Lepr Rev (2000) **71,** 226–244

News and Notes

Mycobacterium bovis: Third International Conference, Cambridge UK, 14–16 August 2000

Following the two very successful International Conferences on *Mycobacterium bovis* held in the Republic of Ireland and New Zealand, it has been decided to hold the third meeting in Great Britain at St. John's College, Cambridge, 14–16 August 2000. This event is being hosted by the Veterinary Laboratories Agency, Weybridge, UK.

The year 2000 is an important time in *Mycobacterium bovis* research with the expected completion of the *M. bovis* Genome Project (funded by the Ministry of Agriculture Fisheries and Food and the Wellcome Trust). It is hoped that this milestone might act as a further catalyst for research into the development of improved vaccines and diagnostic reagents to help in the fight against this important zoonotic disease at the start of the new millennium.

The format of the 3-day conference will comprise:

- Papers by invited speakers
- Selected oral communications
- Selected poster presentations

Seminar topics on the agenda will include:

- disease control
- epidemiology
- modelling disease in domestic animals and wildlife
- molecular typing
- pathogenesis
- immunology
- diagnosis
- mycobacterial genetics and vaccinology

The conference is expected to attract 250 delegates from around the world and an impressive line up of internationally recognized speakers has already agreed to participate.

The conference will be residential, 14 and 15 August but extra accommodation can be arranged at the college for the day before, Sunday 13 August (please specify on reply slip if required).

It is also intended to run a number of workshops following the end of the official conference on 17 August but places will be limited.

Topics will include:

- molecular fingerprinting techniques,
- immunodiagnosis,
- comparative pathology
- vaccine development

Further information:

Conference secretary,
Veterinary Laboratories Agency—Weybridge
New Haw, Addlestone, Surrey KT15 3NB United Kingdom
Telephone 01932 341111 Facsimile 01932 347046
Web site http://www.maff.gov.uk/aboutmaf/agency/vla/vlahome.html

Asian Leprosy Congress, Agra, India, November 2000

The message from the Organizing Committee runs as follows:

Dear Colleagues,

During the 15th International Leprosy Congress held in Beijing in the month of Sep '98 there was a strong desire to hold regional congresses in between the quinquennial international congresses in order to promote more frequent interaction among participants and also to highlight on regional issues, problems and achievements. This desire has culminated in the decision to hold the first Asian Leprosy Congress at Agra, India under the banner of ILA from 9–13 November 2000.

It is only appropriate that the first regional congress takes place in Asia in view of the tremendous problem of leprosy which the continent still is facing inspite of the enormous progress made in combating the disease over the past 10–15 years.

The Congress, apart from discussing technical and research issues, is expected to focus more on the problems of the common leprosy worker in combating the disease and in helping them to find solutions to such problems. This should also help in better interaction between researchers and developers of technical solutions on one hand and the ultimate utilizers of such solutions on the other. In order to promote this approach the organizers of the congress would like to encourage and facilitate participation of as many leprosy workers as possible particularly those involved in leading and organizing the fight against leprosy in the field.

Even though the congress is called Asian Leprosy Congress with focus on Asia, it is expected that the Congress would greatly benefit from experiences in other parts of the world and therefore would welcome participation from everywhere.

On behalf of the Organizing Committee, we extend our cordial invitation to all those interested in the fight against Leprosy to participate in the congress, so that together we can progress towards a world without leprosy which is our ultimate goal.

Chairperson Dr. S. K. NOORDEEN
Organising Committee
Secretary Dr. C. S. WALTER
Organising Committee

GENERAL INFORMATION

Date:
9–13 November 2000

Conference Venue:
Japyee palace, Agra, has been selected as the venue of the congress. Set amidst a sprawling 25 acres of landscaped gardens, water bodies and walk ways, this Hotel is a stone's throw away from the beautiful world famous 'Taj Mahal'.

Congress Language: English

Training Sessions:
Training sessions on various topics will be held in the evenings at the Congress Centre and also at the Central JALMA Institute for Leprosy.

Exhibits:
Exhibitions will be arranged for organizations or institutions wishing to display teaching and learning materials, including books, videotapes, compact disks, foot wears, medical supplies and equipment and other items according to interest of the participants.

Social Events:
Special social events/tours will be organized particularly for accompanying persons. There will also be a reception dinner for Congress participants.

Registration and submission of abstracts of papers:
For information on registration, submission of abstracts and other details please contact at the Secretariat address mentioned below.

Conference Secretariat:
Asian Leprosy Congress
C/o TLM India CNI Bhavan, 16, Pandit Pant Marg
New Delhi-110 001, INDIA
Tel: (91-11) 371-6920, 371-8261, 371-8263, 371-8264
Fax: (91-11) 371-0803, E-mail: tlm india@del2.net.in
Website: www.asianleprosy.com

'Drug resistant TB is spreading worldwide'

This is the title of a report summarised in the *British Medical Journal* of 6 November 1999, page 1220. It reads as follows:

Tuberculosis that is resistant to the standard, four drug regimen has now been found in 104 countries, according to a report released last week in New York.

The report, drawn up by Harvard Medical School and financier George Soros's Open Society Institute, estimates that it may cost up to $1bn (£625m) to fight tuberculosis worldwide.

'We were surprised that multidrug resistant tuberculosis was reported so widely. Nowhere was it going away,' said Dr Paul Farmer, professor of social medicine at Harvard and lead author of the report.

'Hot spots'—areas with high rates of drug resistant tuberculosis—are found in the countries of the former Soviet Union, India, China, the Dominican Republic, and the Ivory Coast.

World Health Organisation (WHO) officials said in the report: 'Tuberculosis control is being neglected in most countries worldwide, and ... MDR-TB [multidrug resistant tuberculosis] is a manifestation of this global neglect.

'It clearly shows the effects on tuberculosis control of the dismantling of public health services, compounded by a generalized socioeconomic crisis in Eastern Europe and the former Soviet Union. In the Russian Federation ... tuberculosis cases have almost tripled in less than 10 years.'

Dr Farmer said: 'This epidemic is only briefly local. It will not remain within borders. Forty two per cent of the Russian problem is in prisons. Prison bars and national borders are inadequate to stop transmission.'

General Vladimir Yalunin, head of the Russian prison service, said: 'About 100,000 people confined within the Russian prison system have been diagnosed with active tuberculosis. About 40,000 of them have multidrug resistant tuberculosis. Every year the penal system of Russia releases 30,000 people into the community with active tuberculosis—about 12 000 of them with multidrug resistant tuberculosis.'

In the report, WHO officials committed the organization to rapidly expanding the treatment strategy

known as DOTS (directly observed therapy, short course) and addressing the emerging threat of multidrug resistant tuberculosis by giving expensive second line drugs to patients with drug resistant tuberculosis.

The Global Impact of Drug-Resistant Tuberculosis, is on the internet at www.soros.org/tb

Global tuberculosis control: three documents from WHO

Dr Paul Nunn, Communicable Diseases Research and Development (including TDR), WHO, Geneva has kindly sent copies of the following:

1. *Prospects for Global Tuberculosis control Under the DOTS Strategy.* WHO/TB/98.251 (English only) by Christopher Dye *et al.* (former) Global Tuberculosis Programme, WHO, Geneva. November 1998. The authors developed 'an age-structured mathematical model to explore the principles of tuberculosis control under DOTS, and to forecast the impact of improved case-finding and cure on TB epidemics in different parts of the world. The *Discussion*, which also summarizes the main conclusions, reads as follows:

A recent appraisal of best buys for research on major microbial diseases concluded that the development of strategies to extend DOTS coverage is one of the highest priorities. The results in this paper back that conclusion by quantifying the large number of cases and deaths that could be prevented by improving case detection and cure rates.

We have shown that the potential impact of DOTS on tuberculosis in many developing countries is even greater than the results achieved in industrialized countries when drugs became widely available 50 years ago. Whereas case detection rates above 70% in Europe during the 1950s were associated with a fall in incidence rate of about 10%/year, it should be possible to generate such rates of decline with lower case detection rates in many developing countries with high TB burdens now. A new DOTS programme will have a bigger impact on incidence if it finds more cases sooner, if efforts are made to treat non-infectious as well as infectious cases, if it replaces a poor programme under which cure rates are low and the incidence rate has been falling slowly (or not at all), and if introduced to a relatively young population. The fraction of deaths prevented will generally be greater than the fraction of cases prevented, the more so if cure rates have been low in the past, and if the new programme treats smear-negative cases. We also find that the fraction of cases preventable by DOTS need not be markedly diminished by a large HIV epidemic. This is true provided case finding and cure rates can be maintained which, of course, is more difficult in an area of high HIV incidence which may have suffered a doubling or tripling of tuberculosis case rates.

The cure rate needs to be high in order to avoid prolonged transmission by those who fail treatment. Although treatment of any quality may reduce the number of TB deaths in the short-term, low cure rates could actually increase the rate of transmission, and hence the number of cases. This re-discovery of Styblo & Bumgarner's result is particularly pertinent now that we have a better appreciation of the worldwide distribution of drug resistant TB. If the principal effect of drug resistance is to reduce the cure rate, further careful calculations are required of the cure rate threshold, below which case finding and treatment will make the tuberculosis epidemic progressively worse.

There are numerous uncertainties in making projections with mathematical models, and their effects are only partly reflected in the bounds of our estimates. Most of what we know about the natural history of tuberculosis—which determines model structure and parameter values—comes from studies in industrialized countries, and yet we are most interested here in the prospects for control in the developing world. Apart from the ranges attached to model parameter values, there are critical but unpredictable external variables. We do not know precisely how many TB cases arise each year, and how many are currently found and cured. Nor can we be sure of the course of the HIV epidemics, which particularly affect projections for Africa and Asia. However, the principles of TB control revealed by our analysis do not depend on the exact results of model calculations. And whilst predictions of the *numbers* of cases and deaths between now and 2020 are subject to great uncertainty, we can be more

confident (roughly to the extent indicated by lower and upper bounds) about comparisons of the preventable *fraction* of the TB burden when control targets are not met by different dates.

Even if WHO targets are met by year 2010, three-quarters of the global TB burden would not be averted over the next 23 years. Better diagnostics, drugs and vaccines, plus targeted preventive therapy, would undoubtedly help. But new control measures with the potential to have a major impact may not be available for years. Meanwhile, the most pressing tasks are to find ways of achieving higher cure rates, and reaching more cases, in the principal endemic countries of the world.

2. *What is DOTS? A Guide to Understanding the WHO-recommended TB Control Strategy Known as DOTS*. WHO/CDS/TB/99.270. Original: English. For the Communicable Diseases Cluster, The International Union Against Tuberculosis and Lung Disease and The Royal Netherlands Tuberculosis Association.1999.

This is a 30 page document, with annexes, describing the DOTS strategy in detail. The *Introduction* reads as follows:

For more than 100 years we have been able to use microscopes to detect the bacterium that causes tuberculosis. For almost 50 years we have had effective anti-TB drugs. Yet, this year, more people will die of TB than in any other year in history. How can this be?

The problem has not been the lack of ways to detect and cure TB patients. The problem has been the lack of organization of services to ensure widespread detection and cure of TB patients, particularly the infectious ones.

Today, however, there is a proven, cost-effective TB treatment strategy known as DOTS. A combination of technical and managerial components, DOTS quickly makes the infectious cases non-infectious and breaks the cycle of transmission. Using DOTS also prevents the development of drug-resistant strains of TB that are often fatal and almost 100 times more expensive to cure.

The strategy has been successful in large and small countries, both rich and poor. Countries achieving high cure and coverage rates include Benin, Guinea, Peru, Nicaragua, China and Viet Nam. In China, cure rates rose from below 50% to more than 95% in areas covered by DOTS, and about half the population of China is covered by the strategy today. In Peru, government commitment for the strategy has resulted in almost 100% DOTS coverage in the country and cure rates of up to 83%.

Several challenges, however, impede the implementation of DOTS. The increasing impact of HIV on the incidence of TB in Sub-Saharan Africa is threatening to overwhelm currently effective TB control programmes. After the collapse of the health care system of the former Soviet republics, TB incidence and mortality are on the rise. Eastern Europe is also seeing a surge in drug-resistant forms of the disease.

Today, the strategy must be adapted to fit specific country situations. For example, in areas of high HIV prevalence, partnerships must be forged between TB and HIV programmes. In Eastern Europe, DOTS must not only be introduced and reinforced, but additional programme elements should be developed to more quickly identify and treat drug-resistant cases.

Since the introduction of the strategy almost 5 years ago, great strides have been made in spreading the message to governments, health care workers and the public about the importance of implementing DOTS. As of 1997, 102 countries had accepted the strategy as policy and had implemented it to varying degrees. However, more must be done to ensure the implementation of DOTS more widely.

This document discusses how DOTS was developed, how it is implemented and sustained, how it differs from other control approaches, and its role within a challenging and changing health care system. This document is designed to give decision-makers with health policy and budget authority a good understanding of the strategy so that they can promote effective TB control in their countries.

2. *The Global Tuberculosis Research Initiative: Research to Make a Difference*
Paul Nunn and Jennifer Linkins, (previous) Global Tuberculosis Programme, WHO, Geneva. WHO/TB/98.248. English only.

The *Executive Summary* reads as follows:

Tuberculosis kills more adults than any other single infectious disease, and the epidemic is

worsening. As an international public health authority the WHO, through its Global Tuberculosis Programme (GTB), has a responsibility to promote the equitable and rational use of the world's TB research resources to achieve the greatest possible health gains in TB control. In 1997, therefore, GTB set in motion a Global Tuberculosis Research Initiative (GTRI) to assess global research needs and identify priorities for reducing the epidemic. The initiative is a consultative exercise involving a broad range of external specialists. This position paper represents GTB's initial contribution to the exercise.

Background to the initiative

GTB set up the Initiative following publication of the report of the WHO Ad Hoc Committee on Health Research Relating to Future Intervention Options. The Ad Hoc Committee showed that funds for the world's health research are often allocated in a non-rational and inequitable manner, with the major health problems of the poor majority attracting only minimal funding. The Ad Hoc Committee recommended an analytic process to help decision-makers to allocate resources rationally. This process consists of measuring the scale of the health problem; understanding why the disease burden persists (for example because of lack of tools or failure to use existing tools efficiently); and agreeing a new research agenda to meet the needs identified, taking account of what is being done already about the problem and how likely the proposed research is to result in a useful outcome. The aim of the GTRI is to begin applying similar logic to the specific problem of TB.

The status of the epidemic

Every year, 7 million to 8 million people develop TB. In contrast to most communicable diseases, the burden of TB is expected to grow in the next 2 decades with the risk that, with no extra effort to control it, there will be 10 million new cases per year by 2020. The spread of HIV-related TB and of multidrug resistant strains of *Mycobacterium tuberculosis* are particular causes for concern.

The impact of TB control efforts today and their potential for slowing the epidemic

WHO's recommended strategy to control TB is known as DOTS: Directly Observed Treatment, Short-Course. This five-point strategy brings together the results of previous decades of work into a practical approach to TB control that represents current international best practice. In studies in Asia and Africa, DOTS has been shown capable of curing 80–90% of patients, and is also highly cost-effective, costing only $1 to $3 per year of life saved in low-income countries. Models developed by GTB suggest that the DOTS strategy has the potential to significantly reduce the size of the TB epidemic: if WHO targets for case detection and cure rates could be met by the year 2000, the global burden of this disease could be cut by more than one-third over the next 2 decades and 32 million deaths could be averted using the DOTS strategy alone.

Why does the disease burden persist?

However, despite the existence of the DOTS strategy, the TB epidemic remains. In line with the Ad Hoc Committee's approach, GTB has made a preliminary analysis of the reasons, as a means of identifying research needs.

Poor use of existing tools. Clearly, a major factor is the failure to use DOTS, the principal existing tool, as widely as possible. Worldwide, DOTS is reaching only a fraction of those who need it. Ninety-four of the WHO's 212 member states have implemented DOTS, and within individual countries, implementation is often uneven. For example, of the total global estimate of TB cases for 1996, only 12% were notified by DOTS programmes. These low coverage rates can be explained largely by the low political priority accorded to TB, and the consequent underfunding of efforts to control it. In addition, certain technical limitations of DOTS, such as the length of the treatment period, may weaken patients' adherence to therapy.

Lack of tools. Another reason for the persistence of TB is the simple lack of more effective tools, such as better drugs and vaccines. DOTS alone cannot prevent the development of TB in those already infected with *Mycobacterium tuberculosis*. Even if the WHO global targets for case detection and cure rates are met by the year 2000, it will take 2–3 decades for incidence to fall to a rate of 2 million people per year.

Lack of knowledge. Finally, some of the burden of TB persists because of a lack of knowledge. For example, the impact of drug resistance on treatment is not fully understood; nor is it clear exactly what constitutes immunity to TB in humans, a factor that may delay the development of a TB vaccine. More knowledge may be needed, therefore, before new or better interventions can be developed.

Research needs identified

From this preliminary analysis, the following research needs are apparent.

- research to widen the implementation of DOTS, using health policy research to understand the current constraints better and, according to what is learnt, operational research to improve delivery;
- the development of new tools to control TB—specifically tools that will be appropriate for the needs of poorer populations;
- research to provide the knowledge base for further or better interventions.

Existing research

The WHO Global TB Programme has set out to determine what research is being done on TB already and whether, and to what extent, this research fits the needs identified above. The Programme conducted a preliminary survey of the major research agencies to determine how much they spent on TB research in 1 year. Using the findings of the survey and drawing also on analyses conducted by the Ad Hoc Committee, the programme found that:

a) global resources for research on tuberculosis are disproportionately small compared to the share of the global disease burden;
b) within existing funds for TB research, the areas of activity that attract most resources are (i) the expansion of the biomedical knowledge base and (ii) the development of certain classes of new biomedical tools; the area that attracts least resources is research to improve existing tools, in the health policy sciences and operational research.

Conclusions

The Global TB Programme concludes that:

1. The TB epidemic is among the world's greatest health problems and is worsening.
2. The DOTS strategy has the potential to reduce the TB burden by more than one-third in 2 decades if properly and rapidly implemented. However, at present only 12% of those who develop TB are being notified by DOTS programmes.
3. According to the preliminary analysis of research needs conducted by GTB, a significant portion of the burden of TB persists because of failure to use DOTs as widely as possible. A further portion of the remaining burden may be attributed to a lack of new tools, and a further portion to a lack of knowledge needed to develop further, or better, tools. This suggests the need for several new research agendas:

    a) research to improve the implementation of DOTS;

b) the development of new tools specifically geared to the needs of low-income countries; and
c) strategic research to provide the knowledge base for further and better interventions.

4. Resources for TB research overall are disproportionately small compared to the burden of the disease. An overall increase in resources will be essential to expand research and development activities to meet the needs identified.
5. Using this position paper as a basis for discussion, the participants in the Global Tuberculosis Research Initiative should discuss and reach agreement on unmet research needs, on the relative priority to be accorded to each of those needs, on the rationale for formulating a new research agenda, and the process for doing so.

New adjuvants for vaccines

The following is extracted from page 4 of *TDR News*, No 58, February 1999:

A variety of novel adjuvants are emerging from research and are currently in clinical trials, with some in clinical use. A new adjuvant licensed recently in Italy (MF-59) with an influenza vaccine was the first to be approved for human use in more than 70 years. Judging by the results of clinical trials, some of the new adjuvants appear to be very promising and capable of significantly boosting the desired immune response. The adjuvants are being used in trials with a variety of vaccines against hepatitis, influenza, cancers and allergies, and also with antiparasite vaccines for malaria and leishmaniasis.

A meeting on novel adjuvants, organized jointly by WHO's Global Programme for Vaccines and Immunization (GPV) and TDR, was held in November 1998 in Annecy, France. Participants at the meeting included some 25 researchers involved in adjuvant research and development in academic institutions and 12 different pharmaceutical and biotech companies. An important aim of the meeting was to help researchers identify which adjuvants are ready to be used in clinical trials, and to strengthen their contacts with companies producing new adjuvants.

All the adjuvants discussed at the meeting are capable of inducing both humoral and/or cellular immune responses, and in mouse models can be shown to bias the immune response towards Th1 or Th2 type immunity. They can be 'active', and modulate the immune response, or 'passive', acting as delivery/depot systems. Studies and trials with a dozen or so adjuvants of different chemical types were reported. Of particular interest to readers of *TDRnews* are trials of new adjuvants with malaria and leishmaniasis vaccines:

- For malaria, an adjuvant consisting of an oil-in-water emulsion—Montanide ISA 720—has proved promising in volunteers with a sporozoite-derived antigen (a synthetic peptide of a surface protein), and is also being tested with different merozoite-derived recombinant antigens in children in endemic areas.
- A saponin-derived adjuvant was used in a trial with the synthetic malaria SPf66 vaccine in Colombia; it produced a better response than when alum was the adjuvant. Saponin-derived adjuvants have been shown in preclinical studies to be capable of inducing long-lasting antibody titres and protective responses with low doses of antigen.
- DNA vaccine trials against malaria in humans—using circumsporozoite antigens—have produced potent CD8 + CTL (cytolytic lymphocyte) responses and many strategies are now being considered to improve the immunogenicity of the vaccines, such as constructing mini-gene DNA vaccines expressing epitopes selected from all genes identified in the *P. falciparum* genome sequencing project.
- For leishmaniasis, candidate subunit vaccines—consisting of several cloned leishmanial antigens, one of which is also a powerful adjuvant—were used to treat drug-resistant mucosal *L. braziliensis* in humans in Brazil. A dramatic improvement was seen in six of the eight patients, suggesting that a therapeutic vaccine may even be able to reverse the pathology associated with this disfiguring disease.

Other types of novel adjuvants in clinical trial include cytokines, e.g. interleukin-12 (IL-12) which plays a central role in protection against intracellular pathogens such as *L. major*, monophosphoryl lipid A derivatives, and non-ionic block co-polymers. Selection of adjuvants for specific use with antigens is, however, still largely empirical and requires a pragmatic approach.

[A full report of the meeting is available from TDR World Health Organisation, 1211 Geneva 27, Switzerland]

Progress in the sequencing of *Mycobacterium leprae*

We are grateful to Dr Stewart Cole, Unité de Génétique Moléculaire Bactérienne, Institut Pasteur, Paris for the following 'Progress report on the project to complete the sequence of *Mycobacterium leprae*—November 1999'.

Background

The *M. leprae* genome sequence project, a high priority for both leprosy research and control programmes, is being undertaken with the financial support of the New York Community Trust (NYCT) and ILEP via the Association Française Raoul Follereau. The work is being directed by the Unité de Génétique Moléculaire Bactérienne at the Institut Pasteur, Paris, and high throughput sequencing and assembly performed by the Pathogen Genome Sequencing Unit of the Sanger Centre, Hinxton.

There have been three distinct phases in the project:

- From 1992–1996, ~1.7 million base pairs (Mb) of genomic sequences were generated by the multiplex sequencing group at Genome Therapeutics Corporation (GTC) and the Institut Pasteur team using the ordered cosmid library generated at the Institut Pasteur as template. About 50 cosmids were fully sequenced.
- In 1997, following the withdrawal of GTC from the project, the Sanger Centre took on the task of completing the genome sequence using a set of 45 cosmids covering the remainder of the chromosome. Funding was generously provided by the NYCT. 38 cosmids, representing a total length of 1.4 Mb were successfully sequenced, fully analysed, then annotated and deposited in the public databases (EMBL/GenBank/DDBJ). As expected of the sequencing strategy employed, there was some overlap between the Sanger Centre sequences and those obtained previously by GTC, and this was useful for the purposes of quality control and error correction. Comparison of the two sets of data revealed an average error rate of 1 per 1674 bp in the sequences generated by GTC, probably as a result of the use of inferior technology. This unacceptably high error rate undermined our confidence in the early sequence data and led us to resequence much of the genome.
- In the fall of 1998, a whole genome shotgun approach was implemented in which DNA from the *M. leprae* strain TN, originally used to construct the cosmids, was nebulized and used to generate a small insert library. Forward and reverse reads were then obtained from ~30,000 clones carrying 1·5–2 kb DNA fragments. A complete assembly of all the data is now available. At present this consists of nine contigs totalling 3338 Mb, and these were assembled from 55,028 reads plus selected cosmid sequences. By changing strategy in this way, we have not only corrected all the errors in the GTC sequence but obtained the missing parts of the *M. leprae* genome as well. The exact size of the genome is not yet known but it is clear that it will be larger than our provisional estimate of 3 Mb. This phase of the project was funded mainly by ILEP but with additional funds to the Institut Pasteur from the NYCT.

The next step

To close the nine remaining gaps, we are currently using primer walking, and combinatorial long-range

PCR reactions to generate templates and sequences. In parallel, a shuttle cosmid library is being screened to identify clones that may span the gaps. It is estimated that the sequence will be contiguous in 6–8 weeks time. A further 2 months will then be required to verify its accuracy and for full analysis and annotation. At this point a publication will be prepared to present the findings and compare the genome organisation with that of the tubercle bacillus.

The future

The genome sequence will not only reveal the genes and proteins of *M. leprae* but also provide us with fresh insight into the genetics, physiology, and biochemistry of the bacillus. The availability of a complete genome sequence for *M. tuberculosis*, and a partial sequence for *M. avium*, enables us to perform in-depth comparisons. It is already apparent that the genetic repertoire of *M. leprae* is much smaller than those of other mycobacteria and that many genes have been destroyed by mutation. This downsizing process may have resulted in the loss of one or more important metabolic pathways and thus imposed a stringent requirement for host-derived growth factors. With the help of bioinformatics, the missing genes and functions can be identified and this will facilitate the conception of new media for cultivating *M. leprae*. Likewise, it is also possible that the missing genes could be replaced by those from *M. tuberculosis* thus generating recombinant forms of *M. leprae*. The ability to grow the leprosy bacillus axenically would greatly facilitate drug development and vaccine research.

Other avenues of clinical importance will benefit from the genome sequence. Knowledge of the genes encoding existing drug targets will allow rapid molecular tests to be developed that are capable of detecting drug resistance without recourse to culture. Such a test already exists for detecting rifampicin-resistant *M. leprae* in clinical specimens and is currently undergoing field-trials. Novel drug targets can also be identified from the genome sequence using bioinformatics and database searches, or through structural and functional genomics. Their essentiality can be confirmed by inactivating the corresponding genes in *M. tuberculosis*.

The small insert clones generated by the shotgun approach will be immensely useful for developing whole genome microarrays that can be used as templates in hybridization experiments. These will enable genetic variability resulting from deletion events to be identified and this, in turn, could serve as the basis of a test to distinguish between different isolates of *M. leprae*. A molecular tool that can discriminate between relapse and reinfection would be of immense value to leprosy control programmes.

AIDS cuts life expectancy in sub-Saharan Africa by a quarter

The spread of HIV and AIDS in sub-Saharan Africa has far exceeded the worst projections, according to speakers at the 11th international conference on AIDS and sexually transmitted diseases in Africa. In 13 countries the prevalence of HIV infection is more than 10%, and in some it is as high as 30%. At the conference in Lusaka, Zambia, last week, the epidemic was described as an unprecedented threat to the region's economic development.

At the end of 1998, 22.5 million people out of the region's population of 600 million were living with HIV or AIDS; this number includes 1 million children. The epidemic in sub-Saharan Africa accounts for two-thirds of the worldwide total of 34 million people with HIV/AIDS. About 7500 people are infected daily.

In only two countries, Uganda and Senegal, does the epidemic seem to be abating. Strong governmental leadership in these countries ensures that there is universal health education, that condoms are easily available, and that there is coordinated action from the government.

Life expectancy in the region has decreased from 64 to 47 years. Sixty-five per cent of patients in medical wards in Zambia, and 75% in paediatric wards, are infected with HIV or have AIDS, and the underfunded health system is near to collapse. Even common drugs such as co-trimoxazole are scarce.

In Zambia, a 15 year old has a 60% chance of dying of AIDS. As the epidemic, which is driven largely by poverty, continues to grow, there is little sign of wide-spread change in sexual behaviour, especially among teenagers, one of the most vulnerable groups.

Tsepo Sitali, aged 8, described to the conference the anguish of her friend who will mark her eighth birthday without a mother or a father because both died from AIDS last year.

Tsepo's friend is not alone: the number of children orphaned by AIDS in Zambia is forecast to reach 500 000 by the year 2010. The epidemic affects children not only directly through infection being spread from mother to child but also through the deaths of their parents which results in their being forced into prostitution and other forms of exploitation.

Children, especially girls, are taken out of school to nurse sick relatives or because school fees are no longer affordable. Only an estimated 10% of the predicted illness and death has occurred: the full impact on people, communities, and economies is still to come.

Source: *British Medical Journal* 25 September 1999 page 806.

UN warns that AIDS deaths are set to reach record level

A record number of people will die from AIDS this year despite the improvement in survival achieved with antiretroviral therapies in wealthier countries, a report from the Joint United Nations Programme on HIV/AIDS (UNAIDS) warned this week.

UNAIDS estimated that 2.6 million people will die from diseases related to HIV and AIDS during 1999—a higher global total than in any year since the beginning of the epidemic. With the HIV positive population still expanding—there were 5.6 million new infections during this year alone—the annual number of deaths was expected to continue to increase for many years.

The report estimated that 32·4 million adults and 1·2 million children would be living with HIV infection by the end of 1999. About 95% of those infected live in the developing world, and this proportion was predicted to rise even further as infection rates continued to rise in countries where poverty, poor health systems, and limited resources for prevention and care fuelled the spread of the virus.

Sub-Saharan Africa continues to bear the brunt of HIV and AIDS, with close to 70% of the global total of HIV-positive people. Most will die in the next 10 years, joining the 13·7 million Africans already claimed by the epidemic. Figures suggest that 55% of infected adults in Sub-Saharan Africa are women. UNAIDS director Dr Peter Piot said: 'Today we see the evidence of the terrible burden women now carry in the African epidemic.'

UNAIDS pointed out that HIV also remains a challenge in industrialized countries. Dr Piot said: 'There is evidence that safe sexual behaviour is being eroded among gay men in some western countries, perhaps because of complacency now that life-prolonging therapy is available.' If this was the case, the report warned that the complacency was misplaced: 'The disease remains fatal, and information from North America and Europe suggests that the decline in number of deaths due to antiretroviral therapy is tapering off.'

The report added that HIV infections in the former Soviet Union have doubled in just 2 years, and that injecting drug use gave eastern Europe and Central Asia the world's steepest increase in HIV infection in 1999. Half of all people infected with the virus were infected before they reached the age of 25 and typically died by 35.

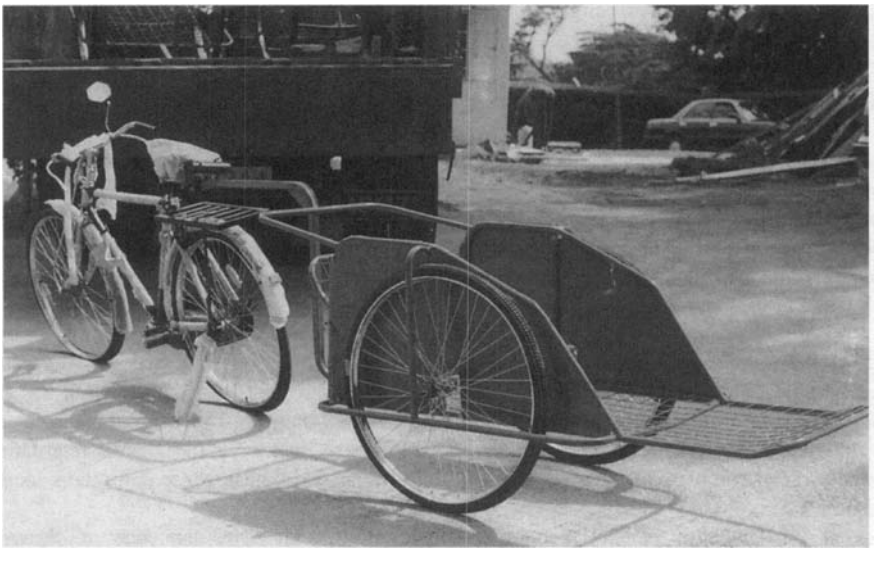
AIDS Epidemic Update: December 1999 is available free from UNAIDS, 20 Avenue Appia, 1211 Geneva 27, Switzerland, or on the internet at http:www.unaids.org

Source: *British Medical Journal* 27 November 1999 page 1387.

A 'bicycle ambulance' from Uganda

A previous issue of *World Health*, 51st year, No 1, January–February 1998 carried the following information:

One of Uganda's responses to the problem is the introduction of the 'bicycle ambulance'. Designed for both flat and hilly areas, health workers in several districts are now trying out this practical vehicle, sponsored by the Ministry of Health, UNICEF and WHO. It consists of an ordinary bicycle with a specially designed trailer attached to it in which health workers can transport a pregnant woman or sick patient. On rugged or smaller village paths or up hills, it may be necessary for more than one person to help pull the trailer. In such situations, it can easily be detached from the bicycle. Maintenance and running costs are small and affordable for most communities. Following an evaluation of the bicycle ambulance, it is expected that the scheme will be extended to other districts in Uganda.



Further information is available from Dr A K Mbonye, Principal Medical Officer, Reproductive Health, Ministry of Health, PO Box 7272, Kampala, Uganda.

The myth of the spread of leprosy with the Crusades

The following is the summary of a paper presented by P D Mitchell, Wellcome Institute for the History of Medicine, University of London, 183 Euston Road, London NW1 2BE, United Kingdom, at a meeting in Bradford (UK) in July 1999 on 'Past & Present of Leprosy':

Many authors have proposed that returning crusaders in the 12th and 13th centuries were responsible for the apparent dramatic rise in the prevalence of leprosy in mediaeval Europe. In support of this view, the European written texts mention leprosy little before this time and leprosaria were scarce but from the 12th century onwards leprosy was the focus of significant sections of medical manuscripts and hundreds of leprosaria were built. However, a more critical assessment raises serious doubts about the interpretation of this evidence. The epidemiology is not suggestive of an epidemic. When leprosy is introduced into an area for the first time and an epidemic occurs, the vast majority of cases are tuberculoid while only a few are lepromatous. In contrast, excavation of 12th century leprosaria in Europe show mostly lepromatous and few tuberculoid cases. While it is not

known what proportion of actual lepromatous and tuberculoid cases were identified and segregated at that time, it can be said that these findings do not support an epidemic theory. Furthermore, it is known that leprosy was present in Europe 500 years before the crusades and any epidemic should have happened then.

While it is true that the number of leprosaria greatly increased at the time of the crusades, the number of general hospitals did too. This suggests a change in social attitudes to caring for the sick, rather than more leprosy patients. The larger sections on the disease in medical texts may have been a consequence of the extra information available from the translation of Arabic manuscripts at that time. In any case, to implement the laws requiring segregation of patients doctors needed good knowledge of the symptoms of leprosy to minimise incorrect diagnosis.

There is little evidence to blame the crusades for a leprosy epidemic. Any true increase in prevalence might be better ascribed to increasing population density and urbanization.

First human chromosome (22) sequenced

Wellcome News (Research & Funding News from the Wellcome Trust, London, UK), Issue 21, Q4, 1999 carries the following:

Researchers from the Sanger Centre near Cambridge, Keio University in Japan and US laboratories at the University of Oklahoma and Washington University, St Louis, have published the complete sequence of human chromosome 22—the first human chromosome to be fully sequenced. The sequence was published in the 2 December issue of *Nature*.

Chromosome 22 comprises 34 million nucleotides, and appears to encode at least 679 genes, of which 55% were previously unknown in humans. The work provides insight into the way genes are arranged along a strand of DNA, and how they might be controlled. Previous research has already revealed that genes on chromosome 22 are implicated in the function of the immune system, and in several inherited conditions, including congenital heart disease, schizophrenia, mental retardation and some cancers. The complete sequence will greatly aid research on these genes and others located on chromosome 22.

Mike Dexter, Director of the Wellcome Trust, commented: 'The sequence of chromosome 22 includes 298 genes previously unknown in humans, which are being released without the constraints of patents and fees. The fact that all of this information is now freely available for scientists to use is of major importance, if the knowledge of our genetic make-up is to be used for the good of humankind.'

A first draft of the full human genome is still scheduled for early 2000. In November, the international Human Genome Project consortium celebrated depositing one billion base pairs of DNA sequence in the public databases—effectively one-third of the entire human genome.'

The summary of the *Nature* publication referred to above (*Nature*, 402, December 1999, 489–495) reads:

'Knowledge of the complete genomic DNA sequence of an organism allows a systematic approach to defining its genetic components. The genomic sequence provides access to the complete structures of all genes, including those without known function, their control elements, and, by inference, the proteins they encode, as well as all other biologically important sequences. Furthermore, the sequence is a rich and permanent source of information for the design of further biological studies of the organism and for the study of evolution through cross-species sequence comparison. The power of this approach has been amply demonstrated by the determination of the sequences of a number of microbial and model organisms. The next step is to obtain the complete sequence of the entire human genome. Here we report the sequence of the euchromatic part of human chromosome 22. The sequence obtained consists of 12 contiguous segments spanning 33·4 megabases, contains at least 545 genes and 134 pseudogenes, and provides the first view of the complex chromosomal landscapes that will be found in the rest of the genome.'

'American Experience With Low-Dose Thalidomide Therapy for Severe Cutaneous Lupus Erythematosus'

The following is a summary of an article recently published in *Arch Dermatol*, 1999;**135:**1079–1087:

Background: There is a renewed interest in thalidomide therapy after its surprising effectiveness in treating erythema nodosum leprosum was first published. Thalidomide has subsequently been reported to be effective in treating a number of dermatoses, including cutaneous lupus erythematosus. We examined the efficacy and adverse effects of low-dose, long-term thalidomide monotherapy in seven patients with various forms of cutaneous lupus erythematosus that were unresponsive to traditional systemic treatments.

Observations: Six of the seven patients treated with thalidomide after discontinuation of other oral agents had complete or marked resolution of their previously treatment-resistant cutaneous lesions, with an average response time of 2·2 ± 0·8 months. Our cohort of seven patients with cutaneous lupus erythematosus was treated with thalidomide therapy for an average of 2·4 ± 3·1 years (range, 1 month to 9 years). The most common adverse effects were sedation, constipation, and weight gain. Two patients reported experiencing intermittent shaking episodes, an adverse effect not previously reported in the literature. Four patients reported symptoms of paresthesia, but none was found to be caused by thalidomide-induced peripheral neuropathy.

Conclusions: A low starting dose of thalidomide as a monotherapy with continued sun avoidance is a safe and effective treatment for the various cutaneous manifestations of lupus erythematosus after traditional therapeutic options have failed to control disease. Our experience with low-dose, long-term thalidomide therapy suggests that peripheral neuropathy is not as common as suggested by other studies (up to 50% of patients treated with thalidomide in some series).

Zinc deficiency; association with reduced immuno-competence and increased rates of serious infectious diseases

Over a period of several decades, the leprosy literature contains articles on the possible importance of zinc deficiency, many of them including reference to its importance in the healing of chronic ulcers. The authors may be interested to know of an article recently published in the *Journal of Pediatrics* 1999; **135:**680–697 in the context of prevention of diarrhoea and pneumonia. Extracts from the commentary published in the *British Medical Journal* of 11th December 1999, page 1521, read as follows:

Zinc deficiency is common in young children in the developing world and is associated with reduced immunocompetence and increased rates of serious infectious diseases. Several trials in poor countries have shown the benefit of zinc supplementation in reducing infection (*BMJ* 1998;**317:**369), but these have varied in the magnitude of the effect and the presence of a differential effect by age and sex. Some trials were underpowered to detect the effects on infrequent outcomes, and others remain unpublished.

A pooled analysis was conducted by the Child Health Research Project, a group of researchers from Johns Hopkins School of Public Health and the World Health Organisation, who had access to the original trial data. Trials were included if they provided oral supplements containing at least half the US recommended daily allowance of zinc for children, and if morbidity surveillance was carried out for at least 4 weeks. Two sets of trials were identified—those in which zinc was given continuously, and those giving only a short course.

For the zinc supplemented children in the seven continuous trials, the pooled odds ratios for diarrhoeal incidence and prevalence were 0·82 (95% CI 0·72 to 0·93) and 0·75 (0·63 to 0·88) respectively. Supplemented children had an odds ratio of 0·59 (0·41 to 0·83) for incidence of pneumonia.

No significant variations in the effects were seen in the subgroups of children stratified by age, sex, and weight, and nor was there a significant difference between short course and long term supplementation.

The authors conclude that 'the development of effective and feasible interventions to improve the zinc status of developing country populations is essential.' One such intervention, zinc fortification of bread, was shown in a randomised controlled trial to reduce diarrhoea, respiratory illnesses, and skin infections in Turkish schoolchildren (*Cereal Chemistry* 1995;**73:**424–426).

Dr Robert Black, of Johns Hopkins School of Public Health and co-author of the study, said: 'Zinc fortification is potentially a powerful tool for settings which produce commercial food, and the idea has been acceptable to food manufacturers. If there's no commercial food, increasing zinc intake is possible by reducing the amount of dietary phytates, which interfere with zinc absorption. This can be done by soaking or fermenting food. Long term, it is possible that plant breeding could be used to increase zinc or reduce phytate content.'

But several questions still remain before zinc therapy can be incorporated into diarrhoeal disease control programmes, including the optimal dosing regime and duration of therapy. Dr Shammim Qazi, from the Division of Child Health and Development of the World Health Organisation, said: 'At present the WHO is not recommending zinc supplementation as routine. We are waiting for the results of larger trials, and we are planning a trial ourselves.'

[The Child Health Research Project's Special Report '*Zinc for Child Health*' is at http://ihjhsph.edu/chr/publicat.htm. An excellent account of zinc deficiency is to be found in Dermatology in General Medicine, 4th edition, 1993, Chapter 146, pp 1826–32].

Second round of modified leprosy elimination campaign (LEC) in the State of Orissa, India, yields fewer cases

A report in the *Indian Express* on 8th March 2000 suggests that the incidence of leprosy in Orissa, based on recent findings in a second LEC, is declining. In a recent press release, the Assistant State Leprosy Officer, Dr PKB Patnaik, reported that 27,197 cases of leprosy were detected during the second LEC, compared with 62,844 during the first—an apparent fall of 57% in 2 years. The second LEC took place between January 30th and February 4th, 1999. Search teams of male and female workers visited each family, with the help of one volunteer for every 600–900 of the population. About 1225 mobile conformation teams, consisting of one medical officer and one paramedical worker (leprosy) examined the 185,548 suspects identified. Eighty-five percent of the population was contacted during the campaign.

TB Alert/TB Focus, London, UK

A meeting of TB Alert in London on 22nd March, 2000 included the announcement of a 'sister' organization called TB Focus, intended to concentrate on medical research and scientific work in TB. Further details and description of projects to be undertaken will be reported at a later date.

The meeting was held in the Post-Graduate Centre of the National Heart and Lung Institute, Brompton Hospital, London and included presentations on the management of TB patients in London; vitamin D deficiency and vitamin D receptor polymorphisms as risk factors for TB among Gujarati Indians (in the London area); TB in the United Kingdom; the *Mycobacterium tuberculosis* genome; problems in TB control in the UK. TB Alert, as previously described in this journal, continues to campaign for better awareness of the TB problem, both in the UK and worldwide, whilst bringing together people in the UK with a common interest in the subject of TB, and the global emergency.

Further information: Paul Summerfield, 22 Tiverton Road, London NW10 3HL United Kingdom Tel: 0181 969 4830 (from outside UK +44 181 969 4830) Fax: 0181 960 0069 (from outside UK +44 181 960 0069) E-mail: tbalert@somhealy.demon.co.uk

Mini Leprosy Guide and NLO Diary 2000

The National Leprosy Association, India has announced the release of their Mini Leprosy Guide and NLO Diary 2000. The Diary is printed in English, Marathi and Hindi. In addition to a calendar and address book, it contains useful information on the diagnosis and treatment of leprosy, MDT coverage in India, case detection and books and journals on leprosy. The price of the Diary is Rs.25/- in India and postage is US$3.00 outside India. Payment is through a banker's draft on any branch of the Bank of Bhilai (cheques not acceptable), made out to 'National Leprosy Organisation, India'. For further information, please contact: National Leprosy Organisation, India, Dhour, Durg, 450 024, India.

IDEA Newsletter

The following extracts are taken from IDEA's Newsletter of March 2000:
'Dear Friends
This Saturday is March 11, the Second Annual International Day of Dignity and Respect. Last year, this day was commemorated at Carville, and also in different ways in China and India.

In reality, every day is a day of dignity and respect as far as IDEA is concerned. But it is also worthwhile to continue to observe this, and encourage others to do the same. This is not to be in competition with World Leprosy Day but something completely different – a day when we think about dignity and respect, rather than focusing on the physical aspect of the disease, treatment, etc.

We are in the process of putting together a book of quotations called *Freeing Ourselves of Prejudice. Thoughts on Dignity, Disability and Discrimination.* We will publish this in many languages. It will not be a thick book but will be something we can use to share words and ideas and thoughts of people around the world with others who have also had the disease. We thing that this will be an important empowerment tool as well as provid(ing) us all with a means of sharing the word of IDEA members with others.

Therefore, as this year's International Day of Dignity and Respect approaches, it would be helpful if you would spend a little time thinking about dignity and respect, and send me your thoughts you have that can be included in this book or other educational materials. We will publish this book in commemoration of the Second International Day of Dignity and Respect.

Also, and this is very important, at the end of the new Quest of Dignity Exhibit we will have a panel that says 'The Quest for Dignity is not over. It has just begun.' (This panel will be) translated into many languages. This quote was originally from Therea Wilson from Carville. So, I need your help to translate this quote into your local language.

Despite the fact that the situation at Carville has changed quite a lot since last March 11, everyone who participated in the First International Day of Dignity and Respect at Carville felt this was so important. It was an opportunity to voice their feelings rather than just passively accept the decisions of the administration and health officials in Washington.

. . . . . we are updating and really changing the Quest for Dignity Exhibit. In the last 2 years, we have received so many new quotes and photos that we now have the voices of 70 different people who had HD from more than 20 countries as part of the exhibit and photos from 28 different countries. The Exhibit is now much more lightweight and easier to transport and also doesn't require a lot of labour to put up. So, it will be able to travel to more places. we are also producing a French version and Italian version. The Nippon Foundation has again provided us funding for the Exhibit. The new Exhibit will be launched in Luxembourg in mid-April.

In conclusion, some words form Bacurau, which are very appropriate for the Second International Day of Dignity and Respect:

'We will no longer bow our heads. We'll hold them high. By our strength of purpose we will no longer feel ashamed or guilty. We will no longer have the fear of rejection. Most important, we will not be denied our human rights. We will maintain our esteem and dignity . . . . . There is no turning back.'

Portraying a positive image of persons (previously) affected by leprosy

The following article, by Wim Van Brakel and P. K. Gopal, was recently published in the *International Journal of Leprosy* and as a communication in *ILEP Flash.*

In the March 1999 issue of *Leprosy Review*, the report of Workshop I on 'Social aspects and rehabilitation', held during the 15th International Leprosy Congress in Beijing, was published.[1] Recommendation 1 (page 86) reads: 'Guidelines for appropriate terminology, taking into consideration cultural differences, should be developed with input from people affected by leprosy. These guidelines should be published and distributed.'

The text below has been adapted from an article published in the *ILEP Flash* last year. While it does not present comprehensive guidelines on the subject of terminology mentioned above, we would like to offer it as a contribution towards the development of such guidelines.

In recent years, many have come to realize the important role of language and terminology in social stigma against people with many chronic conditions.[2–5] People with impairments or disabilities were labelled for life as the 'disabled' or the 'handicapped'. People who were suffering from AIDS were called 'AIDS patients' until their death.[6] Strong appeals, particularly from the affected people themselves, have led to changes in terminology.[7] The 'disabled' are now called 'people with disability' or 'differently abled people'. The blind and deaf, in a dignified way, are called 'visually handicapped' and 'hearing impaired', respectively. Instead of speaking of 'AIDS patients', many publications now talk about 'people with AIDS'.

In the field of leprosy, the situation has been very similar. It is possible that the social stigma against people affected by leprosy has been even stronger than against people suffering from other chronic conditions. The word 'leper' has become almost synonymous with 'outcast'.[2,8,9] In a quest to restore dignity to those who have had leprosy, the affected people themselves, as well as many leprosy workers, have started to call for a change in the language used in the field of leprosy.[1] Particularly instrumental in this is the organisation 'IDEA', the International Association for Integration, Dignity and Economic Advancement. During the 2nd International Conference on the Elimination of Leprosy, a major discussion was held on this topic. Dignity and the use of positive language to promote dignity was also a subject of discussion during the Workshop on People Affected by Leprosy as Working Partners during the 15th International Leprosy Congress in Beijing. Many people who themselves had been affected by leprosy were present at both events.

There is a strong feeling that if someone who has (had) leprosy is always being labelled as a 'leprosy patient' or even just as a 'patient', this will have negative consequences for that person. Given the social stigma against leprosy, this label wrongly gives the impression that an affected person will always remain a patient, and thus is never cured. From a rehabilitation point of view, it would be very desirable to change positively the terminology used in this field. The attitude conveyed by the behaviour of the health worker towards patients as also very important in this context.

To promote the use of positive terminology in relation to people affected by leprosy, we would like to make the following recommendations:

1. The use of the word 'patient' should be context-dependant. It is only appropriate in a medical context of a health worker–patient relationship.
2. The preferred term to use when referring to an affected person, when his/her association with leprosy needs mentioning, is a 'person affected by leprosy (or Hansen's disease)'.
3. In situations when the relation with leprosy is irrelevant, e.g. in many rehabilitation situations, a description such as 'person with disability', or simply 'person' or 'affected person' would be preferable.

4. Recommendations for a change of terminology should be prepared for a wide range of uses, including the media, health training materials, legal documents and medical/technical papers and publications. Manuscripts and other media materials should be reviewed with regard to terminology, where possible by people affected by leprosy themselves.
5. The importance of health workers acting out a positive attitude toward leprosy patients should be emphasized whenever possible. Training to this extent should be included in leprosy courses, particularly those for general health workers.

It is encouraging to see that in several organizations, the term 'person affected by leprosy' has been readily accepted. However, unfortunately, people have started abbreviating this term to 'PAL'. They have now started speaking about 'pals' when referring to people affected by leprosy. This practice is undesirable for two reasons.

First, the word 'pal' is a very colloquial word for 'friend', while it is often used in situations where the use of the word 'friend(s)' would be inappropriate.

The second is the major reason for not using the abbreviation 'pal'. The use of a special word like 'pal' is essentially the same as using the word 'leper'. The use of a special term will label people as different from other people, which is exactly what we want to avoid! We don't do around or write about people with tuberculosis or malaria as 'pals', so why should we do this to people affected by leprosy?

What we try to achieve is that the language and terminology used to describe people who have (had) leprosy is as normalized as possible. If we abbreviate 'person affected by leprosy' to 'pal', we will be using this word all the time. If we use the 'full form', we can be flexible: one time talking about 'the affected person', another time 'the leprosy-affected person', or just 'the person'.

We would therefore like to make a strong appeal to anyone working in the field of leprosy, or anyone otherwise needing to talk or write about leprosy-affected people: for the sake of dignity of the persons affected by leprosy, please do *not* use the word 'pal'!

It is also important to realize that English is not the main language in most leprosy-endemic countries. Rotburg highlighted differences in stigma attached to the word 'leprosy' in South America and Europe.[2] Jeanette Hyland made a strong plea for researching the best word or label in different cultural contexts.[9] It is therefore essential to initiate a discussion in all endemic countries about non-stigmatizing terms that would be appropriate in the different languages spoken. In Nepal, this discussion has led to agreement to use the term 'kustha prabhabit byekti' as the Nepali equivalent for 'person affected by leprosy'.

We hope that our concerned efforts at introducing and using positive language in relation to people affected by leprosy will help to rase their dignity and will slowly push back the age-old stigma attached to the disease!

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Erratum

In the December 1999 Special Issue of *Leprosy Review*, the article entitled 'Leprosy elimination campaign (LEC) in Myanmar, 1997 to May 1999' was erroneously attributed to T. Shwe. The author of this article is Dr Kyaw Nyunt Sein, National Programme Manager, Department of Health, Myanmar. We apologise for this error, and for any confusion that may have arisen.