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Editor's Choice

Many of you will be reading this copy of *Leprosy Review* at the 15th World Congress of Leprosy. Lepra has generously funded the printing of extra copies so that each delegate to the conference has a copy of *Leprosy Review*, and this edition's accompanying poster in their conference pack. I hope that many of you will be persuaded to take out a subscription to the journal or apply for free copies if you come from a resource poor setting.

As befits a conference edition, we have many interesting articles which will be relevant to the issues being debated at the conference. In the Editorial, Dr Ji expresses his confidence in the new 12-month multidrug regime for multibacillary leprosy. Dr Waters, in an accompanying Commentary, suggests a more cautious analysis of the present. I look forward to the readers' response to these two articles.

The original papers range from laboratory techniques to health services research. A study from Indonesia shows that a weak decolorizer can be used for staining both *M. tuberculosis* and *M. leprae*, which will simplify laboratory work. An Indian group demonstrate that fine needle aspirate can be used to assess both bacterial load and cellular morphology of lesions. The sustainability of leprosy services in the next century is a topical issue that will undoubtedly be discussed at Beijing. Here, two health services research papers look at developing effective strategies for leprosy control and the development of sustainable strategies for sustainable and appropriate leprosy services respectively. For me, the key message from both papers is that participation and involvement of providers and users is necessary if effective change and research findings are to be implemented.

It is a pleasure to be publishing reports from two important WHO sponsored meetings that were held in Addis Ababa earlier this year. The first meeting considered the role of leprosy institutes in the future and produced useful reflections on the ways to provide training and support for national and integrated programmes. The scientists who participated in the second meeting concluded that research in leprosy still has important contributions to make at many levels, from aiding elimination to developing new drugs for treating nerve damage. 95% of the *M. leprae* genome has now been sequenced, and the identification of unique *M. leprae* proteins may yield new and useful insights into the biology of leprosy. The review article by Ian Cree and Cairns Smith reminds us of the gaps in our understanding of the transmission of leprosy and revitalizes the idea that chemoprophylaxis may have a role to play in disease control.

'Further Education' is a new section in the journal. Here, we shall be featuring a series of review articles written by experts but aimed at informing general readers. Surgery for non-surgeons seemed a good place to start, and I am very grateful to Dr Dinkar Palande for undertaking the editorship of this series of five articles that will help those of us who have no surgical expertise to understand what surgeons can do and when we should be referring our patients for a surgical opinion.

We also have bulging Teaching Material and News and Notes Sections; all this seems to testify to the many activities going on in leprosy right now.

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Editorial

WHY MULTIDRUG THERAPY FOR MULTIBACILLARY LEPROSY CAN BE SHORTENED TO 12 MONTHS

To overcome the serious threat posed by the widespread emergence of dapsone resistance,[1] and to increase the therapeutic effect in chemotherapy of leprosy, a World Health Organization (WHO) Study Group in 1981 recommended multidrug therapy (MDT) for the treatment of leprosy.[2] It was recommended that, for the purpose of treating different categories of patients with various bacterial loads, leprosy be classified as paucibacillary (PB) and multibacillary (MB), and that two drugs, monthly rifampicin (RMP) and daily dapsone (DDS), be prescribed for the treatment of PB leprosy, and three drugs—daily DDS and clofazimine (CLO) together with monthly RMP plus a supplemental higher dose of CLO—for MB leprosy. The duration of MDT for PB leprosy is 6 months; whereas for MB leprosy, it was recommended that MDT should be given for at least 2 years and preferably be continued up to skin-smear negativity.[2] Because of the promising results of 24-month treatment, the WHO Study Group recommended, at its second meeting in 1994, that all MB leprosy should be treated for 24 months.[3] The MDT regimens have proved to be highly effective and well tolerated by the patients.[4,5] At the beginning of 1997, more than 8·4 million leprosy patients had been cured by MDT.[5]

However, from the operational point of view, the duration of MDT is still too long, especially for MB leprosy. The long duration of treatment has become one of the major obstacles in implementing MDT, particularly in areas where the health infrastructure is poor or the accessibility is difficult. It would facilitate the implementation of MDT among all patients who need treatment if the duration of MDT could be further shortened without significantly compromising its efficacy.

To avoid relapse caused by spontaneously occurring RMP-resistant mutants and to minimize the relapse due to drug-susceptible organisms after stopping MDT, the appropriate duration of MDT for MB leprosy is the time required to reduce the size of viable bacterial population to such an extent that RMP-resistant mutants are completely eliminated and the great majority of drug-susceptible organisms are killed. To date, due to technical constraints, we are unable to determine directly, with any laboratory tool, whether or not the RMP-resistant mutants are still present in the hosts, or whether the drug-susceptible organisms are reduced to a negligible level. However, the following information may be useful to define the appropriate duration of MDT for MB leprosy.

First of all, the definition of MB leprosy has become much broader since 1981, when the Study Group designed the MDT regimen. Originally, MB leprosy referred to those patients

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who had a bacterial index (BI) of ≥2 at any site in the initial skin smears.[2] A few years later, the WHO Expert Committee on Leprosy at its 6th Meeting modified the definition that all skin smear positive cases should be classified as MB leprosy;[4] and the Second WHO Study Group further recommended that, when the classification is in doubt, the patients should be treated as having MB leprosy.[3] Then, because of the lack of dependable skin-smear facilities in most leprosy programmes, the WHO Expert Committee on Leprosy at its 7th Meeting proposed that patients could be classified on clinical grounds only, and that MB leprosy should refer to those having more than five skin lesions.[5] These modifications have resulted in the classification of many cases that would otherwise be PB leprosy as MB leprosy, and the proportion of MB leprosy among newly detected cases has increased from 20·8% in 1985 to 30·9% in 1996.[6] A more important finding is that, unlike in the early 1980s when all newly detected MB cases were skin smear positive, the proportion of smear positive cases among newly detected MB leprosy cases in 1996 was less than half. Among 142,844 newly detected MB cases from the 16 major leprosy endemic countries, it was estimated that 69,449 (48·6%) were skin smear positive, and only 24,216 (17·0%), or one-sixth, of MB cases have a BI of >3.[7] Because the bacterial loads of the majority of MB patients currently classified are significantly smaller than those in the past, the overall requirements of chemotherapy for MB leprosy may also be less.

Secondly, the results from both routine control programmes[8] and from research projects[9] have demonstrated that the relapse rates after MDT were very low, about 0·2% annually, among MB leprosy cases. Similar results have been obtained after 2-year fixed duration MDT.[10–14] The low relapse rates indicate that there is enough room for further shortening the duration of MDT to less than 24 months. Although some reports suggested that relapse rates after MDT could be significantly higher among MB patients with a high initial BI, i.e. the average BI ≥ 4·0,[15,16] because such patients have become relatively scarce in the field,[7] the total number of relapses by them contributed to a leprosy control programme will be small. The programmes should accept the few relapses that may occur from patients with a high initial BI and treat those patients who do relapse with a further course of MDT.

Thirdly, the major role of the DDS-CLO component of the MDT regimen for MB leprosy is to ensure the elimination of the spontaneously occurring RMP-resistant mutants, estimated to be no greater than 10^4 organisms in an untreated patient with lepromatous leprosy,[17] before stopping chemotherapy. The results from both nude mouse experiments[18] and a clinical trial[19] have demonstrated that the bactericidal effect of the DDS-CLO component was significantly greater than expected; 3 months of daily treatment with DDS-CLO component alone killed more than 99·999% of viable *Mycobacterium leprae*,[18] suggesting that all the spontaneously occurring RMP-resistant mutants are likely to be eliminated by 3–6 months of treatment with the DDS-CLO component in the MDT regimen.

Fourthly, in a multicentre, double-blind trial organized by the Steering Committee on Chemotherapy of Mycobacterial Diseases (THEMYC) of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, MB patients with initial BI ≥ 2 were randomized into four groups of about 500 patients each, and two of the four groups were treated, respectively, with 24-month or 12-month MDT. After 4–6 years of follow-up from intake, or 3–5 years after stopping treatment with the 12-month regimen, not a single relapse has been detected among the two groups, which suggests that the 12-month MDT is as effective as the standard 24-month MDT regimen (THEMYC Steering Committee, unpublished data). The efficacy of various durations of MDT has also been compared in a clinical trial in Malawi, in which 305 MB cases were randomly allocated into two groups

and treated, respectively, with 18 or 30 months of MDT.[20] After stopping treatment, the mean duration of follow-up was 3 years, with a maximum of 6 years. In both groups, the BI continued to fall, and fell to 0 by 60 months of follow-up. No relapse was observed in either group and the percentage of patients who developed new disabilities was similar. It was concluded that 18-month MDT may be sufficient for the treatment of MB leprosy.

Finally, information on the clinical and bacteriological progress of defaulted MB cases may shed some light on the efficacy of MDT with duration shorter than the standard one. In one study,[21] 41 defaulted MB cases were retrieved. They had been treated with MDT for a mean duration of 7 months (range 3–13 months), and had not taken treatment after defaulting. By the time the patients were retrieved, from less than 1 year to more than 5 years after drop-out, all 41 patients showed clinical improvement, and 29 (71%) became smear negative, while the BI was stationary in five (12·2%) cases. In another series of patients,[7] who were skin smear positive before defaulting, 139 and 95 of them had been treated, respectively, with <12 months and 13–23 months of MDT before defaulting. By the time the patients were retrieved, after a mean duration of drop-out for 7·6 and 7·5 years, respectively, only 11 (7·9%) patients from the former and six (6·3%) patients from the latter group were still smear positive. Not only were the positive rates very similar between the two groups, but neither differed significantly from those (3·3%) of 761 patients who had completed 24 months of MDT and were examined 4 years later. Although one has to be cautious in interpreting the information from the retrospective analyses, because the records are often incomplete, the sample size is relatively small and the pretreatment characteristics of the patients between the groups may not be comparable, they do suggest that treatment with less than 12 months of MDT exhibited promising therapeutic effects among the majority of MB patients.

On the basis of all the available information, the WHO Expert Committee on Leprosy concluded, at its latest meeting of 1997, that it is possible that the duration of the MDT regimen for MB leprosy could be further shortened to 12 months.[5] This conclusion has been well-accepted by almost all the leprosy control programmes of the major endemic countries and is being implemented. Of course, during the transitional period from 24-month MDT to 12-month, a series of operational issues should be addressed, such as providing guidelines for the transition, revising national manuals, introducing a new reporting system, and improving the detection and treatment of leprosy reactions after completion of treatment. However, compared with the earlier days when MDT was introduced, in most countries now the leprosy control programme managers and their field staffs are more experienced, and they are able to handle these operational issues without too much difficulty.

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COMMENTARY

Is it safe to shorten multidrug therapy for lepromatous (LL and BL) leprosy to 12 months?

M. F. R. WATERS

In some ways, Dr Ji's Editorial is written 2–3 years too soon, as a 7–10 year follow-up is desirable to assess relapse rates after all save very short or weak regimens.[1,2] The WHO ofloxacin controlled clinical trial, which includes the 12 month WHO MB regimen compared with the standard 24 months, only commenced intake of patients in 1992. Moreover, the proportion of patients in each group having a relatively low bacterial index (BI) of 2·0–3·0 has not yet been reported.

Changes in the definition of MB leprosy, first to include all smear-positives, then all with more than five skin lesions, were made for field convenience only, because of the poor standard of skin smears. It was motivated by the fear that borderline patients, misdiagnosed as PB, might relapse if wrongly given PB MDT; yet only a relatively small proportion of such relapse patients are likely to be significantly infectious. The resulting widening of the original MB group has led to a large increase in MB numbers, both proportionately and absolutely, with a corresponding increase in work load, a possible diluting of 'genuine' MB relapse figures and a cry to shorten the duration of MB treatment, which is certainly unnecessarily long for the newly included types of patient.

Transmission of leprosy is largely, if not almost entirely, from active untreated or relapsed LL and BL patients. Although field studies in general have reported very low rates of relapse, relapses reported in carefully studied, highly bacilliferous LL and BL patients have sometimes been unacceptably high after 2 years of MDT. The Institut Marchoux[2] has reported that seven out of 35 (20%) of such patients, or seven out of 18 (39%) of patients with an initial BI of 4.0 or greater, subsequently relapsed, five relapses occurring more than 60 months after stopping MDT; most relapses have been confirmed by mouse footpad inoculation of these strains of *Mycobacterium leprae*. Ji also quotes a personal communication from Girdhar that relapse rates are significantly higher among MB patients with an initial BI $\geq 4{\cdot}0$. Very recently, Ganesapillai (personal communication) has also reported that two of 35 LL and BL patients treated for 2 years with WHO MDT in a controlled clinical trial had relapsed after less than 5 years of follow-up. It is to be hoped that both these latter two workers will present full reports in due course.

These new data, which are beginning to be reported, support the view that more detailed results, obtained over a longer follow-up period, are required before one can safely judge whether it is safe to reduce the duration of MB MDT given to LL and BL patients whose initial BIs are greater than 4·0. It is perhaps ironic that fear of relapse in borderline leprosy has eventually led to medico-political pressure to reduce the duration of treatment in advanced lepromatous leprosy. In addition, relapses–infectious relapses–may well become much

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harder to detect in LL and BL patients, once leprosy services become fully integrated after the year 2000, and therefore could slow down the eventual eradication of leprosy. The WHO Seventh Expert Committee on Leprosy[3] was prepared to complicate MDT by introducing a third regimen (the 1 day MDT for single lesion leprosy); it is strange that it was not prepared to wait another–4 years for the results of the WHO ofloxacin trial before shortening the duration of treatment for highly bacilliferous LL and BL patients.

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Leprosy transmission and mucosal immunity: towards eradication?

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Summary The declining prevalence of leprosy has not been matched by a declining incidence. Widespread adoption of mutliple drug therapy (MDT) in closely monitored control programmes has not prevented transmission of *Mycobacterium leprae*. Despite the rarity of lepromatous patients, most of those living in endemic areas have immunological evidence of exposure to *M. leprae*. This paradox could be explained if, for many such individuals, infection was transient, did not result in disease development, but did allow the transmission of infection to other individuals. There is increasing evidence from nasal PCR studies that such sub-clinical transmission may exist and that mucosal immune responses to *M. leprae* may develop during resolution of initial infection. Sub-clinical infection appears to occur in clusters and may require close contact over a prolonged period for optimal transmission. Control of transmission may be feasible through identification and treatment of individuals within infection clusters, allowing progress towards the eradication of leprosy.

Introduction

Over the last decade, the use of multidrug therapy (MDT) has reduced the estimated world prevalence of leprosy from around 12 million in 1983 to approximately 1·3 million active cases now.[1] This reduction prompted the World Health Organization to aim for 'elimination of leprosy as a public health problem', defined as reduction in prevalence below 1 per 10,000 population.[1] While this may be achievable, leprosy is far from beaten. In some series, up to one-third of patients eventually develop disability due to nerve damage and over 7 million 'cured' cases may still require ongoing care.[1] More seriously, in general, the declining prevalence has not been matched by a declining incidence, except in countries with significant economic development. Widespread use of MDT has not yet prevented continued transmission.[2]

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Source of infection

The transmission of leprosy is poorly understood, but infection from subclinical sources could be more important than infection from active clinically apparent cases.[3–5] Nearly all individuals in highly leprosy-endemic areas have immunological evidence of exposure to *Mycobacterium leprae*,[6–8] despite the relative rarity in most populations of the lepromatous patients thought to be the main source of infection.[5,6] Furthermore, the incidence of leprosy has not fallen dramatically in many endemic countries, despite effective treatment of most lepromatous patients at an early stage of their disease.[2] While early cases of multibacillary or paucibacillary disease may provide the bulk of excreted bacilli in some populations, in others self-healing infections which do not result in disease, but do have a transient period of nasal excretion, could be of great importance.[4,5,9] A case of borderline-tuberculoid leprosy with a 'lepromatous' nodule in the nose[10] might be an example of persistence of an initial bacilliferous lesion. The association of household contact with increased risk of disease[11,12] and an antibody response[5,8,13,14] suggests that direct spread of *M. leprae* from one infected individual to another may be important, although this could also occur by an indirect route as *M. leprae* can survive in nasal secretions.[15] In one study, *M. leprae* has been found in the soil around the houses of leprosy patients by mouse footpad culture.[16] There is also evidence that *M. leprae* may remain viable for some time,[15,17] so it is possible that secreted bacilli in house dust could be a source of infection.

Most new patients have not had contact with leprosy patients who are shedding bacilli from skin lesions, but a reappraisal of Pedley's work on skin–skin transmission[18,19] using PCR detection methods[20] seems appropriate to confirm this work which used tinctorial staining methods to assess shedding of bacilli.

Primary infection and immunity

The route of entry of *M. leprae* to the body is still controversial, but the primary lesion of leprosy is still thought to be in the nose.[21,22] There is little evidence for implantation of *M. leprae* into cuts or abrasions,[23,24] or of transmission by blood-sucking insects.[21,24,25] While occasional animals, notably armadillos and primates, can be infected by *M. leprae*, there is no evidence that they are a major source of infection within the population. However, subcutaneous infection of nine-banded armadillos does result in disseminated infection,[24] albeit using high doses of viable *M. leprae*. While such mechanisms seem unlikely to account for large numbers of patients, they cannot be totally excluded and their validity should be further tested.[23] For instance, the idea of transmission by blood-sucking insects is unproven, but testable by both experimental and PCR survey methods.

Large numbers of leprosy bacilli are excreted from the nose in untreated lepromatous leprosy.[26–28] The nasal lesions in indeterminate cases can be bacilliferous[29] and nasal excretion of leprosy bacilli is much more common than from any other part of the body in leprosy patients.[21,30] It is therefore possible to postulate a hypothesis for early leprosy in which contact with *M. leprae* leads to primary nasal infection (Figure 1). This may be facilitated by nasal abrasions: infection may require the coincidence of infectious bacilli with an abrasion or other pathology of the nasal mucosa.[5] In this model, haematogenous spread to skin and nerves would lead to the eventual development of clinical leprosy (Figure 1). A similar pattern of haematogenous spread has been observed in the nine-banded armadillo,

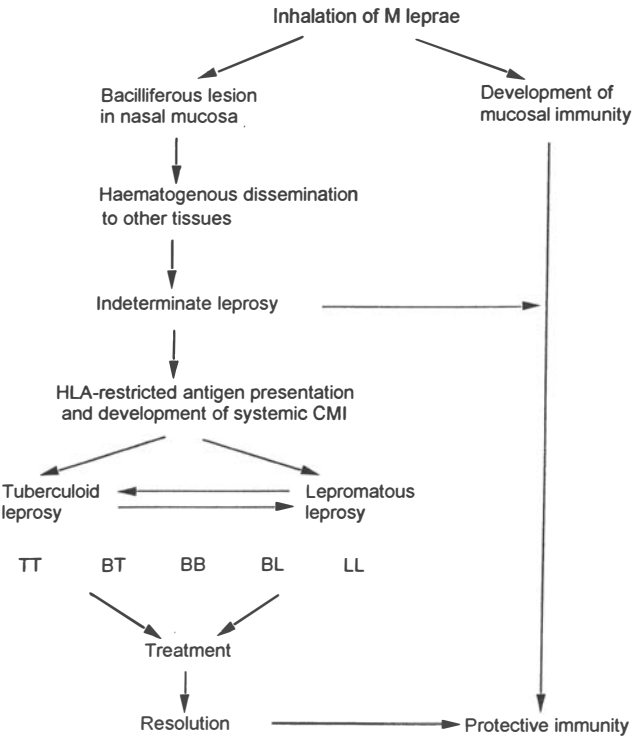

Figure 1. A model for the pathogenesis of leprosy.

although this was following primary subcutaneous inoculation,[24] and in thymectomized mice following nasal instillation of *M. leprae*.[31] Healing of the primary infection would accompany development of protective immunity and seroconversion.[5,9]

If this is correct, frequency of contact with a source of infection would be important in transmission. A large number of studies have shown the risk associated with household contact using both epidemiological and laboratory methods.[5,11–13] However, it is possible that the primary nasal lesion goes through a bacilliferous phase in many infected individuals, accounting for the presence of *M. leprae* DNA in the nasal secretions of those living in endemic areas who have no known contact with leprosy.[3,4,9] It is worth noting that PCR methods for the detection of *M. leprae* require the presence of DNA from at least five bacilli to give a positive result,[20] and it is therefore likely that PCR positivity reflects the presence of substantial numbers of *M. leprae* in the nose. However, PCR positive individuals have not yet been subjected to detailed ENT examination to determine whether they have bacilliferous lesions or not. It is therefore theoretically possible that nasal excretion of *M. leprae* by subclinically infected individuals could be responsible for transmission, but this is by no means proven.

How does the primary lesion heal? The course of the infection (Figure 1) may depend upon the timing of the development of local mucosal immunity. There is evidence that the timing of development of cell-mediated immunity affects the development of indeterminate leprosy.[32] The timing of development of effective immune responses does influence the progression of other infections by intracellular organisms: similar situations occur in the lung

in primary tuberculosis[7,33,34], in Buruli ulcer[35] and in leishmaniasis.[36] It is generally accepted that protection against leprosy and other intracellular infections requires cell-mediated immune responses. Successful immune defence against an initial *M. leprae* infection requires both prevention of dissemination and healing of the primary lesion, and there can be little doubt that an effective cell-mediated immune response could accomplish this.[14,37] The development of cell-mediated responses in the nose is difficult to study, but unlike the systemic immune system, mucosal cell-mediated and humoral immunity may develop concommitantly.[38,39] Since measurement of IgA responses is considerably easier, and all mucosal sites are linked by lymphocyte recirculation,[38] it is possible to measure salivary antibody responses to *M. leprae* as a marker of anti-*M. leprae* immunity. Furthermore, mucosal IgA itself is of interest, since it mediates reduction of adherence of bacilli and opsonization responses which might be protective.[14]

The mucosal immunology of leprosy

Early and seminal studies by Abe *et al.*[40–42] using the FLA-ABS test showed that most lepromatous patients do not have a salivary anti-*M. leprae* IgA (ML-IgA) response and that treated patients are more likely to have an ML-IgA response than untreated patients. The same group showed that a high proportion of contacts of leprosy patients have detectable ML-IgA responses which they hoped might have diagnostic value. In this they were disappointed, but at the same time, we and others were becoming disillusioned with the overconcentration of studies on patients, who have demonstrably failed immunologically by getting leprosy. Initial studies in Bangladesh (253 subjects) and Fiji (163 subjects) showed that the ML-IgA response was least likely to be found in those with untreated leprosy or increased risk (i.e. household contacts), suggesting that, 'the mucosal immune system might be of importance in a putative protective response to infection...'.[14] We were able to confirm that treated patients were much more likely to have a response than untreated patients, and found the highest numbers of ML-IgA positive individuals amongst hospital workers,[14] who rarely get leprosy. Subsequent studies showed evidence of an IgA anti-LAM response in many individuals.[43]

The development of PCR detection of putative early nasal infection[20] gave us the possibility of testing our ideas further. In the MILEP1 study (304 subjects) in Miraj, Maharashtra, we concentrated our efforts on understanding the mucosal immune response to *M. leprae* in defined groups of patients, contacts and control subjects.[9,37] The results of testing for salivary IgA directed against whole *M. leprae* can be interpreted in conjunction with the PCR results (putative infection/excretion of *M. leprae*) to provide a framework for understanding the pathogenesis of primary infection[9] (Table 1). Non-exposed individuals are negative for salivary anti-*M. leprae* IgA (ML-IgA$^-$)[14,37] and do not show an amnestic response to challenge with nasal leprosin A.[37] Nasal swabs are of course PCR negative (PCR$^-$). On contact with *M. leprae*, non-exposed individuals are likely to acquire a primary infection. This will be transient in most individuals, but as a result their nasal excretions may contain *M. leprae*, making them PCR positive (PCR$^+$). At an undetermined and probably variable time after infection, immunity develops leading to IgA positivity (ML-IgA$^+$). Development of a mucosal immune response is more rapid than healing of this initial lesion resulting in PCR$^+$/ML-IgA$^+$ individuals being as common (6/204) as PCR+/MIL$^-$IgA$^-$ individuals (7/204).[9] PCR$^+$ individuals become PCR$^-$ within a year,[4,9] but

Table 1. PCR and mucosal immunity during the pathogenesis of early leprosy infection

1.	Non-exposed	IgA− PCR−
2.	1st exposure	IgA− PCR+
3.	Resolving infection	IgA+ PCR+
4.	Immune (?protected)	IgA+ PCR−

the IgA response is much longer lasting.[9,37] Although salivary IgA anti-*M. leprae* antibody may be absent after a year or so, the capability to produce such a response can be detected by mucosal challenge testing up to 10 years following exposure to *M. leprae*.[37] Other markers of infection such as serum PGL1 IgM antibody levels show a similar pattern within the population,[5,9,13] but correlate poorly with PCR.[5] It is possible that serum antibody levels rise as PCR positivity declines and that the correlation between these two markers is therefore displaced in time.

The most worrying result of the MILEP1 study was the low level of ML-IgA positivity (33%) amongst a group of 58 'control' subjects with no known leprosy contact in comparison with previous studies using the same ELISA protocol in Fiji and Bangladesh (79% and 69%, respectively[14]), despite the continuing presence of nasal PCR positivity suggestive of infection in the community.[9] The numbers are small, but suggest that there may have been a decrease in immunity in the general population in this area while transmission continues, particularly amongst household contacts of leprosy patients.[9] The reasons for this decline, if it is a real phenomenon, are not clear. However, this area has had an effective MDT control programme for 12 years, whereas the previous study was carried out in the pre-MDT era.

The data from the MILEP1 study[9,37] support our hypothesis that mucosal immunity develops during resolution of presumed infection and that it may be related to the development of protective immunity. Since long-term immunity is probably determined by the outcome of initial infection long before clinical leprosy develops, there is a need to investigate the pathogenesis of the primary lesion more thoroughly. We have now embarked on a much larger study (MILEP2) in which PCR and IgA studies are being performed in whole villages near Miraj and in Ethiopia: some 1200 subjects have been examined to date with similar results to those obtained previously (unpublished data). These whole population surveys will define transmission and mucosal immunity within a well-defined epidemiological framework, allowing a strategy for eradication to be developed. Similar studies are taking place in Indonesia (Klatser, personal communication).

Breaking the cycle of transmission

The control of infectious disease requires control of transmission. Since leprosy has such a long incubation period during which the infection can be passed on, development of clinical disease is a poor marker of infection. This makes study of the process of transmission and development of protective immunity difficult, but knowledge of these processes is essential for the design of effective intervention in endemic countries.

We suggest that the key to effective control is the recognition that leprosy infection

occurs in clusters, as do many other infectious diseases.[4] Treatment of all potentially infected individuals in such clusters could be a powerful adjunct to MDT control and might well lead to eradication of the disease. However, PCR requires sophisticated facilities and is unlikely to form part of a practical detection system for field use. Since few of the infected individuals are likely to develop disease and there is already an MDT programme in place, alternative (albeit less specific methods) to identify clusters are appropriate, since all individuals in a cluster could receive single dose therapy with mycobactericidal drugs such as rifampicin or ofloxacin (probably in combination to avoid the theoretical risk of resistance despite the increased risk of toxicity this would entail). Alternatives which may be good enough indicators of recent infection to achieve community-oriented control may include PGL1 serology,[13] which needs to be re-evaluated in the light of studies of the temporal pathogenesis of the primary infection.

Where does first exposure occur? One can only speculate at present. For contacts, the home is probably most important, while for others exposure in childhood may well occur when they start to attend school.[11,44] Public places such as tea houses, buses, factories and hospitals are possibly less likely to be important sources of infection, since in most leprosy endemic populations, individuals will have met *M. leprae* before they encounter these sites and contact may be transient.[44,45] There is of course likely to be variation between communities, and PCR or antigen detection studies to determine where *M. leprae* can be found in the environment would be valuable. However, in many communities, we believe that intervention (drug or vaccine) in school and home might interrupt transmission sufficiently to eradicate infection. The MILEP2 and related studies should provide answers to some of these questions. The finding of reduced levels of immunity in adults with no history of leprosy exposure within a leprosy control area[9] supports the idea that childhood exposure is important and it has long been known that childhood disease becomes rare in societies from which leprosy is disappearing.[46] Understanding of the source of infection and pattern of transmission should allow the design of epidemiological methods to delineate clusters using minimal PCR or serological testing in highly endemic areas.

In populations where numbers of immune individuals decline to about 10% of the population, a screen for immunity may be more appropriate. This would have similarities with the use of Mantoux testing for contact tracing of tuberculosis suspects in areas of low endemicity. Salivary ML-IgA response[9] and skin testing[7] seem the most obvious alternatives. The former has many advantages since it is objective, non-invasive, and can be automated or simplified (development of a dipstick test may well be feasible). There is every chance that it will be possible to identify clusters of at risk individuals. This has considerable implications for the choice of immunoprophylaxis or chemoprophylaxis.

Immunoprophylaxis or chemoprophylaxis?

Rational vaccine design requires knowledge of the protective immune mechanism, which must be shown to confer protection as long as immunity persists. This allows potential vaccines to be tested to ensure that they produce the correct response in unexposed individuals before large vaccine trials are attempted. A vaccine meant for whole population protection may not be required in leprosy if a strategy of targeting recent infection is followed: secondary immunoprophylaxis (i.e. immunotherapy of infection before disease occurs) would be sufficient.[47] Despite the large amount of resources devoted to finding a

leprosy vaccine, there is at present no vaccine which fulfils these requirements and is available for widespread use, with the possible exception of BCG in some areas.[47,48]

The other option is chemoprophylaxis. The recognition that contacts of leprosy patients were at increased risk of contracting the disease led to a number of trials of chemoprophylaxis of leprosy using long-term dapsone treatment. No distinction was possible between primary chemoprophylaxis (protection of uninfected individuals) and secondary chemoprophylaxis (treatment of presumed infection to prevent the development of clinical disease). The results of these studies varied, initially with some encouraging results,[49–51] but controlled trials at Chingleput of this approach were judged less satisfactory[52,53] despite 50% protection levels. There are clearly problems in giving long-term treatment to children with potentially toxic drugs, although at the time the even more extreme measure of separating children of leprosy patients from their parents was commonplace.[49] The results of childhood chemoprophylaxis encouraged Sloan and co-workers[54–57] to attempt whole population chemoprophylaxis in Micronesia (Pingelap atoll), where the incidence was estimated at 7/1000 per annum and the prevalence 6·6%. Lepromin positivity increased with age from 29% at <4 years, 61% in the 5–9 age group, 86% in the 10–14 age group, to 100% in the 15–19 age group. This suggests widespread early childhood exposure to *M. leprae*. A depot preparation of dapsone (Acedapsone or DADDS) was offered to the whole population and actually given to 51% for 3 years (1967-69) at 3-monthly intervals. However, every eligible individual in the population received at least one injection. Six new cases occured during the phase of DADDS administration, but repeated examination in 1969 and 1970 revealed no new cases. The authors[55] concluded, '...the next logical step would be a series of experiments to test how far one must extend DADDS chemoprophylaxis into the web of household and neighbourhood contacts before one runs into serious problems of non-cooperation and/or inefficient benefit.' Despite the success of their approach, this point was largely ignored.[54,55] However, such isolated communities are rare and the problems of giving such long-term treatment as well as the cost lead to a preference for immunoprophylaxis over the next 20 years.

In recent years, chemoprophylaxis has been tried in another isolated community in the Southern Marquesas using a single dose of 25 mg/kg rifampicin given to 98·7% of the population.[58] The rapid occurence of a skin lesion in a boy 3 months after chemoprophylaxis seems to have worried the authors, although this patient may well have been incubating the disease for some time before prophylaxis. A further case was detected at 21 months post-prophylaxis.[59] The authors concluded that their chemoprophylaxis was responsible for 50% protection, but that the costs involved in whole population treatment made chemoprophylaxis unsuitable for leprosy control.[59] The current WHO study of single dose treatment using a combination of ofloxacin, minocycline and rifampicin for single lesion leprosy is based on the premise that there are few bacilli to kill in single lesions and is proving clinically acceptable (V. J. Edward, personal communication). Such multi-agent single dose therapy might be more suitable for chemoprophylaxis. Nasal lesions may be bacilliferous, but they can be quite small[26,27] and single dose therapy with a cidal drug regimen might well result in more rapid healing with development of immunity.

We believe that drug-based intervention studies designed to interrupt transmission of infection rather than to prevent development of the disease might add to the efficacy of MDT programmes. The impact of MDT control programmes on leprosy transmission is largely unknown. However, the likely effect of stopping/reducing such programmes where the prevalence of leprosy has fallen to low levels can be predicted from the evidence of

continuing transmission even in good MDT control programmes[9] and the results of the acedapsone trial in Pingelap[54–57]—leprosy would slowly return. Maintenance of current MDT programmes is financially difficult, but currently available evidence suggests that improving their efficacy might allow eradication.

Conclusion

Since there is no large animal or environmental reservoir of infection, eradication of leprosy is feasible. Adoption of a strategy for control based on the detection of clusters of infection needs more information, but the prospect is an exciting one. Few ENT surgeons have taken an interest in leprosy since the studies by Rex Barton in the 1970s defined the nasal lesions[10,26,27] and there is a general lack of information about the pathogenesis of primary infection which derives in part from the concentration of effort on established disease. Studies of transmission have been unjustifiably neglected for far too long.[2,60] Maintenance of control programmes is expensive and becomes increasingly more difficult to sustain as numbers of cases on treatment fall. Eradication may prove a more attainable long term objective than elimination, but the time to develop the tools is now, while the MDT programmes are still in place.

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Health Systems Research in leprosy control–what contributions can it make?

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Summary The paper describes a Health Systems Research (HSR) training programme which took place at the All Africa Leprosy, Tuberculosis and Rehabilitation Training Centre (ALERT) in Ethiopia. The training consisted of three stages: an initial workshop focussing on protocol development, followed by a fieldwork period and a data analysis and report writing workshop. Twenty participants, divided over four groups, took part in the training and carried out the research alongside their day-to-day professional commitments. Three of the projects were concerned with prevention of disabilities, one with integration of the leprosy programme into the general health services. Based on the findings of their research, each group produced a set of recommendations and a plan of action for the implementation of these recommendations. The contribution of HSR to leprosy control is discussed.

Introduction

Health Systems Research (HSR) is a type of research that is concerned with improving people's health by enhancing the efficiency and effectiveness of the health system as an integral part of the overall process of socio-economic development.

More specifically, HSR may be used to help solve practical problems that are encountered by health programme managers, health staff and/or community members. Problems that can be addressed through HSR may be related to the delivery of specific health services; to proper use or targeting of resources, such as human resources, physical structures, materials and finance; and to the relative merits and demerits of certain health policies or programmes.

The main characteristics of HSR are:

- it is *problem based* and has a strong orientation towards seeking feasible, practical and affordable solutions to these problems;

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- it is *participatory*: there is a close dialogue between those who identify the problems to be studied and who are the main potential users of the results—the health programme managers and policy makers—and those who search for the facts and suggest alternative solutions—the researchers; in many cases, the programme managers are the researchers themselves;
- it is *multidisciplinary*: contributions are obtained from a variety of disciplines, which may include health science, epidemiology, sociology, anthropology, economics, public administration and statistics, through a team work approach.

Because of the variation in types of problems that qualify for HSR studies, there is no single HSR methodology. Each problem requires its own methodology to quantify the problem under study, identify its various direct and indirect causes, measure the relative importance of each cause and explore possible solutions. Efforts have been made, however, to give structure to the process of developing HSR methodologies. One of the best resources that are currently available is the manual *Designing and Conducting Health Systems Research Projects*,[1] which is published by WHO and IDRC. The manual consists of two parts (the first about proposal development and fieldwork and the second about data analysis and report writing) and is the second volume of a five-volume series, issued by WHO/IDRC under the title Health Systems Research Training Series.

In this paper, we describe an HSR module based on this manual, whereby four research projects related to leprosy were developed, implemented and subsequently analysed at the All Africa Leprosy, Tuberculosis and Rehabilitation Training Centre (ALERT) in Addis Ababa, Ethiopia. Possible implications for use in other leprosy control projects will be discussed.

Health Systems Research at the All Africa Leprosy, Tuberculosis and Rehabilitation Training Centre (ALERT)

ALERT was set up over 30 years ago as a leprosy training centre for Africa. The main focus is leprosy and rehabilitation, although in recent years tuberculosis has become an important part of ALERT's activities in both training and service provision. The organization comprises three divisions:

- The Training Division, which organizes and manages all the formal training activities undertaken by ALERT.
- The Hospital Services Division, which runs a 235-bed hospital with medical, surgical and ophthalmology departments.
- The Leprosy/TB Control Division, which manages a control programme in central Ethiopia, an area with a total population of 13 million and a leprosy prevalence of 1·1 per 10,000.

Prevention of disability (POD) activities have become an increasingly important part of leprosy work as the prevalence of registered cases has decreased. One of the major concerns at ALERT is the fact that the rate of disability in both new and treated cases has remained at a constant and unacceptably high level, despite all the resources that have been available to the organization, and the original research that has been conducted over the years. Each division of ALERT therefore sees POD as a central issue, with many problems still to be resolved.

For the Training Division, a major challenge is to develop training guidelines for POD in

the now typical situation in which leprosy work is integrated into the general health services. For the Control Division, there is a need to find out why the disability rate in new cases remains high and then design specific and targeted programmes of health education to reverse the situation. For the Hospital Division, better ways of preventing further disability are needed, whether in the management of acute neuritis or better self care in patients with permanent nerve damage. There is clearly a lot of overlap in the activities of the three divisions, and many of the issues in POD are looked at jointly.

Technical expertise and financial resources were generally not lacking at ALERT, and therefore it became clear that operational aspects of the work would have to be examined in detail if POD activities and outcomes were to be improved. This would involve management issues such as quality, efficiency and motivation on the one hand, and, perhaps more importantly, a greater emphasis on addressing and adapting to the patient's own socio–cultural situation and beliefs, on the other. These operational problems can most appropriately be investigated using the HSR methodology, and this was suggested by the Medical Advisory Committee of ALERT.

A typical HSR training course as proposed in the manual '*Designing and Conducting HSR Projects*' described above, consists of three stages: two workshops and a fieldwork period.

The first workshop, aimed at the development of research proposals, took place during the first 2 weeks of June 1996. Of the 20 participants, the large majority were ALERT staff, coming from all three divisions: Control, Training and the Hospital. Sixteen of the participants were medical doctors (public health physicians, surgeons, dermatologists, and a specialist in internal medicine), two were physiotherapists, one a nurse and one a social worker. There were three facilitators from the Royal Tropical Institute (KIT) in the Netherlands, to introduce the various modules and provide technical guidance during the development of the research proposals.

The participants were divided into four groups. Before the workshop, it had been decided that it would be preferable to limit the area of the research to topics related to prevention of disabilities (POD) in leprosy. Due to the background and specific interest of some of the participants, at the beginning of the workshop integration of leprosy services into the general health services was added as a research topic for one of the groups. The remaining three groups chose topics related to POD in the phase before a patient is started on MDT, the phase during MDT and the phase after release from treatment (RFT). During the workshop, the groups developed a full research protocol each, including a detailed work plan and a budget. All protocols included qualitative as well as quantitative research methods. Qualitative methods to be used were focus group discussions, key informant interviews and semi-structured questionnaires. The final proposals included one case-control study, one retrospective cohort study and two descriptive studies. The total budget was $15,000 US for the four projects together, with costs of individual projects varying between $2000 and $6000 US.

The full titles were:

- Delays in presentation and start of treatment in leprosy patients: a case-control study of disabled and non-disabled patients in Hararge, West Shoa and ALERT hospital.
- Can disabilities be prevented during treatment? A study into the factors involved.
- Analysis of ulcer cases in ALERT and Wollo Leprosy Control Programme and prolonged hospital stay in the ALERT and Borumeda Hospitals.
- Knowledge and attitude of health professionals in relation to the involvement of General

Health Service (GHS) staff in the management of leprosy in Southern Nations, Nationalities and Peoples Region (SNNPR), Ethiopia.

Once funding of the proposals had been secured, the participants carried out the respective researches, alongside their day to day professional commitments. The actual research phase started in October 1996, and lasted until the end of March 1997. All groups utilized a number of research assistants to carry out parts of the research, but it is important to realize that most of the work was done by the group members themselves.

During the last 2 weeks of April 1997, a second workshop aimed at data analysis and report writing was held at ALERT. All groups had implemented their research proposals. Some hypotheses had been confirmed, others rejected, but all groups had come up with unexpected, chance findings. Most of these were very valuable, and enriched the quality and depth of the research.

The research suggested that although ALERT has a well developed Management Information System, certain aspects of the leprosy control programme were not achieving the desired results.

In the case control study which addressed the delays between appearance of the first symptom and start of treatment in leprosy patients, cases were patients with disability grade 2 at the time of diagnosis, and controls were patients diagnosed during the same period, who had a disability grade 0 at diagnosis. The average delay before diagnosis in disabled new cases was over 2 years and seemed to be related to the level of stigma in the community, which remains distressingly high. One striking finding was that on average around 10% of the total delay from first symptom to start of treatment occurred in *general clinics with qualified staff*. Surprisingly, (disabled) cases incurred greater delay in being referred for leprosy treatment within the health services than controls. The full results of this study have been published elsewhere.[3]

In the retrospective cohort study which looked at the factors involved in the prevention of disabilities during treatment, it was found that out of 113 patients who technically fulfilled the criteria for steroid treatment, only 43 were recorded as having received steroids. This was much less than expected. From interviews one possible reason emerged, namely, that health workers in the ALERT leprosy control area are not supposed to start patients on steroids unless their supervisor approves. As the latter is not always present when the patient visits a clinic, this may lead to delays and some patients may even miss treatment for their new nerve function loss altogether.

Further, it was found that according to the patient cards, only 48% of MB patients who were treated with corticosteroids recovered satisfactorily, which is well below the 75% that are assumed to recover by ALERT staff. This may be partly a problem of definition and quantification of the degree of recovery, which needs further study.

Thus a number of important new insights were gained, some of which had important consequences for the programme at ALERT.

One group had had difficulties in carrying out all aspects of the research as planned. Lack of time, and the fact that the group members all worked at different localities were the major reasons for this.

The final output of the second workshop was four research reports, each with a full set of recommendations based on the findings of the research, and a plan of action as to how to implement these recommendations. The reports and the recommendations were presented to the relevant authorities during a meeting at ALERT at the end of the second workshop.

It is expected that the next step will be that the plans of action will be implemented. Some of the recommendations will be implemented directly by the researchers themselves. Others will need to be discussed between the researchers and decision makers. In any case, the fact that the recommendations are based on findings from well designed and implemented research will increase the likelihood that they will be acceptable for these decision makers. It is further expected that findings will be presented at national symposia and seminars. Publication of at least one, but possibly two of the studies in international journals is anticipated.[3]

The future of HSR at ALERT

At the end of the first, as well as the second workshop, written evaluations were held, whereby participants were asked to express their opinions on specific statements and score them from 1 (strongly disagree) to 5 (strongly agree). After both workshops, the participants turned out to be very satisfied with the process of the training. Although all agreed that they had benefitted from the course (mean score 4·6), a common complaint after the second workshop was that the time available for data analysis and report writing (2 weeks) had been too short. The fact that during the second workshop 2 days were 'lost' as a consequence of public holidays will no doubt have played a role in this matter.

The large majority of participants felt confident that 'there is a good chance the recommendations of our research will be implemented' (mean score 3·9), and they were 'looking forward to promote the utilization of our research' (mean score 4·3). Another positive effect of the training was that most participants were 'confident to start other research projects' (mean score 4·4), and in fact 75% already had specific topics for study in mind, not only related to leprosy, but also to tuberculosis and other areas. While many staff at ALERT have had some involvement in research over the years, this was the first time for most participants to be involved in every stage of the research from beginning to end. This has given a much greater understanding of the purpose and process of research, and will incidentally help participants to evaluate other research more critically

A number of participants felt confident to be a facilitator in a possible future HSR training, which will enable ALERT to carry out similar HSR training courses with less (expensive) outside assistance.

It is recognized that it is too early to evaluate the actual impact of the training. Crucial questions which we hope to answer in a year's time are: have the recommendations that resulted from the studies been implemented? Have the problems that formed the justification for conducting the respective studies been solved or alleviated? Are participants applying some of the skills that they acquired during the training course in their day to day work?

Contribution of HSR to leprosy control

The experiences at ALERT suggest that HSR can make a useful contribution to leprosy control. Recently, similar workshops have been organized in other countries as well (e.g. India). The teaching material proved to be well suited for application to subjects related to leprosy, and no special adaptations were needed.

Table 1. Leprosy research priorities for which HSR methodology is particularly suitable

• The development of more effective and efficient POD in leprosy control, primary health care and community based rehabilitation settings;
• The development of more effective self-care and footwear for patients with impairments;
• The development of methods to improve the implementation of MDT in inaccessible areas and to improve MDT completion rates;
• The development of strategies to implement MDT effectively through general health services and primary care in low endemic settings;
• The development of effective rehabilitation for leprosy patients within general rehabilitation programmes, including community based approaches.

Although operational research is not new in leprosy work, the methodology of HSR and certainly the systematic training of health workers in this methodology as well as the implementation of field research is a relatively new development. Training courses like the one described here not only serve to analyse and solve problems in leprosy programmes, but are a good investment in leprosy workers too, as they develop a broader view on the programmes they are working in.

In 1995, a short module on HSR was added to the well known, and widely used WHO training course '*Managing Programmes for Leprosy Control.*'[2] As it is based on the same methodological concepts, it may be useful to use this module as a first step, whereby some participants who show keen interest in the topic are given the opportunity to undergo further HSR training along the lines of the courses described here.

Recently, the Medical Commission of the International Federation of Anti-Leprosy Associations, ILEP, has published a list of topics for future leprosy research. It argues that, as a result of the success of MDT programmes, the priorities of research in leprosy have changed. The Commission set new priorities for research in leprosy according to criteria such as feasibility, cost, time scale and proportion of patients benefiting, as well as the size of the benefit.[4] It is exactly these criteria that can be used to characterize Health Systems Research. Some specific priority items mentioned in the Commission's report for which the HSR methodology seems particularly suitable are presented in Table 1.

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Choosing the decolourizer and its strength to stain *Mycobacterium leprae.* Does it actually matter?

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Summary Leprosy bacilli are more easily decolourized during staining than tuberculosis bacilli, so a weaker concentration of decolourizer is usually recommended. In Indonesia, the same 'strong' decolourizer is used for identifying both organisms. In a study to compare the results using different concentrations of different decolourizers, no difference could be found in the bacterial index (BI). It is suggested that the same staining technique can be used for tuberculosis and leprosy.

Introduction

Ideally, all leprosy patients should have one skin smear examination before starting treatment, if reliable facilities are available.[1] The Ziehl–Neelsen method involves staining with carbol fuchsin, followed by decolourization then counterstaining with methylene blue.[2] If the decolourization process is excessive, bacilli may be rendered invisible. Concerns regarding which decolourizer to use, what strength and for how long, have resulted in several investigations.[3–6]

In Indonesia, the same staining technique is normally used for leprosy and tuberculosis, despite the widely accepted opinion regarding the reduced acid and alcohol 'fastness' of *Mycobacterium leprae*.[2] The objective of this study was again to find out if (i) different decolourizers and (ii) different concentrations of the same decolourizer had an effect on the BI of skin smears.

Although the Ziehl–Neelsen stain is used universally to stain *M. leprae*, there are many modifications.[7] The main difference between the technique for leprosy and tuberculosis is the strength of the decolourizer, but in addition, the duration of decolourizing varies. For tuberculosis, this is usually either 25% sulphuric acid or 3% hydrochloric acid in 70%

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ethanol for 3 min.[8] For leprosy, decolourization or differentiation using 1% hydrochloric acid in 70% ethanol is favoured by most,[2,7,9,10] but 5% sulphuric acid by some.[11] Dharmendra surprisingly recommends 3% acid alcohol.[12] The counterstain is usually methylene blue, although the concentration varies between 0·2%[11] and 1%.[6] Vettom and Pritze found 10 different techniques from 29 projects, the most notable variations being in decolourization time.[13] They ranged from 1% acid alcohol for 5 s to 20% acid alcohol for 1 min and from 5% sulphuric acid for 1 min to 25% sulphuric acid for 10–20 min.[13]

Despite this, several research laboratories use the same concentration of decolourizer for leprosy as for tuberculosis (A. McDougall, personal communication). The Indonesian leprosy manual describes two possible Ziehl–Neelsen methods, one with acid alcohol (concentration not specified) for 3–5 s and the other with 25% sulphuric acid for 8 s.[14]

Materials and methods

Skin smears were taken from 40 multibacillary (MB) leprosy patients, with a range of BI. The selection was by the technician who took the smears, did the staining and read the results. The patients were registered cases and were on WHO MB multidrug therapy (MDT).[1] All patients had smears taken from four standard sites with four identical slides being made from each patient, each slide with the four sites on it.

Apart from the decolourizer, the same Ziehl–Neelsen method was used.[15] The decolourizers were 1% hydrochloric acid in 70% ethyl alcohol (HCl), 3% hydrochloric acid in 70% ethyl alcohol, 5% sulphuric acid (H_2SO_4) and 25% sulphuric acid. Slides were stained in batches. Carbol fuchsin was filtered onto the slide, allowed to act for 2 min, heated gently until steam rose, allowed to act for a further 10 min, washed with tap water until clean, transferred to a staining rack and dipped in decolourizer for 8 s. If any slide was still red, this was repeated, washed, and counterstained with 0·3% methylene blue for 1 min. Most slides only received one immersion in the decolourizer.

The intention was that the examination of the smears would be blind, but it was possible to distinguish immediately between the slides decolourized with HCl and those with H_2SO_4, by microscopy of the smear. It was not possible to distinguish between 1% and 3% HCl or between 5% and 25% H_2SO_4.

The BI was reported for each of the four smears on the slide and the average was calculated. The morphological index (MI) is not routinely used in Indonesia.

The results were compared using the Student's paired *t*-test.[16] Differences were considered significant at the 95% level of confidence.

Results

Forty patients had slit skin smears taken, resulting in 160 slides. Each slide had four smears, except in the case of patient 6, who fainted after smears had been taken from two sites (ears). Thirty-four patients were positive with at least one staining technique. An average BI was calculated for each of the 160 slides (see Table 1). Comparison was also made using individual smears.

Eleven patients had a higher BI with 1% HCl than with 3%. Twelve patients had a lower BI with 1% HCl than with 3%. Eight patients had a higher BI with 5% H_2SO_4 than with 25%. Thirteen patients had a lower BI with 5% H_2SO_4 than with 25%.

When looking at low BIs (i.e. >0 but <2), the same pattern was observed. Eleven patients had a low BI using 1% HCl. In two cases, the BI was greater using 1%, and in five cases, the BI was less. Twelve patients had a low BI using 5% H_2SO_4. In three cases, the BI was greater using 5% and in five cases, the BI was lower with 5%.

Table 1. BI results for 40 patients using four decolourizers

Patient	1% acid alcohol	3% acid alcohol	Difference	5% sulphuric acid	25% sulphuric acid	Difference	Difference between 1% HCl & 5% sulphuric acid
1	1·75	2·25	−0·5	2	1·75	0·25	−0·25
2	1	1	0	0·75	0·75	0	0·25
3	4·75	4·5	0·25	4	4·25	−0·25	0·75
4	1	1	0	1	0·75	0·25	0
5	0	0	0	0	0	0	0
6	4	4	0	3	4	1	1
7	2	1·75	0·25	1	1·25	−0·25	1
8	3·75	3·5	0·25	4	4	0	−0·25
9	4·5	3·75	0·75	4	4·25	−0·25	0·5
10	1·5	1·75	−0·25	1·25	1·25	0	0·25
11	2·75	2·5	0·25	1·75	2·75	−1	1
12	0·5	1·5	−1	0·5	0	0·5	0
13	1	1·75	−0·75	1·25	1·25	0	−0·25
14	0	0	0	0	0	0	0
15	4·5	4	0·5	0	3·25	−3·25	4·5
16	1·75	2·75	−1	0	3·25	−3·25	1·75
17	2·5	2·75	−0·25	0	2·5	−2·5	2·5
18	1·25	1	0·25	1	1	0	0·25
19	0	0	0	0	0	0	0
20	4·25	4·25	0	4·25	3·5	0·75	0
21	2·75	2·25	0·5	1·5	3·5	−2	1·25
22	0·5	0·5	0	0·25	0	0·25	0·25
23	0	0	0	0	0	0	0
24	4·75	4·75	0	4·5	4	0·5	0·25
25	0	0	0	0	0	0	0
26	3·25	4	−0·75	3	3·25	−0·25	0·25
27	2	2·25	−0·25	0	0	0	2
28	3·75	3·75	0	3·75	3·75	0	0
29	4·75	4·75	0	4·5	4·5	0	0·25
30	3·5	3·75	−0·25	3·5	2·25	1·25	0
31	3·5	4	−0·5	3	2·5	0·5	0·5
32	4	3·75	0·25	4·25	4·25	0	−0·25
33	5	5	0	5	5	0	0
34	1·25	0·5	0·75	0·25	0·75	−0·5	1
35	0	0	0	0	0	0	0
36	3·5	4·25	−0·75	3·75	3·75	0	−0·25
37	2	3·5	−1·5	3·75	3·75	0	−1·75
38	0	1·25	−1·25	0·75	1·25	−0·5	−0·75
39	0·5	0·5	0	0	1·25	−1·25	0·5
40	4·75	4·25	0·5	4·75	4·75	0	0
Total	92·5	97	−4·5	76·25	88·25	−12	16·25
Average	2·31	2·43	(0·11)	1·91	2·21	(0·30)	0·41
SD			0·50			0·94	0·98
p value			<0·2			<0·1	<0·02

The average of all the BIs using 1% HCl was 2·31 (with seven negatives). The average BI using 3% HCl was 2·43 (with six negatives). The difference between the BIs was not statistically significant ($p < 0{\cdot}2$ and $>0{\cdot}1$). The average BI using 5% H_2SO_4 was 1·91 (with 11 negatives). The average BI using 25% H_2SO_4 was 2·21 (with nine negatives). Again, the difference between the BIs is not statistically significant ($p < 0{\cdot}1$ and $>0{\cdot}05$). When the differences between the BIs with 1% acid alcohol and 5% sulphuric acid were examined, there was an average fall of 0·41. This was significant at the 2% level ($p < 0{\cdot}02$), suggesting that there might be a real decrease in BI when using sulphuric acid.

There was generally good correlation between the four slide results from each patient. An exception was found in patients 15, 16 and 17, where the slides stained with 5% H_2SO_4 were negative, whereas the other three were moderately or strongly positive. The most likely explanation for this was that these slides were wiped clean on the wrong side of the slide, hence removing all four smears from the slide. If the results from these three patients are excluded, the average BIs are 2·26 and 2·36 for acid alcohol and 2·06 and 2·14 for sulphuric acid. The differences between these figures (between the two acid alcohols, the two sulphuric acids and between 1% acid alcohol and 5% sulphuric acid) all fail to reach statistical significance ($p < 0{\cdot}5$, $p < 0{\cdot}5$ and $p < 0{\cdot}1$, respectively).

In 38 of 158 sites examined, there was a variation of two or more BI units (i.e. more than a 10-fold difference in the number of bacilli) from the same site using different decolourizers. No pattern was observed.

The slides which were stained using an acid alcohol decolourizer were generally easier to examine than those using sulphuric acid. Irrespective of concentration, the bacilli were sharper, clearer, more red, the background had accepted more blue for differentiation and there was little or none of the background pink 'fuzz' that is a feature of the slides which were decolourized using 5% or 25% H_2SO_4.

Discussion

POSITIVITY

This study failed to show that a stronger decolourizer resulted in a lower BI. The BI was slightly higher with the stronger concentration, but not reaching statistical significance (see Figure 1). This was also noted when looking at the results from patients with a low (<2) BI. The BI was slightly lower with sulphuric acid, this reaching significance only when the questionable data from patients 15, 16 and 17 were included.

POSSIBLE BIAS

All patients were purposefully selected. No attempt was made to have a representative sample of leprosy patients, new or otherwise. Since the purpose of the study was to compare results patient by patient, analysis using an average BI for all patients per technique is open to question. The difference in BI from the same site could also be affected by the quality of the smear and within-observer variation. Three patients had results which suggest a major laboratory error. Analysis was also performed excluding results from these three patients.

DOES IT REALLY MATTER?

Most new leprosy patients can be competently diagnosed and commenced on appropriate

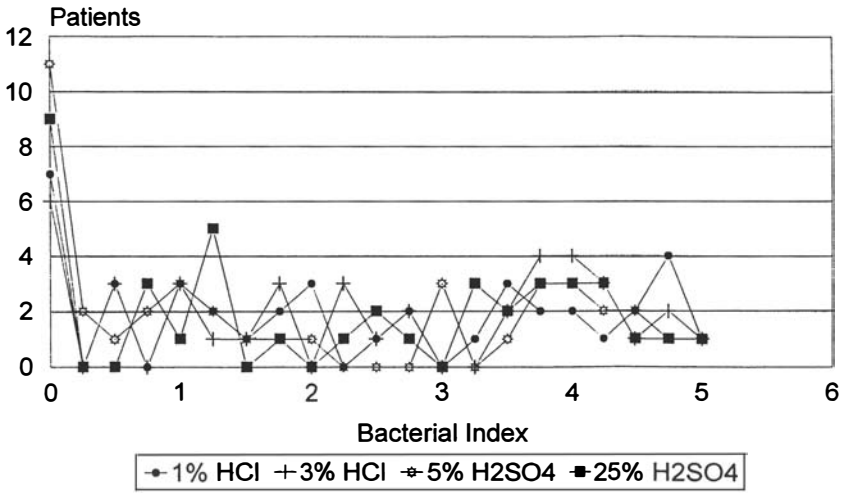

Figure 1. Comparison of BI results using four decolourizers.

treatment without a skin smear. However, there are some patients who present with single or few lesions, but who have early multibacillary disease.[17] There are other patients, either new or old, who have no clearly demonstrable clinical cardinal signs, but who have a positive smear. There are suspicions that some multibacillary patients, who are released from fixed duration treatment but still with a BI of >3, may have a significant relapse rate. It has been suggested that regular clinical and bacteriological review after release from treatment is indicated for these patients.[18] Where communications are difficult, it may not be practical to refer all smear examinations to a referral laboratory.[19] Hence, there is still be a need for skin smear examination to be made available, at least at district level.

The success of the WHO Elimination Strategy suggests that there will gradually be fewer positive smears. Leprosy will not, however, be eradicated by the year 2000. It is therefore essential that there be accessible centres with trained staff who will be able to carry out this procedure accurately. As the world tuberculosis situation deteriorates, it becomes increasingly necessary to have laboratories in peripheral health units capable of bacteriological examination of sputum. Tuberculosis diagnosing centres (possibly one such laboratory per 100,000 of the population[20]), with an established system of quality control, can also be responsible for leprosy microscopy. This is easier if the staining technique for both organisms is identical. From this study, it does not appear likely that the choice of decolourizer or its strength is a major factor in the general unreliability of skin smear services in some parts of the world.

It is possible that this is a much more robust technology than is generally thought. This study suggests that the same technique for staining leprosy and tuberculosis bacilli can be used, furthermore, that acid alcohol is an improvement on sulphuric acid.

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Sustaining leprosy services in the changing context of health sector reform

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Summary National leprosy control programmes currently face a number of changes to the environment within which they operate. This paper examines the issues arising from these. It focuses, in particular, on those arising from changes in the structure of the health sector as a result of policies of health sector reform which are being considered or adopted in many developing countries. These include decentralization, financing strategies, greater role for the private and NGO sectors and the integration of vertical programmes. The paper is structured around a number of key steps in the development of a strategy for sustainability of appropriate leprosy services. These are the assessment of the epidemiological, social and health services context, development of programme objectives, planning of human and financial resources, development of the strategy, mapping the roles of potential actors, development of regulatory and incentive mechanism, action planning and managing change and, finally, re-evaluation of the programme objectives and service delivery organization. The paper stresses the importance of process in developing ownership of a strategy. It concludes with a set of key questions which it suggests need to be addressed by leprosy programme managers in the development of a proactive response to the changes.

Introduction

This paper looks at issues confronting national leprosy control programmes in the face of changes to the environment within which they operate. In particular, it focuses on those arising from changes in the structure of the health sector. It suggests key questions to be asked by each national programme as part of the development of a strategy for sustainability.

There are no universal answers to these questions. They need to be addressed in a context-specific manner. This paper does not suggest responses to these questions or the context of

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any strategy. Many of the questions are not specific to leprosy, and could be asked of other disease control programmes, though the answers would differ.

Underpinning all this is the idea that the proactive and explicit development of a clear and well articulated strategy is critical to sustainability. 'Ad hocery' is unlikely to lead to sustainability. Three preliminary comments need to be made.

First, it is essential that the process be as broad as possible to develop a deep and wide sense of both understanding and ownership of the resultant strategy. This implies the involvement of agencies and individuals who may not traditionally be associated with leprosy. Such a process also requires clear leadership with an obvious role for government planning processes, which have a responsibility for setting the overall policy framework for the health sector, facilitated by the national leprosy programme. In some countries, these government processes may not be well developed. Especially in countries where leprosy services have historically been externally funded, it may be tempting to bypass the government planning process and develop strategies in a tighter (and narrower) fashion. It is, however, important for the long-term sustainability that these processes are fully involved. This may require the development of new facilitation and advocacy skills by leprosy programme managers.

Second, whilst many leprosy experts may feel that the answers to the key strategy questions are well-known, and even self-evident, it is still important to address them explicitly. This is partly as a result of the need to develop a broader constituency. However, the external environment is constantly changing, and truths that were held to be self-evident last year may be less certain this year.

Lastly, there is a need to see strategy development as dynamic and constantly evolving. The pursuit of sustainability is best served by the adoption of clear long-term goals coupled with short-term flexibility. This requires a cyclical process of monitoring and review, rather than the rigid pursuit of a set of targets and activities.

We look briefly at each set of the cyclical steps (summarized in Figure 1) required to develop a sustainable strategy.

Assessing the epidemiological, social and health services context

The first step involves an assessment of the current situation facing leprosy control in a particular country, together with any forseeable changes. The following sets out possible issues for country-based analysis in five broad (inter-related) areas:

- leprosy-related factors;
- health priorities;
- macro-economic factors;
- health sector composition and structure;
- attitudes towards leprosy and leprosy services.

LEPROSY-RELATED FACTORS

There are various factors concerning leprosy which are changing or which are uncertain. This paper does not focus on these, but they are mentioned for completeness and include the following.

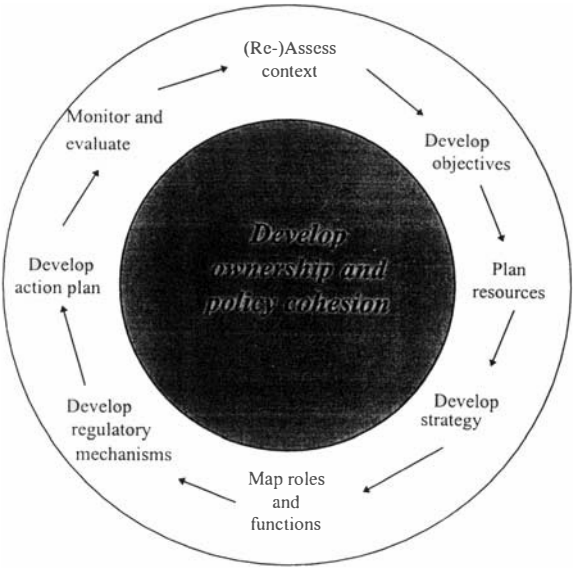

Figure 1. Steps in the development of a strategy.

The formal adoption by the World Health Assembly in 1991 of the goal to eliminate leprosy as a public health problem by the year 2000, and the endorsement of this goal at the first International Conference on the Elimination of Leprosy in Hanoi in1994, provides both opportunities and potential threats to leprosy programmes.[4] While the World Health Assembly resolution has succeeded in putting leprosy elimination on national health agendas, the elimination goal has set up a new dynamic which potentially can divert programmes from the operational challenges of leprosy control. In particular, the choice of a definition of prevalence based on registered cases as a criterion of programme achievement has been criticized by some leprosy experts.[1,5] While the wide use of MDT has certainly reduced the number of cases on treatment, the number of registered cases is not a reliable indicator of disease trends and is easily misused as a measure of disease burden, or as a guide to resource allocation and activity planning. This lack of consensus on the formulation of the goal has created tensions between the donor, technical and research bodies that need to be addressed.

Uncertainty as to the impact of increasing BCG coverage on reducing the future incidence of leprosy,[2] the consequences of changes in the patterns of other diseases such as HIV, and the effects of non-medical factors such as poverty and urban crowding,[3] all make less certain the short-term feasibility of an elimination goal, particularly at the local level, in high endemic countries.

A true reduction in incidence, if not a reflection of less intensive case-finding, will inevitably result in higher unit costs as the proportion of new cases in hard-to-reach subpopulations increases. This discordance between unit costs and progress toward the elimination target may lead to perverse pressures at the operational level if resource planning is too closely tied with numbers of registered cases, and not with the local requirements of improving early case detection and preventing and managing disabilities. The growing recognition of the importance of both functional and social rehabilitation outside long-stay

institutions and leprosaria also has implications for the type and balance of services provided, which may imply additional short-term costs even as case numbers decrease.

HEALTH PRIORITIES

How any particular health problem is viewed has significant implications for the share of what, in most developing countries, are very limited resources available to the health sector. Whilst leprosy may never have been seen as a major priority within national governments, it has nonetheless been relatively successful in terms of fund-raising through the non-governmental organizations (NGO). One effect of the global strategy for elimination is that leprosy is likely to maintain, if not increase, its profile in the short term. However in the medium to long term, a combination of factors may lead to a reduction in its perceived importance. Falling prevalence and incidence will mean that leprosy is perceived more as a rare disease rather than as a public health problem. Furthermore, the growth in relative importance of other health problems, both infectious diseases (in particular HIV, STDs and TB) and non-communicable conditions, will have inevitable implications on the competition for resources.

There are also issues as to *who* sets priorities and on *what criteria*. There are various potentially competing approaches to priority setting which could have implications for the resultant priority given to particular health problems such as leprosy. These include the desire to include greater community participation in priority setting which was a critical component of the Primary Health Care strategy of Alma Ata. Recently, there has been increased emphasis on priority setting based on cost-effectiveness criteria, of which the most explicit is the Disability Adjusted Life Years (DALYs), advocated by the World Bank as a means of measuring the contribution of particular diseases to the overall burden of disease and hence the priority to be accorded to them. The values and assumptions that underpin such approaches may have important implications for leprosy and the resources allocated nationally to it. While the increase in the relative importance of disability versus death, and in the social and economic versus the medical consequences of disease implied by DALYs would logically value leprosy services, the actual effect may be the opposite in some countries if national priorities shift (perhaps under donor pressure) to a narrower range of basic health services deemed cost-effective.

The recent drive to decentralize decision-making and financing has implications for the potential balance between central and local priorities. Again, the impact on leprosy services may depend, for instance, on the mechanisms for financial decentralization, on what conditions may be set by central government to maintain certain services, and on the real opportunities for states and districts to redeploy health staff or reallocate financial resources.

MACRO-ECONOMIC FACTORS

Most developing countries have suffered a severe recession over the last decade, with little prospect of immediate change. This affects the context within which a leprosy strategy has to be developed.

First, and most obviously, the general recession has implications for the level of resources available. For countries which have adopted policies of structural adjustment, this exacerbates the already heavy pressures on the squeezed public sector. This, coupled with

the potential medium-term decline in the perceived importance of leprosy, means that there is likely to be an eventual reduction in public sector leprosy resources.

Second, increasing poverty in sections of society arising both from recession and structural adjustment policies may make these more vulnerable to communicable diseases. Associated with poverty is an increased flow to the peri-urban populations and shanty towns. Continued growth in such densely populated areas may have implications for leprosy transmission. For South East Asian countries, which have managed to attain high economic growth rates, resource constraints are less likely, but the effects of urbanization may still be an issue.

HEALTH SECTOR COMPOSITION AND STRUCTURE

If the 1980s was the decade of Primary Health Care, the 1990s appears to be that of Health Sector Reform. International attention, highlighted, and in part led, by the World Bank 1993 Development Report,[8] has focused on the structure of the health sector in an attempt to attain greater efficiency and responsiveness to public demand. Whilst there is no single Health Sector Reform package, there are common elements which countries are increasingly encouraged to consider. These can be summarized as:

- a conceptual split in the broad functions of health care policy development (including regulation and quality assurance), financing, and delivery of services, with the possibility of different agencies being responsible for different elements;
- a greater role for the non-State sector, including particularly NGOs and the private for-profit sector in the provision of care;
- decentralization of State services to allow greater autonomy and accountability to local areas;
- integration of vertical programmes linked in part to decentralization initiatives;
- the introduction of market approaches to management (performance-related pay and contracting) within the public sector;
- shifts in funding approaches with greater emphasis on individuals (user charges) rather than collective mechanisms (taxation) for financing health care.

The adoption of one or more of these elements of health sector reform is likely to have implications for leprosy programmes which need to be assessed as part of the development of a control strategy.

First, there is likely to be greater diversity of health care providers which may lead to a fragmentation of the sector. This, coupled with decentralization of the state sector, may lead to the danger of less policy cohesion. It may become harder to have an effective leprosy control policy.

Second, the potential reduction in the role of the public sector as a service provider may be mistakenly confused with a weakening of its role in the regulation and financing of health care. Both of these roles are, however, likely to be increasingly important. The increasing diversity of providers suggests the need for *greater* regulation and quality assurance. The particular nature of leprosy also suggests that all aspects of its care should continue to be collectively funded.

Third, and already mentioned, the processes of setting priorities may become more decentralized. This should not be interpreted as a *reduction* in the role of the Centre, but

rather a *change*. There will continue to be a need for a strong central policy framework within which policy towards leprosy is set (this point is discussed further later).

ATTITUDES TOWARDS LEPROSY AND LEPROSY SERVICES

In the development of any strategy, an assessment of attitudes (often now called stakeholder analysis) towards the issue by different groups is essential, though often neglected. Insufficient attention to this critical area can lead to the development of elegant strategies which fail to be implemented due to a misunderstanding or failure to recognize and adjust to opposition to initiatives. Such analysis should identify all the key players in the process including NGOs, the private sector, other programmes of the health service and donors, as well as sections of the community, employers, industry and commerce including, in some countries, the pharmaceutical sector. One set of emerging key groups are leprosy patients' associations operating at both local and national levels.

Developing programme objectives

The second step in the development of the strategy is the setting of clear objectives. There are various issues related to this.

THE ELIMINATION OBJECTIVE

First, there is the country response to the WHO global strategy for elimination. At a basic level, there is the critical question as to whether it is broadly accepted. However, there are other issues, in particular the definition of the elimination goal in terms of the cases under treatment and how small-area denominator populations will be defined in translating the country targets into appropriate local targets. There are also questions as to whether measures of incidence will be used alongside prevalence measures. The development of decentralized priority setting as part of health sector reform may produce significant differences between health districts for the relative priority accorded to leprosy.

BALANCE OF ACTIVITIES

Second, the balance of activity between case detection, treatment and rehabilitation (both functional and social) needs to be reflected in the objectives. Routine programme monitoring should include the proportion of new patients with various disability grades,[7] but as the number of cases decreases, monitoring should focus on delays in case detection and the activities related to the prevention of disabilities.[6] A successful strategy must make explicit these questions of balance between different activities.

WHAT IS TO BE SUSTAINED?

At a broader level, there is the critical need to be clear as to precisely *what* the strategy is trying to sustain. There are at least three possible answers to this, with different implications for the subsequent strategy. The first level concerns the desire for a sustainable *response to leprosy as part of broader health objectives*, i.e. a concern that interest in leprosy does not

diminish. Whilst this is entirely legitimate, particularly from a public health perspective, it is also important that a national strategy recognize that as the incidence of leprosy declines and it attains the status of a rare disease, communities may legitimately see it as of lower priority.

There may also be desire for the sustainability of *dedicated leprosy activities* either in the form of specific specialist services (such as diagnostic services or rehabilitation) or as vertical programmes. This objective, in either form, is hard to justify as a long-term aim, though it may be a necessary component under certain conditions for the attainment of wider health objectives.

Lastly, there may be a desire on the part of particular *leprosy organizations* to sustain their current roles. Leprosy organizations that have existed for some time may find it difficult to recognize when they have, through their own success, reached a situation where their role is either drastically changed or non-existent. It is however important, and the sign of a mature organization, that such organizations do not see their own existence as an objective in itself, but are prepared to reduce their activities or shift priorities. The involvement of leprosy NGOs in TB control or the use of leprosy personnel for TB work, which is happening or planned in several countries as the result of the new priority placed on TB, may be an appropriate response to shifting priorities.

Planning human and financial resources

One of the specific aspects of ensuring the sustainability of any service delivery concerns resources, including human resources. It is essential that any strategy developed is realistic in terms of its ability to raise the resources, both financial and physical, required to implement the strategy.

Whilst international NGOs (INGOs) may have been able to provide a significant proportion of such resources in the past, there is no guarantee that this will continue in the long term, particularly as the leprosy profile diminishes. The public sector's ability, in many countries, to devote resources to particular diseases is clearly limited by macro-economic constraints, the level of priority given (itself a function, among others, of public perceptions) and donor support. Current financing trends, away from tax-funded service provision towards user charges and social insurance, are likely to have implications also for leprosy, given its particular financing characteristics (chronic disease with a long treatment duration, relatively high drug and other treatment costs per individual, danger of defaulting and significant number of unemployed patients). Any strategy needs to examine carefully such issues and, where appropriate, develop arguments for continued public and INGO funding.

The planning and management of human resources is also a key issue. The support of leprosy staff towards changing strategies is likely to be critical to its success and yet a number, particularly those who have specialized in the field for many years, are likely to feel threatened by the changing environment. This may lead to resistance to the strategy. It is important that the development of a broad strategy towards future leprosy services pays particular attention to the implications for staff and any necessary redeployment and or retraining.

Development of a strategy

Once clear objectives concerning leprosy have been set, it is then necessary to develop a

service strategy consistent with these objectives which takes account of the present and likely future external environment. Such a service strategy will specify the level (e.g. first-contact primary care services, general hospital, specialized facility) within the general health service and manner by which particular activities such as case detection or rehabilitation take place. At this stage, the focus should be on services rather than the agencies which will deliver them. The appropriate pattern of service delivery will be affected by a number of issues, including the following.

Reduced case numbers inevitably mean the need for different strategies to target hidden populations. It also raises the critical issue, faced by a number of countries already, as to whether to integrate with other vertical disease programmes or with general health services in order to capture economies of scale and reduce unit costs of service delivery. Such integration does not need to be wholesale and may, for example, be in the area of case detection with separate dedicated services remaining for rehabilitation. Ensuring that sufficient staff with specialized skills for disability management are available may require more flexible working arrangements, whereby certain staff are able to work in more than one health service jurisdiction. Integration may also be phased, with different elements being integrated at appropriate times as community resources for care and social rehabilitation are developed.

Lastly, it is also important to ensure that health sector reform policies of decentralization or integration are not confused with a reduction in the need for a strong technical resource for monitoring and technical policy guidelines. Experience in other fields suggests that decentralization in particular should not imply a weakening but rather a changing of the role of the centre. This may, for example, suggest a move away from managerial control as in vertical programme models, to one of technical leadership or quality assurance. Such a requirement may suggest a new role for former leprosy programme staff and possibly the development of new skills.

Mapping the roles of potential actors in policy, financing and service provision

The preceding step will result in a set of strategies for the delivery of services related to leprosy. From this will result a set of different functions which need to be assigned to different actors in the health care system. Table 1 sets out potential functional roles for the delivery of leprosy services and the likely main actors in the health care sector. The strategy needs to map, from such a set, the appropriate roles for different actors based on their strengths and weaknesses in each functional area. The changing nature of the health sector, and in particular increased emphasis arising from health sector reforms on the provision of services by non-State providers, has implications for this mapping exercise.

Development of regulatory and incentive mechanisms

Following the development of a clear service strategy and identification of roles for different actors, the strategy needs to develop a range of mechanisms to function as incentives and controls which will encourage or discourage the performance of these roles. If the strategy was designed to ensure that the growing diversity of private providers (likely under changing health structures) were able to recognize and refer early cases of leprosy, then appropriate incentives may need to be developed to ensure this. Similarly, if it was felt that an improved

Table 1. Main functions and actors involved in leprosy services

Functions	Potential actors
Policy and regulation • policy development • technical guidelines • quality assurance • regulation • monitoring • surveillance • advocacy • research	*Government* • as policy maker • as financer • as regulator • as health service provider at different levels • specific MOH departments • other government sectors • local councils
Service provision • BCG vaccination • case detection • laboratory services • treatment (including MDT, disability prevention and palliation, management of reactions) • specialist diagnostics • functional rehabilitation (including surgery and prosthesis) • social rehabilitation • health education for patients & families • community awareness • training for public & private practitioners • drug logistics	*NGOs* • local NGOs • international NGOs • volunteer organizations • Leprosy Patients Associations *Private sector* • private hospitals • licensed private practitioners • drug companies & distributors • private pharmacists • traditional practitioners
Financing • government grants • donations (including drugs & equipment) • local fund raising • user charges	*Labour and professional groups* • medical & paramedical associations • employers associations • employee unions *Donors* • local donor • international donors *Others* • technical agencies • health training & research institutes • community and family

and broader information system was required as part of a monitoring process, then legislation to ensure compliance with this may be required.

Action planning and managing change

The implementation of a strategy requires a clear action plan. This needs to specify time-bound activities related to the organization of services and raising of resources. In addition, however, and frequently neglected, is the need for an action plan that deals with the specific issues related to the management of organizational change in organizations such as NGOs whose role is likely to change as a result of the strategy. Managing change is important for at least two reasons. First, the shift in role, unless handled sensitively, may result in resistance to the strategy from key sections within the organization which are anxious, for a wide variety of reasons, to maintain the status quo.

Table 2. Key questions in the development of a sustainable strategy for leprosy services

What is the current and future environment facing leprosy?
- how well are services currently meeting needs?
- how will the country respond to the WHO global strategy for elimination?
- is the balance of activities in the current services appropriate for now and the future?

What are the country's health priorities?
- how are they likely to change in the future?
- what does this mean for leprosy?
- who sets priorities and using what criteria?

What are the prospects for the country's economic situation?
- what are the implications for leprosy?
- what are the implications for general and leprosy-specific resources?

What changes to health sector structures are likely and how would this affect leprosy services?
- are the functional roles (policy, financing and provision) likely to be split?
- what is the role for the non-state sector (NGOs and private-for-profit)?
- what is the likely role for the state?
- is greater diversity of providers likely?
- is decentralization occurring or planned?
- is integration of vertical programmes occurring or planned?
- are changes in funding approaches planned?
- are there adequate regulatory and quality assurance mechanisms?
- is the monitoring and surveillance system appropriate for the changing sector?

What are the attitudes towards leprosy and leprosy services of key stakeholders?
- will they oppose, undermine or support change?

What are the objectives of the leprosy programme?
- what should be the balance of leprosy related activities?
- what are we aiming to sustain?

How will leprosy services be resourced in the future?
What should be the service strategy to meet the objectives?
- what activities should be carried out at what level in the service?
- is (phased) integration of specified elements of the leprosy service with other services appropriate?
- is there a mechanism and provision for adequate technical leadership?
- what should be the balance between case detection, treatment and rehabilitation?

Who are the main actors and what are their appropriate roles?
What regulatory and quality assurance mechanisms are required?
What should be the elements of the action plan for the management of change?
How will the plan be monitored and updated?
How will ownership of the strategy be developed?

Second, staff within such organizations represent an important reservoir of expertise and experience which can be tapped for the benefit of other areas. For example, the experience of leprosy organizations may be well directed towards the strengthening of TB programmes, or more general disability services.

Re-evaluating programme objectives and service delivery organization

The development of any plan for sustainability requires, as an essential element, the development of a *continuous and explicit process of monitoring and review*. This is critical to ensuring that progress towards the achievement of objectives is being made. As such, it

becomes a tool for identifying problems early enough to rectify them. Such a process is also essential to predict any likely changes in the external environment and their potential effects on the strategy in order that any necessary changes to the strategy can be made. Sustainability will depend heavily on the ability to look forward, combined with a willingness to adapt flexibly to potential changes such as those likely to result from changes in the health sector.

Achieving ownership and policy cohesion

Lastly, and closely related to the previous element, is the need to ensure that there is broad ownership of the strategy both within the leprosy-specific organizations and, equally important, outside. Strong policy cohesion is particularly necessary in a situation where there is increasing sectoral fragmentation.

The development of broad ownership is most likely to be successful if involvement in the process of building a strategy starts from the beginning. Consultation amongst outside groups on polished strategies produced by a small internal group is often treated as tokenist, and rarely produces as deep a sense of identification as when there has been broad involvement in all stages of the overall strategic development.

It is important to recognize, however, that involvement in the development of a strategy will not necessarily lead to support for it. There may be groups or individuals who oppose the strategy either on genuine technical grounds or because they have a particular vested interest which may be challenged. Under such circumstances, an advocacy role to challenge such opposition may also be required as part of the strategy.

Government has a unique role to play in providing policy leadership, supported where appropriate by the specialist leprosy organizations. Mechanisms for ongoing co-ordination, once a strategy has been agreed, are also critical.

In conclusion, the preceding has set out a number of issues that face national leprosy programmes, with particular emphasis on the changing nature of the health sector as they enter the 21st century. It has not attempted to provide prescriptions which must be context specific. Instead, it has provided a set of questions that need to be answered in the development of a strategy for the sustainability of appropriate leprosy services. These key questions are summarized in Table 2.

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Fine-needle aspiration cytology of lepromatous leprosy

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Summary A prospective study correlating cytopathology with clinical morphology and histopathology in 22 patients with lepromatous leprosy was performed. Aspirates were taken from skin lesions in all patients. Lymph node aspirates were also performed in four patients with lymphadenopathy. Fine-needle aspirates yielded sufficient cellular material with excellent preservation of morphological detail. Diagnosis and correlation with bacillary index, clinical and histopathological findings was possible in all patients. In addition, the two patterns, partial and diffuse, of lymph node involvement could be recognized. Fine-needle aspiration cytology is a simple method for the laboratory assessment of leprosy.

Introduction

The seminal observations of Marian Ridley[1] on slit smears emphasized the interpretation of the cellular exudate in conventionally stained Zeihl–Neelsen (ZN) smears. In previous papers,[2–4] we expanded on this concept by studying the morphological details of the cellular exudate in MGG stained fine-needle aspiration (FNA) smears and found that precise recognition of cell type was an aid in the appropriate placement of the lesions in the Ridley–Jopling (RJ) scale.[5] We also observed that FNA smears, in contrast to slit skin smears, were free of confounding epidermal squamous cells and therefore better suited for evaluating cell morphology.

In this paper, we present details of new cytological findings on fine-needle aspiration in lepromatous leprosy (LL). The relationship between the cellular infiltrate and the bacillary index (BI) at this end of the spectrum and the cytomorphological correlation with clinical subtypes in 22 patients with LL, viz. macules, plaques and nodules, are defined. Additionally, definitive cytopathological identification of two patterns of lymph node involvement has been described.

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Materials and methods

Twenty-two patients clinically diagnosed with LL presenting with a variety of skin lesions ranging from macules (4), ill defined infiltrated plaques (11) and nodules (7) were studied. Six patients, including four with erythema nodosum leprosum (ENL), had received standard multibacillary multidrug therapy for periods of up to 3 months. Multiple site aspirations of skin lesions and earlobes were done in three patients. In the remainder, a single aspiration was performed. In addition, FNA of cervical (3) and axillary (1) lymph nodes was carried out.

The diagnosis and classification in the RJ scale was based on clinical examination by a dermatologist (S.N.B.) using standard criteria.[6] All patients were subjected to biopsy from the same lesion which had been sampled by FNA. Biopsies were evaluated and classified according to the histological criteria established by Ridley.[7] FNA smears were evaluated independently of the biopsy findings, and the results were classified using the cytological criteria laid down in our previous study.[4]

Smears were specifically evaluated for cellularity (high, moderate, low), morphological details of macrophages (foamy, with negative images), accompanying inflammatory cells (lymphocytes, neutrophils, eosinophils) and BI. Negative images, seen in MGG-stained smears, were cleft-like unstained spaces[8] corresponding to globi seen with modified ZN stain.

The procedures of FNA/cytopuncture have been described in standard textbooks of cytopathology.[9] A syringe holder is commonly advocated as an aid in creating negative pressure while aspirating. However, we have dispensed with this device and employ a 'hand-held' method, the negative pressure being created by lifting the piston with the thumb. The quality and quantity of material obtained were comparable to aspirations performed using a holder. A further modification of the FNA procedure was applied to skin lesions. The lesional skin was pinched, as done for the slit-smear technique, between thumb and forefinger of one hand for about 30 s to blanch it, while aspirating with the other. This ensured a cellular aspirate relatively uncontaminated with blood. The aspirated material was expelled onto glass slides; the flat of another slide being used to smear the material.

All smears were air-dried and stained with MGG and modified ZN stains. Cytological criteria used in the previous study[4] were used to judge the adequacy of the smears and make a diagnosis.

Results

CYTOPATHOLOGY

In all 22 patients, the aspirates were adequate with a dispersed cell population. Bacillary indices were 5+ to 6+.

The cytological features in skin lesions in MGG-stained smears were as follows (numbers in parentheses represent numbers of patients):

Macular LL (4)

Poorly cellular smears.
Occasional macrophage with negative images.
Few lymphocytes.

Plaques and nodular LL (14)

Cellular smears.
Abundant foamy macrophages (AFB) in a fatty background with intra- and extracellular negative images.
Few lymphocytes.

Erythema nodosum leprosum (ENL) (4)

Cellular smears.
Foamy macrophages in a background of numerous intact and fragmented neutrophils (Figure 1).
Numerous fragmented AFB present both intracellularly in macrophages and rarely, in neutrophils; and extracellularly.

Lymph node aspirates (4)

Two distinct patterns were seen:

Pattern I (3)

Cellular smears.
Single or small groups of macrophages in a background of reactive lymphoid cells. The macrophages were foamy and had negative images and intracytoplasmic 'blue' globules

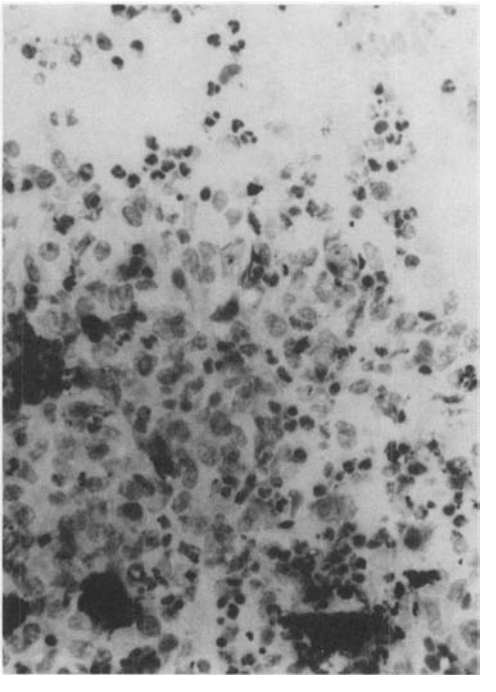

Figure 1. Erythema nodosum leprosum: neutrophils and macrophages with pale, vesicular nuclei. MCG × 400.

(Figure 2) surrounded by haloes. These globular structures corresponded to globi seen with the ZN stain.

Pattern II (1)

Highly cellular smears. The predominant, almost exclusive, cell type was macrophages, similar to those seen in pattern I. Interspersed between these were a few lymphocytes (Figure 3).

HISTOPATHOLOGY

In 15 patients the histopathology correlated well with the cytomorphology. In seven, using morphological criteria alone, the histopathological diagnosis was leprosy; however, the classification in the RJ scale was discrepant by two positions, i.e. BB-BL. These patients could correctly be reclassified as LL only on the basis of high BI in Fite-stained sections. In three instances, repeated Fite stain was required for positive results.

Discussion

In this study, all the FNA smears from macular lesions were poorly cellular, whereas plaques

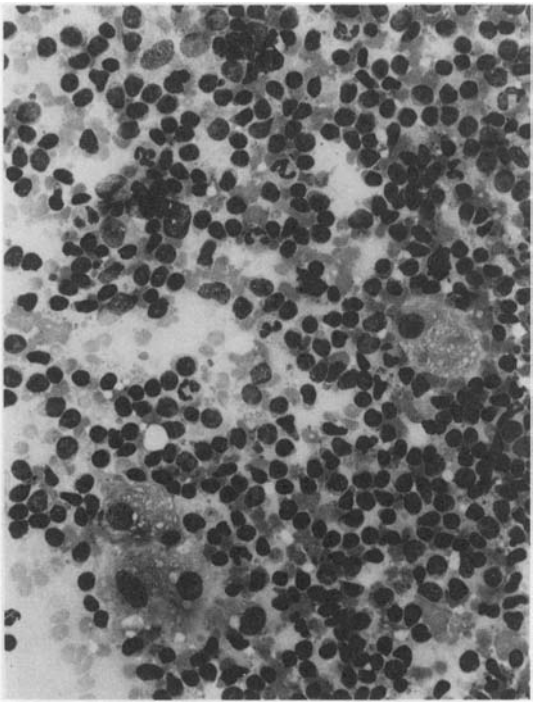

Figure 2. Partial replacement of lymph node: single, dispersed macrophages with negative images in a reactive lymphoid background. MGG × 100.

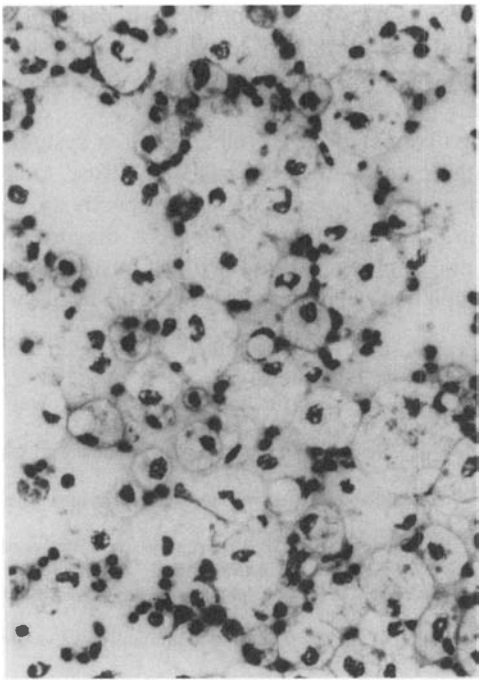

Figure 3. Complete replacement of lymph node: diffuse population of foamy macrophages. MGG × 100.

and nodules had heavily cellular smears. These findings support the observation that cellularity of smears in FNA of inflammatory lesions is proportional to the amount of the infiltrate per unit volume of tissue. This, in turn, correlates with the clinical and histopathological morphology of the lesion, e.g. flat, or macular lesions have very little infiltrate, while lesions with progressively larger amounts of infiltrating cells are raised, i.e. papules, plaques or nodules.

Dispersed macrophages are seen in plaques and nodules of LL. Negative images or foamy cytoplasm correspond to high bacterial load. Mycobacteria do not stain with the Romanowsky dyes. The resulting unstained negative images have been described in other species of the genus *Mycobacteriacae*.[8,10] *Mycobacterium leprae* are also visible as elongated unstained clefts in the cytoplasm which correspond to bundles of lipid rich bacteria.[2] The cytological findings are sufficient independently to categorize the lesion as lepromatous. The AFB findings on the modified ZN stain correlate so well with the cell morphology on MGG stained smears that the two serve as controls to complement each other.

The presence of neutrophils, and occasionally eosinophils, with foamy macrophages points to ENL. Negative images are usually absent because the AFB are fragmented.

Architectural relationships of the inflammatory infiltrate to the various cutaneous structures are undoubtedly better appreciated in histopathological sections; however, cytologic smears are ideal for evaluation of individual cell morphology. Moreover, acid-fast bacilli are more often demonstrable in smears than on tissue section, where the stain is liable, for unexplained reasons, to fail on occasion.[7] Others find biopsies better than slit-skin smears, particularly for paucibacillary leprosy.[11]

The diagnosis of LL in FNA smears is not a problem. Because of the high bacterial load in this type of disease, acid-fast bacilli are easy to find. By establishing distinct cytomorphological correlates to the clinical spectrum, FNA cytology offers a less cumbersome method for calibrating the disease.

There is generalized involvement of the lymphoreticular system, particularly the lymph nodes, in LL. Two histopathological patterns, partial and diffuse, have been described.[12] This is reflected in the cytomorphology as patterns I and II, respectively. Lymph node biopsies are occasionally performed in LL, particularly when the diagnosis is missed on clinical examination, the lymph nodes being excised with a mistaken diagnosis of lymphoma. Accurate recognition of lymph node aspirates can obviate the need for biopsy in this situation.

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Progress in research towards a world without leprosy. Report of a WHO meeting in Ethiopia, February 1998

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Summary A UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases meeting to discuss the future role of biomedical research in leprosy, was held at the Armauer Hansen Research Institute in Addis Ababa, on February 27 and 28, 1998. This was attended by more than 20 scientists from 10 countries, who met to discuss progress towards a world without leprosy.

Leprosy research in the context of immediate leprosy control needs

The meeting was opened by the Chairman of the Board of Trustees of AHRI, who stated that despite the enormous progress made in leprosy control over the last 15 years, new cases of leprosy were still being detected, and that there was a real danger of leprosy research becoming marginalized in favour of TB research.

Dr D. B. Young (St. Mary's Hospital, London) reviewed the challenge that the success of chemotherapy poses for leprosy research. It is important that priorities are set for leprosy research which will support the leprosy elimination programme. These would include the development of tests for leprosy exposure (both skin tests and simple blood tests), tests for the prediction of reactions and better means of prevention of nerve damage. In the longer term, research could provide tools for surveillance of transmission, reactivation of disease, detection of non-human sources of infection and emergence of drug-resistant leprosy strains. Active preventative interventions such as chemoprophylaxis or vaccination of 'at risk' groups, identified by further research, would further reduce the incidence of leprosy. The lessons learnt from leprosy will not only benefit the patient, but provide further insights into the basic process of bacterial genetics, neurobiology and immunology.

Professor P. J. Brennan (Colorado State University) reminded the meeting of the priorities for leprosy research set at a meeting held in Bangkok in 1996, and also by the 7th WHO

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Expert Committee on Leprosy, and the ILEP Medical Commission. These meetings and groups addressed leprosy research from differing viewpoints, including those of individuals working on the genome and immunology of leprosy, the field workers who need tests for detection of early infection, and those who are involved in patient care and management. The purpose of the present meeting was to define further the agenda for biomedical research and to review progress toward the goals set in these previous meetings. The need to conserve resources such as people, laboratories, materials and techniques, training, and funding in leprosy research was also highlighted.

Dr S. K. Noordeen (WHO, Geneva) reviewed the role of research in the fight against leprosy over the past 25 years and suggested three priority areas from the perspective of the leprosy elimination campaign. These were a better understanding of and prevention of reactions and nerve damage, the detection and diagnosis of early leprosy, and the development of simple tools to detect drug-resistant leprosy. The emphasis may need to shift from the broad application of basic care to leprosy patients to a better management of the complications that leprosy causes in a large proportion of patients during and after chemotherapy. Dr Noordeen expressed his optimism that, despite the shrinking size of the leprosy research community, these new tools will be forthcoming in the short term.

Dr W. C. Smith (ILEP, London) gave a view of research needs from an epidemiological perspective. He stressed the need to maintain the dialogue between research scientists, control programmes and epidemiologists and reminded the audience of the difficulties of applying new tests into leprosy care when vertical leprosy programmes have largely been integrated into primary health care services. A number of the current priorities for epidemiological research have biomedical implications. These include the need to measure and monitor leprosy incidence by a more accurate surrogate measure than the new case detection rate, which can reflect the intensity of the leprosy control effort rather than actual disease transmission. The development of simulation models to predict future trends in leprosy incidence under varying scenarios, the evaluation of the implication of detection of *Mycobacterium leprae* in nasal swabs from unaffected individuals and the definition of high risk communities who would benefit from active prophylactic regimens are all areas which require new biomedical tools.

Serology

Dr P. Klatser (Royal Tropical Institute, Amsterdam) reviewed recent serological data from work in Indonesia, which indicate that household contacts of leprosy patients who are seropositive for IgM anti-phenolic glycolipid I (PGL-1) antibodies have an eight-fold higher risk of developing leprosy. Dr Klatser also presented data from a 25-year survey of leprosy cases in an Indonesian village which showed that almost all of the incident cases had some kind of contact (household, work or social) with active leprosy cases. This group of 'contacts' will tend to become the dominant group from which new cases arise as the incidence of leprosy falls and serology can be a valuable tool to identify those at highest risk. Moreover, measurements of anti-PGL-1 antibodies can now be done using a simple 'dipstick' which is cheap (costing about US$1/test), reliable, and well suited to field use. Operational studies in various centres to test the predictive value of the dipstick test should be started shortly. The identification of these seropositive contacts has the potential to identify most of the incident cases of leprosy at a subclinical stage of the disease.

Dr R. Hussain (Aga Khan University, Karachi) emphasized the important information that serological measurements in leprosy patients can give to predict the severity of disease, the response to chemotherapy, the onset of reactions and relapses. The profile of antibody classes and subclasses found in leprosy is not characteristic of the Th2 activation seen in allergic disease or helminth infection, as it is IgG1 and IgG3 antibodies, rather than IgG4, that correlate with the bacterial index. Areas needing further research include the role of cytokines in antibody class and subclass switching in man, and the interaction of these IgG subclass antibodies and immune complexes with macrophage Fc receptors. Many leprosy contacts make an early antibody response to *M. leprae*, and the precise pattern of antibodies and cytokines induced may be predictive of the eventual development of infection, or protection.

Gene amplification techniques

Dr S. Cole (Institute Pasteur, Paris) reviewed the applications of gene amplification techniques to leprosy. Despite grandiose claims for applications of polymerase chain reaction (PCR) technology to leprosy, only a few well conducted studies have assessed the reliability of PCR in detecting leprosy in clinical samples. A multi-centre study in 1994 showed good sensitivity, specificity and reproducibility, using a standardized protocol based on the RLEP sequence. Dr Cole suggested three applications of this technology—to the diagnosis of rare or difficult cases, the diagnosis of drug resistance (to current and future anti-leprosy drugs, such as rifampicin, ofloxacin and minocycline), and the definition of relapse as reactivation or new infection by means of molecular strain typing of *M. leprae* in clinical samples. A further application presently under investigation is the nasal carriage of *M. leprae* by unaffected persons. Studies in India and Ethiopia find a higher rate of nasal *M. leprae* carriage (4·7%) than predicted from the prevalence rates (W. C. Smith) and such carriers may have a higher risk of developing clinical leprosy.

Skin tests and simplified whole blood tests to measure leprosy exposure

Dr H. M. Dockrell (London School of Hygiene & Tropical Medicine) described the first of two new initiatives which hope to develop new leprosy-specific skin test reagents. Four centres in leprosy endemic countries have been testing 193 peptides for their ability to induce T cell proliferation and IFNγ secretion in peripheral blood mononuclear cells (PBMC) from leprosy patients and healthy leprosy contacts, in a study initiated by the WHO IMMYC Steering Committee. These peptide sequences (15 amino acids in length), which were derived from the genome sequencing data now available for *M. leprae*, have been selected from known and unknown proteins which appear leprosy-specific and contain putative HLA-DR binding motifs. Initially, the peptides were tested in 19 pools, each containing 10–11 peptides, most of which elicited strong T cell responses. The individual peptides from eight pools will now be tested, with the hope that a highly leprosy-specific peptide based diagnostic test will result.

Dr P. J. Brennan (Colorado State University) discussed another approach to the development of a leprosy-specific skin test, involving the fractionation of the leprosy bacteria into cytosolic and cell-wall protein fractions, free of immunosuppressive lipid and carbohydrate moieties. The production of these fractions under good manufacturing practice

conditions has been achieved and phase I safety trials in the USA will occur in the autumn of 1998; following certification by the Food and Drug Administration the fractions should be used as skin tests in the field in early 1999. Even if these reagents are not suitable for individual diagnosis, they may be very valuable for epidemiological studies on trends in leprosy transmission, and with further fractionation, may also yield a highly specific diagnostic skin test.

Simplified blood cultures using unfractionated whole blood stimulated by the new leprosy antigenic fractions have been shown to give proliferation and interferon-gamma production equivalent to that shown by peripheral blood mononuclear cells (Dr H. M. Dockrell, London School of Hygiene & Tropical Medicine). The new fractions appear more potent than earlier *M. leprae* sonicates, but further fractionation may be required to achieve the required specificity, as both human and guinea pig experiments indicate that at present the fractions are cross-reactive with antigens in *M. bovis* BCG and *M. tuberculosis*. Studies in TB patients have shown a good correlation between PDD-induced interferon-gamma production in whole blood cultures and skin test reactivity to tuberculin (Dr R. Hussain, Aga Khan University). These simple blood tests may as easy to use in the field as skin tests, as although a basic laboratory is needed, the subject does not need to be recalled for the skin test to be read.

Dr Sengupta (JALMA, Agra, India) and Dr Jim Krahenbuhl (National Hansen's Disease Center, USA) led to a discussion on the role of laboratories in the field diagnosis of leprosy. It is not clear how necessary central laboratories, run by national control programmes, are for the effective running of control programmes, but there is clearly a need for continued training and quality control as leprosy moves towards the post-elimination era. It is important that the skills involved in leprosy diagnosis should not be lost, as even in non-endemic countries occasional leprosy patients need to be accurately diagnosed. As leprosy cases decline, it may also be appropriate to establish central banks of leprosy sera, biopsies, or cells, as a resource for the research community.

Leprosy reactions and nerve damage

Dr G. Kaplan (Rockefeller University, USA) introduced the second day's programme, on future directions in leprosy research, by highlighting some of the unique features of leprosy. These include the development of reactions and nerve damage, which can occur after the completion of treatment and microbiological 'cure'. Nerve damage and reactional complications will remain a problem for leprosy patients even in the post-elimination era. The new knowledge available from the *M. leprae* genome should now allow the identification of the unique features of *M. leprae*. It should also be possible to exploit recent developments in neurobiology and immunology to identify those individuals who will develop nerve damage. Genetic analyses will also facilitate the prediction of which patients are at risk of developing reactions.

Dr E. Sampaio (Fundacao Oswaldo Cruz, Rio de Janeiro) reviewed recent work on the pathology of erythema nodosum leprosum (ENL), mediated by the cytokine tumour necrosis factor alpha (TNFα). High levels of serum TNF have been found to be predictive of ENL reactions and are possibly associated with the development of disability. TNFα is produced by monocytes and macrophages, and both IFNγ and membrane contact between lymphocytes and monocytes increases TNF production. There are also genetic polymorphisms in the TNFα promoter region which may affect an individual's capacity to make TNF. Further work

on the regulation of TNF, its role in nerve damage and the identification of patients at high risk of reactions is underway.

Dr G. Kaplan (The Rockefeller University, New York), discussed the mechanisms of ENL, and its treatment with thalidomide. Thalidomide has been known for many years to be effective as a treatment of ENL, but the mechanism of its action was not clear. As high levels of TNFα are present in the plasma of patients with ENL, it was possible that thalidomide might affect TNFα production. Thalidomide has been shown to inhibit the production of TNFα, which is found at high levels in the plasma of ENL patients, but not that of other cytokines such as IL-1, IL-6 or GM-CSF. Since TNFα can reproduce many of the systemic symptoms of ENL if injected into humans or animals, this cytokine has been proposed to play a central role in the pathogenesis of ENL. TNFα also plays a role in protective immunity: for example, it is required for granuloma formation, and it is therefore both helpful and harmful to the patients. Recently, thalidomide has been shown to induce stimulation of T cells, and in particular, the CD8+ T cell subset. It is hypothesized that thalidomide modulates the host response to mycobacterial infection not only by inhibiting TNFα production but also by stimulating T cells to produce more of the Th1 type cytokines IL-2, IFNγ and IL-12, thus resetting the extreme Th2 cytokine profile of ENL towards a Th1 cytokine profile. Recent work has led to the identification of thalidomide analogues which have enhanced TNF inhibitory activity, but which appear to lack the teratogenic action of thalidomide. It is hoped that some of these new thalidomide analogues might provide non-teratogenic treatments for both ENL and reversal reactions within the next 10 years.

Dr D. Lockwood (London School of Hygiene & Tropical Medicine, UK) discussed new insights into the mechanisms of nerve damage in leprosy. There are at least three types of nerve damage, the acute reactions that occur in reversal (type 1) reactions and ENL, chronic neuritis, and quiet nerve paralysis which may account for the majority of nerve damage. Leprosy antigens can be detected within the nerve granulomas and Schwann cells, and may persist even following the completion of treatment. Both CD4 and CD8 T cells are present within affected nerves, with BT patients in reversal reaction showing the highest CD4/CD8 ratio. Both TNFα mRNA and protein can be detected within nerve granulomas during reversal reactions. There are also increases in the expression of adhesion molecules, inducible nitric oxide synthase (iNOS), IL-2R and IFNγ, suggesting stimulation of Th1 T cells. The need for a more rational treatment of type 1 reactions was stressed as more than one-third of patients do not respond to corticosteroids. New drugs for trial in the treatment of reversal reactions include azathioprine and cyclosporin A, which are available now and the thalidomide analogues, TNFα antibodies and inhibitors of iNOS which should be available for testing in the future. Future research into the molecular pathogenesis of reversal reactions and the reliable measurement of nerve damage should lead to more effective treatments for type 1 reactions, which will result in reduced disability in leprosy.

Dr Rambukhana (The Rockefeller University, New York, USA) discussed the mechanism of entry of *M. leprae* into Schwann cells. *M. leprae* was shown to bind to laminin, present in the basal lamina of Schwann cells, but not to fibronectin. Laminin exists in a number of isoforms, and it is the laminin-2 form ($\alpha 2\ \beta 1\ \gamma 1$) which is expressed by cultured Schwann cells. Within the laminin-2 $\alpha 2$ chain, the G2 domain is critical for *M. leprae* binding. If the $\alpha 2$ chain of laminin-2 is missing, as in the *dy/dy* mouse model of muscular dystrophy, *M. leprae* binding, and the subsequent rearrangement of the cell cytoskeleton to allow bacterial entry, do not occur. This is the first major advance using tools of molecular and cellular biology to understand this unique feature of the leprosy bacteria. Further work may provide new

therapeutic strategies by blocking *M. leprae* uptake with competitive peptides, or other blocking agents.

Drug resistance

Dr P. Roche (Anandaban Leprosy Hospital, Kathmandu) discussed drug resistance in leprosy. The current prevalence of resistance to the three drugs used in the MDT regime is unknown but is thought to be low. Relapses after MDT treatment are rare and seem to be the result of reactivation of drug-sensitive organisms; thus retreatment with MDT is usually successful. The mouse foot pad assay, despite being costly and time-consuming, remains the 'gold standard' for demonstrating drug resistance. New insights from genetic studies have allowed the development of a new gene-based method to detect rifampicin-resistant leprosy. Because of the importance of rifampicin to the success of MDT and rifampicin/ofloxacin/minocycline (ROM) regimens, the monitoring of rifampicin resistance by gene-based assays is considered vital. A pilot study, funded by IMMYC has commenced in India and Nepal to measure the prevalence of rifampicin resistance among MDT relapses using a PCR based line-probe assay developed by Dr S. Cole (Institut Pasteur, Paris). This study will investigate the relationship between the detection of rifampicin resistant mutants in such patients and the response to (re)treatment. The sequencing of the gene associated with rifampicin resistance (rpoB) from all these *M. leprae* isolates may also identify other mutations which may give rise to rifampicin resistance.

Genomics

Dr Stewart Cole (Institut Pasteur, Paris) described the latest developments in the *M. leprae* genome sequencing project. Genomics, the study of the genome, aims to identify all the genes and regulatory sequences that are present, and deduce the functions of these genes using bioinformatics. Since an ordered library of *M. leprae* cosmids became available in 1991, sequencing of the *M. leprae* genome has been underway at the Pasteur Institute, Genome Therapeutics Corporation and the Sanger Centre, and 95% of the genome has now been sequenced.

The preliminary analysis of the genome reveals some surprises, particularly as compared with the recently completed *M. tuberculosis* genome. The *M. leprae* genome is 50% smaller than that of *M. tuberculosis*, and many of the genes present in *M. tuberculosis* have been lost from *M. leprae*. A broad classification of the genes of *M. leprae* into four groups reveals about 1100 house-keeping genes, 300 genes which encode proteins common to other mycobacteria, 50 genes for exported proteins, which would include those inducing protective immunity, and about 60 unique proteins which will be useful for understanding the biology of *M. leprae* and for use as leprosy diagnostics. Data from the genome sequencing initiative are available to investigators via the MycDB database, both in a 'stand alone' UNIX format and on the World Wide Web. The MycDB database has links to other databases such as SwissProt, EMBL and Medline. This valuable database needs to be maintained and improved to gain the maximum benefit from the *M. leprae* sequencing data.

Dr Antoine Danchin (Institut Pasteur, France) who has worked on the *B. subtilis* genome, talked about the potential of such genome information. Genome mapping is an increasingly

common activity in microbiology, with the publication almost monthly of complete genomes from bacterial species; about 300 are expected to be completed over the next decade. Virulent bacteria have often captured extra genetic material, the genes for which may be located on pathogenicity islands. Bacteria can also occupy different biotopes, and have distinct survival strategies, which can lead to individual features or 'styles'. Much information will be obtained by 'in silico' experiments, in which sequence data are analysed for patterns of codon usage, GC content and the distribution of coding regions, TA/GA dinucleotides and the predicted isoelectric point (pI) of encoded proteins. The structure of the genome reveals much about the adaptive biology of the organism and comparisons with other mycobacteria can lead to much useful information on drug targets and immunology.

New vaccines for leprosy?

A round table discussion on the future of leprosy vaccines was led by Dr J. Krahenbuhl, (National Hansen's Disease Center, USA). The large Karonga Prevention Trial in Malawi demonstrated that BCG vaccination induced 50% protection against leprosy, and that the addition of killed *M. leprae* to BCG did not enhance this protection. It seems unlikely that much effort will now be put into the development of new anti-leprosy vaccines, but new vaccines against tuberculosis are in development, and these might confer even greater protection against leprosy than BCG. It will therefore be important to test such candidate tuberculosis vaccines for their ability to protect against *M. leprae* in the mouse foot-pad model. From the field perspective, Dr Noordeen confirmed that it would now be too costly to implement a total coverage vaccine against leprosy, but vaccines with protective efficacy against leprosy could be important as adjuncts to chemotherapy, or for use in high risk groups or areas.

Short term and long term priorities for leprosy research

Dr P. Brennan (Colorado State University, USA) then summarized the priorities identified for leprosy research in both the short term (the next 5 years) and long term (5–10 years). In 10 years time, leprosy will occur at low prevalence especially in isolated communities beyond the reach of control programmes. There is therefore still a need to train new people who will contribute to the final eradication of leprosy as a public health problem. Our lack of understanding about the transmission of *M. leprae*, and whether it has an environmental reservoir, means that even as the number of cases of leprosy fall, there is a real need for continued surveillance. New tools which will have direct practical benefit for the control programme include tests to identify 'at risk' contacts by serology, the use of PCR to detect rifampicin resistance, the development of skin tests and whole blood tests to measure leprosy exposure and new treatments for leprosy reactions. It is also important that facilities such as the mouse foot pad laboratories, slit skin smear services and banks of clinical specimens should be preserved.

Overall, leprosy research is currently in a healthy state, with strong research groups and leadership in both research and control areas. New leprosy research is not required for the current leprosy elimination programme, but it can and should play an important role in the post-elimination era by providing new field-applicable tools to identify areas or groups at

high risk, and in monitoring progress towards the eradication of this debilitating disease. These may include new dipstick assays for antibodies or leprosy antigens, whole blood assays for cellular responses, specific skin test reagents, and PCR tests for the detection of nasal carriers of *M. leprae*. The new knowledge available from the *M. leprae* genome will also lead to new insights into why *M. leprae* behaves as it does, with its predilection for nerves, and its capacity to induce anergy in a proportion of those it infects. Understanding why some individuals develop reactions, and how these can be controlled will also provide new information on the molecular interactions occurring in immunopathology. These challenges will keep scientists absorbed by leprosy and producing insights which will have a fundamental impact in bacteriology, neurology and immunology.

Conclusions and recommendations

1. The decline in leprosy patients and the commitment to leprosy elimination as a public health problem have been matched by a decline in leprosy research, with the majority of active researchers turning to tuberculosis research. Nevertheless, there is a strong core of active investigators, central laboratories, and shared resources. The retention of this pool of expertise and resources is crucial.
2. The discussion of research priorities should be a continuing proposition, and flexible short-term (5 years) and long-term (10 years) global research plans should be defined.
3. In immediate terms, it is unlikely that biomedical research will help in leprosy control. Rather, the agenda should include alternative measures for leprosy control in support of current efforts and bearing in mind the possibility of a breakdown in the elimination program in future years. Control programs should recognize the considerable achievements in research, particularly in diagnosis, and incorporate them into leprosy control measures, especially to the detection of leprosy in isolated populations in the post-elimination period.
4. The full sequence of the *M. leprae* genome and the closure of gaps is a priority in the short term. A concerted effort to express, purify and implement for diagnostic purposes, the full range of *M. leprae*-specific protein and the family of export proteins is a priority. This effort will require co-operation among several global laboratories and sizeable funding.
5. Considerable progress has been made in the simplification of serodiagnosis and application to important clinical issues. Efforts should continue to enhance sensitivity to allow better diagnosis at the tuberculoid end of the disease. Likewise, with PCR and whole blood assays for cytokines. Skin test antigens offer the best prospect for large-scale monitoring of leprosy in a community, and their continuing development is a priority.
6. The preservation of central global leprosy research laboratories is a priority to allow the preservation of expertise and resources for technology such as acid fast staining, skin slit smear, ELISA, dot-blot, PCR, mouse footpad, cytokine profiling, and banks of bacilli antigens, antibodies, cosmids, databases, etc.
7. The continuation of research on the treatment of neuritis and reactions and on the early diagnosis of reactions, is a priority.

In the long term:

1. The preservation of expertise, resources and fundamental research on the immunology of

leprosy, the molecular and immunological basis of the tropism of *M. leprae* for Schwann cells and subsequent damage, the physiology and genetics of the organism, are all crucial. The polarity of the immune response seen in leprosy requires understanding.

2. Experience with tuberculosis has taught us the consequences of the dismantling of specialized research on a major disease. Hence, the preservation of personnel, laboratories and resources is important.
3. The complete eradication of leprosy is unlikely through present measures. The development of a vaccine will always be a priority. However, the plan should be more passive, waiting to see what basic research on the immunology and bacteriology of leprosy will bring, in addition to exploiting the extensive research on tuberculosis vaccine development.

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Future role of leprosy training and/or research institutions. ALERT, February 25–26, 1998

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This meeting, co-ordinated by WHO and ably chaired by Dr Joseph Kawuma, brought together doctors, scientists and managers from over 20 institutions in five continents, involved in leprosy work. The objectives were to review the current activities of specialized leprosy institutions in the light of changing needs; to identify feasible activities for the next 10 years; and to identify leprosy training and research needs for the future.

Ten of the major institutions made brief presentations of their current activities. These were: ALERT, Addis Ababa, Ethiopia; Marie-Adelaide Centre, Karachi, Pakistan; Alfredo da Matta Institute, Manaus, Brazil; SLRTC, Karigiri, India; JALMA Institute, Agra, India; Leonard Wood Memorial Centre, Cebu, Philippines; CLTRI, Chengalpattu, India; ILAD, Dakar, Senegal; Institut Marchoux, Bamako, Mali; and Institute Lauro de Souza Lima, Bauru, Brazil.

There were then two presentations aimed at setting the scene for the discussions. Dr James Krahenbuhl presented a paper by Dr R. R. Jacobson, Director of GWLHDC, Carville, who was not able to attend. He began with a few words about Carville, which, contrary to rumour, is not closing but is relocating to Baton Rouge – the centre remains an active department of Louisiana State University.

Dr Jacobson argued that leprosy will be with us long after the year 2000 and some expertise must be maintained in most areas beyond that date. Future activities will depend on the workload, but leprosy should be covered in all medical and paramedical training and in the appropriate textbooks. The general public should also be kept informed about leprosy through the mass media.

Looking more specifically at workload, Dr Jacobson suggested that with more than 100 new cases per year, a country might consider maintaining regional experts and a referral facility (probably part of a general hospital) for in-patient care of complicated cases. With more than 1000 new cases per year, more than one referral centre would be needed and the whole programme should be regionalized under national guidelines and oversight. This situation already exists in the United States, which may be a useful model for other low endemic countries.

Although any centre could, in theory, provide training and research, it is advisable to have at least five or six world centres of expertise for training, research, rehabilitation and advice on complex issues.

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The second presentation, by Dr Kawuma, Deputy Director of the Ugandan National TB/Leprosy Programme, looked at the relationship between institutions and national programmes. There are significant areas of overlap in both objectives and activities, but they have complimentary roles and responsibilities, with differing expertise and constraints. Even with leprosy elimination and integration, many on-going activities will be benefited by active institutions. Training has often in the past been only loosely connected to the needs of the national programme, so there is a need for better communication between the parties involved. Programme managers are usually not in a position to undertake basic research, but even health systems research would be better co-ordinated by a research institution.

In discussion, Dr Feenstra emphasized that integration did not mean the removal of specialists, but on the contrary, should make other specialists (for example, rehabilitation experts) more available to leprosy patients. Dr Chiang asked whether any success in integrating specialist leprosy services can be quoted. Dr Noordeen suggested that general staff are not reluctant to treat leprosy patients, but we are reluctant to train and hand over the work to them.

Four discussion groups were established, with initial presentations in the plenary session to set the agenda for each group. Each group then met for two sessions before reporting back to the meeting; final conclusions and recommendations were drawn up.

Group A: training

Dr Groenen asked the group to focus on the training needs of control programmes, the end-users of training, given that the current trend in prevalence means that many peripheral clinics will treat one or two cases a year, at most.

The group concluded that after confirmation of the diagnosis, the peripheral health worker should be able to administer MDT and/or steroid therapy. He/she should then be able to carry out case-holding and assist the patient in preventing further damage to hands, feet and eyes. The peripheral health worker should also be able to screen household contacts and identify suspects.

Specific leprosy expertise needs to be available to one or more staff in the general health system at the district level, regardless of the leprosy prevalence. Essential skills required at the district level are as follows:

1. Diagnose leprosy and prescribe proper treatment regimen.
2. Diagnose and manage leprosy reactions.
3. Supervise and provide on the job training to peripheral health workers.
4. Ensure proper recording and reporting.
5. Manage and/or refer other leprosy related complications.

The specific role of leprosy institutions is to provide the specialist training required at the regional and national levels. The added value of these leprosy institutions is that such training can be offered through interaction with leprosy hospital services, leprosy control, research and rehabilitation programmes.

Group B: referral services and field work

Dr Fajardo outlined the future requirements of field work. The group emphasized the

transfer of skills to the intermediate level of the general health services, with effective two-way communication. If achieved, this will enable the referral centres to effectively implement training, research activities and diversification, depending upon the context and resources available.

Group C: prevention of disability and rehabilitation

Dr Virmond introduced the topic in the context of integration, mentioning the need for further research. The group suggested that training of intermediate level staff, better communication and agreed standards of care should be priorities. Networking with centres outside the leprosy field, involved in the management of other types of disability, is recommended.

Group D: research

Dr Ji divided future research priorities into two areas: research for improving patient care (comprising improved implementation of MDT, early detection of nerve damage and management of reactions and neuritis) and research for post-elimination strategies (comprising epidemiology, chemotherapy and basic research). The group stressed operational research, done in conjunction with national programmes, as a priority. They emphasized diversification and increased interaction with other research fields to enrich the intellectual and possibly the financial climate of future leprosy research.

Conclusion

During the final debate, Dr Groenen argued for an expert committee to draw up detailed guidelines for the training of peripheral health workers. The general feeling, however, was that this should be done in each country, taking into account local conditions. Another hotly debated issue was diversification: how important is this for leprosy institutions? Most participants felt it is the only route to survival. Professor Britton felt that public education should be a priority, but the meeting concluded that this is the responsibility of the national programmes, not the institutions. Professor Smith raised the interesting scenario that after elimination and a possible decline in the capacity of the general health services to manage leprosy, the institutions may be required to play a more prominent role than is expected at present.

The conclusions and recommendations of the meeting were summarized as follows:

1. In view of the rapidly changing situation of leprosy and the increasing integration of leprosy work within the general health services, the role of leprosy training and research institutions needs to be redefined.
2. The essential roles of training, service and research need to be retained, with a renewed focus on elimination and post-elimination issues.
3. All future activities must have close collaboration and two-way communication with national leprosy control programmes.

4. Leprosy institutions should network with other centres involved in training, research and rehabilitation, including those outside the field of leprosy.
5. The institutions will continue to provide the required expertise to train leprosy specialists at the national and regional levels and to provide advice to the national programmes on training at district and peripheral levels. The training should be decentralized, task-oriented and as short as possible.
6. In order to preserve expertise and sustain tertiary referral services for leprosy patients in a cost-effective manner, institutions should consider diversifying according to local capacity and needs.
7. The institutions should take the lead in proposing appropriate standards and guidelines for the prevention and management of disabilities, and the rehabilitation of persons affected by leprosy.
8. There remains a need for continued research into improving patient care and operational research into elimination issues. Capacity, particularly for operational research, needs to be built up. Basic research in leprosy should be maintained.

In closing, Dr Noordeen thanked ALERT and the Government of Ethiopia for hosting the gathering.

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Leprosy in Pakistan: Lepra Elective Study

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Summary As part of the curriculum, medical students at the United Medical and Dental Schools of Guy's and St Thomas's Hospitals (UMDS), London, are encouraged to spend an elective period of 8 weeks in their final year anywhere in the world, studying any field of medicine they are interested in. Having lived in Tanzania for 10 years, I have had contact with people suffering from leprosy and my interest in leprosy continued after I moved to Europe to continue my education. I therefore decided to use my elective to gain hands-on experience with the disease so that I could understand and appreciate the impact of leprosy in developing countries such as Pakistan.

Leprosy situation in Pakistan (1996)

Very little has been published about leprosy in Pakistan and the available information is outdated and scanty—a MEDLINE search combining *leprosy* and *Pakistan* as textwords, for example, identified only one brief Japanese article since 1992.[1] 1995 was the latest complete year for which leprosy data were available for Pakistan. The population of Pakistan then was estimated at 118 million, distributed over an area of almost 800,000 square kilometres, with 13 million people living in Karachi, the capital city. The country is divided into four provinces (Punjab, Sindh, North West Frontier Province and Balochistan) and two disputed areas (Azad Kashmir and Northern Areas).

The leprosy control measures in Pakistan are part of the Provincial Health Services, which are administratively integrated and professionally vertical. Each Provincial Health Department works closely with a non-governmental organization (NGO), of which the Marie Adelaide Leprosy Centre (MALC) is the largest. Leprosy prevalence in all provinces declined to less than one active patient per 10,000 in 1993, the threshold below which leprosy ceases to be a public health problem according to the WHO definition.[2] However, the leprosy pattern in Pakistan is very focal, ranging from 35/1000 in Sukkur District in Sindh to less than 0·01/1000 in Punjab. The leprosy belt, which is now well controlled, originally stretched from Azad Kashmir over the Northern Countries to the North West Frontier Province to Northern

This study was undertaken during an 8-week period as a Lepra Elective Student.

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Pakistan and along the seashore to the border of Iran. Hyderabad/Sindh, and especially Karachi, have contributed, and still are contributing, a large portion of the caseload.

There are 11 leprosy hospitals (four of which also admit TB and eye patients) in Pakistan with 377 beds, and there were 2885 admissions in 1995. The country has 104 leprosy field units, of which 91 are run by the government and nine by NGOs. The leprosy programme staffs 803 workers, including 21 medical officers, 412 paramedical and technical staff, and 362 administrative staff.

At the end of 1995, there were 42,800 patients registered in the National Leprosy Register, of whom 2953 were receiving chemotherapy, and 18,119 were under post-treatment surveillance. In all, 1405 untreated cases were detected in 1995 and 2208 were discharged from chemotherapy. At the time, Pakistan had a multidrug therapy (MDT) coverage of 88% (2611 cases) with a treatment completion rate of 97·5% of 1633 multibacillary (MB) and 99% of 359 paucibacillary (PB) cases, with only 17 relapses detected during the year.

The reduction of new leprosy patients to less than 1/100,000 per year had been achieved in four out of seven projects by the end of 1995. However, average disability rate was still 24% in newly detected cases because the annual case detection rate (1·62 patients per 100,000 population) was less than the disease incidence. Unfortunately, like many other countries,[3] the annual incidence rate in Pakistan does not follow the prevalence rate and is only expected to decline after 10–20 years.

By the end of 1995, incidence rate for Pakistan was 1·08 per 100,000 population, and this included (per 100,000) 0·18 in Punjab, 0·65 in Sindh, 1·08 in the Northern areas, 1·09 in North West Frontier Province, 0·51 in Balochistan and 11·98 in Greater Karachi. However, because of the dramatic decrease in the prevalence of the disease in most areas of Pakistan since 1993, the leprosy programme has now undertaken additional tasks. For example, since 1995, leprosy programmes in Azad Kashmir and the Northern Areas also play a major part in tuberculosis control by re-training leprosy staff in tuberculosis management. Similarly, a Prevention of Blindness scheme (in the form of Community Eye Health Care and training of field workers as ophthalmic technicians) has now been implemented in Balochistan and the North West Frontier Province, Punjab and Sindh. In 1995, a total of 90,021 patients were seen by leprosy staff for eye problems, of whom 1154 were operated on for cataracts (79%) or other eye conditions (21%).

Many leprosy control programmes are now also involved in other areas of medicine, education and rehabilitation. For example, homes are now provided to the handicapped in Rawalpindi, Karachi and Faisalabad. Leprosy staff are actively involved in teaching school children as well as children and relatives of leprosy patients, particularly in Karachi and Balochistan. Furthermore, rehabilitation is provided not only for leprosy patients, but also for drug addicts in Sindh. Community-based rehabilitation programmes for children have been implemented in Karachi and income-generating projects for women, such as embroidery and leather patchwork, have begun in many areas of Northern Pakistan. Unfortunately, a large proportion of patients discharged from treatment still need rehabilitation. For example, a survey conducted in rural Sindh in 1995 covering 86% of the entire caseload revealed that 51% of all patients still needed further physical as well as psychological rehabilitation, perhaps for the rest of their lives.

The long-term targets of the leprosy programme in Pakistan include (a) to reduce leprosy prevalence to less than 0·1 per 1000 patients, when the disease is considered to be effectively controlled; (b) to reduce the incidence rates (i.e. the number of new cases found per year to less than 0·01/1000); (c) to discontinue monotherapy and implement MDT in all new leprosy

patients; (d) to enhance health education so that more than 90% of patients voluntarily report their symptoms before disabilities arise; and (e) educate at least 90% of disabled patients to care for themselves so that their deformities do not worsen. While the first three of these targets are likely to be achieved in the near future, targets for prevention of disability and voluntary self-reporting of the disease are not likely to be achieved before the millennium.

In summary, therefore, due to the long and unpredictable incubation period of the disease (3–40 years), there are an estimated 15–30,000 infected asymptomatic persons in Pakistan who will be detected and treated in the next 2 decades. Around 20,000 are still under surveillance to detect and treat any reactions and/or relapses and a similar number require physical rehabilitation.

Leprosy is now better controlled in Pakistan than previously. Preliminary data for 1996 indicate that the disease prevalence in Greater Karachi, the only area in Pakistan with a rate higher than that recommended by the WHO, has now fallen below 1/10,000. This has allowed the leprosy programme to work in other areas, such as prevention and rehabilitation, as well as contributing to the management of affiliated conditions such as tuberculosis.

Leprosy electives in Pakistan (Jan–Mar 1997)

MALC is situated in the centre of the Karachi and is run by Dr Ruth Pfau, honorary advisor on leprosy to the Ministry of Health, Social Welfare, and Population Planning, Government of Pakistan and Azad Kashmir. It caters for most of the leprosy patients in Karachi and its outskirts and is always full of patients. Leprosy sufferers who require treatment are treated free of charge at the MALC. A large proportion of the funding for the Pakistan leprosy control programme comes from Germany, Dr Pfau's home country, but donations are received from charity organizations around the world, including LEPRA and St Francis Leprosy Guild in the United Kingdom. Until a few years ago, much of the country had remained inaccessible, mainly due to political instability—the recent increase in provision of basic health care facilities to these regions has improved the leprosy situation in Pakistan.

MALC is also the national leprosy control centre for funding, data collection and training leprosy staff at all levels. Regular liaison, usually through meetings held at MALC, with officials from other leprosy centres around the country, provides MALC with an overview of the leprosy situation in Pakistan, identifies weaknesses and makes recommendations to overcome them. In smaller towns, there is a trained local worker who can diagnose, treat and report the disease, and has easy access to professional help. The advantage of this system is that the worker is known and trusted by the people, understands their customs and culture and speaks their native language. Around the outskirts of large cities, the main leprosy centre in the area has teams of workers who travel to these regions once or twice a week actively to seek new leprosy cases, correctly diagnose the type and severity of leprosy in new patients, treat the patients, as well as follow-up and rehabilitate known patients who are already being treated.

Working at MALC was an amazing experience, and more dramatic than I had expected. The first thing that struck me as I entered the hospital was the sheer number of people waiting to be treated. Having attended the clinics there, I later realized that some people had been waiting outside the hospital for days before they were seen by a doctor, sometimes having travelled for days from villages as far as away as Afghanistan. There is also an in-patient

facility for ill patients with complications such as severe type I and II lepra reactions or concurrent illnesses such as infections and severe trauma to anaesthetized limbs as a consequence of leprosy. It should be noted that patients seen at MALC do not have to pay for any of the services or treatments.

I was surprised to find few affected people in the city itself. By talking to patients at MALC, I found out that most of the leprosy patients had been banished from the city. The stigma of leprosy was so severe that many voluntarily left their homes and family when they were diagnosed with leprosy. Most of these patients ended up in Mangopir, a small town on the outskirts of Karachi, where they were treated and attached to a rehabilitation programme. This rehabilitation programme, according to the National Council on Rehabilitation, is aimed at restoring the patient to the fullest physical, mental, social and vocational and economical usefulness of which they are capable. Unfortunately, because of the stigma associated with the disease, even after complete rehabilitation, most of the patients remain in Mangopir where they are accepted as part of a community and can help newly arrived patients with their problems. Furthermore, many of these rehabilitated patients are also actively involved in projects for obtaining funds for the country's leprosy eradication programme, such as handmade carpets, jewelry, paintings, and artifacts, and provide for up to 10% of the programme's total income.

In conclusion, initial data for 1996 have revealed that the prevalence of leprosy has now declined below 1 in 10,000 in all areas of Pakistan, including Greater Karachi, where local political unrest had, until recently, isolated and prevented access to patients by health care professionals. With the disease now in control, more attention can now be paid to education, prevention and rehabilitation and linking with other programmes such as tuberculosis.[4] It is only through sheer dedication and team work over 3 decades that such a feat has been achieved, and the programme certainly deserves a lot of credit for reaching the WHO-recommended target despite so much adversity.

Acknowledgement

The author would like to thank LEPRA and St Francis Leprosy Guild for funding his electives, as well as Dr Ruth Pfau and all the staff at the Marie Adelaide Leprosy Centre in Pakistan for allowing him to spend his electives at MALC and for providing the data on the leprosy situation in Pakistan.

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FURTHER EDUCATION

The promise of surgery, its scope and limitations in leprosy

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Introduction

Leprosy is a systemic disease mainly manifested in skin and nerves. The nerves affected are the cutaneous and trunk nerves, especially those located superficially. Early treatment of the disease prevents deformity or disability. Otherwise, the continuing disease process and immune reaction, either by direct involvement of tissues or secondarily through destruction of some trunk nerves, results in deformities and disabilities. All of these complications are amenable to surgical treatment, the results being excellent when the surgery is performed early.

To a deformed patient, appearance means the difference between being an outcast and a normal life in the community. To leprosy control programmes, surgical treatment means the possibility of offering a comprehensive treatment to those cases needing more than chemotherapy. For this reason, surgery is an important part of leprosy treatment and should be available to all control programmes.

Health Education (HE) and Prevention of Disabilities (POD) are also essential activities to all leprosy control programmes. Although these activities show a more adequate cost/benefit ratio, surgery should also be regarded as a *preventive* measure. As examples, surgical correction of drop foot prevents the onset of distorted foot and ulcers in the lateral border which usually leads to a total destruction of the foot. Appropriate surgical correction of clawed hands prevents rigidity of small joints in the affected hand and also improves the grasp, reducing the possibility of wounds in finger tips which, otherwise, would lead to a grossly deformed and useless hand.

- Leprosy may cause motor paralysis and loss of sensation, leading to disabilities and deformities. Surgery can correct most of the disabilities due to motor paralysis.
- Surgery should be available as part of the whole treatment of leprosy patients.
- Doctors should be aware of the possibilities of surgery in leprosy in order to refer cases in need.

The promise of surgery

Surgical treatment of deformities in leprosy ensures optical restoration of function and

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appearance. Proper and adequate surgery done early offers the best results. Surgery is indicated when non-surgical treatment proves inadequate. It is important to note that reconstructive surgery aims to restore some function–that is lost due to paralysis of some muscles–to the affected hand or foot; but no sensory recovery can be expected from such procedures. This must be clearly explained by doctors and understood by patients before any rehabilitation programme is settled, in order to prevent overexpectation in terms of results.

Health Education and Prevention of Disabilities measures must be permanent for patients undergoing reconstructive surgery in leprosy, since reconstructive procedures in leprosy do not aim to restore normal sensation. It aims only to improve the motor function to the paralysed group of muscles and/or cosmetic appearance.

The scope and limitations of surgery in leprosy

Table 1 shows the cause, consequence and the available surgical treatment of these conditions in leprosy, while Figure 1 shows the deformity.

All operations, except tendon transfers, are common procedures and can be done by any surgeon familiar with them. They all give excellent results. Tendon transfer surgery is specialized, not normally available, and its success needs additional input of pre- and postoperative training through physical therapy and a well-motivated patient. The knowledge and methods to prevent ulcer recurrence also need to be specially provided.

Treatment of plantar ulcers is simple; prevention of ulcers and of their recurrence requires special knowledge and skills.

Healing a plantar ulcer is no different from healing any other wound or ulcer. The

Table 1. Cause, consequence and available surgical treatment in leprosy

Cause	Consequence	Surgical treatment
Trunk nerve involvement with compression	Increasing loss of nerve function	Nerve decompression
Loss of sensation secondary to nerve involvement (prevention of ulcers and of their recurrence is a specialized subject)	Ulcers on soles of feet and palms of hand; tendon and bone infection Secondary deformity of foot and fingers	Debridgement, skin grafting, release of focus of infection Arthrodeses etc.
Loss of motor power by nerve involvement		
Facial nerve	Lagophthalmos	Temporalis transfer
Ulnar, median	'Claw' deformity of fingers and thumb	Tendon transfers
Radial and triple nerve paralysis	Wrist drop Completely deformed and dysfunctional hand	Arthrodeses
Posterior tibial nerve	Clawing of toes of grades 1, 2 & 3	Tendon transfer Arthrodeses
Lateral poplitcal nerve	Complete or partial 'foot-drop'	Tendon transfer
Direct tissue involvement	Ear lobe deformities Nasal deformities Gynaecomastia	Plastic surgery (reconstructive)

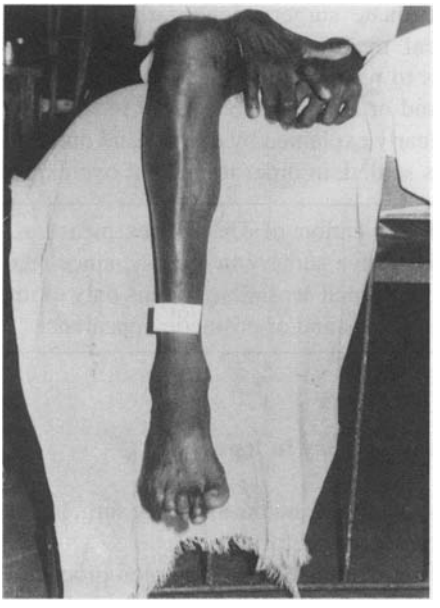

Figure 1. Deformities of hands (ulnar and median paralysis) and foot (lateral poplitcal and posterior tibial nerve paralysis).

principle of treatment is to make a complicated ulcer simple by removing all sources of infection. This can be done by any trained doctor or surgeon. Prevention of ulcer recurrence, a part of any prevention of disability programme, requires the following for implementation: (1) knowledge of *why* ulcers occur on a sole which has loss of sensation and even more so when there is also paralysis of intrinsic muscles; (2) knowledge and skill of a podiatrist and a cobbler to ensure good distribution of weight bearing and protection of any vulnerable part. The methods of prevention of ulcer recurrence are:

1. *Health education* by transfer of knowledge as to why ulceration occurs and how to prevent ulcers by self-care measures.
2. *Provision of simple devices* such as arch support and heel and metatarsal pads to protect vulnerable areas of the plantar surface of the foot.
3. *Provision of specialized footwear and foot care.* The special footwear distributes pressure, protects scars and prevents injury. Thus collaboration with a health educator, a foot specialist, podiatrist and shoemaker is essential.

Tendon transfers

RATIONALE FOR TENDON TRANSFERS

Any movement pattern, e.g. writing, is learned, and involves well orchestrated contraction of different muscles and dynamic play of balance of forces across joints. When some muscles are paralysed, there is an imbalance in these muscular forces. This is corrected by relocation of tendon(s) of normal muscles, called tendon transfer. The function of these transferred

muscles has to be learned by the brain, in order to produce the required movement pattern. This is achieved by a planned training programme using principles of physical and occupational therapy and teaching techniques, not only before and soon after surgery, but also during the periodic follow-up visits for at least 1 year.

SURGICAL PROCEDURE

Tendon transfer surgery, as treatment of motor paralysis, though also performed for non-leprosy patients, is rather uncommon outside the field of leprosy and hence not normally available in an ordinary hospital. A specialized, well-trained team is needed, as in transplant surgery, not only for the operation itself but also for the continued postoperative monitoring, to ensure a sustained long-term result. Its success requires not only a special surgical set-up and technique, but also a learning programme for the patient, with input from physical/occupational therapy and teaching techniques. For this reason, training as a general surgeon is not sufficient, and any surgeon who performs this kind of surgery only occasionally is unlikely to achieve consistently good results. The results of tendon transfer surgery on the hand is shown in Figure 2.

Pre-requisites for surgery for paralytic conditions

1. Well-motivated patient, trained surgeon and physiotherapist.
2. Patient under treatment for leprosy.
3. Normal mobility of fingers or thumb or foot.
4. BI should be 2 or less.
5. Well stabilized disease and reaction free.
6. No focus of infection.

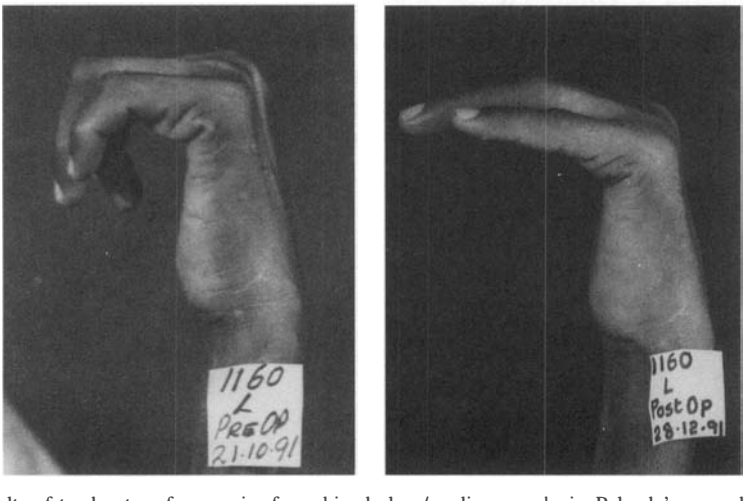

Figure 2. Results of tendon transfer, repair of combined ulnar/medium paralysis. Palande's procedure, five-tailed extensor carpi radialis longus transfer to the intrinsic muscles. (a) Pre-operative; (b) postoperative.

PRE- AND POSTOPERATIVE TRAINING

Special training is exemplified by teaching *isolated contraction* of the muscle–tendon unit to be transferred, before and after surgery. For example, in the transfer of a wrist extensor to the fingers for correction of clawed fingers, the following training steps may be employed:

1. Isolation of the extensor carpus radialis longus (ECRL) before surgery by teaching the patient to contract, see and become aware of the tendon and its action of wrist extension and radial deviation.
2. Postoperatively, at first, the patient is asked to contract the ECRL (as learned pre-operatively) while blindfolded. Only the observing therapist is aware of what is happening when the ECRL contracts.
3. When the action of the tendon is well established, the patient performs the same exercise of contracting the transfer, but with eyes open. The patient is always surprised to find that now, on contraction of the ECRL, instead of wrist extension, the fingers are flexing at the metacarpal joints! Slowly, this new action becomes a part of normal activity.
4. This integration is hastened by training the patient to perform purposeful movements such as writing and picking of objects and, in India, relearning the correct way to eat with the hand.
5. In follow-up visits, all of the above actions are repeatedly reinforced. The patient is first asked to show how the transfer is working, and then the training is repeated each time. The timetable for these visits is as follows:
   i. Pre-operative physiotherapy: 1–3 weeks, depending on the condition of the hand.
   ii. Operation. Postoperative immobilization for 3–4 weeks.
   iii. Postoperative treatment: 4–5 weeks. *No heavy work for another 3 months.* This is to protect the transfer.
   iv. Follow-up visits: 15 days, then once monthly for 6 months, every 2 months for the next 6 months, then every 3 months for 5 years.

The aim of tendon transfer operations is optimum restoration of functional ability, and of appearance. Normal power and function can neither be expected nor achieved. It is essential to maintain normal mobility of the fingers without injuries, scars and contractures until surgery can be done, and similar maintenance and care after surgery in order to obtain and sustain good results. The success of surgery in leprosy requires knowledge and motivation on the part of both the patient and the team managing and treating them. All those working in the field of leprosy need to know the limitations and scope of leprosy surgery.

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CASE REPORT

Reversal reaction, nerve damage and steroid therapy in three multibacillary HIV positive patients

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The progress of three Indian HIV-positive patients with multibacillary leprosy has been recorded.

Case 1

A 38-year-old male gypsy was seen in 1992. On examination, he had multiple hypopigmented and erythematous lesions, some small, some large, on the trunk and limbs. The patches were hypoaesthetic, raised and warm, with well defined margins. He also had swelling of the feet and hands of 3 months duration.

The greater auricular, ulnar, ulnar cutaneous and radial cutaneous nerves were enlarged. The left ulnar nerve was tender. In the lower limbs, the lateral popliteal nerves were enlarged. There was extensive anaesthesia of the glove and stocking type. He had minimal clawing of the little finger of the left hand.

A diagnosis of borderline lepromatous leprosy in reversal reaction with severe ulnar neuritis was made.

FAMILY HISTORY

The patient was heterosexual, he had never used intravenous drugs or received a transfusion. He was married and had a $2\frac{1}{2}$-year-old child. He had had sexual relations with another gypsy woman and subsequently developed a swelling in his groin and an ulcer on his penis, for which he had treatment.

Investigations revealed the following:

HB 11·2 g%
WBC 10,000 mm^3
Differential: neutrophils, 55; eosinophils, 16; lymphocytes, 20; monocytes, 8; basophils, 1; ESR; 12 mm/h

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The liver function tests, blood sugar and blood urea were within the normal range. Chest X-ray showed evidence of chronic bronchitis; sputum was negative for tubercle bacilli. The skin smears were positive for *M. leprae* B.I.1.6. Voluntary muscle testing (VMT) showed complete paralysis in the left ulnar nerve. VMT in the right ulnar nerve was 3, and left ulnar 0.

The lepromin (Mitsuda) reading was 7 mm × 6 mm, and the skin histopathology report (H&E) revealed features typical of borderline tuberculoid leprosy with clumps of bacilli in reversal reaction, while the nerve biopsy was consistent with a diagnosis of borderline lepromatous leprosy with clumps of bacilli in reversal reaction.

Treatment was initiated with prednisolone (60 mg/day) and Dapsone (100 mg/day).

PROGRESS

In hospital, the patient was found to have purulent urethral discharge and a penile ulcer. His VDRL test was reactive at 1 in 2 dilution and serum was positive by ELISA for HIV infection-1 and 2, confirmed by Western blot. The venereal disease responded to a course of penicillin. His hospitalization 2 months after the start of therapy was complicated by herpes zoster of T7 and T8 dermatomes. He made an uneventful recovery from the zoster. Since the patient was ELISA positive for HIV infection, steroids were reduced more rapidly and the patient was started on clofazimine 100 mg thrice daily as an anti-reaction drug for a period of 3 months.

The patient was started on the conventional WHO multibacillary-multidrug therapy (MB-MDT) regimen. His voluntary muscle testing improved gradually, the left ulnar from 0 to 2 and the right ulnar from 3 to normal. While on MDT, he did not develop reversal reaction or neuritis. Since the disease was inactive in the skin lesions and nerves, and he was bacteriologically negative, he was released from treatment after 32 doses of the WHO regimen in March 1995. He has now completed 1 year of follow-up.

Case 2

A 25-year-old commercial sex worker who presented with multiple skin lesions of 2 years duration was seen in 1995.

On examination, she had multiple hypopigmented, well defined, erythematous, infiltrated, medium-sized plaques which were asymmetrical in distribution. The ulnar, radial cutaneous and ulnar cutaneous nerves were enlarged. The left posterior tibial and the left musculo–cutaneous nerves were also enlarged. She had stocking anaesthesia of the feet. She had minimal weakness of the orbicularis oculi muscle on the left side. A diagnosis of multi-bacillary leprosy BT/BB in severe reversal reaction was made.

INVESTIGATIONS

Hb 8·4 g %
WBC 13,000/mm^3
Differential: neutrophils, 52; lymphocytes, 13; eosinophils, 30; monocytes, 5; ESR, 92 mm/h

The liver function tests and blood urea were within normal limits. VDRL was reactive at 1 in 256 dilution. She was positive by ELISA for 1 and 2 HIV infection. Chest X-ray showed

prominent bronchovascular markings and enlarged right border of the heart. The skin smears were negative for *M. leprae*. Her VMTs in right and left ulnar nerves were 4. The lepromin (Mitsuda) reading was 12 mm × 12 mm. The skin histopathology report suggested that the patient was probably upgrading from borderline lepromatous leprosy to borderline tuberculoid leprosy, while the nerve biopsy revealed a borderline tuberculoid picture with single small clumps of bacilli.

Treatment for the reversal reaction was initiated with prednisolone (40 mg/day) and clofazimine 100 mg twice daily for a period of 3 months. She also received benzathine penicillin injection 2·4 megaunits.

PROGRESS

The patient was given haematinics for her anaemia and dapsone was stopped. When her haemoglobin had increased to 10·2 g %. Dapsone was restarted. The patient responded to treatment without any complications. She completed 24 pulses of MB-MDT and was released from treatment. She completed 1 year of follow-up.

Case 3

A 25-year-old male was seen in 1996. On examination, he had many hypopigmented, well defined and ill defined, dry, scaly, medium-sized anaesthetic skin lesions on the extremities. The skin lesions were warm and scaly. His ulnar, lateral popliteal, radial cutaneous, musculo–cutaneous, and posterior tibial nerves were bilaterally enlarged and non-tender. A diagnosis of borderline leprosy (BT-BB) in mild reversal reaction was made.

FAMILY HISTORY

This patient was a married heterosexual and had had sexual relations with a commercial sex worker 1 year previously. He developed a penile ulcer, for which he had received penicillin injections.

Investigations revealed the following:

Hb 11·4 g %
WBC 9000/mm^3
Differential; neutrophils, 54; eosinophils, 7; lymphocytes, 30; monocytes, 9; ESR, 95 mm/h

The liver function tests and blood urea were within normal range and blood VDRL was negative. Chest X-ray was normal. He was positive by ELISA for 1 and 2 HIV infection. His skin smears were negative for AFB. His VMT was normal. The lepromin (Mitsuda) reading was 15 mm × 15 mm, and the nerve histopathology report (H&E) revealed a borderline lepromatous leprosy with epitheloid foci and bacilli singly and in small clumps within the nerve fascicles, while the skin biopsy findings were consistent with borderline tuberculoid leprosy.

PROGRESS

Treatment for the mild reversal reaction was initiated with chloroquine tablets, and he was started on the WHO MB-MDT regimen.

The patient responded well to chloroquine. He completed five pulses of MB-MDT before being lost to follow-up.

Discussion

These three patients were 'high risk' for development of neuritis, as they had borderline leprosy and were in reversal reaction when admitted to hospital. A positive lepromin test was stated to be a risk factor for reversal reaction.[1] HIV sera positivity has been associated with an increased incidence of neuritis and type-I lepra reaction, especially in MB leprosy patients.[2] Histological characteristics of reactional skin lesions were also found to be similar in seropositive and seronegative leprosy patients.[3]

No differences have been reported in the response to steroid therapy among seropositive and seronegative leprosy patients with a lepra reaction.[2] In our case study, the first male patient developed herpes zoster while on steroids, but he recovered from zoster without complications. He did not have delayed bacterial clearance of *Mycobacterium leprae*, or recurrent reversal reaction and neuritis. The second female patient also responded to corticosteroid treatment without complications. The third male patient did not receive corticosteroids, since he responded well to chloroquine.

HIV-infected patients with leprosy have been reported to respond well to anti-leprosy chemotherapy.[4] The down-grading reactions towards lepromatous leprosy due to the combined immune deficiencies of HIV and leprosy[5,6] did not occur in these three patients. Nor did the patients (cases 1 and 2) exhibit the poor outcomes in neuritis shown by the HIV-positive patients with leprosy in Zambia.[7]

The selective tropism of HIV-1 for T-4 lymphocytes leads to T-cell depletion and the lowering of T-cell defences. The development of reversal reactions in these three patients is paradoxical. Presumably, these patients have immunological instability due to lowering of T-cell mediated immunity.

The case reports of all three cases raise several interesting points:

1. All three patients displayed clinical and histological evidence of reversal/upgrading reaction.
2. Though there is histological discordance between clinical and histological staging, all of them required the WHO MB-MDT regimen and responded promptly to conventional therapeutic treatment. The outcome was rewarding in terms of preventing permanent and progressive nerve damage. The first two patients responded well to corticosteroid therapy.
3. Concurrent HIV infection appears to result in anergy to lepromin, but in these three patients the lepromin test was strongly positive.

These patients will need to be followed up for years, since they may relapse, perhaps with unusual features.

Acknowledgement

We thank Mrs Glory Davidson for secretarial assistance.

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Seizures following chloroquine treatment of type II lepra reaction: a case report

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Summary A case of tonic–clonic seizures following chloroquine treatment for leprosy reactions in a Nigerian male is reported. Seizures were controlled with phenytoin sodium capsules. A causal relationship between the seizures and chloroquine is suggested. There have been no previous reports of this adverse reaction in leprosy patients receiving chloroquine for treatment of reactions. The author recommends that chloroquine be used with caution especially in patients with seizures.

Case report

In December 1990, a 42-year-old Nigerian male presented with a 20-year history of untreated leprosy in the outpatients' department of the leprosy referral centre for Akwa Ibom State, south-east Nigeria. Clinical signs included ill-defined hypopigmented macules with loss of sensation to tactile and thermal stimuli, multiple nodules on the chest, bilateral infiltration of the ear lobes, supercilliary madarosis and collapse of the bridge of the nose. He suffered bilateral loss of sensation of the soles of the feet and loss of sensation with absorption of the index finger and thumb of his right hand. A clinical diagnosis of borderline lepromatous leprosy was made. Skin smears showed a bacillary index (BI) of 4+. He was started on WHO multibacillary regimen (MD MDT) with dapsone, rifampicin and clofazamine. He made good progress but defaulted from multidrug therapy (MDT) 12 months after starting treatment.

In March 1994, he reported to the hospital with a 6-week history of fever, joint pains and eye pain. Clinical findings revealed pyrexia of 38°C, tender deep-seated subcutaneous nodules of various sizes on the face and chest, and chronic iritis with fixed nonreacting pupils. No nerves were enlarged or tender. A voluntary muscle test and sensory test (VMT.ST) showed full strength in all muscle groups and a complete loss of sensation in his right hand and the soles of both feet. A diagnosis of erythema nodosum leprosum (ENL) reaction was made. BI showed 2+. He was hospitalized and managed with: i, chloroquine base 150 mg three times daily for the first week; chloroquine base 150 mg twice for the second week; chloroquine base 150 mg daily for the third week; ii, prednisolone beginning

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with 60 mg daily and tapering down to 5 mg over a period of 2 weeks; iii, atropine 1% eye drops and Terracortril® eye suspension (a combination of polymyxin B, oxytetracycline hydrochloride and hydrocortisone acetate) for the iritis; and iv, MDT treatment of MB leprosy. he improved on the above treatment, and his fever and the joint pains subsided.

On the morning of the ninth day of treatment for ENL, he suffered generalized tonic–clonic seizures lasting about 3 min. There was no evidence of postictal paresis. History revealed no aetiological risk factors for epilepsy, no previous history of seizures, and no family history of epilepsy. He suffered a second episode of seizures 8 h later, which lasted about 7 min. He lapsed into a postictal sleep for about 5 min. Postseizure physical and neurological examination were normal. Cardiovascular assessment including pulse and heart sounds were normal. Laboratory investigations of CSF, blood for malaria parasites, urinalysis and blood sugar were normal. X-ray of the skull showed no abnormalities. Electroencephalogram (EEG), electrocardiogram (ECG) and CAT scan facilities are not available at Ekpene Obom.

Following the second episode of seizures, he was placed on anticonvulsive therapy (phenytoin sodium capsules, 100 mg three times daily) with good effect for 6 days. We temporarily suspended phenytoin on the seventh day, while continuing antileprosy and antireaction drugs, and monitored the patient closely for signs of seizures. He suffered a third episode of seizures 5 days after phenytoin treatment was suspended.

After the third episode of seizures he was placed back on phenytoin capsules (100 mg three times daily) for 6 weeks. He did not suffer further seizures over that period. He was slowly weaned off phenytoin when the ENL reaction resolved. VMT.ST showed marked improvement, with full power in all muscle groups and restoration of sensation in his hands and soles of the feet until only the toes were anaesthetic. He was discharged to a peripheral leprosy clinic where he received monthly MDT until he was released from treatment in February 1996, at successful completion of 24 monthly doses of MB MDT. He is now on surveillance, and has remained seizure free to date (May 1997).

Discussion

Chloroquine, a 4-aminoquinoline, is most popularly used in the treatment and prophylaxis of malaria fever. Other uses[1] include hepatic amoebiasis and the employment of its anti-inflammatory effect in rheumatoid arthritis, lupus erythematosus and leprosy reactions (type I and type II).

Adverse effects of chloroquine include gastrointestinal disturbances, headache, ECG changes, visual disturbances, depigmentation, loss of hair, and skin reaction.[2]

The literature contains reports of adverse CNS effects including transient dyskinesias,[3] dystonias[4] and transient global amnesias.[5] Tonic–clonic seizures in three Nigerian students, following therapeutic doses of chloroquine for malaria fever,[6] have also been reported. Interestingly, seizures associated with the treatment of leprosy or its complications have not been reported in the literature.

The patient in question, a 78 kg male leprosy patient, received chloroquine tablets in doses commonly used in the therapeutic regimen for the treatment of acute inflammatory reaction in clinical leprosy. Hastings[7] states that starting chloroquine in a dose of 250 mg three times a day should be sufficient to control type II reaction within a week. The dose is then lowered to 250 mg twice daily for a week, followed by 250 mg daily to maintain control

of the reaction. However, our patient suffered three episodes of generalized tonic–clonic seizures without evidence of focal onsets while receiving treatment for ENL reactions. The possible aetiology of seizures in the above patient includes: intercurrent infections, hypoglycaemia, space occupying lesion of the brain, adverse drug reaction or interaction, and idiopathic epilepsy.

It is unlikely that the seizures were caused by intercurrent infections as revealed by laboratory investigations. The absence of symptoms and signs of hypoglycaemia (anxiety, shakiness, palpitations, coma, hypothermia and irritability)[8] before and after seizures, and a normal fasting blood glucose concentration rule out the possibility of hypoglycaemia inducing seizures in the patient. Furthermore, one would expect subsequent seizures over the past 3 years since discontinuing phenytoin, if seizures were due to a growing space occupying lesion or idiopathic epilepsy. However, the author acknowledges an EEG and CAT scan would settle the above suspicion.

A likely explanation for seizures in the patient would be a drug-induced adverse reaction. Prednisolone, dapsone, rifampicin and clofazamine have not been associated with seizures. Of the drugs used in the management of reactions in leprosy, only chloroquine has been reported in the literature to be associated with seizures, especially in susceptible individuals. Tonic–clonic seizures have been reported following prophylactic,[9] therapeutic[10] and toxic[11] doses of chloroquine used either alone or in combination with other antimalarial drugs or antibiotics for the management of malaria or amoebiasis.

From the above, it is logical to suspect chloroquine, acting alone or interacting with MDT or prednisolone, as inducing seizures in the patient for the following reasons:

He received chloroquine while on treatment for ENL reactions.
He suffered seizures during the period of treatment for ENL.
Seizures were controlled with phenytoin sodium capsules but recurred when the phenytoin was temporarily suspended while he was still taking chloroquine, prednisolone and MDT. We continued chloroquine treatment in spite of the seizures because we were unaware of chloroquine-induced seizures prior to our literature search.
Seizures stopped when chloroquine was withdrawn after the third week of treatment.
No further seizures were observed even when phenytoin was finally stopped and ENL resolved.

The mechanism of seizure induction by chloroquine in the above patient is unclear. Chloroquine inhibits glutamate dehydrogenase activity[11] and could reduce concentrations of the inhibitory neurotransmitter gamma aminobutyric acid (GABA).[9] Torrey states that seizure induction by chloroquine could be due to an idiosyncratic adverse reaction in sensitive individuals.[11]

Seizure induction in this patient is thought to be an idiosyncratic adverse reaction to chloroquine and not due to toxic effects, as he was receiving chloroquine in doses (of 150 mg base given up to three times daily),[12] compatible with therapeutic regimen for the management of leprosy reactions in adults. Deliberate ingestion of an overdose of chloroquine by the patient is unlikely, as his antireaction drugs were administered by a nurse.

This report highlights the potential risk of seizures in patients receiving chloroquine for the treatment of leprosy reactions. The author recommends that health workers use chloroquine with caution, especially in patients with a history of seizures. Patients who suffer chloroquine-induced seizures may require alternative antireaction drugs.

Acknowledgement

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Lepr Rev (1998) **69,** 182–185

Letters to the Editor

FOOTWEAR FOR FARMERS AFFECTED BY LEPROSY

Editor,

We recently reported on a study of footwear carried out at ALERT which showed that commercially produced canvas shoes are a cost-effective method of achieving ulcer healing and/or preventing new ulcers in anaesthetic feet, and are readily accepted by leprosy patients.[1]

We have subsequently carried out a study to compare two commercially available types of footwear for use by farmers. One was the canvas shoe, made by the Ethiopian canvas shoe factory, used in the previous study. The second was a PVC boot, made by the Ethiopian Plastics Factory. This PVC boot is deep enough to accommodate an MCR insole (shore 15°, thickness 8 mm) without any modification, so can be bought 'off the shelf'. In appearance, it is a typical 'Wellington' boot or gumboot, and is used by many people in wet or muddy conditions. Both types of footwear now cost about US$ 6·2 per pair.

Methods

One hundred and ten male farmers working in various parts of central Ethiopia were randomly assigned to the canvas shoe group or the PVC boot group. The study commenced at the beginning of one rainy season (June 1996) and all clients were followed for 1 year. All were former leprosy patients who either had one or more plantar ulcer(s) at intake, or had the scar of a healed ulcer; all had loss of sensation (LOS) as tested by a 10 g monofilament. Many had clawed toes and bone loss.

At follow-up (at 3, 6 and 12 months) any ulcers were measured and the condition of the shoes or boots was noted. The acceptability of the footwear was also determined by a standard set of questions.

Results

Table 1 shows the sample characteristics and the outcomes after 1 year of follow-up.

Durability is mainly a problem of the 'uppers'; the soles and insoles generally remain in good condition. PVC boots were much more durable than the canvas shoes. Table 2 shows the number (percentage) of 'uppers' remaining in good condition after different periods.

At each follow-up visit, more than 80% of the farmers rated the PVC boots as 'excellent' for social acceptability and suitability for work. The canvas shoes were socially acceptable, but 85% of farmers rated them as 'good' for their work, rather than 'excellent' (8%) at the first follow-up, which occurred just at the end of the rainy season.

One adverse comment was that the PVC boots could become very hot in strong sunlight, with the possibility of burning the feet.

Conclusion

PVC boots are more suitable for the agricultural working environment in Ethiopia than canvas shoes.

Table 1. Sample characteristics and results at 1 year. Differences are not significant

	Canvas shoe group	PVC boot group
Total analysed	52	58
Average age	46 years	45 years
Age range	20–70 years	20–65 years
Number with complete LOS	34	39
Number with partial LOS	18	19
Number with ulcers at start	25	13
Of these, number with ulcers after 1 year	4	4
Number with healed ulcers	20	9
Lost to follow-up	1	0
Number with scars at start	27	45
Of these, number who developed new ulcers during the year	0	0

Table 2. Number (percentage) of 'uppers' remaining in good condition after different periods

	Start	3/12	6/12	12/12
PVC boots	58 (100)	58 (100)	58 (100)	25 (43)
Canvas shoes	52 (100)	24 (46)	21 (40)	17 (33)

They are also more durable and have as good a protective effect on insensitive feet as canvas shoes. They are well liked by farmers and are not stigmatizing.

People affected by leprosy in our programme now have the choice of receiving either two pairs of canvas shoes or one pair of canvas shoes and one pair of PVC boots per year at a subsidized price. They currently pay 25% of the cost of both types of footwear.

Acknowledgement

The footwear programme at ALERT is generously supported by ALM and NSL.

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INVOLVEMENT OF NON-ALLOPATHY MEDICAL COLLEGES IN CASE DETECTION

Editor,

A questionnaire analysis[1] of medical competitive examination held by us in allopathy and non-allopathy

medical colleges in Mumbai indicates that teaching of leprosy is grossly inadequate in all colleges, reference books on leprosy are not available in college libraries and proper information about national leprosy programme explaining the existing leprosy status in the country is not available to the students. Though improvement in the standard of teaching of leprosy in medical colleges is a high priority in India against the background of the WHO target of leprosy elimination in 2000 AD, no systematic efforts are being made in this direction at the national level. A few sporadic efforts in this context have been documented by some voluntary organizations.

Hind Kusht Nivaran Sangh-Maharashtra Branch attempted to involve non-allopathy medical colleges in Maharashtra in leprosy work. Leprosy teaching in such colleges is virtually negligible or not up to acceptable standards. Medical graduates passing out from these medical colleges generally set up their private medical practice at the grass roots level, catering to low socio-economic groups, among which the possibility of detection of leprosy cases is relatively greater.

In Maharashtra, there are 37 ayurvedic, 37 homeopathic and five unani medical colleges where approximately 4000 new admissions take place every year. In 1992, collaboration with these medical colleges by organizing teaching sessions on leprosy to medical students was initiated. The teaching was 'task oriented', giving greater emphasis on diagnosis, treatment of leprosy with special reference to elimination strategies and practical clinical demonstrations of leprosy patients. In the initial stages, teachers were leprosy experts and dermatologists practising in local situations. Subsequently, training in leprosy for teachers in non-allopathic medicine colleges has been completed and adequate teaching material has also been provided to them. This has helped to maintain the continuity of teaching of leprosy in those colleges which were willing to cooperate. As such, 39 medical colleges have been covered during the last 5 years and almost 1200 students have received the benefit of leprosy teaching every year.

Follow-up of these students was maintained by correspondence. These young, enthusiastic medical personnel were kept in touch with the subject by the provision of literature on recent developments in leprosy. A questionnaire study revealed that graduate students who succeeded in obtaining jobs, as well as those who started private practice, detected 351 new leprosy cases during the last 5 years. Help with diagnosis and treatment has been provided for all cases by trained staff belonging to the government and non-government sectors. This experiment indicates that involvement of non-allopathy medicine colleges is a fruitful method for case detection in India.

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COMMENT: SENSORY TESTING OF THE HANDS IN LEPROSY

Editor,

I have been reading the letter to the editor by Saunderson, Currie, Gabre and Byass [*Lepr Rev*, 1997; **68:** 252–254] and comments by van Brakel and Anderson [*Lepr Rev*, 1997; **68:** 382–383] with interest.

What is missing in the letter from Saunderson *et al.* is a clear description of the history and clinical findings of the 11 out of 12 patients, of which they present the results of long-term follow-up. Had those 11 patients at diagnosis a history of recent nerve function impairment (NFI) or one of longer duration (more than 6 months)? Were there other complaints like nerve pain, numbness, paraesthesia, recent

weakness? Were there other signs of a severe reaction? Were there signs of atrophy? From the data available, it seems that at least some of these 11 patients did not suffer from a recent NFI, but most likely had already an NFI of longer duration. As such, in general, no major changes in nerve function are expected (except of course when developing new signs of a severe reaction or silent neuritis). The point they want to make would have been better served if only patients with a recent NFI would have been selected for follow-up.

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Editor,

Thank you for the opportunity to respond to Dr Schreuder's comments.

At issue in this discussion is the definition of nerve function impairment (NFI) in leprosy and its correct management. When patients have unequivocal signs of recent NFI, such as nerve tenderness, weakness or sensory loss, with or without signs of a reversal reaction, it is clear that steroids are the treatment of choice. It is possible, however, to use more and more sophisticated techniques to look for early or minimal signs of NFI: these include the assessment of autonomic nerve function and better methods of sensory testing, especially the use of standardized nylon monofilaments.

The question we are interested in is: how important are minimal signs of NFI discovered by these newer techniques? Do they indicate the imminent onset of more serious NFI which could be prevented by steroid treatment, or do they suggest a common, but mild and perhaps self-limiting neuritis with a good prognosis? It is conceivable that every leprosy patient would show some degree of nerve involvement if we had tools sensitive enough to detect it.

The clinical details of the 12 cases we reported are available. At diagnosis, four had normal hands and eight had some degree of loss of sensation (LOS) to the 10 g filament. Three received steroids at diagnosis for recent NFI. Thus many of the study group had previous NFI, but during the study they developed new NFI detected by the 1 g filament.

The filament study itself was not started at the time of diagnosis, but looked at patients already enrolled in another long-term study of the results of MDT. We believe that all patients on MDT are at some risk of developing neuritis, and the original study examined 159 patients prospectively for several months, with 19 meeting the standard criteria for steroid treatment for recent NFI.[1]

The 12 patients we re-examined 5 years later were chosen precisely because they did not fit the standard criteria for NFI and were not treated with steroids, but they did show signs of new sensory loss when tested over a period with the much more sensitive 1 g filament. Thus we were looking at cases of presumed recent, minimal, silent neuritis. We found that 11 of the 12 did not develop further damage on long-term follow-up. The 12th patient did develop more sensory impairment and was treated later with steroids.

Our main point is that the use of very sensitive methods of nerve function assessment may lead to unnecessary over-treatment with steroids.

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Reference

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Lepr Rev (1998) **69,** 186–187

Book Reviews

Essential surgery in leprosy: Techniques for District Hospitals. H. Srinivasan and D. D. Palande, World Health Organization 1997

After reading this excellent handbook, most doctors who have worked in remote places, leprous or not, would readily extend its title to *Essential Surgery in Leprosy—and in many other conditions.* It is more than just a handbook, but rather a fundamental basic text, and a genuine refresher course to lighten, and enlighten, the endless weary delays which are inevitable in a surgical life. A slim volume, A4 size, 136 pages, well bound on good quality paper, to keep on the shelf in theatre—easy to read and difficult to steal.

The book has relevance and value beyond the field of leprosy, and will be of continuing interest to district hospital doctors and health officers in Africa and other similarly underfunded parts of the world. Few are 'qualified surgeons', to whom the text is primarily addressed, and few have had much formal training nor 'considerable experience in its practice'. It has become increasingly difficult, and in some countries quite impossible, for surgeons 'to be trained in these procedures in a specialist institution'.

The section on the anatomy, pathology and surgery of the infections of the hand and fingers, could not be more clearly presented, and will be of value to doctors faced with neglected, delayed, inadequately treated sepsis in the hand. The descriptions and line diagrams are more realistic than those in the orthodox textbooks of surgical anatomy. There are clearly-illustrated descriptions of the safe drainage of distal pulp infections, paronychia, and sepsis in the digital synovial sheaths, the web and palmar spaces—all common conditions, and all commonly neglected and badly managed.

The descriptions of exploration and decompression of nerves in the wrist, elbow and ankle are sufficiently detailed and clearly illustrated to be a safe guide for the many rural surgeons working on their own, with no referral centre, or whose referral centre is run down, underfunded and understaffed. The authors give a polite warning that such procedures are not for 'the hurried or the ham-handed'.

Tarsorrhaphy is indicated in many clinical situations in addition to lagophthalmos, and is often put off too long in the confusion of priorities in a general surgical ward, or a burns unit, on the assumption that this is a specialized difficult procedure. The description here should encourage the fearful.

For foot-drop, in addition to a step-by-step guide to the two-tailed tibialis posterior transfer operation, there is a timely note on the indications, and contraindications, for this procedure, and with emphasis on pre-operative exercising of tibialis posterior, to ensure the cooperation and understanding of the patient in what is being planned.

It is refreshing to read, incidentally in the section on tendon surgery, that 'there is no need for routine, antibiotic therapy post-operatively', when even in grossly underfunded rural hospitals antibiotics are prescribed heedlessly and inappropriately, for any surgery.

There is a clear account of the pathology of partial and complete claw hand, the innervation of the intrinsic muscles, the inter-relationships of the metacarpophalangeal and proximal interphalangeal joints, and the procedures designed to improve function in the hand.

Four of such procedures are described in detail: transfer of the superficial flexor tendon from one finger of the extensor expansion of all four: transfer of the superficial flexor tendon from one finger to the flexor pulleys of all four: capsulorrhaphy and pulley advancement: diversion of the extensor tendon to the flexor aspect of the metacarpophalangeal joint, mainly to improve the appearance of the hand. All

these procedures are accompanied by precise advice on pre-operative assessment, the type of anaesthesia, axillary nerve block, the indications, or not, for the use of a tourniquet, and the optimal post-operative position for the hand, so often forgotten, or delegated. The importance of getting the full cooperation of the patient is emphasised throughout.

The authors conclude, optimistically, that 'the procedures described here are well within your capability, provided you are sufficiently motivated, reasonably skilful, and familiar with the basic principles of surgery'.

The well intended offer by WHO to provide this book free of charge to any applicant from a rural hospital, may prove too difficult to put into effective practice, but might be helped if it were publicised widely—in Tropical Doctor, the BMJ, and through the missions, and the aid groups like Medicins Sans Frontieres with interests in rural surgery. Sadly however, the main obstacle to any hope for the worthy aims of this book, is economic. The poor countries get poorer, health services deteriorate, surgery more than most. Rural hospitals have now to charge fees, which in subsistence farming communities, just cannot be paid, resulting in the woeful spectacle of empty beds, and half empty wards. Still, this book will raise surgical standards and surgical morale, where they are most needed and will be most appreciated.

James Lawrie
OBE MD FRCS

WHO, Geneva Switzerland, 1997, 136 pp.

A guide to eliminating leprosy as a public health problem

This is a well-produced booklet. Its pages with clear print swivel neatly on the spring spine. It is intended 'to enable every health worker in endemic countries to contribute to the historic task of reaching all leprosy patients with multidrug therapy (MDT) and attain the goal of eliminating leprosy as a public health problem'. The sections on diagnosis, the organization and delivery of MDT, and prevention of disability, including the management of reactions, are clear and practical and will be helpful to all leprosy workers.

My problem with the book is that it comes swathed in WHO propaganda about the elimination of leprosy. WHO is very keen to 'eliminate' leprosy by the year 2000, i.e. to reduce prevalence to less than one case per 10,000 of the population. This goal is being achieved in part by redefining leprosy patients as those that have not completed a course of MDT and by measuring the prevalence of so defined cases, rather than the incidence of the disease. Whilst MDT is a very effective antibacterial combination against *Mycobacterium leprae*, it is noteworthy that so far there has been little impact on the incidence of the disease in countries where MDT has been implemented. Statements that the 'number of new cases detected each year is about half a million' says nothing of change; and what is meant by the statement that 'MDT has dramatically changed the leprosy profile in all endemic areas'? The treatment of leprosy goes far beyond mere dishing out MDT tablets, as this guide recognizes, but to pretend that once a patient has completed a course of MTD he 'should no longer be regarded as a case of leprosy, even if some sequelae remain' and should therefore be removed from the register is to neglect the importance of late onset nerve damage which is such an important cause of disability. Leprosy is a disease, not an infection. This kind of creative accounting is worrying.

While it may be true that MDT 'rapidly cures patients', MTD does nothing to eliminate the silent reservoir of infection in the community, and many would disagree that leprosy is 'acquired through prolonged exposure'. So the word 'eliminate' is misleading, however defined.

If this little guide succeeds in encouraging and training leprosy workers to do a better job, it will have served a useful purpose; but if it misleads them into believing that MDT will on its own get rid of the problem of leprosy it may lead to disappointment and disillusionment.

Anthony Bryceson

Action Programme for the Elimination of Leprosy, WHO

Lepr Rev (1998) **69,** 188–200

Teaching Materials and Services

A video documenting the history of Lepra's involvement in Malawi is now available. Produced by Peter Garland, the video can be obtained from: Lepra, Fairfax House, Causton Road, Colchester, Essex CO1 1PU, UK. Tel: +44 1206 562285; Fax: +44 1206 762151; e-mail: 100657.2556@compuserve.com

LEPRA/TLM Ophthalmic Course, Karigiri, India 1998

The thirteenth annual five-day ophthalmic teaching module was held at the Schieffelin Leprosy Research and Training Centre, Karigiri from the 2nd to the 7th March 1998. The course, which was sponsored jointly by LEPRA through the Barclays Bank/English Speaking Union International Training Scheme and The Leprosy Mission was designed to give instruction to leprologists on the detection, prevention and management of the ocular complications of leprosy by means of a series of lectures and clinical and surgical demonstrations, augment 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.

A preference was given this year to clinical demonstrations and discussions dealing with important aspects of ocular leprosy such as the diagnosis and management of lagophthalmos, intra-ocular inflammation and infiltrative lesions, and 'hands on' teaching methods were employed more than in previous years.

The course was attended by seven sponsored participants working in India, and was organised 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 and Dr Kirsteen Thompson from Purulia, West Bengal were invited members 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.

International Course on Rehabilitation and Prevention of Impairment & Disability in Leprosy (RPOID)

The second international RPOID course was conducted at the Green Pastures Training Centre in Pokhara, from 10 November to 12 December 1997. Twenty-five experienced professionals from seven countries contributed to the course as teachers and facilitators. We very gratefully acknowledge the contributions made by TLMI, NSL and the Gastmann-Wichers Stichting to enable Ms Jean Watson, Dr Margreet Hogeweg and Dr Wim Brandsma to be teachers on the course. The 14 participants represented no fewer than six nationalities and eight rehabilitation-related professions. The multidisciplinary nature of the participant group emphasized an important aim of the course, namely, that rehabilitation is a multidisciplinary task.

The curriculum was based on the concepts of the International Classification of Impairments, Disabilities and Handicaps (WHO, 1980). These were expertly introduced by Dr H. Srinivasan. The course addressed prevention and treatment of impairments, prevention of disabilities and handicaps (the social consequences of impairment or disability), and the rehabilitation of individuals with disability or handicap. This included teaching and practice on nerve function assessment, impairment grading, eye, hand and foot examination, disability assessment, psychological assessment and socio-economic assessment. Recording, reporting and monitoring and evaluation of POID activities was also covered, using the ILEP guidelines. The teaching programme aimed at knowledge as well as skill acquisition. The 1997 course also incorporated a 1-week field trip, which helped greatly to practice the knowledge and skills learned during the preceding weeks. A new feature was a 3-day module on community-based rehabilitation, facilitated by Dr Maya Thomas from India.

Much more attention than in the first course was given to psychosocial aspects of leprosy, counselling and socioeconomic rehabilitation. The latter included principles of marketing research and vocational training.

Throughout the course, the participants worked in multidisciplinary groups on a plan for an RPOID programme for their own area of work. These assignments, together with the results of the field assignments and a written exam, formed the basis of the course examination. Feedback from participants and facilitators was again very positive.

ANNOUNCEMENT FOR THE INTERNATIONAL COURSE ON REHABILITATION AND PREVENTION OF IMPAIRMENT AND DISABILITY (RPOID) IN 1998

Venue: The Green Pastures Training Centre in Pokhara, Nepal.
Dates: 9 November to 18 December 1998 (2 + 4 weeks)
Expected course fees (including board & lodging and field trip): $150 per week

The 1998 RPOID course will be run in two modules. The first one 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 second module will aim at RPOID-related assessments, such as nerve function assessment, psychosocial assessment, ADL assessment, impairment assessment and socioeconomic assessment, treatment and rehabilitation interventions. The second module will therefore concentrate on skills acquisition. Through optional courses the second module will offer the opportunity to study certain topics in more depth.

The modules can be taken as separate units of, respectively, 2 and 4 weeks, or can be taken together as one 6-week course.

Target group

- For the first module: managers of rehabilitation and/or POID programmes, senior hospital staff, senior leprosy control staff and doctors with managerial responsibilities for RPOID activities.
- For the second module: physiotherapists, occupational therapists, social workers and field staff will take responsibility for the assessment, treatment and/or rehabilitation of people needing RPOID interventions.
- Experience in leprosy work will be an advantage, but is not essential.

Teaching/learning methods

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.

Further information

Detailed information can be obtained from:

The Training Officer, GPTC, PO Box 28, Pokhara 33701, Nepal.

Topics in International Health

Dr Neil Pakenham-Walsh, Wellcome Foundation, London, United Kingdom

The following article is taken from the Topics in International Health Series published by CAB International.

Europe's largest medical charity, the Wellcome Trust, is introducing a new electronic educational tool and information source for health professionals worldwide.[1,2] Topics in International Health (TIH) is a computer-based learning programme that provides reliable, up-to-date information on major issues in tropical and international health. The emphasis is on quality of content, clinical relevance, and ease of use. Previous computer experience is not necessary and the text has been carefully edited so that it is easily understood by students with English as their second language.

Running on Windows, TIH has evolved from the highly acclaimed DOS-based prototype, the Tropical Medicine Resource (TMR), which has been evaluated in over 200 medical institutions in 60 countries.

The first four CD-ROMs of the TIH series will be launched in March 1998 and will cover malaria, sexually transmitted diseases, sickle cell disease, and trachoma. Each CD is a learning tool and will include a number of interactive tutorials and a large collection of quality images. Four more CDs will follow in September 1998 (leprosy, diarrhoeal diseases, tuberculosis, and schistosomiasis). Further CDs will be introduced regularly, so that by the year 2000 the series will provide a comprehensive information and training resource for centres of learning around the world.

THE POTENTIAL OF CD-ROM

Budget cut-backs and rising costs are making it increasingly difficult for medical libraries in developing countries to purchase up-to-date textbooks and journals. Meanwhile CD-ROM is becoming more available and is already having a substantial impact in many parts of the world.

A single CD is 12 cm across, weighs only a few grams, and can contain more information than a whole shelf of textbooks. They can be expensive to develop, but post-production costs of manufacture and distribution are relatively low (as compared with print media), making them ideal for worldwide distribution. Furthermore, the master copy can be modified and updated with ease.

That said, CD-ROM products such as TIH are intended to complement, not replace, conventional printed materials. TIH is emphatically not a 'book on computer' but an educational experience that combines visual impact and interactivity to help make learning effective and stimulating.

Access to CD-ROM hardware is clearly a key issue. Although increasing worldwide, access continues to be limited in some parts of the developing world, some libraries have no information technology facilities at all, others have only a single CD-ROM station that might already be heavily used for database searching. The emergence of innovative educational products such as TIH emphasizes the potential of CD-ROM as a training tool. Continued international funding and support for appropriate IT development will help to bring such products to an ever-wider audience and is to be encouraged.

IMAGES AND TUTORIALS

The TIH offers two main activities: users can explore a 'virtual gallery' of high-quality images or they can work through interactive tutorials in a subject area of their choice.

The images are selected from a central image library at the Wellcome Trust, a growing collection which currently contains more than 45,000 images relating to tropical and international health. Images can be selected and retrieved instantly by typing in a 'searchword' relating to the field of interest and/or by selection of terms from a hierarchical menu.

The tutorial section of the CD-ROMs uses maximum visual impact and minimum text to emphasize the key points of a subject quickly and easily. They are ideal as a general introduction to a subject, or for revision, with each tutorial consisting of 30 to 40 screens. Throughout, students are invited to 'click' on various parts of the screen ('hot spots') to reveal further information or to test their knowledge with a variety of self-assessment questions. Users can work alone at their own pace, in small groups, or as a whole classroom (images and tutorials can be projected on a large screen). The information in the tutorials can be used to produce printed materials for private study and outreach use at primary care level.

Librarians will no doubt be playing a role in the use of CD-ROM learning materials for medical education—they are the managers of information resources. More and more such products are being issued in this format which can pose problems for the teaching faculties: they do not necessarily have computers with CD-ROM drives in their departments and often the library is the only place where they are available. However the computers and CD-ROM drives in medical libraries are probably in constant use for the searching of bibliographical databases such as MEDLINE and POPLINE. If each student takes about an hour to work through an interactive tutorial on the one CD-ROM drive in a library, hardware resources can be severely immobilised. Can a medical department or a library afford to make a machine available just for these inter-active resources? Should the provision of the necessary hardware be part of 'the package'?

The management of these important information resources needs to be discussed between medical faculty staff and the librarians especially in developing countries where funds for hardware are scarce.

The first series of four CDs will be marketed and distributed in collaboration with CAB International (CABI) and will be available from March 1998. The CDs are intended to be accessible to as many health workers as possible worldwide, and will therefore be available at a subsidized price for developing countries. The Wellcome Trust and CABI will also be working with funding agencies and government departments to provide some areas of the developing world with free copies of the materials through CABI's Information for Development (IFD) Programme. The IFD will also act as a focus for the Trust and CABI to explore the possibility of further development of the Series to include other resources through partnerships with donors and information providers.

To order the TIH series please contact:

Tania Fisher, Marketing, CAB International, Wallingford, Oxon OX10 8DE, United Kingdom Tel: +44 (0) 1491 83211, Fax: +44 (0) 1491 826090, E-mail: marketing@cabi.org

Further details on the IFD Programme are available from:

Stephen Rudgard (Head, Development Projects Unit) at the same address, fax: +44 (0) 1491 833508; Email: s.rudgard@cabi.org

Acknowledgement

This article has been adapted, with permission, from an article in the journal *Africa Health.*

References

[1] Young R. 1995 The Wellcome Tropical Medicine Resource;: 19th century principles, 21st century technology, and distance learning with global horizons. *Trans Roy Soc Trop Med Hygiene*, 1995; **89:** 465–466.

[2] Young R. 1995 Electronic training and resources in tropical medicine: the Wellcome Centre experience. In: Health, Information Society and Developing Countries. Sosa-ludicissa MC, Levett J, Mandil SH, Beales PF (eds). Amsterdam: IOS Press, pp 277–293.
[3] Rhodes James R. 1994 Henry Wellcome. London: Hodder & Stoughton.

Continuing Medical Education in Uganda—a different approach

The latest issue of *Liaison*, Newsletter of the WHO Office of Library and Health Literature Services, Volume 8, Numbers 2–3, August–November 1997, carries the following article by Dr P. C. Bowes, Continuing Medical Education, c/o Uganda Medical Association, Plot 8, Katonga Road, PO Box 2243, Kampala, Uganda.

When relative peace came to Uganda in the 1980s much of the medical work of the hospitals had suffered badly and morale in the service had fallen to very low levels. Contributing significantly to the woes of the medical staff were professional isolation and the lack of access to any form of reference material to which staff could turn when faced with medical or surgical problems. Thus the 'libraries' that had been built into many of the hospitals were largely empty of useful books, journals or pamphlets. There were no academic meetings at which problems could be discussed or new protocols described and, as some of the staff were in 'one doctor' hospitals, there were few colleagues with whom to discuss problem patients. A condition of 'Continuing Medical Ignorance' was setting in and some imaginative measures were called for.

Unfortunately the amount of money available was strictly limited. Support was raised by the Tropical Health and Education Trust in London and other charities as well as about $3000 worth of books donated by Book Aid International. Local assistance from the British Council in the form of subscriptions to the journal *Tropical Doctor* for 30 hospitals for three years and some extra needed books, and from the British High Commissioner to supplement those books, completed our support.

We purchased a 386 microcomputer, a bubblejet printer (which we run on 'Quink' ink when the cartridges run out!), a tiny electric generator, a portable photocopier, overhead projector, and (essential) a long wheelbase version of the tdi Diesel Land Rover Station Wagon equipped with long range fuel tanks and an electric winch.

The original vision was for a programme of Distance Learning, using the eleven Distance Learning Modules produced by the Wellcome Foundation. A 'Workshop' was set up to launch the first twelve doctors in this method of learning. However, before long, the shortcomings of the 'Workshop' became quite clear. Some of the participants seemed more interested in the 'per diem' and travel expenses than in the actual course content, and interest died out once the workshop was over. In the end only one of the original twelve we had hoped to recruit got anywhere near completing the course. Since then we have had a total re-think and have abandoned writing to hospitals to suggest names for Distance Learning in favour of selecting doctors of our own choosing for this method of learning. This has a much lower drop-out rate.

But more importantly we concluded that most doctors do not wish to embark on a Distance Learning project to acquaint themselves with only one aspect of medicine. In the rural areas they have to cope with the whole range of medical, surgical, obstetric, psychiatric and community health problems that come their way; they need a much broader educative programme targeted more at their real needs. So the present thrust of the programme rests on four main planks:

PROVIDING BOOKS ON THE SPOT FOR RURAL HOSPITAL DOCTORS

To this end we have used the books available from the sources listed above and distributed them as fairly as we could to the needy hospitals. Every hospital in the country has now received at least the books which they told us were those most urgently needed—books on surgery and obstetrics and anæsthesia. Some hospitals have received as many as 50 books—few have received less than six. A little spare cash

has been used to purchase 'one-off orders' for special circumstances. We are happy to say that the books chosen by Book Aid International were specially selected with the needs of the rural hospital doctor in mind.

CIRCULATING WHAT WE GRANDLY CALL A 'JOURNAL' TO ALL THE 88 HOSPITALS OF UGANDA

This is in fact a monthly newsletter, together with locally relevant abstracts from selected journals (*Tropical Doctor*, the *British Medical Journal*, the *Lancet* and so on), a 'Wrinkle Corner' in which tips are passed on as to how to manage in difficult circumstances: how to make wax stencils of diagrams so that they can be cheaply duplicated, how to re-use charts like partograms, and so on, and finally including one or two review articles written or commissioned by us with the rural hospital doctor in mind. We repeatedly request suggestions as to what these articles should target, so that we 'scratch where it itches' and don't waste effort. These articles are drafted on a simple word processor; then typesetting and the addition of diagrams is effected using a DOS-based Desktop Publishing programme 'Timewords Publisher II'. The fair copies from the Bubblejet printer are then taken to a commercial photocopy shop to produce just over 100 copies of every sheet in the month's mailing (typically 16 sides per monthly issue). The issue is then collated, put in large A4 envelopes so as to avoid folding which so damages literature, and sent out to the 88 hospitals and 29 other recipients in various countries. To be sure that the mailings do not go astray, we use various stratagems:

- *We are in close contact with the Catholic and Protestant coordinating bodies and use their services to reach the more distant NGO hospitals.*
- *The Government has kindly offered to send our materials to the Government hospitals at express letter rates free of charge to us.*
- *One or two hospitals have indicated some preferred method of communication—viz: hand the envelope to the daily bus going to the hospital in question, together with a Coca cola!*
- *As we are constantly travelling ourselves to some more or less isolated part of the country, we carry the packets ourselves to the hospitals in that area.*
- *We constantly meet people like ourselves who travel around a lot and then hand them packets for the hospitals in the towns they are visiting.*

Our review articles now amount to 70. They include stab wounds of chest and abdomen, hand infections and injuries, meningitis in children and adults, ordering supplies and equipment, epilepsy and acute psychosis, blood transfusion in the AIDS situation, strangulated hernias, anastomosing bowel, empyema, head injuries, ante- and post-partum haemorrhage, ruptured uterus, halofantrine in malaria, fractures of the lower limb, penetrating injuries of the foot, the management of wounds, suppurative arthritis of the hip in children, osteomyelitis, principles of asepsis, the red eye, simple methods of local and general anæsthesia, suppuration in the ear, making peg legs in 'the bush' and things like that. Their popularity seems to reflect the fact that there is nothing else that reaches them in their isolated places and they don't have the money to attend central workshops. These basic articles can be used as personal files for each doctor or health worker as they are easily photocopied and distributed.

VISITS TO HOSPITALS

Using our Land Rover, we equip ourselves with 35 mm projector, video tape deck, TV screen, generator, spare copies of our monthly mailing sets, a few books and booklets, and (having written to them for confirmation as to what they want), visit two or three hospitals over the course of a week or so. During such visits we show videos, such as the recent ones on upper limb fractures, anti-personnel mine injuries, the ABC of resuscitation, theatre asepsis, the management of wounds, or 35 mm slides of (say) burn management, lower limb fractures, skin grafting, etc. We also look round some of their problem patient (although as I am a surgeon they tend to show me the more surgical ones), give advice, and have

a look at their hardware (x-ray machine, autoclaves, theatre equipment and so on), giving advice on that too. Sometimes they ask for a 'Skills transfer workshop', in which case we equip ourselves for that. Once, for instance, they asked for one on spinal anæsthesia, so we took an anæsthetist with us and some equipment, and taught on their own patients, in their own hospital—a great improvement on centralised workshops.

DISTANCE LEARNING

Instead of having centralised workshops this is now done on the spot—at the student's own place of work—and the literature and references are again provided on the spot. Tutors supervise the students regularly so that there is encouragement and support 'face-to-face'. This supervision is complemented by the individual CME papers that we issue.

ARE WE MAKING ANY HEADWAY?

It is difficult to evaluate a programme like ours. We are working to improve Uganda's hospitals services hand in hand with other government departments—quality assurance, support supervision, and so on. So any improvements that may happen must give proper credit to those departments. Our main contribution is to make the knowledge available for the improvements to become possible. And some changes are beginning to appear which suggest real improvement. These include:

INCREASE IN RANGE OF OPERATIONS OR PROCEDURES DONE AT ANY ONE HOSPITAL

Examples are a hospital where the doctor(s) can now take x-rays whereas previously no x-rays were being taken; in another hospital, after reading our brochure, an effective treatment is being used for femur fractures; two hospitals have changed their method of doing Cæsarean section as a result of watching the video we showed.

IMPROVEMENT IN SAFETY OF PROCEDURES CARRIED OUT

An example is one hospital that can now give outpatient injections with autoclaved syringes and needles–one fresh set for each patient—whereas previously unsterile needles and syringes, provided by patients, were used.

IMPROVEMENT IN MEASURABLE INDICES OF SURGICAL AND MEDICAL PRACTICE

For example, one hospital that had a totally unacceptable postoperative sepsis rate has, as a result of the manual of aseptic procedure which we wrote for them (and also distributed to all 88 Ugandan hospitals), reduced its sepsis rate to a far more satisfactory level.

DOCTORS GETTING INTERESTED IN RESEARCH, FURTHER EDUCATION, OR PUBLISHING THEIR WORK

Already many hospitals keep our literature available in a loose leaf binder for study, some using it for Journal Club discussions. Indeed one hospital has now started its own internal CME meetings, written and circulated a brochure on 'Continuing Medical Ignorance', and currently is teaching all its staff the principles of such topics as fluid balance using brochures from our CME literature.

[It is not surprising that, at the end of this article, the Editor of Liaison calls for information or further input from readers who know of work or projects similar to that of Dr Bewes and his colleagues. The approach described is fairly demanding in terms of time, energy and dedication, but it is far from expensive and appears to be highly successful and greatly appreciated in Uganda].

Information packs on leprosy produced by WHO

Dr D. Daumerie, *Action Programme for the Elimination of Leprosy*, WHO, Geneva has kindly supplied examples of materials/documents produced by the Programme and already widely distributed through *Leprosy Elimination Campaign* (LEC). This approach has been extremely successful and well received in many countries. Several evaluations have shown that the material is available at the most peripheral level. Those received include—

1. *Posters*: 'Got leprosy?—Get MDT' Colour, 48 × 68 cm. Six pictures of clinical leprosy on the skin. Blister-calendar packs of multiple drug therapy (MDT) for pauci- and multi-bacillary leprosy.
   'How to cure leprosy.' 'Before and after' pictures of a patient with multibacillary leprosy (showing marked improvement with treatment) together with the blister-calendar pack for this type of leprosy.
2. '*How to recognize leprosy*'. Pictorial guide especially for health workers at the peripheral level to help them in case-finding activities. Thirteen colour pictures of clinical leprosy on the skin. Back page lists the cardinal signs of leprosy.
3. *Pocket Edition of 'A guide to eliminating leprosy as a public health problem'* (WHO/LEP/95.1) (see Book Reviews in this issue) One hundred and two pages covering all important aspects of leprosy to '... enable every health worker in endemic countries to contribute to the historic task of attaining the goal of elimination'.
4. '*Recognising and curing leprosy*'. Expanding folder of 11 pictures (8 × 11 cm), including pauci- and multibacillary blister-calendar packs.
5. *Leprosy: Diagnosis and Treatment*. Expanding folder of 11 pictures (8 × 11 cm) including guidance on clinical classification and details of pauci- and multibacillary regimens.

Further information Action Programme for the Elimination of Leprosy WHO, 1211 Geneva 27, Switzerland.

Libraries at WHO Headquarters and Regional Offices

WHO Headquarters

Office of Library and Health Literature Services	Tel: (41-22) 791 20 62
20 Avenue Appia	Fax: (41-22) 791 41 50
1211 Geneva 27, Switzerland	e-mail: library@who.ch

African Region

Regional Office for Africa Library	Tel: (00242) 83.90.31/32/33
P.O. Box No. 6	Fax: (00242) 83.94.30
Brazzaville, Congo	e-mail: afrobibl@htsd.mail.com
(Temporary address):	
P. B. BE773	
Belvedere	Tel: (00263) 4 707 493
Harare, Zimbabwe	Fax: (00263) 4 705 619

Region of the Americas

Regional Office for the Americas/	Tel: (001) 202.974.3000
Pan American Sanitary Bureau Library	Fax: (001) 202.974.3663
525 23rd Street, N.W.	e-mail: library@paho.org
Washington, D. C. 20037, USA	

Eastern Mediterranean Region

Regional Office for the Eastern Mediterranean Library	Tel: (00203) 48.202.23
P.O. Box 1517	Fax: (00203) 48.39.916
Alexandria–21511, Egypt	e-mail: postmaster@who.sci.eg

European Region
Regional Office for Europe Library
8, Scherfigsvej
DK-2100 Copenhagen

Tel: (0045) 39.17.17.17
Fax: (0045) 39.17.18.52
e-mail: msb@who.dk

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

Tel: (0091) 11.331.7804
Fax: (0091) 11.331.8607
e-mail: postmaster@who.ernet.in

Western Pacific Region
Regional Office for the Western Pacific Library
P.O. Box 2932
1099 Manila, Philippines

Tel: (00632) 528.80.01
Fax: (00632) 52 11 036
e-mail: postmaster@who.org.ph

AFROPAC: WHO Regional Office for Africa

The following information appeared in the latest issue of *Liaison*, Newsletter of the WHO Office of Library and Health Literature Services, Volume 8, Numbers 2–3, August–November 1997.

The World Health Organization Regional Office for Africa has recently launched a new Health Information Package entitled 'Coping with common diseases' dealing with 11 major diseases prevalent in the African continent.

The AFRO Health Information Package (AFROPAC), the first in a series of packages, has been produced in print in English, French and Portuguese versions. It consists of a folder with separate pages for each disease explaining, in simple language, what the diseases are, how they are caused, how to prevent them, the symptoms to look out for and what to do. Information on therapy is not included as the package is intended for patient use—to empower people with the information to protect their own health and contribute to the improvement of the health situation in their community.

It is intended that national governments translate the packages into the local languages and that they be adapted for use by all available modern and traditional means of mass communication. The media use them as a basis for radio programmes and newspaper articles, audio cassettes have been distributed and videos can be made from the information provided. Theatre production is suggested as well.

As a health promotion tool for the community, AFROPAC complements the expertise of health professionals in their work.

For copies of the AFROPAC files, please contact the WHO Regional Office for Africa which is temporarily at the following address: WHO Regional Office for Africa, att: DCP, P.O. Box BE 773, Belvedere, Harare, Zimbabwe.

'A library without walls' Office of Library and Health Literature Services, WHO, Geneva

The following article by Yvonne Grandbois and Barbara Aronson was published in *World Health*, the magazine of the World Health Organisation, No 6, Nov–Decv 1997.

The popular image of a library is of hushed rooms lined floor to ceiling with books through which people leaf in search of information. But this image is out of date. Today's libraries are at the forefront of the information revolution, busily transmitting knowledge to colleagues and clients around the world using

the latest technology. WHO's library is no exception. Our librarians based in Geneva and six regional offices are involved in a wealth of communication activities with a wide variety of clients, from ministries of health, hospitals and international organizations to individual scientists, researchers, students and general enquirers. Our services include sending ready-packaged mini-libraries of vital health information to clients worldwide, running a free exchange service of books and medical journals for other libraries, and training librarians around the world in the latest health science library technologies.

Every week we receive masses of queries and requests for information. Here is a typical selection of questions and the answers we give:

Our library budget is very limited, and we can't convert it to foreign hard currencies. How can we subscribe to international journals for our researchers and purchase the latest textbooks for our medical students?

You can order your books and medical journals through WHO Library's **health literature purchasing service**, and pay through WHO's **Revolving Fund** with your local currency. WHO Library will ensure that you get the best value for your money. You may even be able to find some of the items you are looking for free of charge through our **International Health Literature Exchange**.

Our documentation centre has just been connected to e-mail, and our country should have full Internet capacity by next year. What services can we already have access to, and what can we look forward to when we can enter the World Wide Web?

Through e-mail you can already use our services, including **WHOLIS** (for bibliographical records), **WHODOC** (for information about new WHO publications and documents), and entire issues of our Library **newsletters** (for professional updates on new technologies and trends). These same services are also available through the World Wide Web (**http://www.who.ch**), where they are even easier to find.

Of special interest to our colleagues in Africa are **AHILANET** (African health sciences librarians discussion group on e-mail), our full text **WHO Library Digest for Africa**, and the **African Index Medicus** bibliographic database, both on the Web and gopher.

We receive WHO publications at the Ministry of Health. How can we know which one to look in to find the answer to a particular question?

Consult the **WHOLIS** database and its **WHODOC** updates available on diskette, paper, or the Internet (gopher and the Web). Write, telephone or e-mail the WHO Library closest to your country for guidance.

Our health dispensary is in a rural area several days' journey from any library. How can our personnel get the information they need to provide the best possible medical services?

Our **Blue trunk Libraries/Bibliothèques bleues** and **WHO Documentation Modules** can meet your need. They contain basic manuals and are designed as 'instant libraries', ready for use on arrival. The WHO Library can help you get started.

We know that the health conditions and problems in our area are similar to those in other districts and in neighbouring countries. Is there any way we can share knowledge resources locally and regionally?

WHO's **Regional Office libraries** organize health information and literature services programmes including training, expert counsel and advice. They also publish indexes—topics, authors and titles each arranged in alphabetical order–to the health and medical literature published in countries of the region. Some indexes are already on the Internet, others are on CD-ROM, or on paper. Regional libraries also run networks for sharing resources. Contact your Regional Office library to find out more about its activities.

Our institute does research on public health topics. How can we know what WHO has written on these subjects?

Consult **WHOLIS** on the Internet, CD-ROM, diskette, or paper. This international database indexes all WHO-produced knowledge and information (books, unpublished technical documents, official records, journal articles, CD-ROMS, videos, press releases) from all WHO offices and projects worldwide.

HOW DO WE COMMUNICATE?

Besides answering queries the conventional ways—by post, telephone and fax—WHO Library communicates with clients:

- by e-mail:**library@who.ch**
- through its home page on the WHO Website **(http://www.who.ch);**
- through its electronic database, **WHOLIS**, which enables clients to find out what WHO's view is on any health-related topic;
- through its newsletter, **Liaison**, distributed to health science librarians in developing countries;
- through its **WHO Library Digest for Africa**, transmitted by satellite to ground stations in Africa;
- through the AHILANET e-mail discussion group for health science librarians in Africa.

Ms Yvonne Grandbois is Chief, and Ms Barbara Aronson is Librarian, Office of Library and Health Literature Services, World Health Organization, 1211 Geneva 27, Switzerland.

Current Awareness in Biomedicine: SUBIS, Sheffield, United Kingdom: Mycobacteria

Volume 4, Number 22, late November 1997 of *Current Awareness* from SUBIS, Mansion House, 19 Kingfield Road, Sheffield S11 9AS, United Kingdom, lists 35 recently published books, reviews, original articles and letters on mycobacteria. SUBIS is described as 'a world-wide, current-awareness service in biology and medicine established in 1967. It has become a world leader in the provision of information in the fields of biotechnology, cell biology, immunobiology, neuroscience and physiology.

Manual searching by trained scientists means that the titles of relevant papers, which may be missed by computer searches, can be on your desk only 5–8 weeks after publication.'

Current catalogues are available on request or via the World Wide Web-**http://www.shef-ac-press.co.uk**

Bengali edition of 'Leprosy; basic information and management' (Ciba-Geigy/Novartis Foundation for Sustainable Development) distributed in Bangladesh, Calcutta and West Bengal, India

Dr D. S. Chaudhury, Grecaltes Training Centre, 23 Market Street, Calcutta 700 087, has kindly written to report that over 12,000 copies of the above booklet, published by Ciba-Geigy in Basle, Switzerland (recently changed to Novartis), have been distributed to Bangladesh, Calcutta and West Bengal in India in the last few years. The main recipients in Bangladesh have been The Leprosy Mission, The Damien Foundation and the Ministry of Health and Family Welfare. The booklet, translated into Bengali by Dr and Mrs Chaudhury, has been used extensively in training programmes for various grades of health staff in Bangladesh and plans are now in hand to produce a further 5000 copies of a revised edition. The booklet has also been used by the Health Department of the Government of West Bengal, the School of

Tropical Medicine and the All India Institute of Hygiene and Public Health, Calcutta, medical colleges and hospitals, district leprosy officers, The Leprosy Mission, Calcutta and the Grecaltes Training Centre. Copies in Bengali are available from Dr D. S. Chaudhury at the above address and in English from The Novartis Foundation for Sustainable Development, CH 4002, Basle, Switzerland.

Schieffelin Leprosy Research and Training Centre, Courses in 1998

Facilities: Hostel: 60 Men, 16 Women
Guest House: Single & Double Room

I. Courses Recognised by The Government of INDIA

Courses	Qualifications	Duration	Commencing Date
Medical Officer	Medical Personnel engaged in Leprosy work	6 weeks	Jul 27–Sep. 05
Physiotherapy Technician	+2 passed or P.U.C. (with science subjects)	12 months	Jul. 01–Jun. 30
Laboratory Technician	+2 passed. Science graduates preferred	12 months	Jul. 01–June 30
Smear Technician	+2 passed (with science subjects)	3 months	Sep. 07–Dec. 05
Para Medical Worker	+2 passed. Graduates preferred	6 months	Jul 01–Dec. 31
Shoe-Maker	V-standard with knowledge of English preferred	6 months	Jul. 01–Dec. 31
Diploma in Prosthetic & Orthotic Engineering	+2 passed. Graduate preferred (with science subjects)	30 months	Jul. 01–Dec. 31 (2000)
Ophthalmic aspects in leprosy	Medical Personnel	1 week	Sep. 07–12
Eye care in Leprosy	Non Medical Personnel	1 week	Sep. 14–19

II. Other Courses Offered by the Institution

Courses	Qualifications	Duration	Commencing Date
Medical Records Technologist (CMAI)	+2 passed	15 months	Jul. 01–Oct. 31
Community Based Rehabilitation Worker		12 months	Jul. 01–Jun. 30
Refresher Course in Skin Smear	Trained Laboratory Technician	2 weeks	Apr. 20–May 02 Aug. 17–29
Condensed Course in Leprosy	Medical Personnel Non-Medical Personnel	1 week 1 week	Nov. 02–07 Nov. 23–28
Research Methods in Leprosy		1 week	Nov. 09–14
Programme Management issues in Leprosy Control	Project Officers & Supervisory level in Leprosy Control Project	1 week	Nov. 23–28

III. In-Service Training

Courses	Qualifications	Duration	Commencing Date
In-service training in Medical Surgery. Surgical rehabilitation, Pathology, Laboratory Technology, Opthalmology & Epidemiology and Leprosy Control	For qualified Medical personnel/ Health professionals	3 months	By arrangement
Medical Students Course	Clinical Medical Students	1 week	By arrangement
Medical Record Keepers	+2 passed with proficiency in typing and good English	2 months	By arrangement
Basics of Physiotherapy in Leprosy	Under graduate in Physiotherapy	1 week	By arrangement
Basics of Occupational therapy in Leprosy	Under graduates in Occupational therapy	1 week	By arrangement
Psycho-social aspects in Leprosy	Medical/Non-Medical Personnel working in leprosy field	1 week	By arrangement
Ophthalmic Nursing Care	Nursing Technician students/Staff Nurse	2 week	By arrangement

Courses:- English fluency essential. Recognised by WHO and Indian Government (all Paramedical & Technical courses are fully recognised by the Indian Government).

How to Reach Karigiri: Karigiri is situated about 130 Km West of Chennai (Madras), which is connected to all the major cities of India by Air, Train and Road. From Chennai Airport the fare for Taxi is approximately Rs. 800/= route–Ranipet–Tiruvalam–Sevoor–Karigi Hospital. There are also many buses which operate between 05:00 Hrs and 22:00 Hrs from Chennai to Vellore. From Vellore take any Taxi or Auto which costs Rs. 150/- and Rs. 100/- respectively or else you can take a prepaid Taxi or Electric Train to the City Railway Station (Central Railway Station) about 20 Kms away from Airport. From there take any Train to Katpadi Railway Station (13 Kms away from Karigiri). From Katpadi to Karigiri an Auto will cost Rs. 100/-. If you want to be met at Katpadi or at Chennai Airport, please let us know well in advance.

Mailing Address: Director or Registrar,
Training Unit,
Schieffelin Leprosy Research & Training Centre,
Karigiri-632 106, Vellore District, Tamil Nadu, INDIA.

Contact Institution: Mr T. Jayarajan, Registrar,
Schieffelin Leprosy Research & Training Centre,
Karigiri-632 106, Vellore District, Tamil Nadu, INDIA.

Telephone: 91-(0)416-74227, 74229, 74251, 74221 (Director)
Fax: 91-(0)416-74274, 25035, 32103, 32788

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News and Notes

20th Biennial Conference of Indian Association of Leprologists

The 20th Biennial Conference of Indian Association of Leprologists was held at the Gandhi Medical College, Bhopal from November 28–30, 1997. About 316 delegates from different parts of the country and a few delegates from abroad were registered for the conference. Dr S. K. Noordeen, WHO consultant on Elimination of Leprosy inaugurated the conference and delivered the key note address. He spoke of the prospect for elimination of leprosy as a public health problem within the deadline of the year 2000 and the three pronged strategy of 1) Leprosy Elimination Campaign (LEC), to reach hidden cases and bring them under treatment; 2) Special action approaches for the elimination of leprosy (SAPEL) to reach patients in in-accessible areas and 3) Making MDT available in every general health facility so as to make leprosy treatment universally acceptable.

There were two state of the art lectures on 'Vaccines against leprosy', by Dr B. R. Chatterjee and 'Pathology of nerves in leprosy' by Dr Vanaja Shetty. Dr Chatterjee stressed the need for a vaccine with dual potential—the ability to boost the immune system thereby protecting against infection and the ability to suppress misplaced immune and auto immune responses thus preventing nerve damage. Dr Shetty through her detailed light, semi-thin and electron microscopic work elegantly described the various pathogenic mechanisms involved in nerve damage and the frontiers for research in the prevention of nerve disability.

There were 11 scientific sessions spread over the three days with both oral and poster presentations. Areas covered included Microbiology and Biochemistry, Immunology and Pathology, Clinical Leprosy, Treatment, Reconstructive surgery, Epidemiology and leprosy control, disability prevention and social aspects.

A special session was held on 29th November '97 to address the issue of mono-lesion treatment with ROM and shortened MDT for MB leprosy. Dr Noordeen introduced the discussion and Dr Ganapathi outlined the magnitude of the problem of mono-lesions. Brief reports on ROM were presented from different centres involved in the Multi-centric WHO Trial. Dr Katoch, Dr Diana Lockwood and Dr B. N. Reddy gave short presentations on the advantages and limitations of WHO ROM treatment.

Dr Britto from TRC, Chennai was chosen for the best publication award for the paper entitled 'Regional lymphadenitis following a leprosy vaccine' and Dr Anurag Tiwari received the best presentation award for his case report entitled 'Punch grafting for trophic ulcers'.

The main conference was preceded by pre-conference Symposia on 'The Relevance of Leprosy Research in the present Scenario' and 'Leprosy Scenario in low endemic areas'. The Chief Guest at the closing session was Dr Kamlakar Singh of University Grants Commission. Dr J. A. Ponnaiah was elected president and Dr Porichha as Secretary of the Association for the next Biennium.

The conference honoured two great personalities in the field of Leprosy—Dr S. K. Noordeen and Dr G. Ramu for their doyen services.

LEPRA INDIA was one of the voluntary organisations who contributed by way of sponsorship for the conference.

Dr Sujai Suneetha,
Dhoolpat Leprosy Research Centre,
Hyderabad, India

New tools for leprosy control

Taken from *TDR News*, no. 55, February 1998

With regard to leprosy, WHO's goal is 'elimination as a public health problem', i.e. reduction in prevalence of the disease to below one per 10,000 head of population in all endemic countries, by the year 2000. This implies that leprosy will exist well into the next century, although at a much reduced level. One reason for having a current goal of elimination as opposed to one of eradication (complete disappearance of a disease from the face of the earth, as has been achieved for smallpox and is currently being undertaken for poliomyelitis) is the current lack of tools suitable for eradicating leprosy.

In order to eradicate a disease, amongst other prerequisites, we must know how many people are carriers of the pathogen, in this case *Mycobacterium leprae*. So-called skin test reagents (e.g. Mantoux test, lepromin) are used to estimate the number of people exposed to the mycobacterium and hence the number who may be carriers of the pathogen. The reagents are bacterial preparations which, when scratched into the skin of a person who has been exposed to the pathogen, produce a skin swelling which is immune-dependent. The major problem with existing skin test reagents is that they lack specificity and often cross-react, detecting exposure to all kinds of mycobacteria other than the one used for production of the skin reagent. This is a particular problem in leprosy endemic countries, where people may be confronted by a whole range of mycobacteria which are closely related to *M. leprae*. With a long-term view to eradication of leprosy, TDR has been supporting the development of a skin test that would be specific for leprosy only. An immediate benefit would be easier monitoring of the effect of multidrug therapy on the circulation of *M. leprae* in a given community.

The rationale for the TDR leprosy skin test initiative is that, although most individual proteins of *M. leprae* will cross-react with other mycobacteria, certain short fragments of them (peptides) are likely to contain *M. leprae*-specific epitopes that may induce immune reactions comparable to those provoked by the intact proteins. To be useful in a leprosy-specific skin test, the peptides must not only be sufficiently different from peptides of other infectious organisms, especially other mycobacteria, but they must also be recognized by the immune systems of individuals previously infected by the bacterium. Two hundred 15-mer peptides fulfilling these prerequisites were selected as candidate antigens for a leprosy-specific skin test. Selection was based on empirical algorithms which predict association with antigen-presenting (HLA) molecules and on gene-library comparisons between *M. leprae* and *M. tuberculosis*. Ultimate proof of immune recognition however will have to await clinical testing in humans.

A potential problem for peptide-based skin tests, however, is the genetic variation in antigen recognition that may exist in different human populations. Although antigen recognition by each human being is unique, population-specific antigen recognition patterns have been described for other infectious diseases such as malaria and are suspected to be at work in leprosy. Therefore, testing of candidate peptides will be carried out in different leprosy-endemic areas of Asia, Africa and Latin America. Should the project confirm that such genetic differences exist, the skin test will ultimately be tailor-made for a given geographical area or, alternatively, will contain a mixture of several peptides representing all regional 'preferences'.

Currently, the peptides are being tested *in vitro*, using blood lymphocytes from leprosy patients and controls (healthy people from non-endemic areas). Once the laboratory tests are completed and the most reactive peptides have been infected, skin testing will begin in humans. It is hoped that the laboratory tests will be completed by the end of 1998 and that human trials will begin in 1999. Apart from the obvious focus on safety and freedom from side effects, the human trials should determine whether peptides known to react with blood lymphocytes are also capable of stimulating a skin reaction *in vivo* and whether or not they cross-react.

Vaccine discovery research converges to focus on products

Taken from *TDR news*, No. 55 February 1998

Vaccine discovery in TDR has changed. The three disease-specific vaccine committees have become one (the Vaccine Discovery Research Committee [VDR], see *TDR news* No. 54, October 1997); there are revised priorities, sharply focused on goals, objectives and products.

Vaccines for malaria, leishmaniasis and schistosomiasis are the end-point. Research will focus on the identification and evaluation of candidate antigens, adjuvants and delivery systems. For malaria and leishmaniasis vaccines, the objectives and product profiles are clearly defined in terms of percentage reduction in mortality and/or morbidity, reduced incidence, duration of immunity and target populations. For schistosomiasis vaccines, the objectives and product profiles are defined in terms of percentage resistance to infection/re-infection and duration of this resistance.

Safe and effective vaccines would represent one of the most cost-effective interventions amongst the present range of control strategies for these diseases. In the last decade there has been considerable progress in understanding immunity to parasitic diseases, identifying vaccine candidate antigens and their genes, and demonstrating the protection afforded by vaccine candidates in animal models. However, due to the complexity of parasitic diseases and the cost of vaccine development, relatively few candidate vaccines have so far progressed to clinical trials; and it has proved difficult to develop *in vivo* and *in vitro* assays for predicting protection. Today we stand on the verge of the post-genome era. There is currently a mass of new information available on genes and their products but a shortage of research funds and a relative lack of commercial interest in parasite vaccines. Thus, at the global level, there is a need for parasitic vaccine discovery, development and clinical testing to be coordinated, organized and executed in collaboration with leading scientists and institutions in disease endemic countries.

The first meeting of the VDR will take place in May 1998; new and innovative proposals in vaccine discovery research are now being solicited. Please send your pre-proposals to the Manager of the Steering Committee on Vaccine Discovery Research (VDR), Dr H. Engers (engersh@who.ch), for advice as to the suitability of topic.

ALLF

Leprosy Review has received the first two issues of *Bulletin de l'Association des Léprologues de Langue Française* (ALLF). We believe that this publication will be particularly useful for French-speaking African workers. For further information and subscriptions, please contact: Association des Léprologues de Lange Française (ALLF), 4 rue Jean Jacques Bel, 33000 Bordeaux, France.

HIV and TB in children

The following is taken from '*Tuberculosis and children: The missing diagnosis*', published by AHRTAG, Farringdon Point, 29–35 Farringdon Road, London EC1M 3JB, United Kingdom, 1996.

Children with HIV are at higher risk of TB infection and of rapid progression to disease than children without HIV. It makes sense to always consider the possibility of TB in a child with HIV infection.

DIAGNOSIS

Diagnosis of TB in children with HIV can be difficult because:

- children who are HIV positive may be tuberculin test negative even when they are infected or ill with TB, because their immune system is not functioning well;

- several features are common to both infections. Failure to gain weight, weight loss, intermittent fever, chronic cough, and history of recurrent illness are seen in children with TB and in children with HIV.

Accurate diagnosis is important because:

- children with HIV without TB should not be given TB treatment unnecessarily;
- children with HIV and TB need treatment.

PROGRESSION AND TREATMENT

The natural history of TB in an HIV infected child depends on the stage of HIV disease.

- If the child is still well and the immune system is working properly, the signs of TB will be the same as in a child without HIV infection.
- If HIV is more advanced, TB can spread to other parts of the body and progress to serious illness more rapidly. Disseminated disease, tuberculous meningitis and general enlargement of the lymph nodes are more common in HIV positive children.
- A sick child with HIV and TB will respond well to anti-tuberculosis treatment.
- Children with HIV should NEVER be treated for TB with thiacetazone because this drug can cause severe and sometimes fatal side effects in patients with HIV.

Scientists discover how HIV enters cells

The following appeared in the *British Medical Journal*, Volume 312, 29 June 1996.

A new, recently discovered cofactor that allows HIV-1 to enter and infect human cells could prove a useful future therapeutic target, according to US scientists writing in the 28 June issue of *Science* (272; 1955–8).

HIV-1 infects cells by binding to the cell surface molecule called CD4. Although this mechanism has been recognised for the past decade, researchers had noted that the presence of CD4 alone was not sufficient to guarantee infection. It became clear that a cofactor was needed.

One of the authors of this recent paper is Edward Berger, chief of the molecular structure section at the National Institute of Allergy and Infectious Diseases at the National Institutes of Health in Bethesda, Maryland, United States.

Berger said: 'We knew that the basic mechanism was rather like two soap bubbles: a large one representing the cells, and a small one, the virus. They stuck to each other, but their contents did not mix. It was this mechanism of viral mixing which we all knew to be crucial, but no one understood how it was achieved.'

Last month scientists from Dr Berger's team identified the cofactor as fusin, a molecule that allows HIV to fuse with its target before entry (*Science*; 272: 872–7). However, only certain strains of HIV-1—those identified in the late stages of HIV infection—seemed to need this cofactor. Other strains, most commonly passed between individuals in the early stages of the infection, seem to have a different mechanism for entering cells.

Along with other teams of colleagues, who published an article in the 20 June issue of *Nature* (381; 667–673), part of the same research group has identified a second fusin-type molecule called CC CKR5. Unlike fusin, which is found on T cells, CC CKR5 is found on macrophages.

CC CKR5 is a receptor for chemokines known to inhibit HIV infection. Chemokines have been shown to stop in vitro replication of HIV. They may achieve this by blocking HIV's access to their receptors, which act as viral docking sites.

'The number and distribution of these cofactors may help to explain why some individuals stay asymptomatic for a long time, while others become rapidly infected with HIV and progress to full blown AIDS faster,' said Dr Berger. The race is now on to create transgenic animal models that have not only human CD4 receptors but also the two newly identified cofactors, fusin and CC CKR5.

'Many of the therapeutic implications of this discovery remain speculative, but we have reached a better understanding of a vital process in HIV infection which has remained unclear until now,' said Dr Berger.

WHO: proactive role in advancing policy of health for all

Under the heading 'Future of international health', the following letter, with the above title, appeared in the *British Medical Journal*, Volume 315, 1st November 1997.

Editor,

A recent article on the new world order and the future of international health and an editorial on reform of the World Health Organisation are valuable contributions to discussions about the future of international health.[1,2] Within the WHO substantial progress has been made over the past 18 months in addressing issues raised in the renewal of the Health for All process.[3] However, the richness and breadth of this process were not captured in Fiona Godlee's editorial, which focused on selected internal and external debates without indicating that they have been formally and informally linked to the renewal process.[2]

The WHO regards the renewal process as integral to the future course of world health. This view is shared by its member states and its governing bodies. During the 50th World Health Assembly in May, discussion on renewal overlapped with the issues raised in the article and the editorial.[1,2] Furthermore, during the subsequent session of the executive board, members expressed support for fundamental actions that should form the basis of the new policy and for specific future roles for the WHO (box). These fundamental actions include the establishment of a universal Health for All value system that explicitly considers the pursuit of human rights and health security, equity, ethics, and a gender perspective, thereby making health central to development. The complexity of future health demands requires consideration of a broader agenda for global health action, not one that is narrow and disease specific.

The Health for All consultation process has been deliberately wide. The early call for dialogue, both through formal consultative documents[4] and through the World Health Forum round table (which drew on a wide range of global reviews[5]), has resulted in a draft policy. This policy incorporates the views of countries, non-government organisations, leading academics, United Nations bodies, and the private sector. The guidelines contained in this draft, however, will need substantive discussion at country level before specific priorities for action can be decided. The draft policy is now available on the WHO's web site (/www.who.ch). Consultations planned until late October include meetings with countries during the meetings of the regional committees in September and October, and with UN bodies, the World Bank, the World Trade Organisation, and a wide range of non-government organisations.

The WHO is taking a proactive role in defining actions that will advance the policy and ensure that it leads to tangible improvements in the health of populations. It is committed to continue working with all who share a common vision of Health for All.

F. S. Antezana *Assistant director general*
World Health Organisation, CH-1211 Geneva 27, Switzerland

References

[1] Frenk J, Sepulveda J, Gomez-Dantes O, McGuinness MJ, Knaul F. The new world order and the future of international health. *BMJ*, 1997; **314:** 1404–7. (10 May).
[2] Godlee F. WHO reform and global health. *BMJ*, 1997; **314:** 1359–60. (10 May).
[3] Antezana FS. Health for all by the year 2000. *BMJ*, 1996; **313:** 1331.
[4] World Health Organisation. *Renewing the health-for-all strategy. Elaboration of a policy for equity, solidarity and health.* Geneva: WHO, 1995 (WHO/PAC/95.1).
[5] Yach D. Renewal of the health-for-all strategy. *World Health Forum*, 1996; **17:** 321–6.

Eliminating World Poverty. 'White Paper' on International Development, Presented to Parliament in the United Kingdom, November 1997

This momentous and potentially far-reaching document was presented to Parliament in London by the Secretary of State for International Development by Command of Her Majesty, November, 1997. The Foreward by the Secretary of State reads as follows.

This White Paper sets out the Government's policies to achieve the sustainable development of this planet. It is first, and most importantly, about the single greatest challenge which the world faces—eliminating poverty. It is about ensuring that the poorest people in the world benefit as we move towards a new global society. It is about creating partnerships with developing countries and their peoples, on the basis of specific and achievable targets, to bring that about.

We can succeed. The overall successes of development in recent decades have been remarkable—people live longer; fewer mothers die in childbirth; fewer infants die from preventable diseases. But the numbers living in poverty are continuing to grow. Too many people—1·3 billion too many—live in extreme poverty. The major UN Conferences of recent years have drawn together an agenda that could deliver sustained progress. There are good reasons for optimism. But to succeed we need to mobilise greater political will across the international community.

It is our duty to care about other people, in particular those less well off than ourselves. We all have a moral duty to reach out to the poor and needy. But we also owe it to our children and our grandchildren to address these issues as a matter of urgency. If we do not do so there is a real danger that, by the middle of the next century, the world will simply not be sustainable. The combination of population growth, environmental degradation and the conflict and disease to which this will lead could impose catastrophic pressures upon the planet. This White Paper outlines the ways in which we can make progress. To succeed, we need the active support of the people of Britain. In this area we could give a lead which would make us all very proud of our country and also secure a safe and decent future for all of us.

The detailed text is interspersed with a number of 'panels' on key issues. That on *Essential Health Care* reads as follows.

THE CHALLENGE

The poorest billion people in the world are ten times more likely to die young (under 15 years of age) than the richest billion; they are nine times more likely to die of communicable diseases (diarrhoea, malaria, pneumonia and TB) and twice as likely to die from accidents and injury. Women, who are more at risk in all cases, are also at least ten times more likely to die of causes related to pregnancy and childbirth. This massive burden of ill-health affects poor people's chances of escaping from poverty and taking advantages of opportunities to do better.

Tackling high death and disability rates among poor people poses real challenges. For example, millions of people throughout the world cannot access sufficient water for personal use. As many as half the world's population lack access to effective means for disposing of excreta. Water, sanitation, shelter, food and education, as well as essential health care, are all vital requirements if efforts to improve poor people's health are to succeed.

Recent studies have indicated that a spend of just £9 per person per year on essential health care is sufficient to make a real difference to the suffering of poor people. This would allow a basic package of immunisation and nutritional supplements and public education of family planning, prevention of AIDS and sexually transmitted diseases and substance abuse, to be provided. Currently, many developing countries spend less than £3 per person per year for all health needs, and these funds are not distributed in a way that ensures equitable service provision.

OUR RESPONSE

The UK has signed up to a series of relevant international targets to be achieved by 2015—specifically

halving proportions of people in poverty, halving child mortality rates, reducing maternal mortality by three quarters and ensuring accessible reproductive health services. These call for coherent action to improve the livelihoods and well-being of poor people in poor countries.

We are committed to:

- helping ensure that all the world's people—particularly those in the poorest countries of Africa and Asia—can access and benefit from essential health services;
- establishing long-term partnerships for better health with countries, international organisations and UK-based groups;
- supporting local (as well as global) initiatives on specific issues—for example, to help young people improve their sexual health and reduce HIV, enable all to lessen dangers for women associated with pregnancy, to reduce poor people's suffering due to communicable disease—especially malaria, tuberculosis, diarrhoea and the like, to access clean water and sanitation, and promote health environments;
- working with governments to develop sector-wide approaches to better health;
- increasing our support within the United Nations system to promote international standards for human health and health care;
- the better application of scientific knowledge and techniques to the health and well-being of poor people.

Available from Her Majesty's Stationery Office, HMSO Publications Centre, 51 Nine Elms Lane, London SW8 5DR.

The Nippon Foundation (formerly The Sasakawa Foundation) Tokyo, Japan

Readers of the 6th June 1997, No. 23, issue of *Weekly Epidemiological Record* (WHO, Geneva) may have noticed a reference on page 168 to the supply of multiple drug therapy (MDT) by WHO, but through a contribution from The Nippon Foundation, for more than 1·7 million leprosy patients living in 35 endemic countries.

Mr Koichi Takagi, until recently Director of International Affairs for The Nippon Foundation, has kindly written to clarify the relationship of his Foundation to the Sasakawa Memorial Health Foundation (SMHF), which may be better known to many of our readers. The essential information reads as follows.

'The Nippon Foundation, formerly the Sasakawa Foundation, is a private, non-profit organization. It was founded in October of 1962 when it was written into law that a portion of revenues from motorboat racing would be channeled to philanthropic activities. According to the rules and regulations governing the motorboat racing industry, 75% of revenues must revert back to the public in the form of winnings. Of the remaining 25%, the bulk of which is slated to cover organizers' costs, 3·3% becomes the operational funds of the Foundation.

In keeping with the late Chairman Ryoichi Sasakawa's motto, 'The World is One Family, All Mankind are Brothers and Sisters,' the Foundation's activities are geared toward the alleviation of human suffering, the advancement of human welfare, and the promotion of world peace. The scope of its activities transcends politics, ideology, religion and race.

The Foundation has the largest operating budget of its kind in the world. Funds are allocated to support both domestic and international projects, including those implemented by the United Nations. In 1995, 65 billion yen (US$650 million) was available for disbursement; of this amount, 8·5 billion yen (US$85 million) was earmarked for overseas assistance.

The Foundations's overseas support covers a broad range of areas, including welfare, human resource development, academic and physical education, health care, population, agricultural and rural development, human rights, environment, hunger relief, refugee aid and international understanding.

Some of the Foundation's major projects have been:

- agricultural development in Africa to foster self-sufficiency in staple food production (since 1986);
- establishing fellowship funds at major universities throughout the world to enable promising young scholars to pursue post-graduate studies;
- leprosy control, in collaboration with WHO (since 1975);
- promotion of primary health care in developing countries, in collaboration with UNICEF and local governments (since 1992).

'Over the last 22 years, the Nippon Foundation and the Sasakawa Memorial Health Foundation have been closely involved in the global leprosy control program through our contributions of more than US$100 million to two organizations: the Sasakawa Memorial Health Foundation (SMHF) and the World Health Organization (WHO).

Although only slightly infectious, leprosy has been feared and misunderstood globally because of its tendency to produce visible deformities, and consequent physical and social disabilities, through peripheral nerve damage. This in turn has resulted in extremely unjust treatment of victims throughout the ages.

With the use of effective drugs, however, leprosy is no longer an incurable disease. Deformities can now be prevented, provided that the patient receives early treatment.

Since its establishment in 1974, SMHF has been closely collaborating with health authorities in countries where leprosy is endemic. Beginning in East and Southeast Asia, and then expanding into Southern Asia, Africa, and Latin America in the mid-1980s, we have helped countries strengthen their national leprosy control activities by supplying drugs, medical instruments, training materials, transport equipment, technical expertise, and funding.

In 1982, WHO published a recommendation for multi-drug therapy (MDT), a new approach to an effective leprosy control scheme in the field. Thanks to MDT, the number of cases of the disease worldwide dropped from 10 million to 12 million in the mid-1980s to fewer than 2 million in 1995. Encouraged by these remarkable results, the World Health Assembly passed a resolution in May 1991 calling for the elimination of leprosy as a public health problem by the year 2000. In numerical terms, this means reducing the rate of the disease to no more than one case per 10,000 people in every country where it is now endemic.

In order to support the Leprosy Elimination Program, we are providing the WHO with an additional $50 million over a five-year period for the purchase of necessary MDT drugs. Our commitment is firm: We will continue to support this program until its successful conclusion in the year 2000 by strengthening our cooperative ties with both WHO and health authorities in each country.'

Further information about The Nippon Foundation: Mr Takashi Ito, Director of International Affairs, The Nippon Foundation, Senpaku Shinko Building, 1-15-16, Toranomon, Minato-ku, Tokyo 105, Japan.

Bangladesh Rural Advancement Committee (BRAC)

Sadia Chowdhury, Director, Health & Population of BRAC, has written with information about this remarkable organisation in Bangladesh, originally created in Sulla (Sylhet) as a relief agency.

When BRAC was born in 1972, its initial aim was to bring succour to affected people in the genocidal war of 1971. Starting its work in the Sulla area of Sylhet district in the north-eastern part of the country, BRAC provided relief and rehabilitation for war ravaged victims who had lost all and had no means of livelihood. Although BRAC began its operations with relief work it eventually underwent two basic transitions, first from relief to development work, then from a community development effort to development oriented to target groups only. In the first approach, adopted in 1972, while basic human needs were met by providing welfare assistance to the village poor, a state of utter dependency crept in amongst them. Thus in 1973, BRAC shifted its approach towards community development. However, lack of access to resources also continued to create a situation of dependency for the poor on the rich people of the village. Despite being well-intentioned and meant to benefit the poorer community, this

strategy was misused by the influential and by-passed the resourceless. Based on better understanding of the dynamics of the rural power structure, in 1976 BRAC underwent its second transition towards the target group approach. The target populations consist of the poorest of the poor: day laborers, fishermen without fishing tools, *rickshaw* pullers, farmers working on land that is share cropped, service or petty traders and craftspersons. These people sell their manual labor to earn an income, lack adequate leadership and have low status in society. By organizing landless people with programmes directed towards their development, BRAC operates as a self-help initiator, and tries to make them aware of their own problems, and provide them with the tools to improve their socio-economic status. Through various shifts in its approaches BRAC's goals became clear:

Learning by doing, in developing the target group approach BRAC aimed not only to change the conditions of the poor in the village through microeconomic growth oriented programmes, but also to educate the poor about the mechanisms of exploitation and the basic causes of poverty through a process of conscientization. BRAC believes development programmes should not be focused on felt needs only. BRAC programmes, therefore, do not only meet the immediate needs of the rural poor, they also generate new demands. In all its efforts BRAC is careful to encourage and to ensure participation and involvement of the group members.

Since 1993, BRAC has been focusing its programmes specifically on women and children. The experience that BRAC gained by observing rural women through their long-term involvement with the organization brought the realization that the reason for rural women being placed in a helpless position is their continuous state of powerlessness both economically and socially. Female members of the household receive less nutrition, lack health care, and have little or no access to education. Employment opportunities are limited for them with the few seasonal jobs available offering low wages. Yet, women are responsible for the lion's share of the work within and outside the domestic sphere. Women provide food for the family, perform household chores and assist the male members in farming or other activities in the public sphere. Furthermore, the growing number of female headed households as a result of death, divorce, desertion and male migration have left many women as sole providers. Looking at these factors, BRAC felt that it would be most beneficial to focus mainly on rural women, giving priority to their needs. This will ensure a meaningful transformation of women's lives. Recognition of these facts led BRAC to develop gender perspectives in its programmes.

Numbers give a sense of the magnitude of BRAC in 1997: the organization has almost 18,000 staff and more than 33,000 part-time teachers in villages through Bangladesh. By the beginning of 1997, there were 1·8 million members in almost 54,000 village organizations, most of them women. Collectively they had saved over one *billion* taka—about US$30 million. And in 1996 they borrowed over five billion taka (US$128 m) for productive enterprises, repaying virtually all of it on time. A million women were actively involved in poultry projects. And 25 million mulberry trees had been planted to support a sericulture enterprise which produced 43·5 metric tonnes of silk between 1992 and 1995, half the entire national production. Twelve million notebooks, 21 million textbooks and readers, and more than three million pencils were purchased in 1996 for BRAC's 34,000 nonformal primary education schools. Every three years, these schools convert a million dropouts into literate children ready to enter the formal education system. In 1996, BRAC purchased 42 tons of corn seed, 200 tons of corrugated iron sheet and 120 motorcycles. Every month, BRAC buys one million day-old chicks. An estimated 12 million people are covered by BRAC's health and population programmes.'

Further information: Sadia Chowdhury, BRAC Centre, 356 Mohakhali, C/A, Dhaka 1212, Bangladesh.

The Jaipur Limb Campaign

The latest issue of *Jaipur Limb Campaign News*, issue 2, August 1997, includes the following information.

The Jaipur limb was developed and perfected over the last 20 years by Dr P. K. Sethi, an eminent

orthopaedic surgeon in Jaipur, India. Dr Sethi, then Head of Orthopaedics at the SMS Hospital in Jaipur noticed that more and more amputees he had treated were discarding their prostheses and reverting to crutches. He found that limbs based on Western designs were proving unsuitable to the needs of the mostly rural population and set about designing a prosthesis which would suit their needs. His ideas were brilliantly translated by local craftsmen and after many trials, the Jaipur Foot was born. The Jaipur Limb can also be worn by the shoe wearing urban amputee and is now used by over a hundred thousand people in many developing countries.

THE DESIGN CRITERIA

- flexibility at the ankle, allows user to sit crosslegged, squat and even to climb trees;
- strong, durable and waterproof, permits walking on uneven ground and in wet fields;
- utilises locally available labour, skills and materials;
- the production process and technology is easily transferable;
- can be worn barefoot or with shoes;
- low cost and rapid-fit (takes about 50 mins to fit with ready made feet);
- aesthetically excellent, matching skin colour, lifelike appearance;
- once established, projects can be sustained without long term external aid;
- mobile units can make and fit limbs in remote villages.

The Jaipur Limb Campaign was thrilled to hear on the 20th of May that it was amongst the 130 UK agencies to receive funding from the National Lottery for projects overseas. A total of £25 million was distributed in this, the first round of the Board's international grants programme. The JLC has received funding for 3 of its projects partners in India over a three year period. They are Gandhigram Trust in Tamil Nadu, Mobility India in Bangalore and the Research and Rehabilitation Centre ay Santokba Durlabji Hospital in Jaipur.

The grant over a 3 year period will cover training and salaries for more technicians, and resources and materials to enable our partners to reach more people. Some funds have also been earmarked for follow-up work and feedback into a research and development programme. Our partners can now put into practice ongoing Research and Development strategy and disseminate the outcomes to many other limb fitting projects within India and those being developed in Africa.

Further information: Jaipur Limb Campaign, 7th Floor, Windsor House, 83 Kingsway, London WC2B 6SD.

ILEP: International Federation of Anti-Leprosy Associations

International Federation of Anti-Leprosy Associations
Fédération Internationale des Associations contre la Lèpre
Internationale Vereinigung der Leprahilfswerke
234 Blythe Road, London W14 0HJ, GB
Tel.: +44/171 602 6925, Fax: +44/171 371 1621, E-mail: ilep@ilep.org.uk

THE FEDERATION

ILEP, the International Federation of Anti-Leprosy Associations, exists, as stated in its constitution,

To support medical, scientific, social and humanitarian activities throughout the world for the relief and rehabilitation of persons suffering from leprosy and the prevention and eventual eradication of that disease.

In June 1996, ILEP Member-Associations unanimously adopted the following Statement of Priorities:

ILEP and its Member-Associations are determined to respond to the total and continuing problem of

leprosy. The priority of the Federation over the next few years is, therefore, to assist Members as effectively as possible to achieve:

- Prevention of disabilities for all people affected by leprosy.
- Multi-drug therapy for all who need it.
- Health services capable of sustaining cost-effective anti-leprosy activities under conditions of low endemicity.
- Normalisation of the lives of all people who are or have been affected by leprosy.
- Continuation of essential research into leprosy, especially as regards the development of tools for the prevention of the disease, ever more efficient treatment and the prevention of disability.

This Statement reflects the success achieved in leprosy work in recent years and the view of ILEP Member-Associations that the emphasis is changing from the medical to the social aspects of leprosy for the individuals affected by it.

While retaining their autonomy and making their own decisions the 20 ILEP Member-Associations co-ordinated their grant-giving through the mechanism of the Federation: an Information Network with standardised forms, centralised files and directories and analyses of the information obtained; an annual Working Session in December; and a system of country and project co-ordinators.

These mechanisms help avoid overlap and concentrate resources where they are most needed—a exceptional example of international co-operation by autonomous agencies in the distribution of funds.

STANDING COMMITTEE

Damien Foundation Belgium
President (1995–1997)
Jean-Pierre Schenkelaars
American Leprosy Missions
Chris Doyle
LEPRA
Terry Vasey
DAHW
Horst Franck

CO-ORDINATING BUREAU

The mechanisms of the Federation and its information services are maintained by a small co-ordinating bureau in London.

General Secretary
Angelo Simonazzi
Assistant General Secretary
Dominique Martineau-Needham
Secretary to Medico-Social Commission
Dr Sarah Lacey
Administrative Staff
Andrew Clark
Maryline Delpy
Marilyn Holderness
Pascale Vassie

MEDICO-SOCIAL COMMISSION

The Federation's Medico-Social Commission provides Member Associations with medical and

technical advice on matters of common concern. It is also able to advise on particular projects if so requested by a Member.

The Commission, elected every four years by the ILEP General Assembly, consists of the following members:

Dr Cairns Smith (Chair)
Dr Ju Baohong
Dr Sunil Deepak
Dr Etienne Declercq
Dr Henk Eggens
Dr P. K. Gopal
Mr Ernst Hisch

The Medico-Social Commission holds regular interface meetings with ILEP Member Associations and international multi-disciplinary workshops when appropriate.

MEDICAL PUBLICATIONS

There has been major focus on the availability of Medical Bulletins in Spanish and Portuguese in addition to French and English and the use of leprosy journals to disseminate advice.

Prevention of Disability in leprosy
ILEP Medical Bulletin no. 8, December 1995
The management of Erythema Nodosum Leprosum
ILEP Medical Bulletin no. 9, May 1996
Priorities for leprosy research
ILEP Medica Bulletin no. 10, October 1996
Detecting and treating hard to reach leprosy patients
ILEP Medical Bulletin no. 11, September 1997
Guidelines for the field
Guidelines for writing a healthworkers manual
Volumes 1 and 2, second edition, April 1996
Guidelines for improving the sustainability of leprosy services
July 1997

TALMILEP

An ILEP joint project to produce and distribute teaching and learning materials on leprosy worldwide.

A booklist of English language publications is available from: TALMilep
c/o TLMI, 80 Windmill Road
Brentford, Mddx TW8 0QH, GB
tel.: +44/181 569 7292, fax: +44/181 569 7808
e-mail: friends@TLMint.org

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General Director: Trevor Durston

AHRTAG (Appropriate Health Resources and Technologies Action Group), London, UK

AHRTAG

- believes that every person, whatever their economic or social position, has the right to good health;
- aims to promote policies and practices in health which are appropriate, sustainable and cost-effective;
- provides information on health and disability issues in developing countries, through print and electronic median, and resource centre services;
- provides technical support and training in publications and information management to strengthen human resources and capacities of partner organisations.

AHRTAG (Appropriate Health Resources and Technologies Action Group) is a non-governmental organisation established in 1977.

AHRTAG'S RESOURCE CENTRE

AHRTAG's resource centre houses a unique collection of over 19,000 books, journals, newsletters, training manuals, reports and audiovisual materials focusing on the practical aspects of primary health care and community-based rehabilitation in the South. Subjects include:

- adolescent health
- child health and development
- communicable diseases
- disability issues and community-based rehabilitation
- evaluation
- health education
- health sector reform

- HIV, AIDS and STDs
- information management
- planning and management
- poverty and inequalities in health
- primary health care
- programme implementation
- sexual health and sexuality
- structural adjustment and health
- training
- urban health

Many of the materials in the resource centre are published in the South. Much of the information is not available in academic or medical libraries in the UK.

For more information please contact:

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http://www.poptel.org.uk/ahrtag/

Registered charity no. 274260

UNAIDS: 'HIV epidemic is far worse than thought'

The following is extracted from the *British Medical Journal*, Volume *315*, 6 Dec 1997, page 1486.

HIV infection is far more common than previously thought, according to a report from the joint United Nations programme on HIV/AIDS (UNAIDS) and the World Health Organisation. The new figures show that about one third more people are living with HIV worldwide than was estimated in December 1996.

Dr Peter Piot, executive director of UNAIDS, said: 'We are now realising that rates of HIV transmission have been grossly underestimated—particularly in sub-Saharan Africa, where the bulk of infections has been concentrated to date.'

Over 30 million adults and children are now believed to be living with HIV infection—one in every 100 sexually active adults worldwide. And if current transmission rates hold steady, by the year 2000 the number of people living with HIV or AIDS will reach 40 million.

The pattern of infection had been assumed to be similar in different countries in the same region, but as more data became available it became apparent that there were huge differences in the way the epidemic was developing in different countries. In sub-Saharan Africa, for example, very few countries had reliable data on HIV infection and some, notably Nigeria and South Africa, had virtually none. The country with the best surveillance rates was Uganda, and that showed that infection rates were beginning to level off, with new infections dropping in younger age groups. The situation in Uganda was wrongly taken to be typical of the whole region.

Over 90% of people with HIV live in the developing world, where few facilities exist for voluntary testing and counselling and where, according to UNAIDS, 9 out of 10 HIV positive people will have no idea they are infected. The organisation warns that the full impact in terms of mortality from AIDS is

only just beginning. It is estimated that 2·3 million people died of AIDS in 1997—a 50% increase on 1996. Nearly half of those deaths were in women, and 460,000 were in children under 15.

The report states that in very badly affected countries the development gains achieved over the past few decades are being wiped out by the epidemic. In Botswana, for example, life expectancy, which rose from under 43 years in 1955 to 61 years in 1990, has now fallen to levels found in the late 1960s. On current trends, Zimbabwe's infant mortality can be expected to rise by 138% by the year 2010 because of AIDS.

Clare Short, Britain's international development secretary, said that although recent scientific advances were very encouraging, people in developing countries were unlikely to see the benefit: 'The new advances in drug therapies are prohibitively expensive in societies where expenditure on all health needs is often only £3 a day. It is just not feasible for such therapies to be a solution for the vast majority of people affected by HIV today. The search must continue for affordable means of slowing down the progression of HIV to AIDS and to increase protection, especially for young people.'

'PATH', USA: development of self destructing, single-use syringe

A recent publication from PATH (*The Program for Appropriate Technology in Health*, 4 Nickerson Street, Seattle, WA 98109, USA. Fax (206) 285-6619) includes the following.

A critical problem facing immunization programs is reuse of disposable syringes or the use of improperly sterilized syringes and needles because of inadequate supplies or lack of sterilization equipment. These practices can result in cross-infection with HIV, hepatitis B virus, or other pathogens. In collaboration with the WHO/Expanded Programme on Immunization (WHO/EPI) and with support from USAID and other agencies, PATH has designed and evaluated several nonreusable syringes and other injection devices meant to ensure safe injections.

One device developed by PATH, a self-destructing, single-use syringe called SoloShot®, is now being manufactured by Becton Dickinson and Company and distributed by UNICEF.

UniJect® is a prefilled, single-use injection device that makes it possible for frontline health workers to deliver vaccines, contraceptives, or emergency medications in a safe, easy, and consistent manner. UniJect® has been licensed to Becton Dickinson and Company, which is planning to manufacture and market the device widely in developing countries. A field trial to deliver Cyclofem™, a once-a-month injectable contraceptive, in UniJect® in Brazil demonstrated the acceptability and usability of the device for this purpose. A successful field trial of the device filled with tetanus toxoid and delivered by traditional birth attendants has been conducted in Bolivia, while trials with hepatitis B vaccine for infants and tetanus toxoid vaccine for mothers were carried out in Indonesia.

The Program for Appropriate Technology in Health (PATH) is a nonprofit, nongovernmental, international organization. PATH's mission is to improve the health of women and children in developing countries. To achieve these goals, PATH works with public sector agencies and with private companies.

Further information: Glenn Austin at the above address.

'Diana's fund fails to satisfy all' *Guardian* Newspaper, UK

The following information on the 'Diana fund' appeared in The *Guardian* Newspaper of 11/3/98.

The Diana, Princess of Wales Memorial Fund is unlikely to give away enough money to make it one of the top 20 grant-making trusts, despite claims that it will transform the charity landscape.

Projections suggest that after yesterday's initial one-off payouts, the fund's annual grants will total

about £5 million. That would place it 24th in the Charities Aid Foundation list of grant-making trusts, just behind the Variety Club Children's Charity and 10 places behind the Prince's Trust.

The first grants are worth £13 million. Future grants will be made from the income of the fund, the capital of which is expected to reach £100 million. For the fund to continue indefinitely, as is intended, annual grants will be limited to a small proportion of that.

The foundation said that 5 per cent was considered a safe return on investment, giving the Diana fund £5 million to distribute each year.

Yesterday, Vivienne Parry, one of its trustees, said: 'I think the fund will become the most important grant-giving body in the country, and a lifeline to an enormous number of charities.'

In 1995 the Wellcome Trust gave grants worth £218·6 million, followed by the National Lottery Charities Board (£158 million), the British Academy (£22·5 million), the Royal Society (£21·3 million) and the Garfield Weston Foundation (£19 million). The Diane fund could become one of the most important grant-giving bodies only by using up its capital, which would run out within 10 years and betray its remit to keep the princess's name alive.

Alternatively, it could hit the big league if contributions continued pouring in, but there is a belief that they had probably levelled off.

A spokeswoman for the fund said £40 million was in the bank and another £60 million was due later this year, including the money from Elton John's single, Candle in the Wind. Reaction to the first round of grants was mixed.

Eight causes will share £8 million, and £5 million is to be allocated among 100 more bodies, once they apply for funds.

The favoured eight causes are: the homeless charity Centrepoint; the English National Ballet; Great Ormond Street children's hospital; the Leprosy Mission; the National Aids Trust; the Royal Marsden NHS Trust; the Osteopathic Centre for Children; and various organisations dedicated to the eradication of land mines. Vivienne Parry said: 'There will be so many grant announcements that in the end people will take no notice, even though some of them will be for large sums of money. The Diana, Princess of Wales Memorial Fund will become part and parcel of everyday life in Britain.'

Several charities, including Headway, which helps head injury victims, expressed disappointment that they would have to jostle with more than 100 rival organisations for a share of the £5 million.

Forum for health information providers: steering group meeting, British Medical Association, London, UK, 30th March, 1998

A meeting of potentially far-reaching importance, chaired by Professor K. G. M. M. Alberti, President of the Royal College of Physicians of London, was held in the headquarters of the British Medical Association on 30th March, 1998. This was organised mainly by '*INASP-Health*', a specific programme within the *International Network for the Availability of Scientific Publications (INASP)*, dedicated to the coordination and support of activities of health information providers in developing countries, including universal access to reliable information for health professionals.

A full account of the development and aims of *INASP-Health* has been published in 1) previous issues of this journal, 2) *The British Medical Journal*, volume 314, 11th January, 1997 and 3) the most recent issue of *WHO Liaison*, volume 8, numbers 2–3, August–November, 1997.

Thirty people involved in the provision of health information for developing countries were invited, including representatives of the *British Medical Journal*, *Leprosy Review*, *Africa Health*, *Medicine Digest*, Action in International Medicine (AIM), African Medical and Research Foundation (AMREF), The British Council, CAB International (CABI), Essential Drugs Project, Appropriate Health Resources and Technologies Action Group (AHRTAG), Authors Licensing and Collecting Society, Book Aid International, Department of Information Studies, Sheffield University, Footsteps/Tear Fund, International Health Exchange, London School of Hygiene and Tropical Medicine, Nigerian Medical Forum, Practical Pharmacy, SatelLife, Teaching Aids at Low Cost (TALC), Liverpool School of Tropical

Medicine, Neurology International Partnership Programme, South Thames Library and Information Services, Tropical Health and Education Trust, Tropical Health Technology and The Wellcome Trust.

The main objective of this first meeting was to discuss the advisability (or otherwise) of establishing a group or forum of health providers, essentially from the UK, but with the option of inviting participants from outside, to a) improve the knowledge and understanding of participants on the needs of health information users and the most effective ways of meeting those needs, b) exchange ideas, contacts, information, avoid duplication, c) lobby international organizations and others for more resources to be devoted to health information provision and argue the case for health information needs to be given due consideration in the planning and implementation of healthcare programmes, d) facilitate partnerships between participants and/or the organizations they represent.

The initial round of 'self-introductions' at the meeting revealed a vast pool of experience from many parts of the world in the origination, assembly, publication, distribution and assessment of health information/material, whilst at the same time underlining the need for health information providers in the UK to liaise more closely in order to avoid duplication and ensure that the main activities of all agencies working in this field are mutually well known.

Professor Alberti guided the discussions toward the main question to be addressed at this first meeting, namely the possible justification for the creation of a forum in the UK, with meetings (in London) on a regular basis. This was accepted and the next meeting will be held within a few months to discuss the practical steps to be taken to '.. assist health information providers towards the achievement of a common goal: universal access to reliable health information'.

This may well be the first meeting of its kind held in the UK. It clearly has considerable potential for the identification of appropriate and sustainable channels for the provision of reliable health information to health workers at all levels in developing countries. *INASP-Health* is supported by the *Department for International Development* (UK), the *British Medical Association* (UK) and *Danida* (Denmark).

Instructions to Authors

Article submission. Articles submitted for publication in Leprosy Review should be sent to the Editor at the following address. Diana Lockwood, LEPRA, Fairfax House, Causton Road, Colchester CO1 1PU, England. The name(s) of the author(s) and the place where the work was done should be indicated clearly below the title of the article. Degrees and diplomas are not to be included.

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