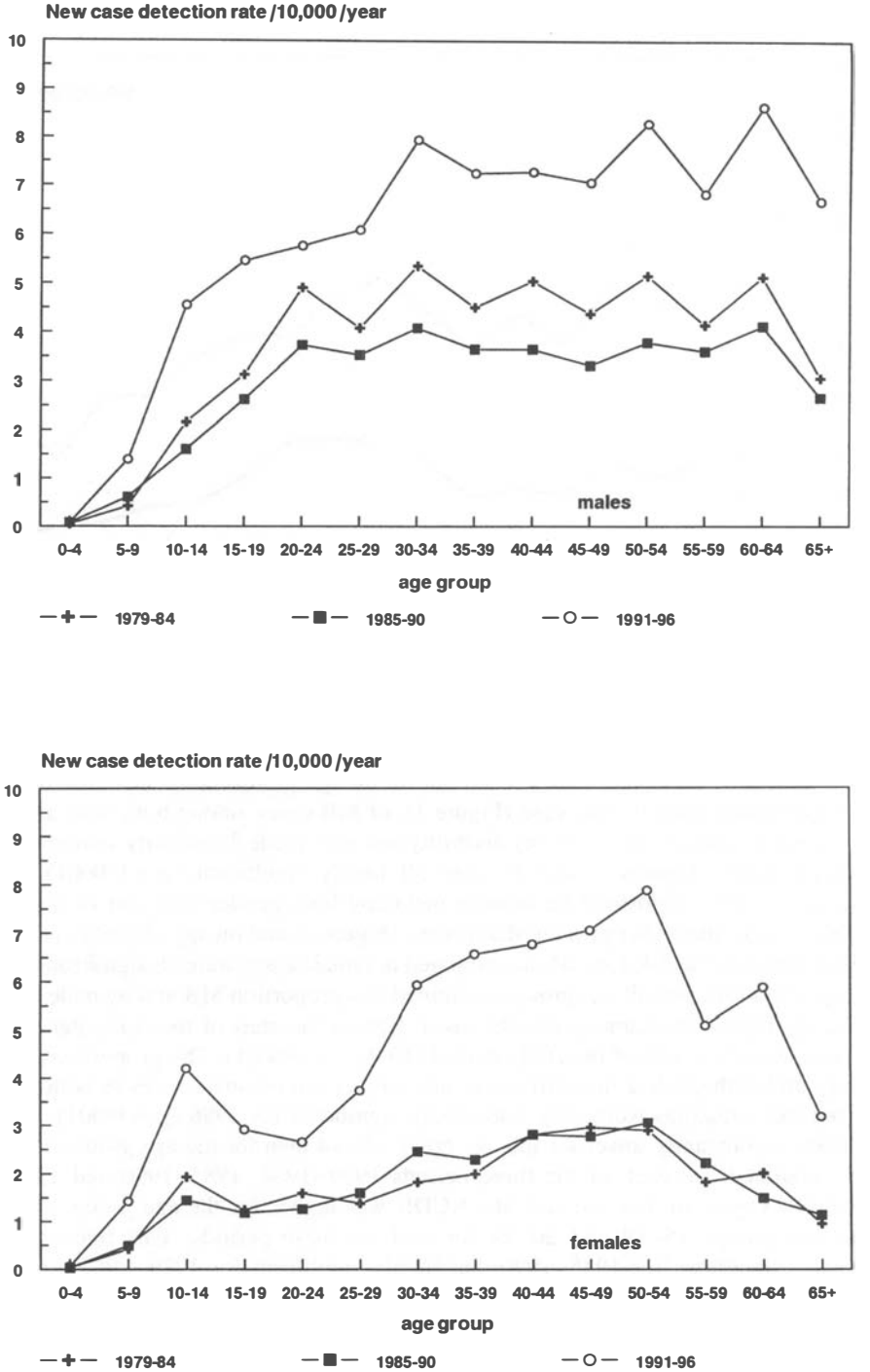

Figure 6. Age specific new case detection rates of leprosy patients in three time periods: 1979–1984; 1985–1990; 1991–1996, according to sex.

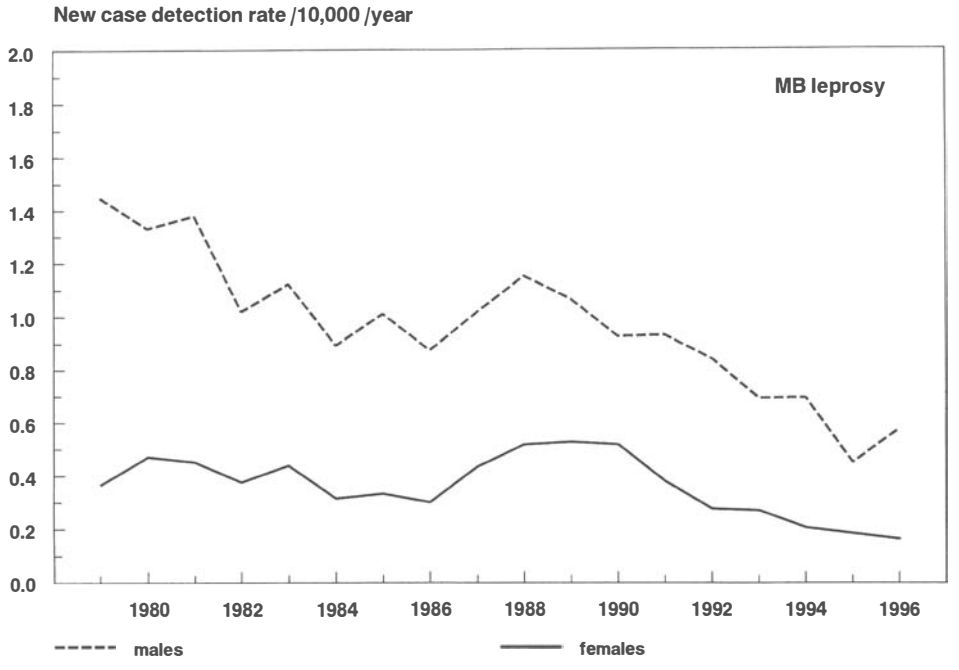

Figure 7. New case detection rate of MB leprosy patients in the DBLM project area per 10,000 general population from 1979 to 1996, according to sex.

Statistical tests for trends were carried out for all age groups combined. The decreasing trends in the proportion of male case (Figure 1), of MB cases among both male and female cases (Figure 2), and of cases with any disability and with grade 2 disability among both male and female cases (Figures 3 and 4) were all highly significant ($p < 0{\cdot}0001$). Logistic regression was also performed for models including both gender and year of registration. For these models, the odds ratios on MB leprosy (Figure 2) and on any disability and grade 2 disability (Figures 3 and 4) for male as compared to female cases were all significantly greater than 1 ($p < 0{\cdot}0001$). For all age groups combined, the proportion MB among male cases was significantly higher than among female cases, both at the start of the study period (1979, $p < 0{\cdot}005$) and at the end of the study period (1996, $p < 0{\cdot}0001$). The proportions with any disability and with grade 2 disability were also higher among male cases in both 1979 and 1996, but these findings were only statistically significant for 1996 ($p < 0{\cdot}001$). The male NCDR was significantly lower for the age group 10–14 than for the age groups 15–19 and 20–24 combined, for each of the three periods 1979–1984, 1985–1990 and 1991–1996 ($p < 0{\cdot}0001$, Figure 6). For females, the NCDR was higher for the age group 10–14 than for the age groups 15–19 and 20–24 for each of these periods. This finding was not statistically significant for 1985–1990, but highly significant for 1979–1984, ($p < 0{\cdot}001$) and 1991–1996 ($p < 0{\cdot}0001$). Logistic regression showed a decreasing trend in NCDR for MB leprosy which was highly significant for both males and females ($p < 0{\cdot}0001$, Figure 7). A statistically significant increasing trend in NCDR for leprosy with any disability was observed from 1988 onwards for males ($p < 0{\cdot}0001$) but not for females ($p = 0{\cdot}27$, Figure 8).

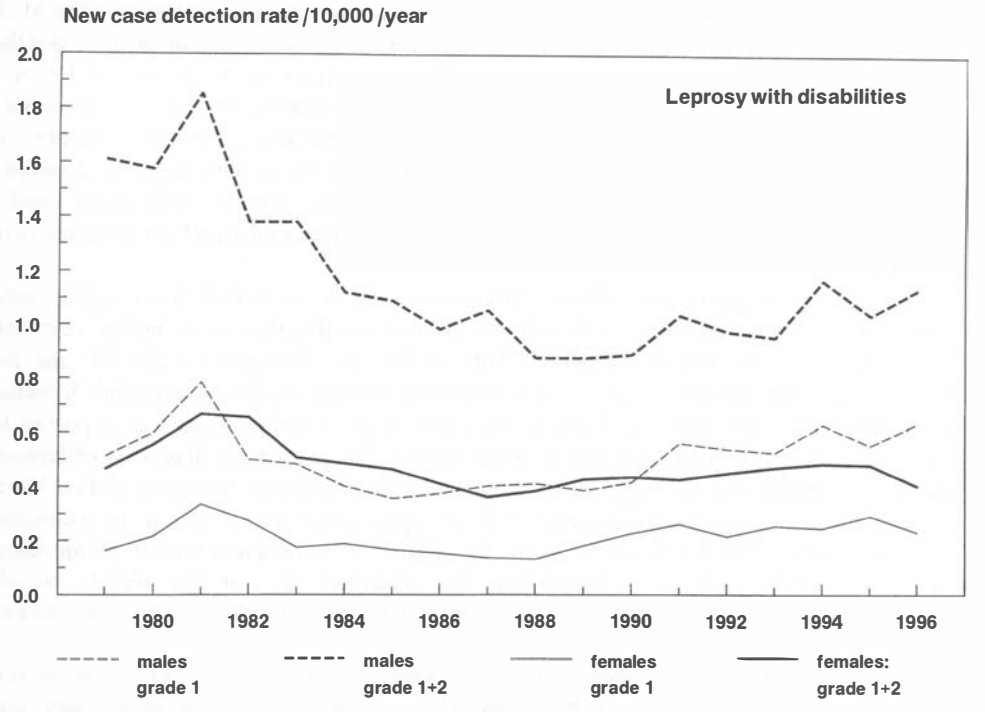

Figure 8. New case detection rate of leprosy patients with disability (grade 1 and grade 1 + 2) in the DBLM project area per 10,000 general population from 1979 to 1996, according to sex.

Discussion

In the 18-year study period the findings at numerator level are largely determined by operational factors in leprosy control activities. Initially, there were few clinics, distributed unevenly over a large area. The number of newly detected cases increased with the expansion of the programme in the last 6-year period. Over-representation of MB leprosy cases in the initial stages was primarily caused by a backlog of easily identifiable leprosy patients, with high deformity rates. Over the last 6-year period, increasing numbers of patients (mainly PB) were detected earlier. The reduction of grade 2 disability also reflects the intensification of case finding. This intensification reduced delays in diagnosis, so preventing patients developing grade 2 disability before treatment.

Caution is warranted in interpreting the declines in MB proportion and proportion with disability in newly detected cases. The NCDR for MB leprosy has also declined over the study period, especially in males. An impact of this decline on the transmission of leprosy in terms of a reduction in the case detection rate of new cases has not yet been observed. In fact the NCDR increased, due to the intensification of case finding. Furthermore, the decreasing percentages of new cases with disability may falsely suggest that shortly this phenomenon will disappear and therefore no additional efforts are needed to detect and treat nerve function impairment and maintain prevention of disability (POD) programmes. As can be seen in Figure 8, the NCDR of leprosy patients with nerve function impairment and disabilities has not decreased from 1988 onwards, and even shows a clear increase for males.

This study reveals important gender differences in both detection and disability. The M : F ratio in new case detection decreased considerably over the study period, suggesting that the chance of females being detected has increased. To what extent the M : F ratio of 1·4 over 1994 to 1996 reflects a gender difference in biological predisposition of males to contract leprosy, exposure-related differences, or operational shortcomings in the detection of females, is still unclear. The observed difference in proportion with grade 2 disability among new cases at the end of the study period (males: 10%, females: 4%) raises similar questions; perhaps earlier detection occurs in females, as well as biological sex differences in the incidence of nerve function impairment.

Additional information on gender differences can be obtained from age-specific NCDRs. These reveal that the socio-cultural context of Bangladesh is highly relevant. The interruption in the rise in female NCDRs in the ages between 15 and 30, and the absence of this interruption in males, is an important finding. Maybe young adult females, who in Bangladesh are more confined to their homes than males, have less exposure to leprosy. Also, they might be reluctant to come forward for fear of the diagnosis of leprosy affecting their chances of marriage, or causing separation from their husbands and children. In the Bangladeshi sociocultural context, it is not appropriate for women to be examined by men, and particularly for young women. There may be insufficient female paramedical workers to examine women. Summarizing, the observed 'dip' in the female NCDR probably does not have a biological explanation, but arises from the social circumstances in Bangladesh.

Undoubtedly, females have gained from the intensification of leprosy control. However, more effort is needed to understand the underlying incidence patterns in females, and methods should be developed and tested to reach out to females in the ages range 15–30 years. However, the decrease in M : F ratio and the low proportion grade 2 disability in new female cases (4%) at the end of the study period are positive signs. However, the higher proportion of grade 2 disability in males (10%) does not indicate that females fare better. In the DBLM area, it was shown that the social stigma for females with leprosy disabilities (including skin lesions) is higher than in males.[9]

It has been pointed out that under comprehensive and consistent leprosy control conditions, NCDRs are the nearest approximation of true incidence rates.[10] NCDRs are therefore a vital indicator for understanding the epidemiology of leprosy. Obviously, control conditions over time in the DBLM programme diverge from this ideal. Nevertheless, this study demonstrates that the application of general population statistics is essential for understanding the dynamics in leprosy control programmes in non-ideal circumstances. Calculation of NCDRs helps to identify population groups that are not benefiting sufficiently from the services provided, and to clarify the dynamics in control programmes and the future trends and programme requirements.

Acknowledgements

The dedicated work of the Danish Bangladesh Leprosy Mission staff is gratefully acknowledged. Their consistent and skilful performance in often-difficult circumstances has resulted in a model leprosy control programme in a large, remote leprosy endemic area of Bangladesh. Their meticulous record keeping has made it possible to provide this review.

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Leprosy elimination through integrated basic health services in Myanmar: the role of midwives

S. BARUA*, S. WAKAI†, T. SHWE‡ & T. UMENAI*
**Department of Health Policy and Planning, Graduate School of International Health, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo Ku Tokyo, 113-0033, Japan*
†Department of Neurosurgery, Dokkyo University School of Medicine, 880 Mibu, Tochigi, 321-02, Japan
‡National Leprosy Elimination Program, Department of Health, 36, Theinbyu Road, Yangon, Myanmar

Summary Myanmar is one of the top 16 countries identified by WHO as being hyperendemic for leprosy. Multi-drug therapy (MDT) was introduced in 1988 as a vertical programme and gradually integrated into the basic health services (BHS), achieving 100% coverage over the registered cases by 1995. To achieve maximum coverage of and benefit for patients, both leprosy vertical staff and BHS staff were trained to implement MDT whilst performing routine BHS activities. This included a total of 8615 trained midwives who were mobilized for the nationwide leprosy elimination programme (LEP). They worked at village level in various parts of the country and were willing and able to carry out basic tasks in leprosy management, such as the implementation of MDT using blister-calender packs carrying a month's supply of drugs. This study was performed to assess the workload of midwives and their attitude towards LEP. The authors conclude that midwives in Myanmar show a high level of commitment and reliability, which are essential contributing factors to achieve the current goal of leprosy elimination by the year 2000. Along with the present trend of decreasing prevalence rate, leprosy could no longer be considered as a public health problem at national level by the year 2000 in Myanmar. However, because of its long incubation period, new leprosy patients may arise even after the elimination target is achieved, whilst many other patients may become disabled. A community-based sustainable approach for the post-elimination phase, after the year 2000, will be essential and the contribution of the midwives may be of considerable importance.

Correspondence to: Sumana Barua

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Introduction

Since the introduction of multi-drug therapy (MDT) in 1982 by the World Health Organization (WHO),[1] more than 8 million patients have been cured at global level with this treatment. Within 10 years since its introduction, MDT has been adopted by all endemic countries as the standard treatment for leprosy.[2] MDT is provided in monthly-basis blister packs, making the distribution system easier at different levels of health care services with less workload in the part of the community health workers.[3,4]

Myanmar (population 46 million) has a significant leprosy problem and is included by WHO in a list of the top 16 endemic countries worldwide.[5,6] MDT was introduced in Myanmar in 1988 as a vertical leprosy elimination programme (LEP), which was gradually integrated into the basic health services (BHS) from 1991 and covered the whole country by 1995 (Department of Health, National Leprosy Elimination Programme, Yangon, Myanmar, unpublished Government Report, 1995). At the village level, actual implementation of LEP activities is performed by the Midwives and the Public Health Supervisors II. All the midwives (8615 in 1993–94) nationwide received training on LEP. They gradually adopted LEP in their responsible areas in the integrated BHS services by 1995 (Department of Health, Basic Health Services, Unpublished Government Document, Yangon, Myanmar, 1995). LEP activities such as case finding, confirmation of diagnosis, drug distribution and follow-up of patients became feasible for the midwives and could be performed in conjunction with other BHS activities. The registered prevalence rate of leprosy in Myanmar was reduced from 39·9 in 1988 to 2·91 per 10,000 population in 1997, whilst the MDT coverage over the registered cases was sharply increased from less than 20% in 1988 to 100% in 1995 (Figure 1). This achievement was made through the combined effort of both vertical (specialized) leprosy and

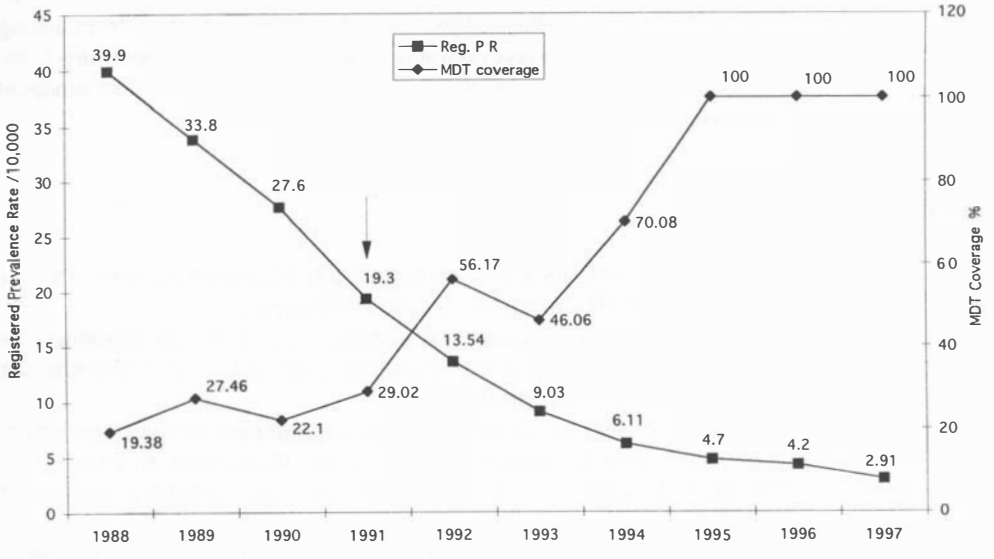

Figure 1. Registered prevalence rate (Reg. P R) and multi-drug therapy (MDT) coverage rate of leprosy cases in Myanmar, 1988–1997. Arrow indicates the time (year) of the integration of the vertical leprosy control activities into BHS and intensive training of BHS staff on leprosy. Source: National Leprosy Elimination Program, Myanmar, 1998.

BHS staff with midwives playing a vital role (Tin Shwe: Progress Towards Leprosy Elimination in Myanmar; paper presented at the joint Department of Health/World Health Organization meeting inaugurating an Independent Evaluation of the National Leprosy Elimination Programme, Yangon, Myanmar, 4 November, 1997).

Significant contributions of midwives in leprosy elimination activities of Myanmar[7] are mentioned in several WHO reports that evaluated the overall LEP national programme of Myanmar (Department of Health, Myanmar, final report of the joint Government/WHO Independent Evaluation of Leprosy Control Program, Myanmar, 1993. Unpublished Government Report, Feenstra P. Leprosy Control in Myanmar; Expanding MDT Coverage, Unpublished WHO assignment report, Yangon, Myanmar, 1993).

However, a detailed assessment of the role of the midwives has not been done in terms of performing the LEP activities. This study was thus carried out to analyse the leprosy situation in Myanmar over time: 1) to investigate the role and contribution of the midwives in LEP; 2) to analyse the perceptions of the midwives regarding leprosy activities. We also discuss their possible future contribution to leprosy control beyond the year 2000 in Myanmar.

Subjects and methods

In Myanmar, under the integrated LEP, three categories of BHS staff are considered as implementers, namely, midwives, public health supervisor grade II and multipurpose health workers, of whom the majorities are midwives.

In order to analyse the LEP workload of the midwives, a survey was conducted by trained interviewers by using pretested standard questionnaire from July to November, 1995 in three of the six Divisions of Myanmar where MDT was introduced in 1988. A total of 188 midwives were interviewed. They were selected by a simple random sampling from among the midwives assigned in three divisions (Ayeyarwaddy, Bago and Yangon), totalling 2349.

The study did not include any analysis of the quality of the leprosy services rendered by the interviewed midwives.

Results

Of the 188 midwives interviewed, 185 (98·4%) were female and 3 (1·6%) were male. The age ranged from 22 to 59 years old, with a mean of 41·2 (SD ± 9·4 years).

One hundred and eighteen (62·8%) midwives responded that MDT was introduced in their areas in 1991, 48 (25·5%) in 1989, three (1·6%) in 1995, two (1·1%) in 1987 whilst the remaining 17 (9·0%) did not answer this question.

With regard to the duration of services in the respective areas during the interview, of the 188 midwives, 12 (6·4%) have been assigned in the area for less than a year, 61 (32·4%) for 1–5 years, 41 (22·0%) for 6–10 years, 23 (12·2%) for 10–15 years, and the remaining 51 (27·0%) for 16 years and more.

Thirty-nine midwives (20·8%) had no cases, 124 (66·0%) had one to five cases, 15 (7·9%) had 6–10 cases and three (1·6%) interviewed midwives had more than 10 cases to be taken care of, whilst the remaining seven (3·7%) did not mention their caseload. Thus, the average leprosy patient load was 2·2 cases per midwife per month. During the survey period, basic

health services were provided by one midwife; an average of 15 patients per day. Thus, 2·2 leprosy patients count for only 0·75% of midwife's total caseload for a month.

All the interviewed midwives perceived that leprosy activities were not an extra workload. Ninety-four (50%) of them were able to perform leprosy activities with other BHS activities. Seventy-three (38·8%) presumed that it was a part of their routine activities under BHS since its integration with LEP (11% gave no answer).

Out of the 188 midwives interviewed, 149 (79%) responded that they spent less than 10% and 18 (10%) spent more than 10% of their monthly working time for LEP activities (11% gave no answer).

Regarding the case finding activities, during the last 6-month period, the midwives conducted the routine contact survey, school survey and other methods (such as mass survey or cases detected during the physical examinations for other complaints). A total of 132 cases were suspected as leprosy by the interviewed midwives and 113 cases confirmed by their supervisors with an average accuracy rate of 85·6% (Table 1).

For contact survey, out of the 188 midwives interviewed, 147 (78·2%) used this method and 41 (21·8%) did not. Ninety-three cases were suspected as having leprosy. Of the 93 suspected cases, 80 were confirmed as having leprosy by their supervisors with the accuracy rate of 86·0%.

For school survey, out of the 188 midwives interviewed, 147 (78·2%) used this method, 40 (21·3%) did not. (One gave no answer). Six cases were suspected as having leprosy. Of the six suspected cases, five were confirmed as having leprosy by their supervisors with an accuracy rate of 83.3%.

For other surveys, out of the 188 midwives interviewed, 72 (38·3%) used these methods and 102 (54·2%) did not [14 (7·5%) gave no answer]. Thirty-three cases were suspected as having leprosy. Of the 33 suspected cases, 28 were confirmed as having leprosy by their supervisors with the accuracy rate of 84·8%.

A midwife spent 2·1 days during the last 6-month period for the surveys. The figure equals 1·9% of the total working days during half a year for each midwife.

In regards to the location of MDT drug delivery, 165 (87·8%) of the 188 interviewed midwives delivered MDT drugs in the patients' homes, seven (3·7%) at the clinics (Health Centre/Sub-Centre), two (1·1%) either in the homes or at the clinics, whilst the remaining 14 (7·4%) were through other means, such as through the village health workers, or through another patient. It should be noted here that the distribution of MDT blister-packs containing 1 month's

Table 1. Leprosy cases detected by the interviewed midwives during last 6 months by different survey methods in the study areas of Myanmar in 1995

Case detection methods	Midwives used the method[a]	Total number of suspected cases	Total number of confirmed cases	Percentage of case detection accuracy
Contact survey	147 (78·2%)	93	80	86·0%
School survey	147 (78·2%)	6	5	83·3%
Other surveys[b]	72 (38·3%)	33	28	84·8%
Total		132	113	85·6%

[a] Some midwives used more than one case detection methods.

[b] Other surveys include mass survey and case detection during the physical examinations for other complaints.

drug was easier for the midwives to handle. They routinely collect the used blister-packs of the previous month from the patients whilst distributing the new supply of MDT drugs.

Periodic training was conducted for the midwives to implement the LEP activities. Out of the 188 interviewed midwives, 164 (87·2%) responded that they had training whilst 24 (12·8%) had no training on LEP activities by the time of the interview. With regard to the duration, of the 164 who received training, 26 (15·9%) for 1 day, 30 (18·3%) for 2 days, 103 (62·8%) for 3 days, 3 (1·8%) for more than 3 days [2 (1·2%) gave no response].

With regard to any extra allowance for performing the LEP activities, out of the 188 interviewed midwives, 182 (96·8%) responded did not receive any extra allowance, three (1·6%) responded received occasional extra allowance. The remaining three (1·6%) did not mention either.

The midwives were required to submit a monthly report to their field supervisors. To prepare such a report, they kept records of all activities that they carried out. Out of the 188 interviewed midwives, 177 (94·2%) responded that they maintained a separate stock book, patient charts and records of leprosy cases. Ten (5·3%) did not keep such records and one (0.5%) did not respond either.

All the interviewed midwives responded that their LEP activities were supervised by both LEP and BHS staff at the different levels. In all, 81·4% of the total supervisory visits were by the BHS staff and the remaining 18·4% by the LEP staff.

Discussion

The MDT implementation guidelines of WHO simplified the LEP activities such as case detection and drug distribution in the endemic countries. LEP activities were distributed to the BHS staff through an integrated approach to implement the MDT. This study revealed that an average of 2·2 leprosy patients count only 0·75% of a midwife's total monthly workload among those interviewed. Moreover, all midwives perceived that leprosy activities were not an extra burden, as 94 (50%) of them were able to perform these activities with other BHS activities and 73 (38·8%) presumed that it was a part of their routine activities under BHS since its integration with LEP. Thus, LEP is implemented by the BHS midwives without hampering other basic health services of the country and without any extra allowance for the LEP activities. Training on LEP activities was one of the essential task which is strengthened by regular supervisory visits and on the job training of the midwives.

Along with the present trend of decreasing prevalence rate and maintenance of 100% of MDT coverage over the registered cases, it is evident that leprosy will not be a significant public health problem at the national level by the year 2000 in Myanmar. However, because of the long incubation period of the disease, new leprosy patients may present long after the elimination target is achieved, whilst many other patients may develop disability. Thus, a community-based, sustainable approach for the post-elimination phase, after the year 2000, will be essential and the contribution of the midwives may be of considerable importance.

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Grading impairment in leprosy

WIM H. VAN BRAKEL*, NAOMI K. REED** & DARREN S. REED+
**INF Leprosy Project, Pokhara, Nepal*
***Green Pastures Hospital, Pokhara, Nepal*
+Western Regional Hospital, Pokhara, Nepal

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Summary The aim of the paper is to discuss the concept of 'severity grading' in relation to impairment in leprosy, and to describe the use of an impairment sum score, the Eyes, Hands, Feet (EHF) score, as an indicator of the severity and the evolution of impairment over time. The use of an impairment sum score, the EHF score, is illustrated using data on impairment at diagnosis and after a 2-year interval from MB patients released from MDT in the Western Region of Nepal. The WHO 1988 'disability' grading scale (0–2, for both eyes, hands and feet – six sites) was used as a measure of impairment. For the analysis, the WHO grades for the six sites were summed to form an EHF score (minimum 0, maximum 12). The sensitivity to change over time of the EHF score was compared with that of the 'method of maximum grades'. Using the 'method of maximum grades', 509/706 patients (72%) appeared not to have changed in impairment status, compared with only 399 (56·.5%) with the EHF score. Improvement or deterioration of impairment status was missed in 113 patients (16%). In 216/706 patients (30·6%), the changes detected with the EHF score were bigger than those revealed by the method of maximum grades. The six components of the WHO impairment grading may be added up to form a EHF sum score of impairment. This score can be used to monitor changes in impairment status in individuals or in groups. It should be recorded and *reported* at least at diagnosis and release from treatment. Reporting could be done as the 'proportion of patients with improved EHF score', 'stable EHF score' and 'EHF score worse', and 'proportion of patients without impairment', 'proportion with WHO grade 1' and 'proportion with WHO grade 2'. It is recommended that the concepts and terminology of the WHO International Classification of Impairments, Activities and Participation (ICIDH-2) be adopted in the field of leprosy, particularly for the areas of prevention of impairment and disability and rehabilitation. The 'WHO disability grade' should be renamed 'WHO impairment grade'.

Correspondence to: Wim H. van Brakel, c/o INF LP, PO Box 5, Pokhara, Nepal. Fax: +977-61-20430, e-mail: wvbrakel@iname.com

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Introduction

In the rehabilitation of people with impairment, limitations in activities of daily living and/or restrictions in social participation, the question is often not '*how or why* did the condition occur', but '*what* is the nature and severity of the problem for the person affected?' In other words, a problem-oriented rather than a diagnosis-oriented approach is needed. Rehabilitation needs to be directed at solving the problems experienced by the individual patient.[1] The same is true in prevention of impairment and disability (POID). To decide what kind of rehabilitation or POID intervention is needed, the health worker needs to 1) *assess and classify* the problem(s), and 2) *grade* their severity.

A 'disability classification' for use in leprosy has been advocated by WHO since 1960.[2] It was developed into its current form in 1988.[3] The original purpose was to record a baseline 'disability' status to monitor changes during follow-up.[2] The grading system was therefore quite elaborate. However, by 1988 the main purpose of the grading had changed to being a case finding indicator, to estimate delay in case finding.[3]

Classification helps to decide what kind of problem one is dealing with and what kind of treatment protocol or intervention should be used. It also provides a uniform language for communication between health workers and health centres and for research purposes.[4] A classification is defined as 'a system of concepts (terms) connected by generic relations'.[4] Each category of a classification is determined by certain predefined characteristics. A very simple example is the multibacillary/paucibacillary (MB/PB) classification in leprosy.[5]

A classification for use in rehabilitation medicine was introduced by WHO in 1980, the International Classification of Impairments, Disabilities and Handicaps (ICIDH).[5] It defines the concepts of impairment and disability (see below; handicap has been left out because it falls outside the remit of this paper) and then subdivides each into categories and subcategories. Its use in leprosy has been recommended by Brandsma *et al.*,[6,7] Pönnighaus *et al.*[8] and Smith.[9] Adoption of the ICIDH framework and terminology in leprosy would greatly help to clarify the current confusion in terms and concepts. The terms 'impairment', 'disability' and 'deformity' are often used interchangeably. Anaesthesia is sometimes referred to as a 'deformity' and a plantar ulcer as a 'disability'. The term 'disability' is used without any reference to rehabilitation.

The ICIDH defines impairment and disability as follows:

Impairment: 'Any loss or abnormality of psychological, physiological, or anatomical structure or function'.[5]

Disability: 'Any restriction or lack of ability (resulting from impairment) to perform an activity in the manner of within the range considered normal for a human being'.[5]

Deformity may be defined as 'visible impairment'.

According to these definitions, the well-known 'WHO disability grading scale' does not grade disabilities but impairments.[7,9] This confusion has also been found with other similar scales. Molenaar *et al.* noted that the 'neurologic disability score' 'is in fact an impairment measure'.[10]

In 1997, a draft of the revised edition of the ICIDH was published: the ICIDH-2.[11] In this revised classification, the terms 'disability' and 'handicap' were replaced by the more intuitive and positive terms 'activities' (of daily living) and (social) 'participation'. Problems in these areas are described as 'activity limitation' and 'participation restriction'. We propose that the concepts used in the new ICIDH-2 be used throughout in leprosy work. Besides providing a uniform language for the area of prevention of impairment and disability, it offers

a client-oriented framework for rehabilitation. In this paper we will use the terms 'impairment' and 'disability' only according to the above definitions. We will therefore refer to the 'WHO disability grade' as the 'WHO impairment grade'.

Besides classification of the problems a person experiences, it is often important to grade their severity, for example, if progress over time is to be assessed. The purpose of this paper is to discuss the concept of 'severity grading' and to describe the use of an impairment summary score, the Eyes, Hands, Feet (EHF) score, as an indicator of the severity and evolution of impairment over time.

Materials and methods

To illustrate the use of the EHF score, data are used from a retrospective cohort study on impairment in multibacillary (MB) patients in West Nepal. The methods are described in detail in a separate paper by Reed *et al.*[12] In summary, a record review was done of 1082 multibacillary patients (MB) registered between 1980 and 1993 and released from treatment (RFT) between 1983 and 1994 at nine mobile clinic treatment centres in the Western Region. From each patient card, the following information was collected: registration and RFT dates, age, sex, leprosy type, WHO grades at diagnosis and any other recorded at yearly intervals.

The summary score used is the sum of the WHO impairment grades of both eyes, hands and feet (EHF score, minimum '0', maximum '12'). The EHF score was calculated at diagnosis and for annual follow-up examinations for which the patient had attended. To assess whether the patient had improved, stayed the same or deteriorated, the difference in EHF scores between diagnosis and annual follow-ups was calculated. The same was done using the WHO maximum impairment grades.

Results

Table 1 compares the impairment status as measured with the WHO maximum impairment grade with the result of the 0–12 grade EHF score. It can be seen that the EHF score gives a much fuller picture of the extent of impairment. Of the 1082 patients, 478 (44·1%) had no impairment (a score of 0) at diagnosis. This left 55·9% of patients scoring one or more (at least one hand or foot with sensory impairment, or one eye affected by leprosy).

Table 1. Comparison of the maximum WHO impairment grade and the impairment sum score of eyes, hands and feet (EHF score) at diagnosis in 1082 MB patients registered in field clinics in the Western Region, Nepal

Maximum grade	Summary impairment score (EHF)													
	0	1	2	3	4	5	6	7	8	9	10	11	12	Total
0	478													478
1		87	81	24	85		3							280
2			100	21	45	44	44	21	32	4	5	2	6	324
Total	478	87	181	45	130	44	47	21	32	4	5	2	6	1082

Table 2. Changes in maximum WHO impairment grade between time of diagnosis and 2-year follow up in 706 MB patients registered in field clinics in the Western Region, Nepal. The impairment status of the patients who appeared to have remained stable are shown in bold (509 or 72%). Those above the diagonal (top-right segment) deteriorated

Maximum grade at diagnosis	Maximum grade after 2 years						
	0	%	1	%	2	%	Total
0	**279**	90·0	19	6·1	12	3·9	310
1	86	45·7	68	36·2	34	18·1	188
2	25	12·0	21	10·1	**162**	77·9	208
Total	390		108		208		706

In Table 2, the WHO maximum grades at diagnosis and at 2 years follow-up are cross-tabulated. Only 706/1082 patients had a WHO grading recorded at 2 years. 509/706 patients (72%) appeared not to have changed in impairment status. Table 2 also shows that grade 2 impairment cannot be equated with 'irreversible' impairment: 22% of patients with a maximum grade of 2 improved during the study period. Table 3 shows a similar comparison for the EHF scores. This time only 399 (56·5%) appeared unchanged, with only three showing changes in the maximum grade.

Table 4 compares the difference in maximum WHO grade between diagnosis and 2-year follow-up with the difference in EHF sum score during the same period. Of the 509/706 patients who had a stable WHO maximum grade, 113 showed changes in EHF score. Improvement or deterioration of impairment status was thus missed in 113 patients (16%)

Table 3. Changes in EHF scores between time of diagnosis and 2-year follow up in 706 MB patients registered in field clinics in the Western Region, Nepal. Patients below the diagonal (bottom-left segment) improved; those above deteriorated (top-right segment)

EHF scores at diagnosis	EHF scores after 2 years													Total no. patients
	0	1	2	3	4	5	6	7	8	9	10	11	12	
0	279	7	17		6		1							310
1	36	11	11		1									59
2	41	15	44	7	8	2	3	1						121
3	6	5	4	2	4	2	2	1						26
4	21	4	12	5	31	7	4	3	2					89
5	2	1	1	3	4	7	6	1	4					29
6	4		2		5	4	9	3	2		1		1	31
7					1		1	5	2	3				12
8				2			2	4	2	8			1	19
9										1	1			2
10												1		
11											1	1		
12	1												4	5
Total	390	43	93	18	59	25	34	13	20	1	2	2	6	706

Table 4. Comparison of responsiveness to change between the method of the maximum WHO impairment grade and the EHF sum score during 2 years of leprosy treatment in 706 patients in West Nepal. Positive 'difference scores' indicate an improvement; negative scores a worsening. The bold numbers refer to patients in whom the changes detected with the EHF score were bigger than those detected with the maximum WHO impairment score (216/706 = 30·6%). In 113/509 patients (22%) the EHF score detected a change of between 1 and 6 points while the difference between maximum scores was zero

Difference in EHF score	Difference in maximum WHO impairment grade					
	−2	−1	0	1	2	Total
−6	**1**		**1**			2
−5		**1**				1
−4	**1**	9	**4**			14
−3		6	6			12
−2	10	**13**	**10**	**1**	34	
−1		19	**29**	1		49
0		2	396	1		399
1		1	**28**	48		77
2		**2**	**26**	**31**	12	71
3			**7**	**2**	**4**	13
4			**1**	**22**	**2**	25
5					**2**	2
6			**1**	**1**	**4**	7
12					**1**	1
Total	12	53	509	107	25	706

with the method of the maximum grade. In 216/706 patients (30·6%), the changes detected with the EHF score were bigger than those revealed by the method of maximum grades. One patient recovered completely from having an EHF score of 12 at diagnosis to not having any impairment after 2 years. While there may have been mistakes in his original grading, he was also suffering from ENL reaction at the time. Successful treatment of the reaction may explain this dramatic recovery.

Discussion

In the current study, the WHO maximum grading system was compared with a simple sum of the WHO impairment grades of both hands, feet and eyes, the EHF score. This idea is not new. De Rijk *et al.* used a simple sum of the WHO grade of each hand and foot in the AMFES project in Ethiopia.[13] They omitted the eye grade, because only 5% of the patients in their sample ($n = 286$) had eye impairment at diagnosis.[13] In our sample ($n = 1082$), this was 4·3% (95%CI 3·1–5·6). However, we consider eye impairment very important, particularly in people who may also have hand or foot impairment. Furthermore, the prevalence of eye impairment varies greatly in different patient populations and the score results should be comparable between different projects and centres.

It is clear from the data presented that the EHF score provides a much more detailed picture of the impairment status of individuals than does the maximum WHO grade. Watson remarked that the maximum grade method was not sensitive enough to change.[14] We have

shown that the maximum grade method failed to detect changes in impairment status in 16% of patients compared with when the EHF score was used. In 30·6%, the changes were underestimated when only the maximum grade was used as indicator.

SEVERITY GRADING

In the management of people with impairment, activity limitations and/or problems with social participation, one often needs to grade the severity of the problem. This will help to assess the urgency of intervention and provide a measure to monitor progress over time. Severity of impairment can be graded by:

1. Assigning different grades for different levels of a given type of impairment.
2. Assigning different weights to different impairments, i.e. a hierarchical system in which certain impairments are more severe than others.
3. Using a summary score of the grades assigned to separate impairments in one individual, i.e. grading the *extent* of impairment, assuming that more extensive impairment, will be more severe to the patient.

In 1960, WHO adopted a 'classification of disabilities' for use in leprosy,[2] based on a 6-point scale (0–5), separate for hands, feet and face. The scale graded only impairments according to the ICIDH terminology and was a combination of an impairment severity grading of type 2 above and an impairment classification. Two revisions of this grading system were subsequently published, a 4-point scale in 1970[15] and a 3-point scale in 1988.[3,15] These have become widely accepted in leprosy control programmes, although their use is often restricted to grading of impairments at diagnosis. Modifications of the WHO grading scale and forms have been proposed by Hasan,[16] Kulkarni *et al.*,[17] Watson,[14] Brandsma *et al.*[18] and Thappa.[19]

Two major difficulties faced are:

1. The widely varying needs: a simple system for use in prevention of impairment activities in the field and a detailed system to be used for physical rehabilitation in referral centres.
2. The fact that impairments in leprosy do not always follow set patterns and that the relative severity of different impairments varies among individuals and is related to the resulting activity limitations and/or restriction in social participation.

For example, some people develop sensory impairment before contractures, while others have contractures without sensory impairment. For a person who depends for his daily living on his ability to feel, anaesthesia of his hands may result in a more severe disability than a contracture of one or more fingers. This raises the question whether impairment measures are the most relevant in this situation, or whether activity (disability) measures should be used instead. Discussing outcome measures in peripheral neuropathies, Molenaar *et al.* stated 'We believe that impairment measures give information on the biological effect of treatment, whereas disability and handicap measures give clinically important and patient relevant information showing whether a treatment improves the patient's functional health'.[10] In leprosy, physical rehabilitation efforts have mainly centred on prevention and treatment of primary and secondary impairments.[20] To assess the severity of the impairment in a given individual and to monitor the success of prevention and treatment of impairment, an impairment measure is therefore appropriate. At the same time, measures to assess activities of daily living and social participation relevant for people affected by leprosy should be developed.

IMPAIRMENT SEVERITY SCORES

It is convenient if the person's condition can be summarized in a single score. Until now, two main approaches have been used: a 'disability' index and the 'maximum WHO disability grade'. The former was first introduced by Bechelli and Martinez Dominguez in 1971.[21] They proposed three different ways of calculating a disability index (DI) from the grades of the 1970 WHO disability grading. The most commonly used is the DI(2), in which the index is the average of the sums of impairment grades for each hand, foot and eye.[22,23] The Bechelli DI(2) is a comprehensive summary measure, but, because it is based on the WHO 1960 grading, it requires fairly extensive recording of impairments and is complicated to calculate.

The use of the maximum WHO disability grade to summarize a person's impairment status has been popularized by the inclusion of this indicator in ILEP and WHO statistics.[3] With this method, the *maximum* grade of the six individual sites is taken as an overall indicator of the person's impairment status. The validity of the severity weights assigned to different impairments in the WHO grading system, used in both methods, is questionable (Jean Watson, unpublished discussion document on disability grading, 1995). To our knowledge, none of the WHO grading scales has been subjected to reliability testing. This should be urgently done, as an increasing importance is attached to the results of the WHO impairment grading.

SUMMARY SCORES

The use of sum scores has been criticized by several authors. Van Gijn and Warlow warned strongly against attempting to reconstruct a patient from separate 'functions': 'A patient is more than the sum of his signs'.[24] They argue that numerical changes in (impairment) sum scores of individuals may be meaningless and advocate the use of handicap or disability scales with only few categories, as these are much more meaningful from the patient's point of view.[24,25] Another criticism of summary scores is that one cannot tell whether a change in score was a major change in one component or only minor changes in several components (Watson, unpublished discussion paper on disability grading, 1995). While this is true, this disadvantage can be reduced by ensuring that only significant changes in components contribute to changes in the sum score.

For example, the EHF score is made up of the components of the WHO impairment grading. A change of one point at any site usually constitutes a major change in impairment status and, therefore, a change of even 1 point in the sum score should be considered clinically significant. In a sum score such as the EHF score, changes may be masked if different components of the score change in opposite directions. For example, if the anaesthetic hand of a patient recovers, but he develops sensory impairment on the sole of one foot, the sum score will show no change. The same occurs when using the maximum grade method.

It should be pointed out that sum scores such as the EHF score are not intended for clinical management of individual patients. They serve as indicators of whether a patient or group of patients is improving, deteriorating or remaining stable. For clinical management, a system such as the Impairment Summary Form, using separate impairment indicators, such as a wound count, a count of sites of bone loss, sites with sensory impairment or changes in voluntary muscle test will be much more useful.[26]

We do not advocate the EHF score as an ideal impairment indicator. It is a simple sum of

very crude components. Its reliability has to date not been established and its responsiveness to change over time needs further prospective study. However, its main strength lies in the availability of the components. According to a recent survey of the ILEP Medical Commission on prevention of disability activities in ILEP-supported projects, 99% of the responding projects recorded the WHO impairment grade.[27] Adding up the six components to form the EHF score makes, in our opinion, much better use of the available data than does the method of maximum grades. Such a score should be calculated at diagnosis, at release from treatment and at other times as needed. Changes should be *recorded* as 'improved', 'stable' or 'deteriorated' and *reported* as 'proportion of patients improved', 'proportion of patients remaining stable' and 'proportion of patients deteriorated'. In addition, the 'proportion of patients without impairment', 'proportion with WHO grade 1' and 'proportion with WHO grade 2' should be reported at diagnosis and RFT. Where possible, these data should be based on cohort calculations. Such indicators would provide at least a crude measure of the effectiveness of prevention of impairment activities, until better measures become available.

RECOMMENDATIONS

1. The concepts and terminology of the ICIDH-2 should be adopted in the field of leprosy, particularly for the areas of prevention of impairment and disability (POID) and rehabilitation.
2. We suggest that the term 'POID' is more appropriate than 'POD' (prevention of disability), given that most activities are aimed at preventing primary or secondary impairments.
3. The 'WHO disability grade' should be renamed 'WHO impairment grade'.
4. Besides the use of the 'proportion of new cases with WHO grade 2' as a case finding indicator, the six components of the WHO impairment grading may be added up to form a E(yes)H(ands)F(eet) sum score of impairment. This score can be used to monitor changes in impairment status in individuals or groups of people.
5. The impairment status of patients should be recorded and *reported* on a cohort basis at least at diagnosis and release from treatment, and more frequently if indicated. This could be done as the 'proportion of patients with improved EHF score', 'stable EHF score' and 'EHF score worse', and 'proportion of patients without impairment', 'proportion with WHO grade 1' and 'proportion with WHO grade 2'.

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Factors associated with impairments in new leprosy patients: the AMFES cohort

A. MEIMA[+], P. R. SAUNDERSON*, S. GEBRE*, K. DESTA*, G. J. VAN OORTMARSSEN[+] & J.D.F. HABBEMA[+]

[+]*Department of Public Health, Erasmus University Rotterdam, The Netherlands*

**All Africa Leprosy, Tuberculosis and Rehabilitation Centre, Addis Ababa, Ethiopia*

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Summary Data on the importance of the delay between onset of symptoms and registration as a risk factor for impairment are sparse. This study investigates the quantitative relationship between this delay, other risk factors and the impairment status in new leprosy patients. It reports on 592 new leprosy patients enrolled in 1988–1992 in the prospective ALERT MDT Field Evaluation Study in central Ethiopia (AMFES). The influence of the risk factors sex, age, delay, PB/MB classification in relation to BI, and prior dapsone treatment on the impairment status at intake is analysed. Estimates for the delay are based on patient recall. For the risk factors, odds ratios on impairment and on severity of impairment were calculated using both univariate and multivariate logistic regression. The registration delay was 2 years or more for 44% of new patients. The prevalence of impairment (WHO impairment grades 1 and 2 combined) increased continuously from 36% for new patients with a delay of 0–1 year to 81% for new patients with delays of 4 years or more. This prevalence also increased continuously with age; it rose from 26% in children to 80% for the age group 60 and over. In the multivariate regression, the odds ratios for new patients to be impaired were statistically significant for all delay categories (baseline 1–2 years) and age groups (baseline 15–29 years). No statistically significant differences in odds ratios were observed with respect to sex and PB/MB classification in relation to BI. Overall, 31% of new patients presented with WHO impairment grade 1 and 23% with grade 2. The risk on grade 2 also increased with the registration delay amongst the impaired new patients. Relatively few impaired males and relatively few impaired MB patients with a BI value of 3 or higher had grade 2 impairment. Registration delay and age are the main risk factors for presentation with impairment. Reduction of delay in central Ethiopia requires re-thinking of control methodologies. The search for ways to reduce delays in diagnosis and treatment should receive high priority in leprosy research and in leprosy control programmes.

Correspondence to: Abraham Meima, M.Sc., Department of Public Health, Faculty of Medicine and Health Sciences, Erasmus University Rotterdam, PO Box 1738, 3000 DR Rotterdam, The Netherlands. Fax: +31 10 408 9449; e-mail: Meima@mgz.fgg.eur.nl

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Introduction

The implementation of effective antibacterial treatment for leprosy has shifted the focus in leprosy programmes to prevention of disability. However, many new cases already have impairments and disabilities. Amongst major endemic countries, the proportion of new cases presenting with WHO disability grade 2 was reported in 1995 to range from 6% to 21%.[1] Several studies showed that the majority of patients who were impaired at release from MDT already had nerve function impairment at the time of registration.[2–4] This paper documents risk factors for impairment in new cases, which may contribute to the improvement of prevention of disability activities in leprosy control programmes.

Various factors might be associated with the presence of impairment at registration. For example, differences in impairment status at registration have been observed with respect to gender, age at registration, and leprosy type according to clinical classification systems or the WHO paucibacillary/multibacillary (PB/MB) classification.[2–9] At the same time, higher proportions of MB cases amongst male patients have been documented,[2,7–10] and different age distributions for new PB and MB cases have been reported.[9,11–14] This implies that interrelations must be taken into account when analysing which factors are associated with the impairment status at registration.

In addition, it is generally believed that a longer delay between onset of disease and registration, here called registration delay, is associated with more impairment. The proportion of new cases with impairments at registration is, for instance, much higher in passively, as compared to actively, detected cases in Malawi.[2] Richardus *et al.*[3] concluded that early diagnosis (and subsequent activities for prevention of disability) could prevent impairments in more than 30% of all patients in a control programme in Bangladesh, more than any intervention at a later stage could achieve.

Registration delay has been documented in several studies.[7,8,10,15–22] A study on long term leprosy trends in Thailand showed that important declines in the registration delay coincided with a declining trend in the proportion of cases presenting with grade 2 disability.[17] A recent study from another area in Thailand[4] revealed a highly significant linear trend in the proportion of new cases with grade 2 disability in relation to the registration delay. Bekri *et al.*[22] concluded that the median registration delay was more than twice as high in disabled as compared with non-disabled patients from Ethiopia. Wittenhorst *et al.*[7] found a highly significant association between registration delay and presence of impairments in new leprosy patients from Zimbabwe. It is beyond doubt that the presence and severity of impairments are associated with duration of disease (e.g. [23–27]). Surprisingly, knowledge on the quantitative relationship between the registration delay and the impairment status at registration in *new* leprosy patients—while simultaneously considering the impact of other, interrelated factors—is very limited.

This paper therefore examines the impairment status at registration as a function of several potential risk factors and their interaction for patients who were enrolled in a long-term prospective study of the effectiveness of the WHO-recommended MDT regimens under routine leprosy control service conditions. This study, the ALERT MDT Field Evaluation Study (AMFES), is carried out in a selected area within ALERT's leprosy control programme in central Ethiopia. Details of the design of the AMFES study and preliminary results for the new patients who were registered in the first 3 years have been reported upon before.[28,29]

Materials and methods

Case-finding in ALERT's control programme was almost exclusively passive. All new cases from the selected area were eligible for AMFES, but not all patients presenting during the intake period were enrolled, mainly because of limitations in the accessibility of leprosy clinics. The AMFES intake period was April 1988 to March 1993.

Cases who were relapses from previous chemotherapy treatment and newly detected cases with errors in diagnosis or in enrolment procedures were excluded from the present study. The present study involves all remaining newly detected cases who were enrolled in the AMFES study. Patient characteristics included are age, sex, classification, bacteriological index (BI), duration of prior dapsone treatment, impairment status and registration delay. PB and MB patients who received no more than 4 weeks and no more than 16 weeks of dapsone, respectively, were regarded as 'new, untreated', and were included in the study. Impairments are in this paper expressed in terms of the 'WHO disability grades' and are, following Reed *et al.*,[30] referred to as 'WHO impairment grades'.

The type of treatment (PB or MB) was chosen on the basis of clinical classification and skin smears. Skin smears were routinely taken from both earlobes and from at least two skin lesions for all patients, and were repeated after 4 or 8 weeks in case of doubt. For some patients, the smear was either not done, or the result was not available for logistic reasons. For clinical classification, the simplified system for field workers recommended by Jopling[31] (which adds BB to the BL group) was used. Tuberculoid (TT) and borderline-tuberculoid (BT) patients with a negative smear at all sites were normally given PB treatment. Until July 1989, BT patients with BI not exceeding 1 were included in the PB group. Borderline-lepromatous (BL) and lepromatous (LL) patients and those with a positive smear at one or more sites were given MB treatment. For patients with nerve involvement only, lacking skin lesions and whose skin smears were (repeatedly) negative (neural leprosy, NL), assignment of treatment regimen was based on the extent of nerve involvement or on the finding of acid-fast bacilli in a nerve biopsy. In case of any controversy, patients were referred to the AMFES medical officer. In practical terms, many patients correctly classified as PB within this study, would be classified as MB if now used criteria focussing on number of skin lesions or number of body areas affected had been applied.[32] The assignment of treatment regimen was straightforward for most patients. More detailed information on procedures for diagnosis, classification and treatment is given by de Rijk *et al.*[29]

The registration delay was based on patient recall. Health workers first asked what the patient's complaint was, and then tried to find out when any symptoms (e.g. skin lesions, neurological problems, weakness or numbness in hands and feet) were first noticed, relating them to known events if necessary. The health worker recorded the calendar year of the first notice of symptoms, and the registration delay was calculated from the mid-year of this calendar year and the date of registration. For example, a patient who registered on March 5, 1992 and who recalled having first noticed symptoms in 1990 was assigned a registration delay of 1 year and 8 months. In the Results, we have denoted this as 1–2 years; this category includes all calculated delays between 1·0 and 2·0 years. If this patient had registered on September 5, 1992, he would have been assigned a delay of 2–3 years. Individuals registering in the same year as or before July 1 of the year following the year in which symptoms were first noticed, were assigned a delay of 0–1 year (i.e. less than 1 year).

The factors associated with increased risk for impairments at the time of registration were analysed both separately and in combination. In the data analysis, odds ratios for risk

factors for presentation with impairments at the time of registration were calculated using univariate and multivariate logistic regression. Statistical significance refers to the 5% level. The data analysis was carried out in SPSS.

Results

A total of 603 new cases were enrolled in the AMFES project. Out of these, four individuals were wrongly diagnosed as having leprosy, and seven had improper enrolment procedures. Thus, 11 new cases had to be excluded from the present data analysis. This paper reports on the resulting 592 newly detected patients.

PROFILE OF AMFES AND ALERT PATIENTS

The 592 included patients and the new cases detected in the same period by ALERT's routine control programme[33] were compared for age, sex, classification and WHO impairment status. Important discrepancies were not observed, and the patients involved in this study are thus considered to be sufficiently representative for new case detection by ALERT in the same period.

Out of the patients involved in this study, 92% reported voluntarily. This confirms the passive nature of case finding by ALERT's control programme in the late 1980s and early 1990s. Table 1 shows that the number of males in the study population was almost twice as high as the number of females (male:female ratio: 1·8). The child proportion was 14%, and for approximately half of the patients the age at registration was between 15 and 34 years. The most common clinical classifications were BT and BL. TT and NL cases were rarely seen. Skin smears were taken from all but 14 (13 BT and one BL) patients. None of the TT, and 13 BT patients had positive smears (10 with BI 1 and three with BI 2). Forty BL patients had a BI of 1 or 2, and 132 had a BI of 3 or more. The BI was 3 or more for all 84 LL patients but two. Overall, almost half of the patients were smear positive, and more than one third of the patients had high bacterial loads ($BI \geq 3$). The group of patients who received MB treatment consisted of two NL patients, 12 BT patients (including nine smear-positives with two with BI 2), and all BL and LL patients. Overall, almost equal numbers of patients received PB and MB treatment. For data analysis, patients were re-classified according to a composite classification with four categories (PB; MB: $BI = 0$; MB: $BI = 1 + 2$; and MB: $BI = 3 + 4 + 5 + 6$). At intake, about 16% of patients had received dapsone treatment (39 PB for at most 4 weeks and 54 MB for at most 16 weeks). The registration delay was above 2 years for 44% of the patients. The mean registration delays for males and females were 2·4 and 2·3 years. Figure 1 presents a frequency distribution of the registration delay. Leprosy induced impairments are very common in the study population: 31% of new patients presented with grade 1 impairment and 23% with grade 2.

UNIVARIATE ANALYSIS OF RISK FACTORS FOR PRESENTATION WITH IMPAIRMENT

Table 2 gives details on risk factors for presentation with any impairment (either grade 1 or grade 2). The six cases without information on the registration delay were excluded from the analysis. The univariate results indicate that the risk for presentation with impairment

Table 1. Characteristics of new patients at intake. Percentages are given in proportion to the numbers of patients for which information is available. Numbers of patients for which information is available are given in brackets if information is not available for all newly detected patients

Total patients				
592				
Gender				
Male	*Female*			
377 (64%)	215 (36%)			
Age at registration in years				
0–14	*15–29*	*30–44*	*45–59*	*60+*
83 (14%)	240 (41%)	127 (21%)	97 (16%)	45 (8%)
Ridley–Jopling classification				
TT	*BT*	*BL*	*LL*	*NL*
6 (1%)	297 (50%)	202 (34%)	84 (14%)	3 (1%)
Bacteriological index (BI) ($n = 578$)				
0	*1+2*	*3+4*	*5+6*	
311 (54%)	53 (9%)	97 (17%)	117 (20%)	
PB/MB classification				
PB	*MB*			
292 (49%)	300 (51%)			
Subdivision of PB and MB				
PB	*MB: BI = 0*	*MB: BI=1+2*	*MB: BI = 3–6*	
292 (49%)	37 (6%)	49 (8%)	214 (36%)	
Registration delay in years ($n = 586$)				
0–1	*1–2*	*2–4*	*4+*	
156 (27%)	174 (30%)	168 (29%)	88 (15%)	
Duration of prior dapsone treatment in weeks				
0	*1–4*	*5–16*		
499 (84%)	70 (12%)	23 (3·9%)		
WHO impairment grading				
0	*1*	*2*		
268 (45%)	185 (31%)	139 (23%)		

strongly increased with both age and registration delay. The proportion with impairment was much smaller for delays below 2 years than for longer delays (42 versus 72%). The overall associations between presence of impairment and age and between presence of impairment and delay were both highly significant ($p < 0{\cdot}001$). A strong association was also found between risk for any impairment and classification in relation to BI ($p = 0{\cdot}002$); the risk was highest for MB patients presenting with BI 0, 1 or 2. Males more often presented with impairments than females, but the association was not significant ($p = 0{\cdot}07$). Short term prior dapsone treatment is associated with a higher but non-significant risk of being impaired at the start of MDT treatment ($p = 0{\cdot}17$). The higher risk is even not significant when comparing no prior dapsone treatment with prior dapsone treatment up to a maximum of 16 weeks (i.e. prior durations of treatment of 1–4 weeks and of 5–16 weeks are combined, $p = 0{\cdot}09$).

MULTIVARIATE ANALYSIS OF RISK FACTORS FOR PRESENTATION WITH IMPAIRMENT

Figure 2 illustrates the simultaneous impact of registration delay and other risk factors on

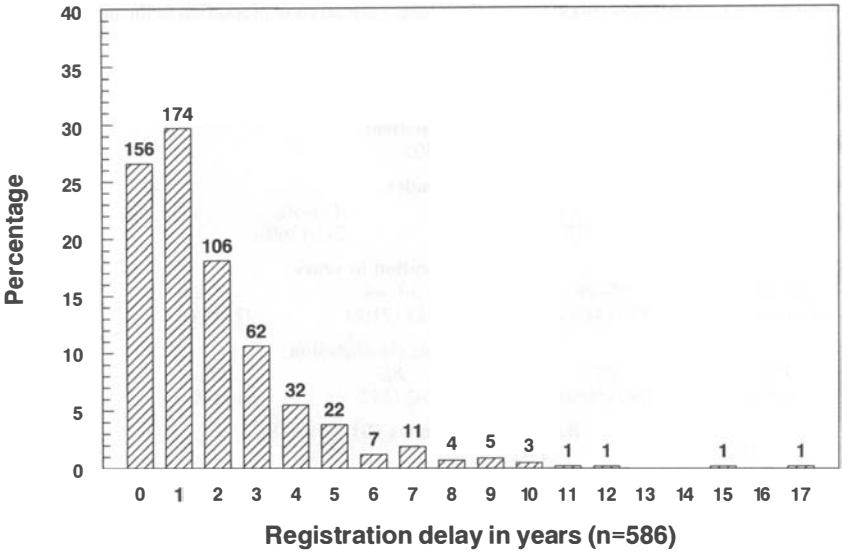

Figure 1. Frequency distribution of the registration delay. Numbers of patients for the respective registration delays are given on top of the bars. Years are truncated, e.g. 2 years means between 2·0 and 3·0 years.

impairment. With increasing delay the proportion presenting with impairment increases in both males and females, in each age group, and in PB and MB patients irrespective of BI. Only 15% (four out of 27) MB patients with BI 0 and with a delay of 1 year or more presented without impairment. Age influences impairment independently of the registration delay: the proportion with impairment increases with age for all registration delays. An effect of MB in relation to BI on impairment which is independent of the registration delay does not come out clearly.

Table 2 gives the results of multivariate logistic regression for a model with all risk factors included. The odds ratios for the significant risk factors in the univariate analysis are pulled towards the no influence value of 1 in the multivariate logistic regression. Details below refer to the multivariate logistic regression. A statistically significant increase in odds ratios is found both for delay and for age. None of the odds ratios for the other risk factors is significant. In particular, the odds ratios for BI 0 and for BI 1 + 2 have lost their category-wise statistical significance in the multivariate regression; however the differences in risk for the factor classification in relation to BI, with relatively higher risks for MB with BI 0 and MB with BI 1 or 2, are overall significant ($p = 0{\cdot}04$). The model which includes all risk factors was compared with a multivariate model that was obtained by backward selection of risk factors on the basis of the Wald statistic. Little difference was observed: the odds ratios and confidence intervals for the risk factors included in the model obtained by backward selection (age, registration delay and classification in relation to BI) are very close to those presented in Table 2.

LEVEL OF IMPAIRMENT

Table 3 gives the results of univariate analysis for the risk for impaired new cases to have

Table 2. Impairment at intake according to various risk factors with odds ratios for presentation with impairment obtained by univariate and multivariate regression for the 586 new cases with known registration delay

Risk factor	No. impaired (% of all cases)	Univariate odds ratio (95% confidence interval)	Multivariate odds ratio (95% confidence interval)
Gender			
Male	215/372 (58%)	Baseline	Baseline
Female	107/214 (50%)	0·7 (0·5–1·0)	0·8 (0·6–1·2)
Classification i.r.t. BI			
PB	150/286 (52%)	Baseline	Baseline
MB: BI = 0	28/37 (76%)	2·8 (1·3–6·2)	2·2 (0·9–5·3)
MB: BI = 1 + 2	35/49 (71%)	2·3 (1·2–4·4)	1·6 (0·8–3·2)
MB: BI = 3 – 6	109/214 (51%)	0·9 (0·7–1·3)	0·8 (0·5–1·2)
Age (in years)			
0–14	21/81 (26%)	0·4 (0·2–0·7)	0·4 (0·2–0·7)
15–29	112/238 (47%)	Baseline	Baseline
30–44	85/127 (67%)	2·3 (1·5–3·6)	1·9 (1·2–3·0)
45–59	69/96 (72%)	2·9 (1·7–4·8)	2·6 (1·5–4·5)
60+	35/44 (80%)	4·4 (2·0–9·5)	4·2 (1·8–9·6)
Registration delay (years)			
0–1	56/156 (36%)	0·6 (0·4–1·0)	0·6 (0·4–1·0)
1–2	82/174 (47%)	Baseline	Baseline
2–4	113/168 (67%)	2·3 (1·5–3·6)	2·1 (1·3–3·4)
4+	71/88 (81%)	4·7 (2·6–8·6)	4·5 (2·3–8·5)
Prior dapsone treatment (weeks)			
None	264/494 (53%)	Baseline	Baseline
1–4	42/69 (61%)	1·4 (0·8–2·3)	1·0 (0·6–1·9)
5–16	16/23 (70%)	2·0 (0·8–4·9)	2·5 (0·9–6·9)

grade 2 impairment. The multivariate results are not given, because they hardly differed from the univariate results. The risk is higher for long registration delays, but odds ratios for the longer delays are only just significant. The proportion with grade 2 impairment among impaired cases was 31% for delays below, and 52% for delays above 2 years. Figure 3 shows that longer registration delays are particularly associated with a higher proportion of grade 2 impairment. The apparent limited influence of longer delays on the proportion with grade 1 impairment must partially be due to an increase in grade 2 resulting from worsening of grade 1, which is largely 'compensated' by individuals who were free from impairment but who develop grade 1 with increasing delay.

Other factors show differences with respect to their influence on the risk of any impairment and on the severity of impairment in impaired cases. Firstly, MB with BI 3 or more gives a significantly lower risk for grade 2 impairment (baseline: PB leprosy). Secondly, there is no increase in the risk of grade 2 impairment with age. In fact, the risk appears to be highest for children and lowest for individuals of age 45 and older. No decrease was found in the mean registration delay with age in impaired new cases. Finally, while overall having less impairments, females with impairment more often had grade 2 than impaired males (53 versus 38%). Figure 4 shows that the excess in grade 2 impairment in impaired females as compared with impaired males exists for registration delays above 1 year and for all age groups. Gender, age, registration delay and classification in relation to BI were all statistically significant risk factors, but prior dapsone treatment was not.

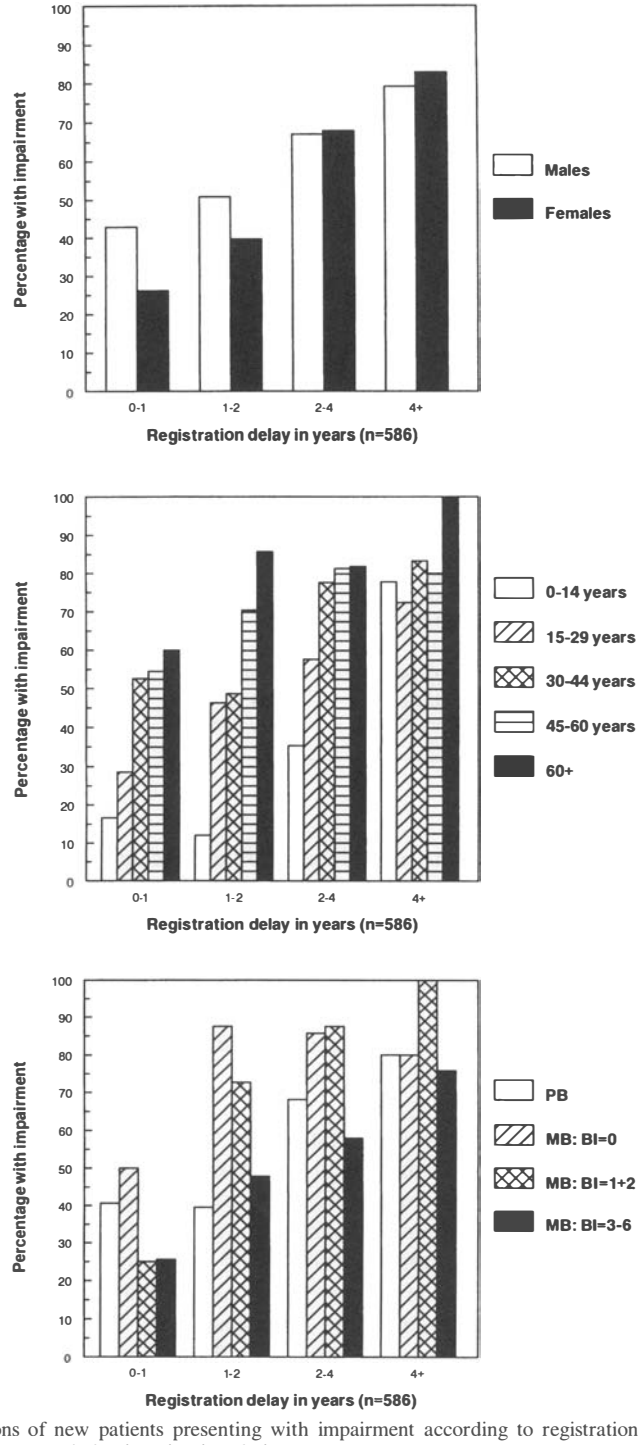

Figure 2. Proportions of new patients presenting with impairment according to registration delay in relation to respectively gender, age, and classification in relation to BI.

Table 3. Grade 2 versus grade 1 impairment at intake according to various risk factors with odds ratios for presentation with grade 2 impairment obtained by univariate regression for the 322 impaired new cases with known registration delay

Risk factor	No. with grade 2 impairment (% of all impaired cases)	Univariate odds ratio (95% confidence interval)
Gender		
Male	82/215 (38%)	Baseline
Female	57/107 (53%)	1·8 (1·2–3·0)
Classification i.r.t. BI		
PB	72/150 (48%)	Baseline
MB: BI = 0	14/28 (50%)	1·1 (0·5–2·4)
MB: BI = 1 + 2	19/35 (54%)	1·3 (0·6–2·7)
MB: BI = 3–6	34/109 (31%)	0·5 (0·3–0·8)
Age (in years)		
0–14	15/21 (71%)	3·5 (1·2–9·6)
15–29	47/112 (42%)	Baseline
30–44	46/85 (54%)	1·6 (0·9–2·9)
45–59	19/69 (28%)	0·5 (0·3–1·0)
60+	12/35 (34%)	0·7 (0·3–1·6)
Registration delay (years)		
0–1	16/56 (29%)	0·8 (0·4–1·7)
1–2	27/82 (33%)	Baseline
2–4	58/113 (51%)	2·1 (1·2–3·9)
4+	38/71 (54%)	2·3 (1·2–4·5)
Prior dapsone treatment (weeks)		
None	116/264 (44%)	Baseline
1–4	17/42 (40%)	0·9 (0·4–1·7)
5–16	6/16 (38%)	0·8 (0·3–2·2)

Discussion

The objective of this study was to examine the impairment status at registration as a function of registration delay, age, classification in relation to BI, gender and prior short term dapsone treatment.

RISK FACTOR: DELAY IN REGISTRATION

This study clearly shows a heavy impact of long registration delay on the impairment status of new leprosy patients from central Ethiopia. Patients with delays of less than 2 years had a much smaller chance (42%) of being impaired than patients with longer delays (72%). Among the impaired, similar differences were observed: their chance of grade 2 impairment was 31% for delays below and 52% for delays above 2 years.

The role of registration delay was also addressed in recent studies from Zimbabwe and Thailand. A strong association between delay and grade 2 impairment was shown in the study from Zimbabwe.[7] Further analysis of the dataset underlying that study revealed that 41% of patients with a registration delay below 2 years presented with impairment against 60% of patients with longer delays. The proportion with grade 2 impairment among the impaired new patients from Zimbabwe increased from 60% for delays below 2 years to 73% for delays above 2 years.

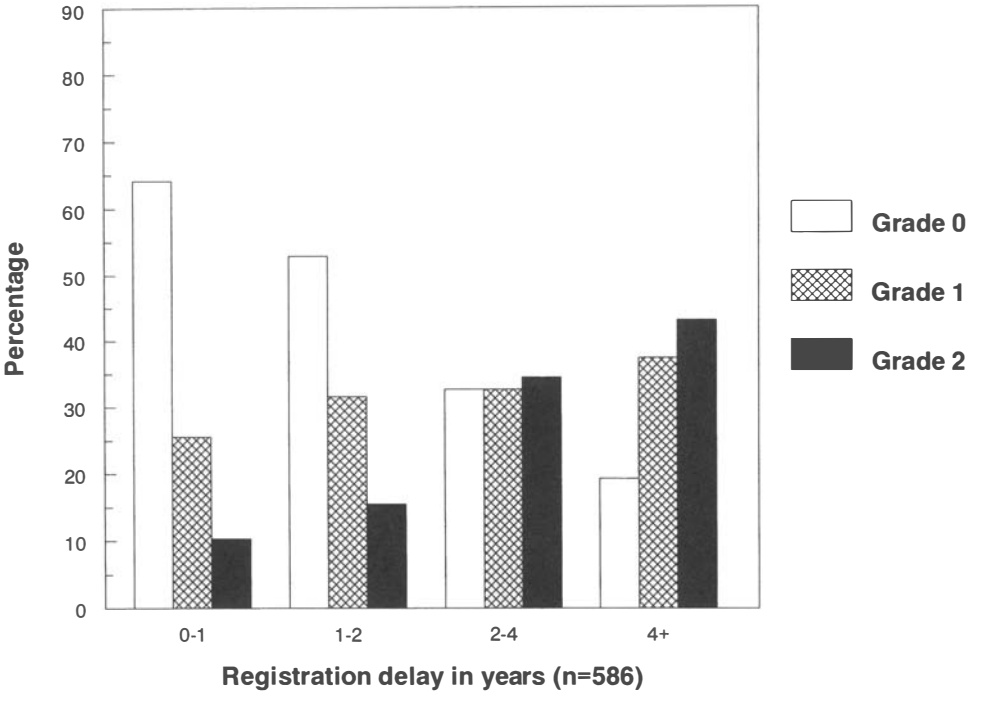

Figure 3. Impairment status of new leprosy patients according to registration delay.

For Thailand[4] also, a significant association with delay was found: 17% of patients with a delay below 2 years had impairments against 23% of patients with longer delays. The association between delay and the proportion grade 2 impairment amongst the impaired was particularly strong: 30% for delays below 2 years and 58% for longer delays had grade 2. Biological differences between populations and differences in case detection and assessment methods, methods of interviewing patients and calculation procedures may all underlie differences in results from studies on the importance of the registration delay as a risk factor for impairment. Nevertheless, all the above results are remarkably consistent.

RISK FACTOR: AGE

Several studies have reported that the risk of impairment in new cases increases with age.[2,5,7,8] However, such a univariate association does not occur in the study from Thailand,[4] and observed univariate associations between age and impairment may be confounded by the registration delay. In the present study, the multivariate analysis shows that the risk of impairment increases with age independently of other risk factors including registration delay. Interestingly, a different effect of age was shown for the risk of grade 2 impairment amongst impaired new cases: this study showed this risk to be lowest among the individuals of ages 45 and above. We do not have a straightforward explanation for these age effects. Additional examination of the data presented in the Thailand study[4] and of the data sets underlying the Zimbabwe study[7] and another recent study from Bangladesh[9] did not give further evidence for the finding of a lower risk of grade 2 impairment in impaired new cases of older ages.

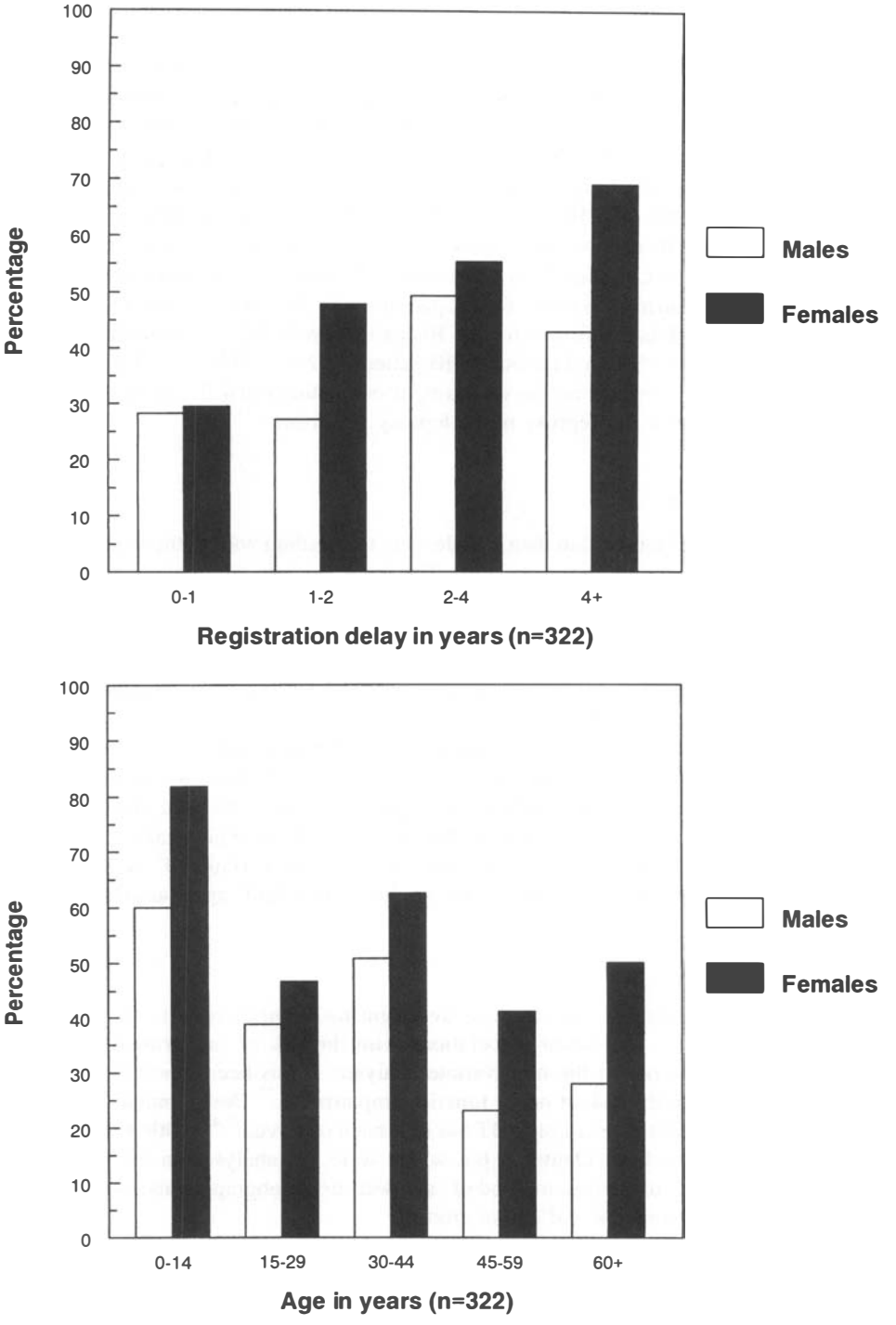

Figure 4. Proportion of impaired new leprosy patients presenting with grade 2 impairment according to gender in relation to both registration delay and age.

RISK FACTOR: CLASSIFICATION IN RELATION TO BI

MB patients with BI 0, 1 or 2 had the highest risks of impairment. The lower odds ratios in the multivariate analysis are largely explained by the relatively high age of these MB patients. MB patients with high bacterial loads (BI $\geq$ 3) had relatively few impairments, and had a significantly lower risk of grade 2 once being impaired. Further investigation showed that this risk was significantly lower only for LL patients with BI $\geq$ 3 in univariate analysis, and for both BL and LL patients with BI $\geq$ 3 in multivariate analysis. In the present study, all LL patients but two had a BI of 3 or more. Gilbody stated that borderline leprosy is 'potentially the most widespread and crippling form of leprosy'.[34] This is in line with our observation that the risk of grade 2 impairment is lower for LL patients with BI 3 or more, but does not explain our finding that the risk is also lower for the BL patients with BI 3 or more than for the PB patients (all but seven are BT) and the other MB patients (12 BT, 70 BL, two LL and two NL). This finding, however, may not be too surprising if one realizes that BL leprosy with BI 3 or more is very close to true LL leprosy in the leprosy spectrum.

RISK FACTOR: GENDER

Males had impairments more often than females, but this finding was neither significant in the univariate nor in the multivariate analysis. The mean registration delays for males and females were almost identical (2·4 versus 2·3 years). The finding as such that impairments are more common in males than females (although with a non-significant difference) is in line with many reports in literature (e.g. [2,4,5,8,9,18]). The data underlying the study from Zimbabwe[7] not only show a higher risk in males, but also longer mean registration delays for males as compared to females (3·1 versus 2·1 years).

A significant excess in grade 2 impairment in impaired females was found in the univariate analysis. This excess is difficult to explain (see also Figure 4), and its significancy disappeared in the multivariate analysis. Comparison with published data[4,8] and data underlying published reports[7,9] revealed that the proportion with grade 2 impairment among the impaired was higher in males than females from Thailand[4] and Zimbabwe,[7] whereas equal proportions were found for the studies from Chad[8] and Bangladesh.[9]

OTHER RISK FACTORS

In this study, 92 patients received dapsone treatment for a duration of 1–16 weeks before inclusion. In the cohort, significant associations with the risk of impairment were neither found in the univariate nor in the multivariate analyses. It has been reported that dapsone treatment may enhance the risk of nerve function impairment.[35] Development of new nerve function impairment after the start of MDT has also been observed.[3,4,36] Other risk factors for impairment which have been identified but which were not analysed in the present study include occupation, site of lesions, method of case detection, geographic and socio-economic factors, educational attainment and ethnic group.[6]

SOURCES OF BIAS

Registration delays are obtained by asking the patient when he or she first noticed symptoms. In his or her mind, a patient might advance this moment in time, especially in cases of long

duration of disease. On the other hand, patients or staff could presume that the duration of disease is of long duration when impairments are present. Clearly, the fallibility of patient's recall of first awareness of symptoms can bias the relationship between delay and risk of impairment, although it is difficult to judge the direction of the effect.

In the present study, the date of registration was combined with the recorded calendar year of first notice of symptoms in estimating the registration delay. We used the mid-year of this calendar year. This inaccuracy will lead to underestimation of the strength of the association between delay and impairment.

Other sources of bias also cannot be excluded. Case detection was of a passive nature and differences in awareness of symptoms and in self reporting behaviour can exist. Recall of onset of symptoms may also vary between groups of patients. It may be possible that certain findings from this study (in particular the lower risks of grade 2 impairment amongst the impaired in males and in patients of ages 45 and above) are to some extent related to these sources of bias. On the whole, we still found strong associations between impairments status and risk factors in this cohort. Studies comparing routinely obtained registration delays with delays obtained by carefully designed in depth interviews might give valuable information on the reliability of the registration delay.

SIZE OF THE PROBLEM

Individuals with grade 1 impairment are at risk of developing more severe impairments and subsequent disabilities. This study has shown that short registration delays are associated with less grade 1 impairment. The size of the impairment problem in new cases is usually only expressed in terms of the proportion with grade 2 impairment. In a report from 1995, this proportion was above 20% in four out of fifteen major endemic countries that together contributed 95% of the world wide new case load with grade 2 impairment.[1] From this perspective, the 23% grade 2 impairment observed in this study is disturbingly high. It is encouraging that the proportion with grade 2 impairment reported by ALERT's control services in central Ethiopia was somewhat lower in 1995, 1996 and 1997 than in the early 1990s.[37] Considering ALERT's presence in the area for a period of over 3 decades, re-thinking of control methodologies is definitely required, although it is also clear that public attitudes towards leprosy cannot be changed easily.[22]

IMPLICATIONS FOR RESEARCH AND CONTROL

The search for ways to reduce delays in diagnosis and treatment should have high priority in leprosy research and in leprosy control programmes. Research addressing this challenge has recently been conducted in Ethiopia. It was shown that ex-leprosy patients were important advisors for seeking early treatment. Also, 21 out of 31 patients (68%) initially presenting with grade 2 impairment versus 11 out of 48 non-impaired patients (23%) had first sought help from traditional healers instead of directly contacting the general health services (unpublished data from the All Africa Leprosy, Tuberculosis and Rehabilitation Centre (ALERT), Addis Ababa, Ethiopia).

A second study[22] broke down the delay until start of treatment into several components. It was shown that just over 50% of the delay occurs before the patient seeks any help. Use of some form of traditional medicine accounted for just under one-third of the delay, and delay after attending a recognized clinic accounts for over 10% of the total delay. The delay until

the patient's first action and the delay between first action and the first visit to a recognized clinic were significantly longer for impaired patients. High levels of stigma and use of traditional medicine were found to be associated with more impairment when comparing two rural areas of Ethiopia with different impairment rates in new patients.

It is highly questionable whether a shift to active methods of case finding can be cost-effective. In addition, there is already a tendency to integrate leprosy services into the general health services. This calls for proper management of leprosy suspects, and delays in referral for leprosy treatment within the general health services should require special attention. In view of problems with referral, Bekri *et al.*[22] suggest that in the Ethiopian context, it would be ideal for diagnosis and the start of treatment to be done at the rural clinic, with examination by a specialist at a later stage. They also state that reducing stigma is far more complex than imparting knowledge alone, and that health education campaigns must be well planned and sufficiently sophisticated in order to have any impact. A recent review already indicated that gender inequalities should be a point of concern to health services and in health education.[38] A national advertising programme involving mass media was an integral part of a successful campaign against leprosy in the early 1990s in Sri Lanka.[39] The potential benefits of well-researched media campaigns need to be investigated.

In conclusion, a better understanding of factors determining delays is of eminent importance for the development of strategies that minimize impairment at registration and thus minimize permanent disability in those who develop leprosy. This has also been recognized by the Medico–Social Commission of ILEP, which identified investigation of factors influencing delay in diagnosis and treatment for different communities as a major research priority in the context of prevention of disability in leprosy (ILEP: Development of an ILEP co-ordinated programme of research on nerve damage and reactions in leprosy. Internal Report. Draft, June 1998).

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FURTHER EDUCATION

Ulcer surgery for non-specialist surgeons

ROLAND O. KAZEN
ALERT, Addis Ababa, Ethiopia

Introduction

Despite prevention of disability efforts in the management of leprosy, a high proportion of patients are still presenting with nerve damage of hands and feet. Considerable numbers of cured leprosy patients will for a long time in the future be developing ulcers and septic conditions on their feet in need of surgical treatment.

Surgical interventions in addition to conservative ulcer care play an important part in the prevention and treatment of plantar ulcers.

Many programmes have no access to surgeons trained in leprosy surgery. Traditionally, surgical treatment has been provided only in leprosy institutions. With the increasing integration of leprosy management in general health care, there is a need for integration and decentralization of surgical activities. The work must be shared by many.

In developing countries, where most leprosy patients are, non-specialist surgeons mainly perform surgery in peripheral units. Surgical interventions can be classified into different levels and delegated to different grades of qualified persons in peripheral health units. What is required is adequate planning and training.

This article describes some basic and simple procedures that can be performed by non-specialist surgeons. Trained paramedical workers, provided the rules of the health system permits, could do some of the simple methods.

The basic principle is that after a surgical intervention the quality of the foot should be upgraded, and the risk for a recurrence of the ulcer diminished; the procedure should be preventative and rehabilitative.

A basic understanding of how ulcers are caused, and the diagnosis of the type of ulcers is essential for proper management.

GENERAL PRINCIPLES OF ULCER MANAGEMENT

1. Discuss the cause of the ulcer with the patient.
2. Is there an infection? (Sequestrum, osteoarthritis, tendovaginitis?)
3. Is surgical intervention necessary?
4. Does the patient need hospitalization? (Deep ulcer, severe infection, poor general condition.)
5. Does a specialized surgeon need to be consulted?
6. Immobilize (bed-rest, crutches, POP).
7. Discuss further ulcer prevention with patient.

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Indications for surgery

1. To drain a septic focus.
2. To speed up healing.
3. To resurface the sole.
4. To reduce pressure points.
5. To diminish the effect of deformities.

Deep ulcers require surgery. If there is a septic condition, (heat, swelling tenderness, fever, anaemia), the case is an emergency and should be sent without delay to a clinic that has facilities for surgery.

Patients with early signs of tarsal bone disintegration (TD) need urgent attention. A specialist surgeon should preferably see them, who, after evaluation may put the leg in a plaster cast for a long period. Surgery may be needed at a later stage.

Basic procedures

INCISION, DEBRIDEMENT AND SEQUESTRECTOMY

Procedure

- Incisions should be adequate and long enough to ensure that the cavity becomes funnel shaped so that it heals from the bottom.
- Avoid incisions on the sole, Incise on the dorsum of the foot whenever possible. Longitudinal incisions on the forefoot are preferable (Figure 1).
- Incisions on the lateral and medial border of the foot should preferably be dorsal to the border of the glabrous skin.
- Devitalized tissue should be removed. This could include fascia, tendons, joint capsules, ligaments, cartilage and bone. Resection of joints is permitted, even recommended. No attempt to 'fuse' the joint should be made.
- Bone removal should not leave potential new pressure points.

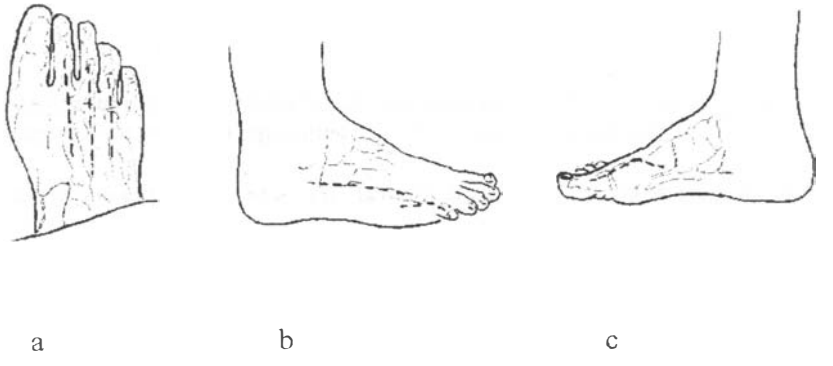
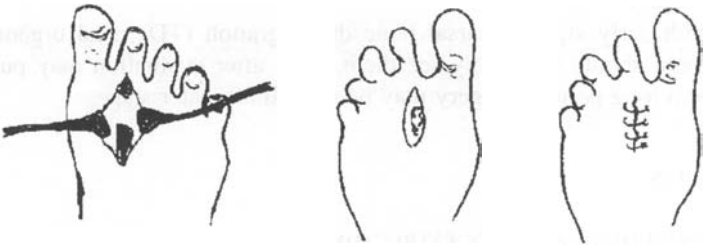


Figure 1. (a) Longitudinal incisions, long enough to ensure enough exposure and proper drainage. (b) Incision for reducing pressure points and excising ulcers caused by the fifth metatarsal head or base should be dorso-lateral and well above the border of the glabrous skin. (c) A dorso-medial incision well above the border of the glabrous skin allows good access to the first metatarsal head and tarso-metatarsal joint, and allows reduction of pressure points and infected tissue without reducing more of the bone length than absolutely necessary.

Aftercare

- Daily cleaning and deep packing. Keep on packing, thus allowing the ulcer to heal from the inside, avoiding a 'funnel shaped' cavity to become 'barrel shaped'. Simplest possible cleaning techniques should be used.
- Soaking is recommended after a few days.

DRAINING OF A PLANTAR ULCER TO THE DORSUM OF THE FOOT (FIGURE 2)



a b c

Figure 2. Draining of a plantar ulcer to the dorsum of the foot ('ulcer deviation'). (a) The incision must be long enough to create a funnel shaped cavity to secure drainage. Remove all infected tissue. Do not remove more bone than necessary, but enough to secure good drainage. Do not leave tendons and other tissue exposed which can form sequestra and delay healing. (b) Excise the ulcer and the scar allowing fresh edges to meet without tension. (c) Suture, and keep the dorsal cavity open till the plantar wound has healed properly.

Whenever a plantar forefoot ulcer is debrided, it should be with the aim of upgrading the plantar surface. An ulcer under a metatarsal head, which on healing will leave a hard scar underneath a bony prominence, is better excised so that the scar is better located. Even better is reduction of the bony prominence as well.

Procedure

- A dorsal incision, from the proximal interphalangeal joint in a proximal direction to the middle of the metatarsal bone and down to the bone through the extensor tendon should be made.
- Dissect the tissues from the metatarsal joint all around. Do not denude more bone of periosteum than necessary.
- With a bone cutter or a small osteotome, cut the bone just proximal to the metatarsal head. Resect the joint surface of the base of the phalanx at the insertion of the joint capsule and remove the joint with capsule, ligaments, fibrocartilage and tendons are now exposed. Remove all infected structures.
- Excise the plantar ulcer and scar tissue with perpendicular, oval cuts from the sole aiming at a wound were the edges are easily brought together without tension. The aim is to bring the edges of the sole-wound together to allow the defect to heal to a linear, soft, scar without any underlying pressure point.

- The plantar edges are adapted with a fairly thick suture (2-0 or thicker) without any tension.
- The wound is packed with gauze from the dorsum. The cavity should be funnel shaped, the widest point being the incision of the skin.

Aftercare

- Daily dressing with careful cleaning and packing down to the plantar pad and the suture line is done.
- Do not allow the dorsal incision to close before the plantar wound has healed, which will take a minimum of 2 weeks.
- Take great care to instruct and supervise the dressers.
- Standing or walking ((on the wound)) is not allowed.

'SAUCERIZATION' AND SKIN GRAFT

a b

Figure 3. (a) An ulcer with undermined edges must be trimmed before a skin graft is attempted. In case there is delayed healing and undermined edges because of movements in the area (lateral and medial malleolus, metatarsal heads), the limb also has to be immobilized. (b) After excision, the saucer shaped wound is ready for a skin graft.

Ulcers with undermined and fleshy edges may benefit from being cut into the shape of a saucer, and resurfaced with a split thickness skin graft (Figure 3). A skin graft will speed up healing and give a better covering epithelium than secondary healing, but will not improve the plantar pad. A skin graft is of no advantage where there is no reasonable remaining pad. If a skin graft is not done the wound is dressed and left to heal by secondary intention. Immobilization with a plaster cast can be considered to promote healing if the wound is in an area exposed to movements.

Procedure

- The ulcer is trimmed, undermined edges are cut. Scar tissue is removed till there is a soft bed of viable tissue. The bed is covered with wet gauze to stop bleeding.
- Granulation tissue transforms into a fibrous scar by time and should be removed. A skin graft on a scarred surface is easily torn open by shearing forces during walking.
- It is technically easy to take a split thickness graft from the anterior and lateral surface of the thigh, a donor site usually accepted by the patient. The area is infiltrated with a local anaesthetic. A large scalpel blade or a skin graft knife using a razor blade gives acceptable grafts. The graft should be larger than the defect to cover.

- Meshing the graft with a knife blade allows expansion and prevents blood and tissue fluid to accumulate under the graft. Meshing lowers the risk of infection.
- The graft is applied, the excess resting on the border of the bed. A very wet gauze is used to press on the graft to get a good contact with the bed.
- The graft is held in place by one layer (only!) of Vaseline gauze, is covered by a wet gauze and some absorbing layers of dry gauze, cotton wool and an elastic bandage to give a gentle compression.
- A plaster of Paris cast can be a useful protection.

Aftercare

- Rest the skin-grafted area in elevation for 10 days.
- Walking is not allowed.
- Leave the dressing on for 10 days. Some prefer to change the dressing already after 3–4 days. After the first inspection, redressing is done as needed.
- After the skin graft has taken, the new skin has to be conditioned gradually (skin care, gradual weight bearing) during a period of a few weeks. In case of failure, the grafting can be repeated when the bed is free from infection.

PINCH GRAFT

a b c

Figure 4. Pinch graft. (a) Insertion of the injection needle superficially into the skin. The skin is lifted up and cut off with a knife. (b) The small split thickness graft, still on the needle, is transferred to the recipient site. (c) It is tempting to put too many grafts too close together. The procedure is easy to perform with a minimum of equipment and resources.

In situations with higher risk of infection, a 'pinch' graft is recommended (Figure 4). This method is easily performed under field conditions. It gives a better epithelium than secondary healing and it speeds up healing. But the donor site sometimes heals with an ugly scar.

Procedure

- The donor site is infiltrated with a local anaesthetic.
- An injection needle is inserted intradermally and used to lift up the skin slightly.
- A sharp knife is used to cut a small piece of the skin from the tip of and along the inserted needle giving a small piece of split thickness graft of 5–6 mm diameter.

The graft (still on the needle) is placed on the prepared bed as a seedling for new epithelial growth. Only a few grafts should be transplanted. They should in no way cover the whole surface.

- The grafted wound is covered.
- With a thin layer of Vaseline gauze and dressed as for the spilt thickness graft.
  Aftercare is the same as for a split thickness graft.

CORRECTION OF STIFF OR SEMI-STIFF CLAW TOES

When ulcers on the tips or the dorsum of the toes occur due to fixed clawing of toes and footwear does not solve the problem, the foot can be upgraded by a resection of proximal interphalangeal joints.

Procedure

- Anaesthesia, if necessary, is given by blocking the digital nerves of the toes (infiltration at the base of the toes).
- A dorsal longitudinal incision is made over the proximal interphalangeal joint down to the bone.
- The joint is freed from surrounding tissue and resected with a small bone cutter or bone nibbler. The ends are trimmed.
- If there is no ulcer the wound can be closed with a few sutures, otherwise it should be left open for secondary healing.

Aftercare

Reduced walking for 10–14 days, or till the would has healed. Then removal of the stitches and later adjustment of footwear is done.

PROCEDURES FOR ULCERS ON THE FIFTH METATARSAL BASE

Procedure

- A longitudinal incision is made along the lateral border of the foot, and above the border of the glabrous skin.
- The pad is freed along the bone and down to the ulcer.
- The ulcer and scar is excised. A bipedicled flap has now been created. Make sure the pedicles are wide enough to guarantee proper circulation.
- The bone underlying the ulcer is trimmed (too vigorous trimming may open the tarso-metatarsal joint, which should be avoided).
- The wound is closed without any tension.

Aftercare

- Dressing is applied, care taken to avoid pressure on the flap.
- The lateral incision is kept open by packing till the suture line has healed.
- If the remaining lateral wound does not heal easily, a split thickness skin graft can be applied.

PROCEDURES FOR HEEL ULCERS

Ulcers on the heel are very difficult to heal, because of destruction of the important heel pad. The scars often adhere to bone and recur. The heel is difficult to resurface. Chronic ulcers cause reactions of the heel bone that exaggerate the underlying pressure point. Destruction of the heel bone may occur and will lead to a foot that even the most skilled orthopaedic shoemaker cannot accommodate in a functioning device. Any ulcer on the heel should be given great care as early as possible to avoid further deterioration. Heel ulcers that cannot be healed by simple rest should be referred to a specialist. Plastic surgery procedures using different kinds of flaps are the best way to treat heel ulcers.

AMPUTATIONS

An amputation may include anything from a part of a phalanx to a whole leg. When malignancy is suspected or there are deformities, which may be correctable, it is better to consult a specialist. For larger amputations (forefoot, Syme's, below and above knee) a close co-operation between the surgeon and the prosthetist is essential.

Some basic principles

- The patient should be in full agreement with what is being removed. Counselling should be offered before any amputation.
- Devitalized tissue must be removed.
- Place scar lines away from weight bearing surfaces.
- Weight bearing surface should be preserved.

Indications

- Contracted toes preventing the wearing of a 'non-stigma carrying' protective shoe.
- Cosmetic reason (to reduce stigma).
- Uncorrectable severe deformity not permitting weight bearing.
- Gangrene.
- Chronic ulcers with risk of developing a malignant change:
  Extensive infection with destructive osteoarthritis.
  Severe, life-threatening septicaemia caused by an extensive infection.

Comments

- Toe amputations, total or partial: endeavour to place suture lines away from the sole and the tip of the remaining toes. Remaining skin, especially plantar skin, can be useful as a flap to cover plantar or dorsal defects.
- *First and fifth toes*: try to save as much of the metatarsal bones, provided the remaining pad is sufficient. Shortening significantly alters the shape of the foot and the mechanics of walking, inviting new problems.
- *Forefoot amputation* is best done by a trained surgeon.
- *Syme's amputation* has a high failure rate, and should only be attempted by a trained surgeon. The prosthesis is more complicated and difficult to produce. Patients who refuse below knee amputations may sometimes accept Syme's amputation.

- *Below knee amputation*: any surgery trained medical or paramedical person may perform a below-knee amputation after proper instructions. The choice of the shape of the stump should be made in co-operation with the prosthesis makers. The end result, the patient's ability to walk, is more dependent on the skills of the prosthesis maker than the skills of the surgeon.

VARIOUS FLAPS (RESURFACING PROCEDURES

Due to the special properties of the skin pad of the sole of the foot, it is very difficult to substitute lost pad. Attempts to substitute lost skin with skin flaps from outside the sole itself do not give satisfactory results. Successful resurfacing is best accomplished by flaps within the sole of a foot (rotation flaps, island flaps). Such techniques require some training and experience and patients in need of such surgery should be referred to the specialist, except for forefoot flaps using skin from the toes, which can be done with success by workers in peripheral units.

VARIOUS STRUCTURAL CORRECTIONS BY SURGERY

Deformities, mobile or fixed, increase the risk of ulcer formation. In some cases, corrections are possible such as claw toe correction, tendon transfers for foot drop, lengthening of the Achilles tendon for equinus deformity, corrections osteotomies for fixed inversions. Tendon transfer for foot drop and claw toe correction may be performed by surgeons and general practitioners trained in the procedure. More advanced bony corrections may be necessary for the patient to remain free of ulcers. Such cases should be referred to the specialist.

Summary

In the majority of cases, plantar ulcers in need of surgical intervention can be treated by very simple procedures. Patients benefit from treatment facilities near to their homes. In the process of integration surgery could be made available to leprosy patients in peripheral health units near their homes by training non-specialist surgeons in peripheral health units in basic surgical procedures, aiming at ulcer healing as well as preventing reoccurrence of ulcers.

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Letters to the Editor

IMPROVED METHOD OF REPORTING DISABILITY GRADES IN POD PROGRAMMES

Editor,

Leprosy will soon be eliminated from the globe, perhaps by 2000 AD. If the new multidrug (MDT) programme is going to be successful, new patients will no longer suffer from deformities. However, some unfortunate patients who are already disabled need to be cared for, and for them the Prevention of Disability Programme (POD) will go on.

The grades of disabilities for individual patients are recorded in various registers, which are used in National Leprosy Elimination Programmes (NLEP) all over, for monitoring the programme. On examining some of these records, it was noted that disabilities were recorded in hands, feet and eyes, and the patient was labeled by the highest grade of deformity. The NLEP Guidelines from India[1] (1994) state that 'the highest value for any part should be taken as the overall disability grading of the patient'.

On perusal of several such records, it was noted that this system of recording does not give the correct picture. This will be more clear from the examples shown here.

In Table 1, four different patients are shown who have different problems but have all been labeled as grade 2. Patient 1 is unlikely to benefit much from the POD programme and practices because his foot is deformed, his fingers are absorbed and he is blind. This means that his grade will not change in the register. Patients 2 and 3 could achieve a change in disability grade with effort. Patient 4 will not be able to change his overall grade because he has loss of vision in one eye. Even if sensory recovery occurs he will continue to remain in grade 2.

Since grade 2 disabilities, at least in extreme situations, will not change in the registers (because the

Table 1. Grading of disabilities assigned to patients using three different systems

Patient no.	Actual disabilities		Individual disability grades			Overall disability grade		
			Hand	Foot	Eye	WHO system	EHF system	Proposed system
1.	Blind with malformed foot and absorbed fingers	R	2	2	2	2	10	H2 F2 E2
		L	0	0	2			H2 F0 E0
2.	Anaesthesia sole and small ulcer over feet	R	0	2	0	2	2	H0 F2 E0
		L	0	0	0			H0 F0 E0
3.	Clawing of fingers and anaesthesia of sole of foot	R	2	1	0	2	3	H2 F1 E0
		L	0	0	0			H0 F0 E0
4.	Loss of vision in one eye with anaesthesia in palm and sole	R	1	1	2	2	4	H1 F1 E2
		L	0	0	0			H0 F0 E0

patient is going to be awarded the highest overall grade), the same information will continue to be reported, as a consequence of which the true impact of POD activities cannot be evaluated by mere inspection of records. The programme managers evaluating the reports will have no option but to screen the original records of the individual patients. This will often not be feasible, for obvious reasons.

More recently Reed *et al*.[2] and Saunderson *et al*.[3] have evaluated the EHF score as a measure of change in impairment over time. The EHF score is a number obtained by adding together the impairment grades of eyes, hands and feet on either side in a patient. A patient can have a maximum score of 12. The drawback of the EHF score is that it only gives a partial idea of the severity of the problem. One has to scan the records to get the actual picture about the three vital and commonly impaired organs of the body. EHF score is nothing but a consolidated, glorified form of expression of the WHO impairment grades.

To overcome this, a modified method of reporting is suggested. Instead of mentioning the overall grade, disabilities in hands, feet and eyes can be individually reported in the records, each side having been represented separately. For this, symbols can be used, e.g. hand denoted by letter 'H', foot by 'F' and eyes by 'E'. the highest grade for these can then be recorded in the notes, as shown in Table 1.

The report for different blocks or areas can be tabulated and disability grades finally added up to give the exact disability load in that area. Subsequent reports can then be more meaningful and will indicate the success or otherwise of the POD programme. This is going to be more informative and will provide a true picture in any given situation to the programme managers.

Central Jalma Institute for Leprosy G. N. MALAVIYA
Tajganj, Agra, India
Address for correspondence:
Post Box 25, GPO,
Mall Road, Agra,
India, Pin 282001

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NERVE GROWTH FACTOR (NGF) CONCENTRATIONS IN CULTURED HUMAN KERATINOCYTES EXPOSED TO *MYCOBACTERIUM LEPRAE* CELL FREE EXTRACT

Editor,

The classical neutrotrophic factor, nerve growth factor (NGF), is a small protein normally produced by cells in the target organ, such as skin; NGF is taken up by sympathetic and small sensory nerve fibres via a high-affinity receptor (trkA), and retrogradely transported to the cell body. In adults, NGF is necessary for the survival of sympathetic fibres, and for phenotypic properties of small sensory fibres, including expression of neuropeptide substance P, and their response to noxious stimuli.[1] Our recent studies showed decreased NGF staining in keratinocytes in leprosy skin patches, as well as mirror-image clinically unaffected skin in the same patients: we postulated that a sub-clinical decrease on NGF immunostaining may explain lack of pain in this condition.[2] However, the mechanism of the decrease of NGF immunostaining is unknown.

In vitro studies of NGF production may help in understanding the cellular and molecular mechanisms involved in changes observed in the clinical studies. A number of potential agents, including cytokines and growth factors, have been shown to affect NGF expression in different cultured cells,[1,3] but it is not known whether these mechanisms operate in leprosy skin. Although infection of human keratinocytes has not been observed, it may be possible for *Mycobacterium leprae* and substances derived from them to interact with keratinocytes to affect NGF production. Despite multidrug therapy, *M. leprae*-derived antigens persist in skin,[4] and keratinocytes may be therefore exposed to them for long periods. In the present study, we have challenged normal human keratinocytes in culture with *M. leprae* cell free extracts, and measured keratinocyte NGF concentrations using a specific NGF immunoassay, and immunocytochemistry.

Keratinocytes were obtained with permission from patients ($n = 3$) undergoing surgical resection of normal skin, and grown at a minimum starting density of $1{\cdot}25 \times 10^4$ per well on a mouse fibroblast 3T3 (gamma irradiated) feeder cell layer in keratinocyte medium for 5 days until established. To eliminate any possible influence of medium-soluble molecules, the cells were transferred to serum and calcium-free medium for a further 3 days. Cells were cultured, in duplicate, for a further 24 or 48 h with or without *M. leprae* cell free extract (kindly provided by Dr M. J. Colston, National Institute for Medical Research, London) at a concentration of 10 μg/ml. Cells from at least two wells per culture were detached with trypsin, washed in medium, centrifuged and re-suspended in 1 ml phosphate-buffered saline (PBS). A 900 μl aliquot was taken for NGF assay and the remainder for protein assay. Both of these samples were centrifuged and supernatant removed. The samples for immunoassay were then re-suspended in NGF extraction buffer (100 mM Tris-HCl, 0·2 M NaCl, 2% BSA, 0·05% sodium azide, 1% Triton X-100, 1 mM phenylmethylsulphonyl fluoride, 4 mM ethylenediaminetetracetic acid, 7 μg/ml bovine aprotinin, pH 7·0) and stored frozen at −80°C. NGF immunoreactivity in extracts of keratinocytes was measured in duplicate by fluorometric, enzyme-linked immunoabsorbant assay (ELISA) using recombinant human NGF as standard and biotinylated anti-NGF and a streptavidin-β galactosidase detection system (Genentech, Inc., USA), as previously described.[3] Protein concentrations were determined colorimetrically with a commercially available kit (Bio-Rad Labs, UK). NGF concentrations in keratinocyte extracts are shown in Figure 1. There was no significant difference (Student's t-test, $p > 0{\cdot}05$) of NGF content for keratinocytes cultured with or without *M. leprae* extracts at either 24 or 48 h of exposure. NGF levels for 3T3 fibroblast control cultures were below the detection limit (5 pg/ml) of the assay at all times, with or without *M. leprae* extracts.

Replicate cultures on glass slide wells were frozen for NGF immunostaining. The slides were

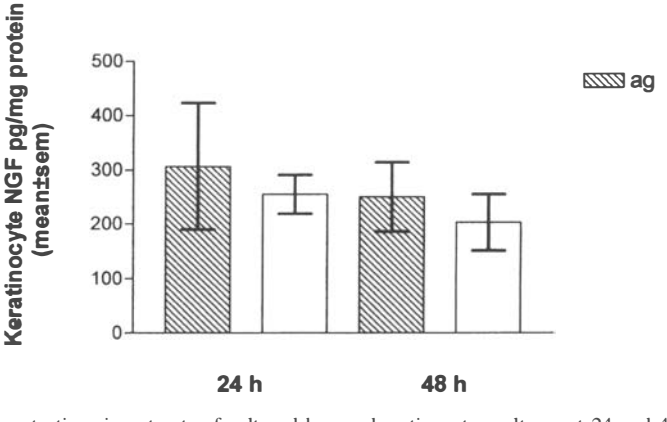

Figure 1. NGF concentrations in extracts of cultured human keratinocytes cultures at 24 and 48 h. The effect of *M. leprae* cell free extract ('ag') at a concentration of 10 μg/ml is shown in shaded columns, while the clear columns show NGF concentrations without addition of *M. leprae* cell-free extract.

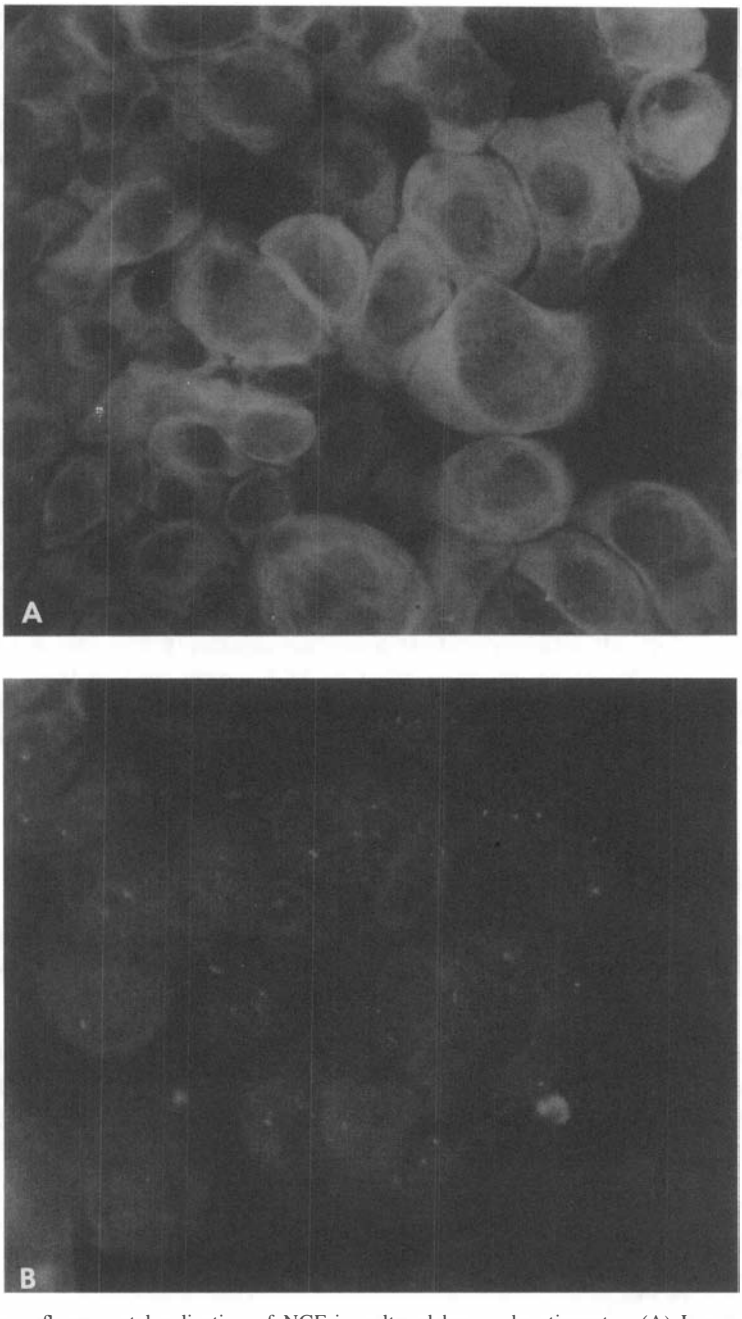

Figure 2. Immunofluorescent localization of NGF in cultured human keratinocytes. (A) Immunopositive cells incubated with anti-NGF; (B) negative control cells incubated with non-immune serum. ×300 magnification.

immersed in 0·4% w/v paraformaldehyde in PBS for 30 min at room temperature, rinsed in PBS then de-ionized water, and air dried for 2–3 h. Cells were then soaked in 0·2% v/v Triton X-100/PBS for 30 min. After washing in PBS, cells were dehydrated and re-hydrated through graded (70–100%) ethanol and returned to PBS. Cells were then incubated overnight with either normal non-immune rabbit serum (1:30 in PBS; negative control) or rabbit antibodies to rhNGF at 1·6 μg/ml. To detect antibody-binding sites, the slides were washed in PBS and incubated with goat anti-rabbit IgG conjugated to fluorescein isothiocyanate (FITC) for 60 min. After a further wash, slides were mounted in glycerine-PBS including anti-fade reagent (Vector Labs, UK), assessed by an independent observer without knowledge of the identity of each slide, and photographed using epi-fluorescence. Specificity of immunoreaction was determined by pre-incubation of rhNGF antibodies with rhNHF antigen. There was substantial NGF-like immunoreactivity seen throughout the cytoplasm in the majority of keratinocytes (Figure 2A). However, there was no detectable difference of NGF immunofluorescence intensity at 24 or 48 h of incubation with or without *M. leprae* extracts. Control cultures, in which primary antibodies were replaced with non-immune serum or pre-incubated with homologous rhNGF, showed little or no immunofluorescence, and only a few scattered granular deposits which were non-specific (Figure 2B). Fibroblast feeder cell (3T3) cultures showed no immunostaining with anti-rhNGF antibody.

The present study is the first to demonstrate NGF immunoreactivity cytochemically in cultured human keratinocytes, and is in accord with earlier work which described keratinocytes as a major source of NGF in skin.[1,2] The intensity of NGF immunofluorescence appeared not to change with exposure to *M. leprae* cell-free extract. The measurement of NGF in keratinocyte extracts by immunoassay showed only a slight decrease of NGF content with time, and no significant effect of exposure to *M. leprae* cell free extract. The decreasing NGF concenrations with duration of culture was an expected trend, reflecting the positive relationship of NGF production with rate of proliferation of keratinocytes.

The dose of *M. leprae* cell free extract we used has been shown to be critical for effects on the proliferation of lymphocytes in a recent study.[5] Further studies with a range of antigen concentrations, and with *M. leprae* cell wall antigen or whole *M. leprae*, are necessary. It is possible that *M. leprae* cell free extract, although having no detectable effect on NGF protein concentrations, may influence turnover or secretion of NGF. It is also possible that conditions *in vitro* do not reflect the conditions *in vivo*. In addition, it would be of interest to study the effect of sera from leprosy patients, and cytokines known to be involved in leprosy skin, on NGF concentrations in cultured keratinocytes.

Acknowledgements

We thank the Wellcome Trust for support, Dr D. V. Sinicropi, Genentech Inc., USA, for providing reagents and helpful discussion and Dr M. J. Colston, National Institute for Medical Research, UK, for providing the *M. leprae* cell-free extract.

Academic Department of Neurology,
St Bartholomew's and
The Royal London School of Medicine and Dentistry,
Whitechapel,
London E1 1BB, UK
**Blond McIndoe Research Centre,*
Queen Victoria Hospital,
East Grinstead, Sussex, UK
Fax: +44 171 377 7286
e-mail: P.Anand@mds.qmw.ac.uk

P. FACER
D. MANN*
G. TERENGHI*
P. ANAND

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THE TRAGEDY OF DEFORMITY IN CHILDHOOD LEPROSY

Editor,

It is the deformity resulting from late or inadequate treatment which sets leprosy apart from other diseases in the minds of both the public and patients. Deformity is a preventable complication, given the powerful drugs available for cure, and is especially distressing when it occurs in children. Delay in seeking appropriate care being compounded by the social stigma of leprosy is mostly responsible for the continued incidence of deformity. The intention of this paper is to highlight the plight of the substantial number of children who must carry the burden of deformity lifelong despite widespread efforts to 'control' the disease.

Methods

All cases of child leprosy (under 15 years of age) attending Karigiri Hospital for diagnosis and treatment in 1997 were reviewed retrospectively. Information regarding age, sex, leprosy type, duration of symptoms, household contacts, deformity and details of any previous treatment was gathered. Information on subsequent therapy received from this institution was also noted, as well as any development of deformity during this period. Deformity for the purpose of this study included grade 2 of the WHO disability grading 1995[1] as well as muscle weaknesses objectively assessed.

Results

In all, there were 46 child leprosy patient charts. These were reviewed and the results summarized in Table 1.

Fifteen of 46 children (33%) had deformity ranging from abductor digiti minimi weakness to gross claw hand. Six of the 15 (40%) had grade 2 deformity, constituting 13% of all children: one while on treatment, one after being released from treatment and four presented for the first time.

Nine children had developed weakness of abductor digiti minimi, six presented for the first time with weakness while three developed weakness after RFT. MB patients and those above 10 years had significantly higher deformity rates ($p < 0{\cdot}05$). Detailed findings are summarized in Table 2. Just two of these had been referred for corrective surgery from other institutions.

Another patient demonstrated worsening deformity whilst on MDT, initially presenting with a deep fissured anaesthetic right heel and started on PBR, returning 3 months later in reversal reaction with weakness of both hands and right foot drop.

Thirteen children reported a household contact with leprosy (28%), three of whom had deformity. A summary of these is given in Table 3.

The mean duration of symptoms before presentation amongst those without prior treatment was 172 months (range 3–60) in the nine with deformity and 99 months (ranges 1–48) in the 18 without deformity. Interestingly, two sisters whose mother and father were also leprosy patients had a duration of symptoms of only 2 and 12 months and presented without deformity.

Discussion

As this was a hospital-based study, the results may not reflect the status of leprosy as it affects children in a community. However, some conclusions can be drawn.

It is well recognized that generally, the lower the grade of disability at induction of patients for MDT, the lower the chances of new disability development.[2] Clearly, it is a preventable catastrophe if factors operate to dissuade children or their families from seeking help at an early stage. Anyone presenting with a grade 2 disability without previous treatment represents a serious shortcoming in the system of detection; nine cases in this series. Those whose first presentation to leprosy services was recorded in 1997 were those who had received no previous treatment; amongst these patients there was a significant difference in mean duration of symptoms between those with deformity and those without. The incubation period, although unknown, is in the order of years and hence diagnosis should be possible before deformity results in most instances.

Reaction episodes and disabilities are reportedly rare in children[3] but are 30% and 32%,

Table 1. Deformity in children by age, sex, leprosy type and previous treatment

		Deformity			
				Total	
Characteristics	No. studied	Gr. 2	Other	No.	%
All	46	6	9	15	33
Age (years)					
0–4	1	–	–	0	0
5–9	14	–	2	2	14
10–14	31	6	7	13	42
Sex					
Male	23	4	4	8	35
Female	23	2	5	7	30
Type					
PB	28	2	4	6	21
MB	18	4	5	9	50
Prev. Rx with MDT*					
Yes	19	2	4	6	32
RFT	11	1	3	4	36
UT	4	1	–	1	25
Incomplete	4	–	1	1	25
No	27	4	5	9	33

*RFT: patients released from treatment; UT: patients under MDT at time of presentation; Incomplete: patients received an incomplete course previously (1–4 pulses); Prev. Rx: previous therapy.

Table 2. Nerve trunks involved in children with deformity by previous treatment and presentation in reversal reaction

	No previous RX*		Previous Rx*	
Nerve trunk involved	No.	No. RR**	No.	No. RR**
Facial only	2	1	0	0
Ulnar only	4	3	4	1
Median only	1	1	0	0
Ulnar & median	1	0	1	1
Ulnar, median & radial	0	0	1	1
Ulnar & post-tibial	1	1	0	0
Total	9	6	6	3

*No prev. Rx: Children presenting at initial diagnosis with no previous therapy.
*Prev. Rx: Children having received some previous therapy (MDT).
**RR: Reversal reaction.

Table 3. Deformity among household contacts

	Contact		
Contact	Disease type	Disease status	Patient symptom duration (months)
Mother	BT	UT	60 (Pat. no prev. Rx)
Father	Unknown	UT	48 (Pat. prev. incomplete Rx)
Brother	TT	RFT	48 (Pat. already RFT)

respectively, in this limited series. Not all these children are from the local district, but must represent a need not being met in their respective areas.

As with other infectious diseases, the rates of childhood leprosy are a helpful marker of incidence and prevalence trends in the population as a whole as they demonstrate current transmission. Larger proportions of children presenting at later, deforming stages of disease, even at a lower incidence, would suggest a certain reluctance to come forward and/or inadequate pick-up of early disease. Concern has certainly been expressed about hasty 'integration' of leprosy services in India to the detriment of patient care.[4,5]

In the popular rush to declare leprosy 'eliminated', planning effective programmes to bring down the incidence of leprosy and its complications in children should become a top priority. The current scenario of a high deformity rate among children, and especially those with a household contact of leprosy, presents a grim picture. Greater vigilance should therefore be maintained not only as part of the health system but of any other child care programmes in nutrition, development etc. Prevention is always, and particularly in this situation, vastly superior and cost effective to curative or rehabilitation services.

Epsom, Surrey, UK P. J. HAMMOND
Director, S.L.R. & T.C., Karigiri, India P. S. S. SUNDAR RAO

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OPHTHALMIC COURSE, KARIGIRI, INDIA. MARCH 1999

The 14th annual 5-day ophthalmic teaching module was held at the Schieffelin Leprosy Research and Training Centre, Karigiri from the 1st to the 6th March 1999. The course, which received sponsorship from LEPRA through the CfBT/English-Speaking Union International Training Scheme was designed to give instruction to medical officers on the detection, prevention and management of the ocular complications of leprosy by means of a series of lectures and clinical and surgical demonstrations, augmented by videos and a field trip. Teaching included formal didactic presentations on the basic anatomy, physiology and pathology of the eye with a special emphasis on leprosy; in addition, there were lectures on the pathogenesis and treatment of corneal ulcers, rehabilitation, community ophthalmology and global aspects of blindness in the disease.

Preference was given to problem-based clinical instruction concentrating on the identification of sight-threatening complications of the disease, their prevention and management.

The course was attended by 12 sponsored participants working in India, and was organized by Dr Ebenezer Daniel of Karigiri, with the assistance of members of the Staff of the Centre. Mr Timothy ffytche from St Thomas's Hospital, London was invited as a member of the Faculty.

The Director of Karigiri, Dr P. S. S. Sundar Rao, is to be thanked for his continued support for this important and popular contribution to teaching.

The Hospital for Tropical Diseases T. J. FFYTCHE
Mortimer Market
off Tottenham Court Road
London WC1E 6AV
United Kingdom

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Teaching Materials and Services

Announcement for the International Course on Management of Rehabilitation and Prevention of Impairment and Disability (RPOID) in 1999

After the successful introduction of the modular concept into the RPOID course 1998, we have now decided to run a separate 2-week course in RPOID management, which will be followed by a 4-week RPOID skills course in January/February 2000.

The 1999 **RPOID management course** will aim at teaching concepts in rehabilitation and POID, approaches to rehabilitation, rehabilitation and POID management, including monitoring and evaluation of activities in these areas. The course will be based on the concepts and terminology used in the International Classification of Impairments, Activities and Participation (ICIDH-2) published by the WHO.

For a limited number of participants an opportunity will be offered for additional in-service training during the week following the management course (29 November to 3 December 1999). Selected participants will be assigned on a one-to-one basis to a tutor who will guide them through a self-learning programme.

Available topics include institutional rehabilitation, CBR, expanding the services of a leprosy hospital to serve people with other rehabilitation needs, agricultural rehabilitation, statistics and information systems, footwear, prosthesis and orthoses, physiotherapy and occupational therapy. These placements will be available strictly by arrangement prior to the course only.

Dates: 15–26 November 1999 (2 weeks)

Target Group: Managers of rehabilitation and/or POID programmes, senior hospital staff, senior leprosy control staff and doctors with managerial responsibilities for RPOID activities.

The RPOID skills course will aim at RPOID-related assessments, such as nerve function assessment, psychosocial assessment, ADL assessment, impairment assessment and socio-economic assessment, treatment and rehabilitation interventions. The second course will therefore concentrate on skills acquisition. Through optional workshops the second course will offer the opportunity to study certain topics in more depth. The course will include a 1-week field trip to practise the learned skills in a real programme setting.

Dates: 10 January to 4 February 2000 (4 weeks)

Target group: Physiotherapists, occupational therapists, social workers and field staff with responsibility for the assessment, treatment and/or rehabilitation of people needing RPOID interventions.

Teaching/learning methods (both courses): Lectures, group discussion, group assignments, individual assignments, practical work in small groups, problem-based learning, self study, presentations, and simulation exercises. The teaching medium is English. Because of the complicated nature of the subject, a high fluency in both spoken and written English is required. Experience in leprosy work will be an advantage, but is not essential.

Venue: The Green Pastures Training Centre in Pokhara, Nepal.

Course fees (including board and lodging): $175 per week.

Further information: Detailed information can be obtained from: The Training Officer, GPTC, PO Box 28, Pokhara 33701, Nepal. Tel: +977 61 24562, Fax: +977 61 20430, e-mail: gptc@inf.org.np.

Forum on leprosy up and running

After many painful experiences, the Internet 'Forum on Leprosy' is now up and running. There are various 'categories' where those who already are on-board and those thinking about joining, will be free to post articles. When posting articles, look for the 'Send New Message' on the top browser bar and hit that button. Then 'Choose a category' under which to file your message.

The categories embrace most of the various aspects of leprosy—'Clinical Pathology', 'Research', 'Immunology', 'Leprosy Organizations', Reconstructive Surgery', Rehabilitation/Occupational Therapy', 'Immunology', 'Reactional States', 'Diagnosis and Differential Diagnosis', 'Bookshops on the Net where leprosy books are available', 'Prevention of Disability', 'Epidemiology', 'Control', 'Social and Psychological Aspects', 'Chemotherapy/Drugs', 'Treatment' etc. There is a department where everyone may feel free to contribute out of their expertise. If you would like to join, forward your details and e-mail address to: Keith Skillicorn, International Benevolent Services, 'Rosehaven', Unit 4, 953 North East Road, Modbury, South Australia 5092, Australia. Your e-mail address will be sent to 'DELPHI' (the organization which provides this facility), who will e-mail you the Registration Form. It takes only minutes to fill in the details and e-mail it back to DELPHI. There is no charge.

TALC (Teaching Aids at Low Cost) 1999 Newsletter

Despite difficulties in many countries, TALC's books, slides and accessories continue to get through to health workers to ease suffering. In the health field malaria remains more prevalent than any other disease so it is disappointing that the book on malaria, which we had hoped to include in the 1998 catalogue, is still not ready and will be unavailable for some time.

The need for TALC books, slides and equipment, which help to save lives and prevent suffering, has never been greater.

'To prevent this downward trend of ''continuing medical ignorance'', from which no-one is immune, we need continuing medical education. For this we need books, journals, etc'. Wrote Dr Tekolla Belaingh Desalegn, Head Dept. Surgery, Deder Hospital.

This year we have a number of new books and slide sets which we feel meet an urgent need. You will find them in the 1999 catalogue.

We would like to draw your attention to a new venture for TALC. This is a range of books listed under '*Speciality Titles*'. These do not come in the normal TALC low-cost range, but are well established text books written for doctors, nurses and midwives, which we can distribute at an affordable price. They include the comprehensive 20th edition of *Mansons Tropical Diseases* which runs to over 1700 pages; *Hutchinsons Clinical Methods, Myles Textbook for Midwives* and *Tropical Medicine & Parasitology*, also the excellent *Bailiere's Nurses and Midwives dictionaries.* There is also a colour illustrated book on **dermatology** and two books on **first aid**. Perhaps if you need a speciality item, or library pack you might approach a local NGO who could fund your needs for ongoing education.

TALC has always played a major part in the battle against AIDS and HIV. The Strategies for Hope series of books and videos which we distribute on this subject, is widely acclaimed. Dr Sandra Anderson of the UNAIDS Regional office in South Africa: comments 'The content of the books are superb and they are so captivating and user friendly. The conclusions are both insightful and helpful. In brief, the books are inspired and inspirational'. The latest **Strategies for Hope** book, *Under the Mupundu Tree*, addresses the dual epidemic of HIV and tuberculosis and is accompanied by a video. *Clinical*

Tuberculosis has now been translated into 17 languages. Most are available in the country of origin. TALC distributes the English, French, Spanish and Portuguese editions. The new 1999 English edition has been totally revised and includes the effects of HIV.

TALC is the major distributor of Child-to-Child publications which include a number of reading books each with a health message incorporated in the story. A new reading book for the 1999 catalogue is *Five Friends of the Sun* designed to raise children's awareness and recognition of land mines.

Our District Hospital and Clinic/Health Centre libraries continue to be popular with over 1400 orders, which gives an indication of the need they are fulfilling. We have now decided to add two new libraries, one on surgery and one on womens' health, and we anticipate a considerable demand for these items. It is interesting to note that the World Health Organisation's Blue Trunk Library project to set up libraries in hospitals and clinics resulted in over 5000 books being ordered from TALC.

On another topic, if you are in London you will be very welcome to visit the resource centre situated at the Institute of Child Health, 30 Guilford Street, London WC1N 1EH. This is located on the 2nd floor in the Library. There you will find a large amount of health information including a section on each country. You will also find the TALC sales corner, (open 10 am until 4 pm) where you can look at and buy TALC books and accessories and view and order our slide sets.

You may not know that TALC has partnership organizations that assist us to market our books and equipment in local currency in both South Africa and Australia. We are interested in forming new partnerships in other countries and if you feel you might be able to help we would be pleased if you could contact us.

On the staff side TALC has had a number of changes and new appointments. Our long-serving chairperson, Judy Arthur, has retired as has credit controller Margaret Wilson. Each of them has contributed over 10 years valuable service to TALC.

With the appointment of our new Chairman, Gerry Dingley, from the commercial world, the opportunity has been taken to re-organize the management structure.

Operations: Maggie Fowler will be responsible for the overall day-to-day operations of TALC. This will encompass sales, distribution and administration.

Development and Planning: Indira Benbow will undertake this area aimed at our future growth.

Management Accounts: We have appointed Stephen Mawle to this new position.

We are confident that our new structure will ensure that TALC remains at the cutting edge of meeting demands from the developing world for healthcare education and flexible enough to meet the changes of the future.

Finally we are always looking for good quality low cost primary health and medical materials and TALC would also like to hear more about what materials you find most useful and what medical teaching materials you would like us to provide in the future.

Further information—TALC, PO Box 49, St Albans, Herts AL1 5TX, United Kingdom. Tel: +44 (0) 1727-853869. Fax: +44 (0) 1727-846852. e-mail: talcuk@btinternet.com.

Fellowships and Grants from The Wellcome Trust, London

From an extensive list of fellowships and grants available from The Wellcome Trust in London, the following appeared in the latest issue of *Wellcome News*, Issue 17, Q4, 1998:

Training fellowships for research into infectious diseases for scientists from tropical and developing countries

The Trust recognizes the continuing threat of infectious diseases in tropical and developing countries

and wishes to develop sustainable research expertise in these countries in order to address health problems arising from infectious diseases. The awards are intended to provide both training and research experience for applicants, who must be based in a developing or tropical country. The training will be obtained at international centres of excellence in the UK, Republic of Ireland, or any country in the developing or restructuring world, and a substantial period of research will be undertaken in the applicant's home country. For instance, a 4-year award would normally include a minimum of 2 years' research in the home country over the period of the award. AIDS/HIV-related studies relevant to tropical regions are fully supportable.

ELIGIBILITY

Applications are invited from postdoctoral basic scientists or medical graduates with up to 6 years' research experience (postdoctoral) who are nationals of developing countries. Applications may be considered in exceptional circumstances from those who are educated to first-degree or Master's level, who are able to demonstrate substantive potential for research and operational leadership and have research experience equivalent to a PhD, as evidenced by their publication record. Applicants will wish to become independent research scientists through high-quality research into infectious diseases of regional significance to their home country. The research proposal must include a clear argument outlining the relevance of the project to the home country. Applications will be assessed on the basis of the candidate's achievements in research, the scientific merit of the proposal and the appropriateness of the research for the proposed location. The nature of the training component and the training site chosen must be appropriate for the proposed research.

FUNDING

Awards will be for a maximum of 4 years, and are non-renewable. Fellowship support may include a salary/stipend appropriate to the countries in which the candidate will be studying/working, as well as project-dedicated and travel expenses. All expenses must be fully justified. Cosndideration may also be given to the expense of attending a course leading to a recognized qualification in a discipline relevant to the fellowship research programme.

APPLICATION PROCEDURE

The preliminary approach to the Trust should include an outline of the proposed research, an approximate budget and curriculum vitae of the applicant, together with a written guarantee of subsequent employment from the host institution in the applicant's home country and a letter of support from a suitable sponsor at the training institution. Applications will be considered throughout the year.

Further information about the initiative can be obtained from: The Grants Section (Tropical), The Wellcome Trust, 183 Euston Road, London NW1 2BE, UK. Tel: +44 (0) 171 611 8409. Fax: +44 (0) 171 611 7288. Web: www.wellcome.ac.uk.

NB: *Applicants may not apply for more than one Trust fellowship scheme at any one time.*

Project grants in tropical health services research for medicine in developing countries

The Trust has a long-standing interest in tropical medicine research and awards are offered to encourage research into the effectiveness of health interventions in developing countries. Applications for these awards may relate to any disease, infectious or non-infectious, that is of importance in tropical regions. Cancer research and HIV-related studies relevant to tropical regions are also acceptable.

Health services research is defined as the identification and quantification of healthcare needs, and the quantitative study of the provision and use of health services to meet them. Such research is usually multidisplinary and should preferably involve formal links to ministries of health or non-governmental organizations, and provide evidence that the research findings might be adopted in policy and practice.

The awards will provide research costs for up to 3 years for studies that focus upon issues relating to the effectiveness of health services in tropical countries. Applicants must hold an established academic post in an appropriate university or research institute in the UK, Republic of Ireland or in a developing country.

Enquiries should be directed to: The Grants Section (Tropical), The Wellcome Trust, 183 Euston Road, London NW1 2BE, UK. Tel: +44 (0) 171 611 8641. Fax: +44 (0) 171 611 7288. E-mail: tropical@wellcome.ac.uk.

The Trust offers a range of awards for UK and overseas nationals who wish to undertake research in any branch of the natural or clinical sciences that has a bearing upon human or animal health. Further schemes that may be relevant to individuals with an interest in tropical medicine are available. Details of all awards are available upon request from the Trust or can be viewed on www.wellcome.ac.uk.

Tuberculosis: Important International Media

The following information is based on a list of media published by WHO in '*TB Advocacy. A Practical Guide*'. 1999, page 21. WHO Global Tuberculosis, Programme, WHO, CH-1211 Geneva 27, Switzerland. The e-mail details may represent individuals or offices within the main organization and thus be of limited value.

TUBERCULOSIS (TB): Important International Media
(Expanded from 'TB Advocacy. A Practical Guide' 1999, page 21. WHO Global Tuberculosis Programme, CH-1211 Geneva 27, Switzerland).

	Name	Address	Telephone/Fax/www/e-mail
1	Associated Press (AP)	12 Norwich St., London, EC4A 1BP United Kingdom	Tel: 0171-353-1515 Fax: 0171-353-8118 www: www.ap.org e-mail: info@ap.org
2	Agence France Presse (AFP)	11–15 Place de la Bourse, Paris 75002, France	Tel: 33-1-40-41-4646 Fax: 33-1-42-33-4466 www: www.afp.com e-mail: contact@afp.com
3	International Herald Tribune	181 avenue Charles de Gaulle, Neuilly, 92521 France	Tel: 33-1-46-37-9300 Fax: 33-1-46-37-5212 www: www.iht.com e-mail: iht@iht.com
4	Washington Post	1150, 15th Street, NW Washington DC, 20071, USA	Tel: 202-334-7470 www: www.washingtonpost.com
5	New York Times	229 West 42nd Street, New York, NY, 10036, USA	Tel: 212-556-1234 www: www.nytimes.com
6	Cable News Network (CNN)	1 CNN Centre, Atlanta, GA USA	Tel: 404-827-1503 www: www.cnn.com
7	Economist	25 St James Street, London SW1A 1HG, United Kingdom	Tel: 0171-839-7000 Fax: 0171-839-2968 www: www.economist.com

TUBERCULOSIS (TB): Important International Media *(Continued)*

	Name	Address	Telephone/Fax/www/e-mail
8	Financial Times	Number One, Southwark Bridge, London SE1 9HL United Kingdom	Tel: 0171-873-3000 Fax: 0171-873-3084 www: www.ft.com
9	British Broadcasting Corporation (BBC)	76 Bush House, The Strand, London WC2B 4PH, United Kingdom	Tel: 0171-240-3456 www: www.bbc.co.uk e-mail: worldservice.letters@bbc.co.uk
10	Centre for Disease Control	1600 Clifton Road, Atlanta GA, 30333 USA	Tel: 404-639-3311 Fax: 404-639-8960 www: www.cdc.gov e-mail: rfp5@cdc.gov
11	Reuters	Reuters Group plc, 85 Fleet Street, London EC4P 4AJ United Kingdom	Tel: 0171-250-1122 Fax: 0171-542-9780 www: www.reuters.com e-mail: health@rtrlondon.co.uk

TALCS Partnership Book Programme

Since the mid 1960s TALC has distributed over 7 million slides (colour transparencies), accompanied by a variety of written suggestions as to how the slides can be used to improve their teaching. And from the early 1970s, TALC has provided about 1 million low-cost books, every effort being made to identify and, where necessary, develop books which would be particularly appropriate for those in primary health care.

Recently we have become more concerned with what use is made of the books that we distribute. Two experiences illustrate the need for this. It is likely that these experiences could have occurred anywhere in the world, but the first was from South America.

When visiting one of the best community health workers in a South American programme, the worker was asked to use his copy of Where There is No Doctor to find out what action he would take if a case of poliomyelitis occurred in a village. He thumbed through the book, threw it down and said he would send the child to hospital—although some of the villages are cut off for many weeks in the wet season. This worker, like many others, had not been trained 'around' a book. He had never been taught how to use the index of a book, and how to use a book to extend his knowledge and ability.

The second experience is related by a well experienced doctor who teaches medical assistants in central Africa.

'We tried to create a reading culture amongst our students, particularly as we got more into problem based learning. However, we discovered that students who had been in schools that use the ''parrot fashion'' style of teaching had no inclination and little ability to read. We therefore reduced our reading list to five essential books, and included the price of them in school fees. Students were given the books, and all problems were confined to the tests within these books, apart from problems in the community. Other sessions were given to specified reading. Without such discipline, books were carried around to protect papers carried inside them—or to look important.'

TALC believes these experiences are common to many countries in the developing world. This has led us to develop three initiatives:

1 Encourage programmes around a book. If less well educated health workers are to use books regularly then training programmes need to be developed which involve the trainees using the book. TALC hopes to identify those who could make use of books such as Where There is No Doctor, Disabled Village Children, A Book for Midwives and Nutrition for Developing Countries. All of these

and some other TALC books are appropriate for use where health workers are literate and can read English. TALC would also encourage those who are running the courses to undertake a refresher weekend after 6 months to see how well the books are being used. Working in partnership with such teachers TALC hopes to obtain grants to supply the book for training and also for continuing use by the trainee.

2 Small Libraries in Health Centres and District Hospitals. Even the low cost books provided by TALC are equivalent to a week or more salary for many health workers. For this reason it is unlikely that many will be able to 'own' more than one or two books. We looked at experience from around the world in running small libraries and found that except for schools there was almost none. Unfortunately unless the small library is planned it so often ends up locked in the senior worker's office or the books rapidly disappear from open shelves. For this reason TALC considers it is necessary to develop libraries run by small democratic committees representing all levels of workers in the health unit. So far TALC has sent out over 1200 library packs but we have not yet managed to develop a research programme to find out what happens to these books.

3 Develop local NGOs to provide books and other low cost material for local currency. TALC works closely with an organization in Nigeria providing books and has also helped in the development of a small TALC in South Africa. However, TALC considers that to widen this approach we need to work with other organizations and we were happy to join a small loose consortium with Healthlink (formerly AHRTAG), a nonprofit organization that reaches some 2 million health workers around the world with their free health newsletters, and FSG-MediMedia, which produces Africa Health and Medicine Digest, two of the most widely read journals in the developing world. The consortium hopes to develop small offices in the capitals of developing countries which can respond to local needs for health education from the mass of such information available (but so far poorly organised) in the North to areas in the South where it is so desperately needed.

For further details please contact: Professor David Morley, Teaching Aids at Low Cost, PO Box 49, St Albans AL1 5TX, United Kingdom.

The Research Training Programme of the London School of Hygiene & Tropical Medicine

A recent summary of a pamphlet on the Research Programme by Professor Harrison C Spencer, Dean, reads as follows:

The London School of Hygiene & Tropical Medicine has an internationally excellent reputation in public health and tropical medicine, is a leading postgraduate medical institution in Europe and is Britain's national school of public health. A special strength of the School's research is its multi-disciplinary nature with leading researchers having a very wide range of backgrounds including public health medicine, epidemiology, clinical medicine, infectious diseases, parasitology, medical microbiology, virology, chemotherapy, biochemistry, immunology, genetics, molecular biology, entomology, statistics, demography, health economics, public health engineering, medical anthropology, health promotion, environmental health management, psychology, sociology, and health policy.

The School has been providing advanced and interdisciplinary training for future senior academics, policy makers, practitioners, and research workers, in the international medical and public health community, for nearly 100 years.

This leaflet tells you about the School's research training programme and the opportunities for research study leading to the University of London degree of DrPH (Doctorate in Public Health), MPhil (Master of Philosophy), and the PhD (Doctor of Philosophy). It provides an overview of the work being carried out within departments and of the possibilities for research study.

The degree of DrPH offers experienced professionals in the field of Public Health an opportunity to pursue doctoral level studies relevant to their interests and needs. The course develops high level

professional, research and enquiry skills, and is best suited to those who wish to further a career in professional, operational and management aspects of public health.

The British MPhil and PhD research degrees involve the presentation of a thesis on a research topic, which will be in a field appropriate to student's or their sponsor's needs. Under the supervisor's guidance, students develop the intellectual and technical skills required for research and gain insight into the nature of research, which will provide the foundation for a future research career.

The diversity of our students and staff is exceptional; staff come from 35 countries and our 600 postgraduate students from 95 countries and this provides a rich environment for students to learn and to learn from each other. School alumni are now working in more than 140 countries; many former students hold prominent positions in health ministries, universities and international organizations throughout the world.

I am delighted to report that the School's excellence in all departments has been recognized in the UK's Research Assessment Exercise, a peer review exercise to grade research activities at all UK academic institutions.

The London School celebrates its centenary in 1999, after 100 years it remains an exciting place in which to train, please join us.

The Department of Infectious & Tropical Diseases in the school is described as follows:

The Department encompasses all of the laboratory-based research in the School as well as research on the clinical and epidemiological aspects of infectious and tropical diseases. The Department is headed by Professor Peter Smith and the range of disciplines represented is very broad and inter-disciplinary research is a feature of much of the activity. The spectrum of diseases studied is very wide, including major research groups with a focus on malaria, tuberculosis, HIV/AIDS and other sexually transmitted diseases, vaccine development and evaluation, and vector biology and control. The Department is organised into five large research units comprising: Immunology, Pathogen Molecular Biology & Biochemistry, Disease Control & Vector Biology, Infectious Disease Epidemiology and Clinical Research. There is close interaction between scientists in different research teams and thus research students have excellent training opportunities across a wide field. The Department has strong overseas links which provide a basis for field studies and international collaboration in developed and developing countries. Students are encouraged to broaden their education through participation in specialist courses on the School's Masters programme, which has a modular structure, and by attending and participating in the many and varied research seminars that take place in the School. The Department provides a stimulating environment for postgraduate students and an excellent preparation for an international research or practical career. The description of the work of the Units within the department which follows will help identify where students would most appropriately carry out their research degree training.

If you would like further information about research opportunities leading to MPhil, PhD or DrPH degrees, or taught courses (MSc and short programmes) please contact the School for a Prospectus.

The School Prospectus, which is available on the internet (www.lshtm.ac.uk/prospectus), contains detailed information about entry requirements, application details, tuition fees, the costs of living in London, accommodation, and medical and postgraduate study in London, one of the world's great capital cities.

If you would like a Prospectus or have other queries please contact or send the form below to: The Registry, London School of Hygiene & Tropical Medicine, 50 Bedford Square, London WC1B 3DP. Tel: +44 (0) 171 927 2239. Fax: +44 (0) 171 323 0638. e-mail: registry@lshtm.ac.uk. internet: http://www.lshtm.ac.uk.

TALMilep: Teaching and learning materials for leprosy

TALMilep is an Action Group of ILEP—the International Federation of Anti-Leprosy Associations which produces and supplies teaching materials on leprosy and related subjects free or at low-cost.

Leprosy: A. Bryceson and R. E. Pfaltzgraff (1989)—a readable reference book for medical students, general practitioners and physicians. £2.00.

Essentials of Leprosy: Dr Leo Yoder (1996)—this booklet contains information on leprosy care and treatment suitable for a range of health workers. FREE.

A Guide to Eliminating Leprosy as a Public Health Problem (1997), WHO—a pocket guide to diagnosis and management. FREE.

Leprosy for Field Staff: Alison Summers (1993)—this excellent book is aimed at health workers in specialized leprosy programmes or general health workers who see leprosy on a regular basis. FREE.

Atlas of Leprosy: Guinto *et al*., Sasakawa (1997)—this book of colour photographs is most suitable for use in areas such as East Asia where leprosy is seen in lighter skins. FREE.

Leprosy in Africans: Jacyk (1986)*—an booklet containing colour photographs with short notes in English and French. Arabic translation available on request. A popular and practical reference guide for health workers. FREE.

Care of the Eye in Hansen's Disease: M. Brand (1993)*—outlines the management of eye complications in leprosy for ophthalmologists and other health workers FREE.

Insensitive feet: P. Brand (1994)—a good background to the problems of insensitive feet. FREE.

Prevention of disabilities in patients with leprosy a practical guide: H. Srinivasan (WHO 1993)–for those involved in patient assessment, treatment and teaching self-care to people with leprosy. Price (for use in developing countries) £9.50.

Essential action to minimise disability in leprosy patients: J. Watson (1994)*—an excellent book with clear text and illustrations written for general health workers caring for people with leprosy. FREE.

Leprosy Surgery for General Hospitals: H. Srinivasan, WHO.

FREE (for use in developing countries).

Guide to health education in leprosy: P. J. Neville (1993)—contains messages for patient education. FREE.

Don't treat me like I have leprosy: Frist—a book about the history of leprosy and the importance of social issues. FREE.

Tuberculosis Guide for low-income countries: IUALTD—FREE.

***Also available in French**

All of these can be ordered directly from TALMilep. A more detailed list of books can be obtained from TALMilep. TALMilep is currently reviewing and updating the materials it supplies as a result some titles may be replaced by new or revised publications.

TALMilep also distributes a catalogue of training courses and a video catalogue which reviews leprosy related videos and gives information on how to order them.

For people developing health training materials locally for leprosy in general, combined or specialist programmes, TALMilep can help by sharing information on what has been produced elsewhere and can provide technical and editorial advice.

INFOLEP, TALMilep's sister organization, provides a leprosy information service and bibliography through mail and the world wide web (http://infolep.antenna.nl). It is based at the offices of the Netherlands Leprosy Relief (NLR).

For further information and to order books, please contact: The Teaching and Learning Materials Co-ordinator, ILEP, 234 Blythe Road, London W14 0HJ, United Kingdom. Tel: +44 171 602 6925. Fax: +44 171 371 1621. e-mail: ilep@ilep.org.uk. Website http://www.oneworld.org/ilep.

WHO conferences in TB treatment

September 15–18, 1999
Conference on Global Lung Health and the 1999 Annual Meeting of IUATLD
Venue: Palacio de Congresos, Madrid, Spain
Details:
Sophie Aumonier, IUATLD Secretariat, 68 Boulevard St. Michel, 75006 Paris-France
Tel: +33 1 44 32 03 75
e-mail: SophieAumonier@compuserve.com

November 13–15, 1999
Middle East Regional Meeting of IUATLD
Venue: Kuwait City, Kuwait
Details:
Sophie Aumonier, IUATLD Secretariat, 68 Boulevard St. Michel, 75006 Paris-France
Tel: +33 1 44 32 03 75
e-mail: SophieAumonier@compuserve.com

April 10–13, 2000
9th International Congress on Infectious Diseases
Venue: Buenos Aires, Argentina
Details:
International Society for Infectious Diseases, 181 Longwood Avenue, Boston, MA 02115, USA
Tel: +1 517 277 0551
e-mail: isidbos@aol.com

April 13–15, 2000
Future Challenges for Chest Physicians in Europe and the 1st European Regional Meeting of IUATLD
Venue: Budapest Convention Centre, Budapest, Hungary
Details:
Sophie Aumonier, IUATLD Secretariat, 68 Boulevard St. Michel, 75006 Paris-France
Tel: +33 1 44 32 03 75
e-mail: SophieAumonier@compuserve.com

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News and Notes

LEPRA creates new fund in memory of Dick Rees

LEPRA staff, together with over a hundred others from the leprosy world, commemorated the death of Dr Dick Rees with a memorial service at the National Institute for Medical Research in London in February. Dr Rees played such a central role in the leprosy field that LEPRA and its Executive Board have decided to honour his memory by instituting a fund which will allow us to support those working in leprosy to undertake useful training in the UK or elsewhere. In addition to the support already provided to Medical Elective Students from this country, the fund will enable one person each year to undertake a longer period of study aimed at strengthening their capacity to contribute to anti-leprosy work in their country. The new fund will be called the Dick Rees Memorial Fund.

WHO publication: 'Tuberculosis Control and Medical Schools'

WHO/TB/98.236 of the above title is a Report of a workshop, Rome, Italy 29–31 October, 1997 (paperback, 53 pages). Following a Foreword by Sir John Crofton, Emeritus Professor of Respiratory Diseases and Tuberculosis, University of Edinburgh, United Kingdom, the *Abstract* reads as follows:

The Global Tuberculosis Programme of WHO responded to the World Health Assembly's resolution (WHA 48.8) for change in medical education and medical practice by setting up a workshop on 'Tuberculosis Control and Medical Schools'. The workshop, held between 29 and 31 October 1997 in Rome, was attended by 25 participants from 16 countries of the six WHO Regions, and whose disciplines covered microbiology, clinical chest medicine, infectious disease, radiology, public health and medical education. Most of the participants currently hold or have held leading positions in medical schools and/or in National Tuberculosis programmes.

Considering the large spectrum of responsibilities that future doctors should assume, and in line with the evolution of health systems worldwide, discussion was held on what the doctor's position should be in tuberculosis control.

A list of required knowledge, skills and attitudes essential for a doctor to manage tuberculosis was agreed. Various options in educational strategy were considered, the first choice being a comprehensive module integrating all aspects of tuberculosis and tuberculosis control. Taking also into account the accommodation of learning needs relative to other important public health concerns, participants stressed the importance of proper evaluation of practical skills and attitudes before graduation.

To initiate, achieve and sustain the required changes in the medical curriculum and in medical practice, the workshop recommended that a 'task force for tuberculosis' be set up in each medical school. The remit of this task force should extend eventually into medical practice and post-graduate training in close association with the Ministry of Health, the National Tuberculosis Programme, medical professional organizations and other national bodies, organizations and/or institutions in the community.

At all stages, the task force should recognize the importance of partnership in the process of change in health care delivery, medical practice and medical education and should seek to create appropriate partnerships.

It was recommended that WHO should be a catalyst and a resource for developing task forces at regional and country levels.

Towards the closing pages, the *Recommendations* are the following:

1 In each medical school a task force for tuberculosis should be set up in order to produce changes in the curriculum which will ensure that the graduates have the knowledge, skills and attitudes essential to the proper management of tuberculosis in the individual patient as well as in the community.
2 The task force of the medical school should be comprised of representatives of all those groups involved in teaching e.g., Bacteriologist, Histopathologist, Chest Physician or Infectious Disease Physician or General Physician with expertise in tuberculosis, Radiologist, Public Health Physician or representative of the National Tuberculosis Programme and representatives of the medical students.
3 The task force should use this document as the basis for its deliberations and plans of action for improving the curriculum for tuberculosis and the evaluation of the graduates.
4 The task force should encourage partnerships between medical schools, Government Health Authorities, Medical Professional Associations and concerned organizations and groups in the community in achieving, sustaining, evaluating and updating the changes in medical education and medical practice.
5 These partners should extend their remit to include continuing post-graduate education, practice guidelines, and performance assessment for doctors as well as the organization of health care locally and regionally.
6 WHO should act as the catalyst for these plans for change. Ministers of Health, National Tuberculosis Programme Coordinators/Managers, Deans of medical schools, presidents of relevant medical professional associations and relevant NGOs should be sent this report with a covering letter from WHO. WHO Regional Offices will identify and inform other key personnel and organizations, at country and regional level.

These recommendations should, if translated into action, result in improved detection of patients with smear positive tuberculosis, improved cure rates and reduction of the proportion of resistant and multi-drug tuberculosis.

These important recommendations, with great emphasis on the creation and maintenance of 'task forces' in all medical schools, clearly deserve serious consideration. Although this report was not published until 1998, it may not be too soon to say that feedback on progress, including success or failure, with regard to these recommendations, would be valuable. We would be glad to hear from readers, especially those working in, or connected with medical schools.

Editor

Donors fail to meet commitments

Developed nations have failed to come up with the funding they promised for reproductive health programmes in the developing world. Population Action International (PAI), an NGO specializing in reproductive health, says that developing countries agreed to meet one-third of the total costs of the 20-year programme for the developed world, which was drawn up at the 1994 Cairo International Conference on Population & Development. In total the donor nations agreed to provide US$5·7 billion by the year 2000. However, only $1·4 b has so far been paid.

PAI's new study—'Paying their fair share? Donor countries and international population assistance'—profiles 20 major donor nations and concludes that only a few of them (Denmark, the Netherlands, Norway and Sweden) have either reached or are close to meeting their funding goals. The US and Japan account for $2·4 billion of the $4·3 billion shortfall.

One of the report's authors says, 'More than three million women and men die each year from reproductive health-related causes, including HIV/AIDS, and nearly all of them are in developing

countries. Reproductive health needs are growing, due to the AIDS epidemic and the record numbers of young people entering their childbearing years. These are facts that donor community cannot ignore.'

Report of WHO/TDR Scientific Working Group on the Utilization of Genomic Information for Tropical Disease Drug and Vaccine Discovery: Geneva 18–20 February, 1998

This 75-page document (TDR/Genomics/98.1) comes from the *UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases.* The Summary reads as follows:

The meeting reported in this document brought together scientists, administrators and managers from both academia and industry, and from both North and South, to discuss the impact of genomics on the future of drug and vaccine discovery in tropical diseases.

The meeting was timely given the status of functional genomic research into infectious disease pathogens and three of the four components of TDR's mission, namely: (I) to stimulate strategic research, particularly in the areas of genome research and pathogenesis, on tropical disease pathogens; (ii) to promote research capability strengthening in disease-endemic countries; and (iii) to promote the discovery and development of new products (drugs and vaccines) against tropical diseases.

The meeting programme and discussion searched for ways in which the tropical disease scientific community, and TDR, could link the scientific advances in functional genomics, currently occurring in both academia and industry, into a coherent strategy for promoting stronger drug and vaccine discovery research for tropical diseases.

The meeting was divided into five main sessions:

- Sequencing and bioinformatics
- Tools to assist with analysis of genomic information
- Strategic application of tools for drug discovery
- Genetic manipulation of organisms to assess gene function
- Strategic application of tools for vaccine discovery

A round table discussion of these topics focused on several main themes:

- The need for further sequencing efforts
- Appropriate scientific and managerial strategies for functional genomics
- Converting genomic information into drug and vaccine discovery projects
- Training and research capability strengthening in functional genomics

Several key conclusions were drawn from this discussion:

- There is a continuing need to promote genomic sequencing efforts
- There is a need for TDR, together with other agencies, to promote the appropriate curatorship of sequence information and its annotation
- There is a need for TDR, together with other agencies, to create repositories of reagents to assist functional genomic research
- There is a need for TDR to actively promote activities in functional genomics
- There is a need for TDR to fund the development of new and improved technologies that will facilitate functional genomics research in its target diseases
- Within TDR, there is a need to ensure effective coordination between genomic research, pathogenesis research and drug and vaccine discovery
- There is a continuing need to engage with industry where possible and appropriate to maximise the translation of genomics research into appropriate product R&D
- There is a need for appropriate training and institutional strengthening in disease endemic countries in functional genomics, especially bioinformatics

- TDR should investigate the role it has to play in promoting appropriate partnerships in the field of bioinformatics.

This document signifies the importance of functional genomic research for tropical diseases. We hope it will serve as an initial source document for scientists and administrators who are involved, or wish to become involved in this field, and hope that it may help identify appropriate contacts for further discussion between interested individuals.

Many people outside the TDR secretariat contributed to the success of the meeting and the preparation of this document. In addition to those attending, speaking and chairing sessions, the rapporteurs deserve a special note of thanks. All contributors are listed in the appendices documenting the meeting programme and the list of participants. Special mention should go to Jennie Blackwell, who helped tremendously in the initiation, planning and organizing of the meeting.

Anybody wishing further information or wishing to offer suggestions on the general topic of TDR genomic and post-genomic research should contact Dr Boris Dobrokhotov (dobrokhotovb@who.ch) or Dr Robert Ridley (ridley@who.ch).

Deciphering the biology of *Mycobacterium tuberculosis* from the complete genome sequence

The above is the title of a publication of very considerable importance which appeared in *Nature*, Volume *393* on 11 June 1998, by S. T. Cole of the Unité de Génétique Moléculaire Bactérienne, Institut Pasteur, Paris, France and 41 co-authors from centres in the United Kingdom, the USA and Denmark.

The *Summary* reads as follows:

Countless millions of people have died from tuberculosis, a chronic infectious disease caused by the tubercle bacillus. The complete genome sequence of the best-characterized strain of *Mycobacterium tuberculosis*, H37Rv, has been determined and analysed in order to improve our understanding of the biology of this slow-growing pathogen and to help the conception of new prophylactic and therapeutic interventions. The genome comprises 4,411,529 base pairs, contains around 4,000 genes, and has a very high guanine + cytosine content that is reflected in the biased amino-acid content of the proteins. *M. tuberculosis* differs radically from other bacteria in that a very large portion of its coding capacity is devoted to the production of enzymes involved in lipogenesis and lipolysis, and to two new families of glycine-rich proteins with repetitive structure that may represent a source of antigenic variation.

And the *Introduction*:

Despite the availability of effective short-course chemotherapy (DOTS) and the Bacille Calmette-Guérin (BCG) vaccine, the tubercle bacillus continues to claim more lives than any other single infectious agent. Recent years have seen increased incidence of tuberculosis in both developing and industrialized countries, the widespread emergence of drug-resistant strains and a deadly synergy with the human immunodeficiency virus (HIV). In 1993, the gravity of the situation led the World Health Organisation (WHO) to declare tuberculosis a global emergency in an attempt to heighten public and political awareness. Radical measures are needed now to prevent the grim predictions of the WHO becoming reality. The combination of genomics and bioinformatics has the potential to generate the information and knowledge that will enable the conception and development of new therapies and interventions needed to treat this airborne disease and to elucidate the unusual biology of its aetiological agent, *Mycobacterium tuberculosis.*

The characteristic features of the tubercle bacillus include its slow growth, dormancy, complex cell envelope, intracellular pathogenesis and genetic homogeneity. The generation time of *M. tuberculosis*, in synthetic medium or infected animals, is typically ~24 hours. This contributes to the chronic nature of the disease, imposes lengthy treatment regimens and represents a formidable obstacle for researchers. The state of dormancy in which the bacillus remains quiescent within infected tissue may reflect

metabolic shutdown resulting from the action of a cell-mediated immune response that can contain but not eradicate the infection. As immunity wanes, through ageing or immune suppression, the dormant bacteria reactivate, causing an outbreak of disease often many decades after the initial infection. The molecular basis of dormancy and reactivation remains obscure but is expected to be genetically programmed and to involve intracellular signalling pathways.

The cell envelope of *M. tuberculosis*, a Gram-positive bacterium with a G + C-rich genome, contains an additional layer beyond the peptidoglycan that is exceptionally rich in unusual lipids, glycolipids and polysaccharides. Novel biosynthetic pathways generate cell-wall components such as mycolic acids, mycocerosic acid, phenolthiocerol, lipoarabinomannan and arabinogalactan, and several of these may contribute to mycobacterial longevity, trigger inflammatory host reactions and act in pathogenesis. Little is known about the mechanisms involved in life within the macrophage, or the extent and nature of the virulence factors produced by the bacillus and their contribution to disease.

It is thought that the progenitor of the *M. tuberculosis* complex, comprising *M. tuberculosis*, *M. bovis*, *M. bovis* BCG, *M. africanum* and *M. microti*, arose from a soil bacterium and that the human bacillus may have been derived from the bovine form following the domestication of cattle. The complex lacks interstrain genetic diversity, and nucleotide changes are very rare. This is important in terms of immunity and vaccine development as most of the proteins will be identical in all strains and therefore antigenic drift will be restricted. On the basis of the systematic sequence analysis of 26 loci in a large number of independent isolates, it was concluded that the genome of *M. tuberculosis* is either unusually inert or that the organism is relatively young in evolutionary terms.

Since its isolation in 1905, the H37Rv strain of *M. tuberculosis* has found extensive, worldwide application in biomedical research because it has retained full virulence in animal models of tuberculosis, unlike some clinical isolates; it is also susceptible to drugs and amenable to genetic manipulation. An integrated map of the 4·4 megabase (Mb) circular chromosome of this slow-growing pathogen had been established previously and ordered libraries of cosmids and bacterial artificial chromosomes (BACs) were available.

Definitive guide to the United Kingdom charity sector

CaritasData Ltd, Kemp House, 152–160 City Road, London EV1V 2NP (fax: 0171-250-3050: e-mail info@caritasdata.co.uk) are currently advertising their 1999 Guide to the top 3000 charities in the UK, together with a CD listing 10,000 charities. The promotional brochure describes these sources of information as essential to–

- identify grantmakers sympathetic to your cause
- contact key personnel in other charities
- compare your performance to the sector
- locate the top performing charities
- target known corporate donors
- pinpoint and approach professional advisers
- target thousands of named charity executives
- see how your company performed last year
- keep in touch with the sector
- study the top charity performers

New publication: 'Tuberculosis in Childhood'

Publishers from South Africa (see below) have just announced the availability of this book, with the following description:

Tuberculosis is today more prevalent in the world than ever before. Fast-growing populations in

countries with poor resources continue to be the breeding ground for the world's most wide-spread epidemic, which is further aggravated by co-infection with HIV/AIDS and the emergence of multi-drug resistant tuberculosis. Children represent a significant proportion of the case-load, and with the increasing demands on health care services in high-prevalence regions, special strategies to effectively diagnose and manage tuberculosis in this group are required.

In this book a comprehensive overview is presented of tuberculosis in childhood. Although special attention is given to dealing with the disease in high-prevalence situations in Southern Africa, its applicability is universal. Modern approaches to clinical and laboratory diagnosis, prevention and treatment are explained in practical fashion, which allows the book to be used as a manual in both the clinical and public health settings. On the other hand, fully referenced, state-of-the-art reviews on bacteriology, immunology, epidemiology and the pathogenesis of tuberculosis in children make it an ideal textbook for students in medical and related professions.

Further information: J. L. van Schaik Publishers, PO Box 12681, Hatfield, Pretoria, 0028, Attention Mary-Ann Foster Tel +27 12 342 2765, Fax +27 12 43 3563

Does anyone use the Internet?

The Internet information service HealthNet is now being operated in 23 sub-Saharan countries but it seems not to be widely used.

HealthNet is a major initiative run by the SatelLife organization. African health professionals with electricity, a telephone line and a suitable computer can use HealthNet to send and receive electronic mail and gain access to 'Websites' where they can look up information on health topics as required. Telecommunication links are made via satellite.

An Eritrean, Resoum Kidane, who is currently a student in the UK, contacted 130 health professionals and asked them what they knew of HealthNet. Those approached were either African health professionals taking postgraduate courses in the UK or subscribers to AHILA-NET, a discussion group, which also uses the Internet. Only 49 responded, of whom only 19 had ever heard of HealthNet. Most of the 19 were people working in libraries. Those health professionals who used HealthNet gave it a low satisfaction score, although health librarians rated it more highly. The information source most favoured by health professionals was *Child Health Dialogue.*

Mr Kidane believes the lack of information on tropical diseases and rural healthcare available through HealthNet is responsible for the unpopularity of the service. He would like to see HealthNet carry more appropriate information and for steps to be taken to enable health workers in rural areas to gain access to it.

- Mr Kidane's study, though based on a very small sample, raises important issues: can such a service reach the majority of front-line healthcare providers and does the information presently made available match the needs of those for whom it is intended? Readers views and experience would be welcomed.

Editor

More Topics in International Health: The Wellcome Trust

The following is taken from the latest edition of *Wellcome News*, Issue 17, Q4, 1998:

The Wellcome Trust has just released four new CD-ROMs in its 'Topics in International Health' series, covering leprosy, schistosomiasis, diarrhoeal diseases and tuberculosis. The CDs provide interactive and highly illustrated training modules for health professionals in the developing world.

Since the launch of the first four titles in the 'Topics in International Health' series in April 1998,

CD-ROMs have been acquired by more than 1000 users in 52 countries. Critical opinion has also been favourable—writing about the malaria disk in the September issue of *Parasitology Today*, Sylvia Meek commented: 'This CD-ROM is of a very high standard and should be an essential tool for all courses on malaria and for malaria-control programmes.'

One of the most satisfying aspects of the series' success is the integration of the disks into coordinated international disease control programmes. In November, Pfizer and the Edna McConnell Clark Foundation announced the setting up of the International Trachoma Initiative (ITI), which is dedicated to eliminating the world's leading cause of preventable blindness. The ITI's Program Director, Jeff Mecaskey, has taken delivery of 50 copies of the trachoma disc. Speaking from his New York office, Jeff explained how the 'Topics in International Health' series was a part of the strategy to help eliminate trachoma: 'The ITI has a commitment to evidence-based decision making, but we had to find a resource to enable our national and international partners to remain current with the latest thinking about trachoma and its control. We expect that the Wellcome Trust trachoma CD-ROM will do just that. Because it is self-directed learning, the CD-ROM will enable these partners—whether they work in Vietnam or Vienna—to develop a common body of knowledge tailored to their own specific needs.'

As with the first disks, the four newly published titles have all been produced at the Wellcome Trust by the Tropical Medicine Resource team. The content of the disks is designed, written and edited in-house in close collaboration with internationally respected subject experts and advisers. The result is a thoughtfully presented and scientifically rigorous collection of images and tutorials. The development of the series is a dynamic process and the newest titles have evolved in response to comments from users. The new disks include more computer animations and video clips than the first titles.

All eight disks in the 'Topics in International Health' series—malaria, trachoma, sexually transmitted diseases, sickle cell disease, leprosy, schistosomiasis, diarrhoeal diseases and tuberculosis—are available through the Wellcome Trust's publishing partner for this project, CABI Publishing: Tel: +44 (0) 1491 832111; Fax: +44 (0) 1491 829292.

Chris Coyer, Head of the Tropical Medicine resource.

Wellcome News is published 4 times yearly and is available free of charge: apply to Marketing Department, Wellcome Trust, 183 Euston Road, London NW1 2BE, United Kingdom. Fax: +44-171-611-8416. E-mail: marketing@wellcome.ac.uk.

New publication: 'Tuberculosis. An Interdisciplinary Perspective'

Imperial College Press describe this publication, due out in March 1999, as follows:

The fact that the World Health Organization has declared tuberculosis a 'global emergency' indicates the serious inadequacy of the ways in which the control methods at our disposal are used. Several books on tuberculosis have been published in recent years, but none have taken a deep and detailed look at the 'holistic' aspects of global tuberculosis control, even though international agencies are increasingly aware of the importance of the numerous factors other than the design and efficacy of therapeutic drug regimens. This unique book fills that gap. Although it deals specifically with tuberculosis, the principles outlined and discussed are relevant to many other areas of global medicine, including the ever-growing problem of HIV/AIDS.

The book is aimed principally at those involved in the design, establishment and management of disease control programmes at international, national and local levels, and also at a more general readership of epidemiologists, public health officers, community psychologists, and others interested in understanding the human dimension of disease control.

Contents include: the global burden of tuberculosis; the politics of tuberculosis: public health and human rights; current control strategies; the economics of diagnosis and management; sociocultural

dimensions; the impact of HIV; tuberculosis in ethnic minorities; gender issues; health sector reform; educational approaches to tuberculosis control.

Editors: John D. H. Porter (London School of Hygiene & Tropical Medicine), John M. Grange (Imperial College).

200 pp (approx.) Pub date: Spring 1999
1-86094-143-5 US$42 £28

Further information and ordering: World Scientific Publishing (UK) Ltd, 57 Shelton Street, Covent Garden, London WC2H 9HE. Fax: +44-171-836-2020.

AIDS cases soar

World AIDS Day (1st December) saw the publication of new UNAIDS figures indicating that the number of people infected with HIV globally rose 10% during 1998. Sub-Saharan Africa remains the hardest hit region; nearly 12 million Africans have now died in the epidemic. Although AIDS hit southern Africa relatively recently, the most dramatic rise in infections is taking place in this part of the continent.

Amongst the issues discussed in the UNAIDS report is the role of war in the spread of HIV; before the conflict in Rwanda urban and rural infection rates were 10% and 1% respectively but now both exceed 11%.

Also notable is the widespread reluctance of Africans to be tested for HIV. For example, over 13,000 pregnant women in Côte d'Ivoire were offered testing as part of interventions to increase their chances of having a healthy baby, but fewer than half wanted to know their HIV status. Most Africans with HIV/AIDS are also reluctant to admit that they have the infection and, in one study, only 10% of people caring for family members with HIV at home were prepared to admit that they were infected. Dr Peter Piot, head of UNAIDS, said: 'One might think that in a country with a quarter or a third of the population infected people would become more open about the epidemic. Experience teaches us that this doesn't happen automatically. The silence needs to be broken'.

Other issues of great concern include the growing number of orphans and the rise infant mortality which is occurring in many African countries. The impact on adolescents and young adults is also serious; globally half of new infections are in 15–24-year-olds and 10% are in under-15s.

There are some hopeful signs. Condom use is increasing in several African countries; in Senegal the percentage of men under 25 using condoms with non-regular partners has gone up from 5% to 65% within 6 years; amongst women it rose from 5% to 25%. UNAIDS once again singles out Uganda as an example to the whole world for its openness on AIDS and its commitment to action on both prevention and care.

- The progress of AIDS has by no means been halted in the rest of the world. In some regions, for example Eastern Europe and Latin America, it is still largely confined to what UNAIDS calls 'marginalized groups'. However, in India it has moved from these groups, and from urban to rural areas, to be 'firmly embedded' in the population as a whole. In North America and western Europe new infection rates have levelled off but show no sign of declining. In these countries, however, the death rate has fallen dramatically as patients have access to expensive treatments that greatly prolong their lives.

A Directory of History of Medicine Collections, USA

The ninth edition of this Directory, 1999 has recently been compiled, listing information on collections in the USA, and including a few from other countries. The preface reads as follows:

The 93 collections described in this booklet provide research, reference, and interlibrary loan services to

scholars interested in the history of the health sciences, including medicine, dentistry, veterinary medicine, nursing, and pharmacy. While the directory is by no means exhaustive, it serves to draw attention to the depth and variety of history of medicine collections available to researchers. In the future, it is expected that more institutions will agree to be included in this annual publication.

The records on the following pages are arranged alphabetically by US state and city, followed by foreign collections grouped alphabetically by country. For each record, the Abstract field indicates the collection's scope of coverage and services provided. The Holdings field lists the substance of the collection and identifies guides to the collection. Information about the collections has been provided by the person named as Contact. Interested researchers should get in touch with the contact person for more details.

The directory is a print version of the History of Medicine component of DIRLINE® (Directory of Information Resources Online), a National Library of Medicine (NLM) database, which contains location and descriptive information about a wide variety of health and biomedical resources. Developed by NLM's History of Medicine Division (HMD), the DIRLINE® History of Medicine component aims to assist scholars and researchers in identifying useful medical history collections throughout the world. For further information about the DIRLINE® database, including how to access, please consult the DIRLINE® Fact Sheet at http://www.nlm.nih.gov/pubs/factsheets/dirlinfs.html.

We invite libraries, archives, and museums, which include in their collections holdings in the history of medicine, dentistry, veterinary medicine, nursing, and pharmacy, to become part of the DIRLINE® History of Medicine component. Participating institutions must be able to respond to relevant reference questions and, in the case of libraries, interlibrary loan requests.

To ensure that information is up to date, participating institutions are encouraged to keep their records current. New and revised data can be sent to the History of Medicine Division via mail, e-mail or fax.

Please contact: Elizabeth Tunis, History of Medicine Division, National Library of Medicine, Bethesda, MD 20894, USA. Tel: +1-301-402-6134, Fax: +1-301-402-0872, e-mail: elizabeth_tunis@nlm.nih.gov.

WHO target draws veil over leprosy

Sub-titled 'Efforts to eliminate the disease by 2000 do not take into account undiscovered cases', the following report of the Beijing Congress by John Gittings appeared in the *Guardian* newspaper (UK) of September 8th 1998:

The International Leprosy Congress opened yesterday in the Chinese capital with critical questions being asked about the World Health Organisation's goal of eliminating leprosy by 2000.

The WHO points to huge achievements since the beginning of the decade. Treatment with a cocktail of drugs known as MDT has reduced the estimated number of leprosy cases worldwide from 10–12 million in 1998 to 1·15 million last year.

But leprosy campaigners from non-governmental organisations complain that the WHO has 'manipulated data and moved the goalposts in order to claim success'.

They agree that fixing the target was important in mobilising international funds and support, but fear that interest will fade if the WHO announces that the target has been reached. Financial backing already depends heavily on private donors, headed by the Tokyo-based Sasekawa Foundation.

By 'elimination' the WHO means reducing the prevalence of leprosy to less than one case per 10,000 population. And by prevalence it means only cases which are being actively treated and are still infectious.

This leads to a statistical paradox. Because MDT treatment eradicates infection within a year, the number of registered cases is relatively low—it is now less than 900,000 worldwide. Yet the number of cases discovered each year is disproportionately high at nearly 700,000 in 1997.

Specialists suggest that this may be due to an incubation period of five to 10 years. But it could mean that there are many more unidentified sufferers than hitherto believed.

Professor Cairns Smith of the International Federation of Anti-Leprosy Federations said yesterday that more effort must be made to locate cases in vulnerable communities.

These include nomads, those who are geographically isolated, those who lack basic health care, those who are refugees or suffering from war or famine, and urban slum dwellers.

The WHO admits that even by its restricted definition some countries may have to 'continue and intensify activities beyond the year 2000 to reach their elimination targets'.

A campaign launched last winter in India to speed up the detection of unknown cases has produced alarming results. Although its coverage was not complete, it discovered 423,000 people suffering from leprosy. More than half were in the states of Bihar and Orissa.

In China, the host country for the Congress, there are now only 4000 cases under active treatment and fewer than 2000 new cases. But the vice-minister of health, Yin Dakui, admitted that leprosy control was still difficult 'in the remote, poor, mountainous and [ethnic minority] areas'.

There are more than 200,000 people who have been cured in China, of whom 120,000 are disabled.

International leprosy workers argue that the 'cured should still be part of the WHO statistics'. A specialist said: 'Drugs cannot eliminate the persistent effect of nerve damage after the patient has become non-infectious. There are probably five to six million worldwide who still have disabilities such as foot ulcers.'

Voluntary groups at the congress are lobbying hard for more involvement in anti-leprosy work by patients and former patients.

The IDEA organisation, which is based in the United States and runs work projects in several countries, including China, argues that sufferers should be encouraged to 'overcome their sense of helplessness and shame by taking a pro-active role'.

In a written presentation to the congress, the WHO said that if MDT treatment was maintained for the next five to 10 years, 'all transmission of the disease can be terminally interrupted', although it concedes that this may take longer in India.

India, however, is a huge part of the problem: it has more than 500,000 active cases: 60 per cent of the known global total.

FDA approves new anti-tuberculosis drug

The following appeared in the *British Medical Journal*, Volume 317, 4/7/98, page 11:

The US Food and Drug Administration has approved rifapentine (Priftin)—the first new antituberculosis drug to be licensed in 25 years.

Rifapentine is indicated for pulmonary tuberculosis but must be used in conjunction with other antituberculosis drugs. It is expected to increase patient compliance because it has a shorter treatment course than conventional drugs.

Current treatment regimens for active pulmonary tuberculosis require a minimum of 6–9 months of treatment with at least three drugs, which usually include isoniazid, rifampicin, and pyrazinamide. Treatment can last over a year in recalcitrant cases. Because the regimen is complicated and lengthy, patient compliance is problematic and treatment errors are common. These factors contribute to the emergence of multidrug resistant strains of tuberculosis.

Like rifampicin, rifapentine is given twice a week for two months in the intensive first phase of treatment, when daily isoniazid, pyrazinamide, and ethambutol are also required. However, in the next four months of treatment, one dose of rifapentine once a week is sufficient, as opposed to a twice weekly dose of rifampicin. Although this regimen still seems complicated, it is expected to increase compliance and reduce costs associated with directly observed treatment.

Clinical studies on rifapentine in which the drug was substituted for rifampicin in combination therapy showed that the drug was associated with a higher relapse rate than standard treatment, with 10% of patients taking the rifapentine combination relapsing, compared with 5% taking rifampicin. However, this higher relapse rate is expected to be offset by greater compliance.

The United States is the first country to approve rifapentine, but the largest market for the drug is likely to be in developing countries—however they may be unable to afford it.

Changes at WHO: 'Budget set to reflect new priorities'

The following is taken from the *British Medical Journal*, Volume 318, 23/1/99, page 212:

The director general of the World Health Organisation, Gro Harlem Brundtland, will next week ask the organization's governing body to approve radically overhauled spending plans reflecting her programme of reforms.

The WHO's executive board, which meets from 25 January in Geneva, will be presented with budget proposals for the years 2000–1 that require an increase of nearly one fifth in voluntary contributions by donors—that is, an increase in the amount paid over and above membership dues.

Dr Brundtland believes that the reforms already under way within the organization will attract further support from member states.

The proposed budget of $1·8 bn for the next two years allocates $19 m in extra funds to Africa and a smaller amount to the former Soviet republics. There is an overall shift in resources from headquarters and the six regional offices to activities at country level.

At headquarters, spending on communicable diseases continues to account for the biggest share of funds, at $284,000, an increase of 37% on the last budget. But two much smaller areas of the WHO's work will attract the biggest increases in spending: non-communicable diseases, which doubles its budget to $14,000, and data analysing activities known as evidence and information for policy, whose budget climbs by 44% to $48,000. Three new, high profile initiatives to be spearheaded by Dr Brundtland—tobacco controls, malaria control, and health sector development—will each receive extra resources. Managerial and administrative costs have been cut.

The new budget is intended to be more transparent, reflecting the new structure of the WHO. Previously, member states found it almost impossible to work out how their money was being spent because the categories in the budget did not reflect the organisation's structure. Now, 52 disparate programmes have been turned into nine clusters, and these are linked to the budget.

AIDS strains Zambia

The annual cost of caring Zambia's AIDS patients will rise to US$21 million by the year 2005, according to a recent study by the Central Board of Health. The costs, which are expected to rise from $1·7 m in 1990 and $12·9 m in 1995, will impose a strain on the government's budget and divert resources from other sectors.

Zambia's HIV prevalence rate is 20% and if it stays at that level until the year 2000 and then drops to 16%, as experts have predicted, then the number of HIV infected persons in the country (including children) will peak at about 1·1 million and stay at that level until 2010.

The Zambian government has agreed to test the efficacy of an 'AIDS drug' known as Herbiron Tisaniferon, ending a long stand-off with its inventor Professor Mulenga Lukwesa. The drug manufactured by MLN Laboratories of Lusaka will undergo tests but in the meantime Professor Mulenga has been told he can dispense his medicine as a 'herbal drug'. An outright ban on the drug was imposed in 1997 but a number of Zambian scientists have since said that they consider it to have shown positive results in the alleviation of diseases associated with AIDS/HIV, and against cancer, diabetes, arthritis, gout, and hypertension. The Head of Pharmacology at the University of Zambia, Dr Patrick Chikusu, said the drug might reverse trends that encourage the movement of HIV between cells. Dr Chikusu, who is also chief government pharmacologist, said state scientists would conduct trials to determine the drug's efficacy.

'Essential Drugs: Action for Equity'. WHO Action Programme on Essential Drugs

This publication from WHO (A4 size, 27 pages, WHO/DAP 92.5) begins with a 'charter for equity' in essential drugs:

- access for all people to necessary medicines

- prices which society and the individual can afford
- priority for drugs which meet the real health needs of the majority of the population
- fair distribution between cities and rural areas
- assurance that drugs are safe, effective and of good quality
- adequate training of all prescribers
- access to objective information
- real dialogue between patient and prescriber
- empowerment of consumers through education and information
- community involvement and participation
- development of drugs that meet health needs in the third world and not only those of rich countries
- responsible manufacture and export
- ethical promotion and marketing
- a stop to 'donations' of hazardous or ineffective products

The text goes on to describe: The Essential Drugs Concept; How Many Drugs do we Really Need?; The Work of the Action Programme; Key Elements of a National Drugs Policy; Using Drugs Rationally; The Action Programme & Research; Global Partners and Future Outlook. 'Further Reading' is as follows:

WHO PUBLICATIONS

(obtainable from WHO sales agents in each country or Distribution and Sales, WHO headquarters, Geneva)

The World Drug Situation, WHO, 1988
A comprehensive review of the many factors that influence the current availability and consumption of pharmaceuticals throughout the world.

Guidelines for Developing National Drug Policies, WHO, 1988
Addressed to policy-makers and administrators, this book identifies and explains the many complex factors to be considered when planning and carrying out a national drug policy.

The New Emergence Health Kit, WHO, 1991
Explains the historical development of the kit, details the contents and provides assessment and treatment guidelines for diarrhoea and respiratory infections.

Estimating Drug Requirements, WHO, 1989
A practical manual for course work or self study which describes, using working examples, how to estimate drug needs based on previous consumption and/or morbidity patterns.

Ethical Criteria for Medicinal Drug Promotion, WHO, 1988
Presents ethical criteria for the promotion of medicinal drugs, and constitutes a frame of reference for judging proper behaviour in drug promotion.

WHO Model Prescribing Information: Drugs used in Anaesthesia, 1989
Drugs used in Mycobacterial Diseases, 1991
Drugs used in Parasitic Diseases (2nd ed.), 1995
Drugs used in Sexually Transmitted Diseases and HIV Infection, 1995
Drugs used in Skin Diseases, 1997
Provides advice on the safe and correct prescribing of essential drugs in these specific fields.

Indicators for Monitoring National Drug Policies, WHO, 1994
Provides a comprehensive set of simple, objective and reliable indicators that allows assessment of countries' capacities to implement the elements of a national drug policy, monitor implementation and measure progress towards objectives.

Guide to Good Prescribing, WHO, 1994
The training manual gives step-by-step guidance to rational prescribing, explaining the principles of

drug selection and how to develop a set of drugs for regular use in practice. Numerous examples show how to select, prescribe and monitor treatment.

International Nonproprietory Names (INN) for Pharmaceutical Substances, WHO, 1996
The ninth cumulative list covering all currently proposed and recommended INN: a useful aid for drug manufacturers, prescribers and regulatory authorities who must work with generic names.

WHO Expert Committee on Specifications for Pharmaceutical Preparations, Technical Report Series No. 863, WHO, 1996
Sets out 12 international guidelines and other recommendations intended to assist national drug regulatory authorities and manufacturers in the quality control of pharmaceutical products.

The Use of Essential Drugs—Model List of Essential Drugs (Ninth List), Technical Report Series No. 867, WHO, 1997
Incorporates revisions to the Model List agreed upon by a WHO committee of experts, together with updated information on several other components of national drug policy.

UNPUBLISHED REPORTS AND GUIDELINES

In addition to WHO's priced publications in the field of pharmaceuticals, many offset documents, technical reports and guidelines covering subjects ranging from drug donations and financing to research studies and methodologies, are available free of charge directly from the Action Programme on Essential Drugs, WHO, Geneva.

PERIODICALS

Essential Drugs Monitor
Published twice a year in English, French, Spanish and Russian, by the Action Programme on Essential Drugs. It is available free of charge and provides information on national drug policies, rational drug use, supply, research, training and the development of national essential drug programme activities.

WHO Drug Information
A quarterly subscription publication, which communicates pharmaceutical information either developed or issued by WHO, or transmitted to WHO by research and regulatory agencies.

For further information, contact the WHO Representative in your country, or any of the WHO Regional Offices listed below:

World Health Organization
Regional Office for Africa
P.O. Box 6
Brazzaville
Congo

Temporary address:
World Health Organization
Regional Office for Africa
Medical School, C Ward
Parirenyatwa Hospital
Mazoe Street
P.O. Box BE773
Belvedere
Harare
Zimbabwe

World Health Organization
Regional Office for the Americas/Pan American Sanitary Bureau
525 23rd Street, N.W.
Washington D.C. 20037
USA

World Health Organization
Regional Office for the Eastern Mediterranean
P.O. Box 1517
Alexandria 21511
Egypt

World Health Organization
Regional Office for Europe
8 Scherfigsvej
2100 Copenhagen Ø
Denmark

World Health Organization
Regional Office for South-East Asia
World Health House
Indraprastha Estate, Mahatma Gandhi Road
New Delhi 110002
India

World Health Organization
Regional Office for the Western Pacific
P.O. Box 2932
Manila 1009
Philippines

Or you can write directly to:

The Action Programme on Essential Drugs
World Health Organization
1211 Geneva 27
Switzerland
Telex: 415 416, Fax: 791 41 67
E-mail: dapmail@who.ch

Please state in which areas or in what specific information you are interested.

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Electronic submission. Articles produced using a word-processor may also be supplied in electronic format (preferably Word or Wordperfect 5.1). Please submit a disk with the final revised version of the article. The electronic file should correspond exactly to the hard copy.

Illustrations and Tables. Contributors must send the original artwork and two copies on separate sheets. In addition electronic versions may be submitted in the form of compressed tiffs, eps, jpegs or bitmaps. The recommended resolution is 600 dpi or above.

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

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