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

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

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Editorial

LEPROSY AND COMMUNITY-BASED REHABILITATION

Introduction

Leprosy continues to be of major concern in developing countries, not only because of the large number of people affected by it and their potential for communicating the disease to others, but also because of the deformities in a proportion of patients.[1] The gradual decline in the number of registered patients needing multidrug therapy (MDT) in the last few years, has focused the attention towards the problem of disabilities caused by leprosy. The declaration issued at the Hanoi International Conference on the elimination of leprosy includes: 'To ensure that prevention and management of disability become an integral part of leprosy elimination programmes so that all leprosy patients are rehabilitated and reintegrated within their communities'.[2]

The suggestion that community-based rehabilitation (CBR) could be the approach for the rehabilitation of disabled leprosy patients has been put forward for many years.[3] A review of the literature related to 'leprosy and CBR' shows that often CBR is considered to be only an approach for promoting vocational training and economic self-sufficiency.[4–6] During the last ILA congress in Orlando, a workshop was held on CBR. Lastly, during meetings and discussions about leprosy, with increasing frequency, 'CBR' is nominated as the ideal approach for rehabilitation and proposals are made to 'integrate the rehabilitation of disabled leprosy patients in CBR programmes'. All this is done without properly understanding what CBR is and if it is a feasible approach for the rehabilitation of leprosy patients.

Thus before discussing how the CBR approach can be used for rehabilitation of disabled leprosy patients it would be useful to try to understand this approach and analyse its advantages and limitations.

What is CBR?

CBR can be considered as a philosophy of intervention rather than as a rigid system of programme organization. As the name suggests, a CBR programme is adapted to the community needs and communities differ widely from country to country and even

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among the different areas of the same countries. Thus the CBR programmes may seem to be very different in different situations. Having said this it is, however, possible to identify and analyse some basic components of a CBR programme which are common to all programmes.

The joint position paper by the World Health Organization (WHO), United Nations Educational, Scientific and Cultural Organization (UNESCO) and International Labour Organization (ILO) gives the following definition of CBR: 'Community-based rehabilitation is a strategy within community development for the rehabilitation, equalization of opportunities and social integration of all people with disabilities. CBR is implemented through the combined efforts of disabled people themselves, their families and communities, and the appropriate health, education, vocational and social services.'[7]

Analysing the existing CBR programmes in a number of countries, the following common components of a CBR programme can be identified:

1 Multisectoral approach: the CBR approach looks at all the needs of disabled persons starting from participation in family life to self-sufficiency in activities of daily living, schooling, employment, participation in leisure and community activities, etc. This means that apart from the health ministry, other governmental ministries and departments, community representatives, teachers, social workers, labour officials, etc. all need to be involved in the CBR programme. Thus integration of young disabled persons in regular schools, vocational training, support for self-employment, production of orthopaedic appliances, techniques of medical rehabilitation, etc. all need to be organized.

In practice, the multisectoral approach seems to work more easily at the peripheral level while at the higher levels it is more difficult. Evaluation of existing CBR programmes shows that even if the multisectoral approach is accepted in theory, usually the programmes tend to give more prominence to certain aspects. However there are some programmes, as in Guyana where they have managed to involve different sectors, e.g. health, education, community volunteers in an effective way.

2 Community participation: it is important that the programme is developed in a gradual way and with active involvement of community leaders, so that it is not seen as something 'for' the community but is seen as 'of' the community. Right at the beginning, the formation of community committees involving political, social and religious leaders of the community is needed, which takes all the decision for the programme activities. It is also important to ensure that the external aid is limited and used only as a support.

When any new programme is started, the communities expect to receive things and/or aid. While in community development programmes, communities are expected to find their own solutions to their problems. The external support is mainly limited to training. The involvement of a community is strengthened if it can provide volunteers for working with the programme.

If the community is going to be responsible for decision making, it means that sometimes there can be decisions which are not shared by the external agency supporting the programme and this has to be accepted even if it may create difficulties.

3. Role of organizations of disabled persons: although the organizations of disabled persons can be considered as part of the community, for this analysis it has been taken as a separate component because of its importance. The final aim of the programme is

empowerment of disabled persons. Thus a CBR programme has to involve the disabled persons and their organizations in all stages of the programme: as members of community committees, as volunteers, and in planning, implementation and evaluation of the programme activities.

4 Rehabilitation workers: the CBR programmes train personnel at community level as rehabilitation workers (RWs). These workers in turn train disabled persons and/or their family members, in all the rehabilitation activities, with the help of a manual similar to the one prepared by WHO.

Some programmes run under the Ministry of Health may utilize community health workers as RWs; programmes run under other ministries may involve teachers, social workers or community volunteers as RWs. In many countries all of these may be involved. Among the volunteers, disabled persons and their family members often play a prominent role.

5 Referral system: a CBR programme is going to work at community level but it cannot substitute the role of specialists and specialized institutions, especially for severe cases and in the case of complications. Referral support should be seen in terms of all the different sectors that are involved in the programme, e.g. health, education, social services, vocational training.

Needs of disabled leprosy patients and CBR

On the basis of the short information given above, we can consider the needs of rehabilitation for leprosy patients and see if these needs can be satisfied by a CBR programme:

A CBR programme cannot substitute all the rehabilitation services provided by a vertical leprosy programme, especially the identification of at-risk patients and the prevention of disabilities. Unless the RWs are community health workers already working in vertical leprosy control programme, they cannot know which patients have more chances of having neuritis and thus develop disabilities; they do not know how to treat neuritis and anyway do not have any drugs. However, if community health workers are involved in the programme as in Vietnam, Guyana, Indonesia such activities are possible.

Under the CBR programme, training is provided to RWs regarding detection of persons having insensitive hands and soles. However, if the persons do not have any visible deformity, it is possible that they may not be detected by the RWs, or if detected, may not be considered as a priority. In endemic areas studies need to be carried out to find the effective inclusion of leprosy patients benefitting from the existing CBR programmes.

It will be difficult to start new CBR programmes only for leprosy patients, because communities cannot be expected to start it for only one category of disabled persons. However, this can be done in leprosy villages or leprosaria, but in that case it may be impossible to adopt the community approach because the patients are generally passive recipients of everything from others. At the same time formation of community committees in the leprosaria giving them the responsibility for decision making may be unacceptable for organizational reasons to the persons managing the leprosaria.

Can the CBR approach be adapted for rehabilitation of leprosy patients?

The basic principle of CBR is the transfer of knowledge and empowerment of disabled persons, so that they themselves become responsible for their own care. This principle is already used in leprosy programmes for teaching self-care to disabled leprosy patients as well as for the prevention of disabilities. This can be further strengthened by analysing the information which is not given at present to the patients and is known only to the medical and paramedical personnel, to see what other information can be transferred to the patients themselves.

This would require a change of perspective for the medical staff from being 'care-givers' to becoming 'partners' in dispensing care. In the paper entitled, 'A new approach to the challenges of the final stages of leprosy control' Hugo A. Vrakking also proposes a similar change of perspective for leprosy control programmes.[8]

Paramedical staff working for vertical leprosy programmes can be trained to become supervisors or RWs for CBR programmes, after appropriate training.

Leprosy programmes having specialized services and infrastructures for rehabilitation of leprosy patients can provide referral support to CBR programmes in their area.

Links should be made between vertical leprosy programmes and CBR programmes already existing in some countries such as Vietnam, Ghana and Indonesia to make sure that disabled leprosy patients living in the communities benefit from activities such as education, vocational training and orthopaedic appliances.

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Immunohistochemical study of cutaneous neuritis in positive lepromin reactions

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Summary Sixty skin biopsies taken from positive tuberculoid and borderline–tuberculoid late lepromin reaction were studied using histological techniques. The distribution of mycobacterial antigen and nerves was demonstrated using immunochemical methods.

A total of 557 nerve bundles was observed in 51 biopsies; 9 were devoid of nerves in the sections examined; 475 nerve bundles showed some relationship to the inflammatory infiltrate (85%); perineuritis being seen in 144 (30%) and endoneuritis in 5 (0·9%).

Mycobacterial antigens inside the granuloma were detected in 59 of the 60 biopsies (98%). Only one specimen, showing a strong tuberculoid reaction, failed to show these antigens. On the contrary, mycobacterial antigen was absent in almost all nerves. Small deposits were detected in the perineurium of one nerve with perineuritis, and inside a Schwann cell of another, the latter belonging to a previously multibacillary patient.

The neurotropic tendency of the granuloma does not seem to be stimulated by the presence of mycobacterial antigens inside the nerves, as normally these antigens do not penetrate them. The hypothesis of some antigenic fraction of the neural tissue which cross-reacts with *Mycobacterium leprae* antigens, thus eliciting a perineural or near-perineural inflammatory reaction is put forward, but needs further investigation.

Introduction

During the last 70 years, the lepromin test has been widely used throughout the world to assess the immune status of leprosy patients and their contacts. The type of lepromin developed by Mitsuda in 1919,[1] is still used today.

The positive Mitsuda test, or late or delayed lepromin reaction, consists of a nodular induration of the skin, of varied size, at the site of the dermal inoculation of the

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substance, reaching its maximum size between the third and fourth weeks after the injection, slowly involuting afterwards, sometimes leaving an atrophic scar. Ulceration can occur in strongly positive reactions. Its presence is regarded as an indicator of resistance of the host to *M. leprae* infection,[2–5] being the result of a delayed hypersensitivity reaction to the injected antigen.[6–8]

The inoculated antigens can be of human origin, obtained both by the Mitsuda or by the Dharmendra method from human lepromata, or of animal origin, obtained from armadillos experimentally infected with *M. leprae*.

Histologically, the classical positive Mitsuda reaction consists of a dense grouping of epithelioid cells, with multinucleated giant cells and lymphocytes, thus forming a typical tuberculoid structure, similar to that encountered in TT or BT cases of leprosy. The size and type of cells in the granuloma can be variable according to the spectral concept of leprosy.[6,14,18]

The histopathology of the lepromin reaction has been extensively studied.[9,11,13,16] Some authors note the preference for the inflammatory cells to be arranged around blood vessels and skin appendages, without referring specifically to nerves.[7,10] Nerve involvement in lepromin reaction received specific attention in five papers, the authors of these stressing the frequency of neural involvement in the biopsies.[7,12,15,19,20]

Mistry *et al.*[20] have raised the question of why infiltration should be seen specifically around dermal nerves. Desikan *et al.*[7] suggest that nerve tissue could be in some way associated with the immunological process of the lepromin reaction, possibly having some role in delayed hypersensitivity reactions, particularly in view of the special predilection of *M. leprae* for nerves.[21] Serial[15] states that neuritis in lepromin reactions is 'undoubtedly' caused by very specific 'endotoxic' substances released by *M. leprae*, with an affinity for the peripheral sensory nerves.

Cutaneous nerves can be more easily identified in sections by using immunoperoxidase technique with S-100 protein as a Schwann cell marker, as the inflammatory infiltrate in leprosy can make this identification difficult in routine stains.[22] *M. leprae* antigens can also be clearly demonstrated in histological sections by the peroxidase–antiperoxidase (PAP) immunoenzyme technique using rabbit anti-*Mycobacterium bovis* (BCG) as the primary antibody, as most of *M. leprae* antigens cross-react with BCG.[23,24]

In this report we quantify and classify cutaneous nerve damage in positive Mitsuda tests and locate the antigen in the tissue, in an attempt to explain the mechanism of the neural involvement frequently observed in the histology of granulomatous lepromin tests.

Materials and methods

Sixty positive lepromin test human biopsies were studied. In 50 cases, human-derived lepromin (lepromin H) and in 10, armadillo-derived (lepromin A) had been used. Five-micron-thick sections were cut, left to dry in an oven at 56°C, dewaxed in xylene, passed through graded alcohols and into water. Haematoxylin and eosin, Ziehl–Nielssen and Wade–Fite stains were used for classification of the type of granuloma[18] and for demonstration of *M. leprae* at the site of inoculation.

IMMUNOPEROXIDASE METHODS

The Avidine–Biotin–Complex (ABC) method of immunoperoxidase using anti-S-100 protein antibody was used in the study as a marker for Schwann cells to detect nerves in sections, according to the method of Hsu *et al*.[34] Normal goat serum at 1:2000 was used as a negative control, and normal nerve sections stained for S-100 protein as positive controls. To detect mycobacterial antigens in the tissues, a peroxidase antiperoxidase (PAP) method was used, following the method of Sternberger *et al*.,[25] using antiBCG antibodies.

$UCHL_1$ (T cells) and CD_{45} (leukocyte common antigen) methods were used to confirm penetration of inflammatory cells into the nerves, in four selected cases of endoneuritis.

CLASSIFICATION OF NERVES

Nerves were classified according to their histological alterations and location in the granuloma.

Perineuritis was considered present if inflammatory cells penetrated the perineurium or were present in perineural spaces (Figure 1); endoneuritis, only if inflammatory cells were present inside the nerve, at times with nerve destruction (Figure 2 and 3). Nerves were classified as related to granuloma, when surrounded or tangentially touched by the granuloma (Figure 4), and normal distant nerves, when distant and not related to the granuloma.

The size and type of the granulomatous reaction, the number of giant cells, the absence or presence of lymphocytes around or inside the granuloma, as well as the presence of caseating necrosis, or ulceration, were the parameters used together to classify the histological lepromin response as tuberculoid or as one of the variety of positive borderline cases.[14,18]

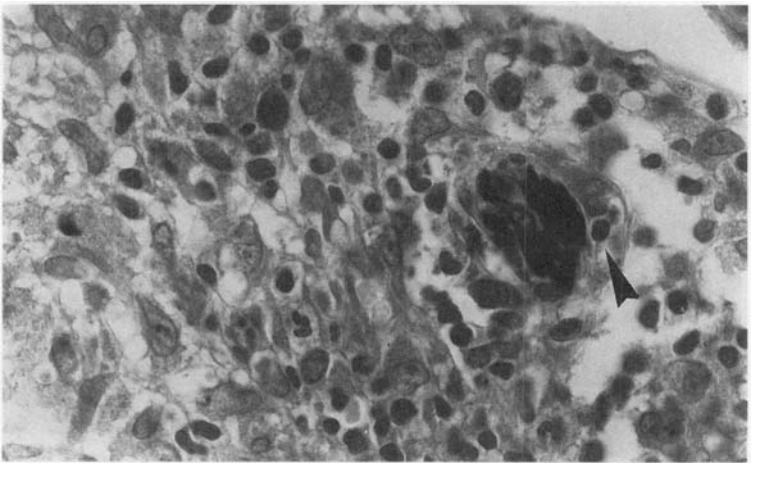


Figure 1. Perineuritis. Inflammatory cells in perineural spaces (arrow) (S-100 ×1000).

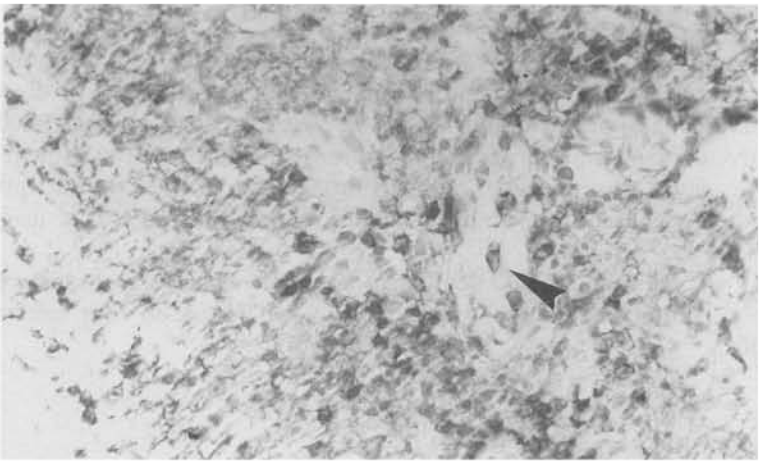


Figure 2. Endoneuritis. CD_{45}+ inflammatory cells inside the nerve (large arrow). Small arrows delimitate nerves. (CD_{45} × 400).

The Bacterial Index (BI) of Ridley[26] was used to quantify the number of acid-fast bacilli (AFB) present in Wade–Fite stains. The quantity of antigen present in the tissues, detected by the antiBCG method was measured on a scale graded from 0 to 3+.

Results

Dermal nerves were present in 51 of the 60 specimens (85%); 557 nerves were identified

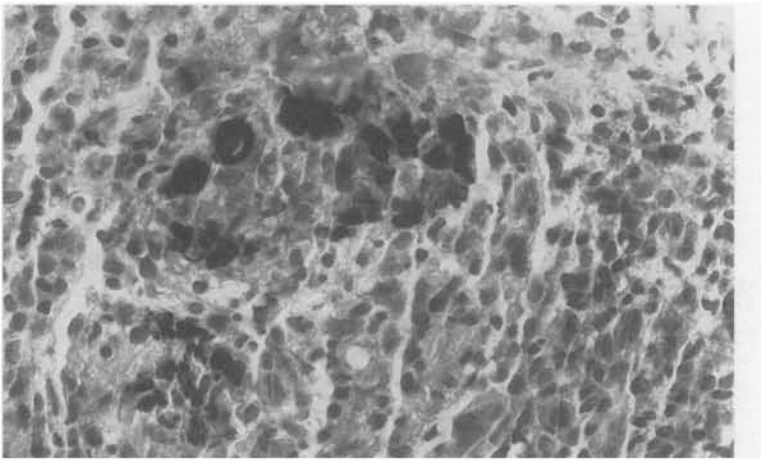


Figure 3. Endoneuritis with nerve destruction. S-100-positive Schwann cells (black granules) delimitate the nerve bundle disrupted by inflammatory cells. (S-100 ×400).

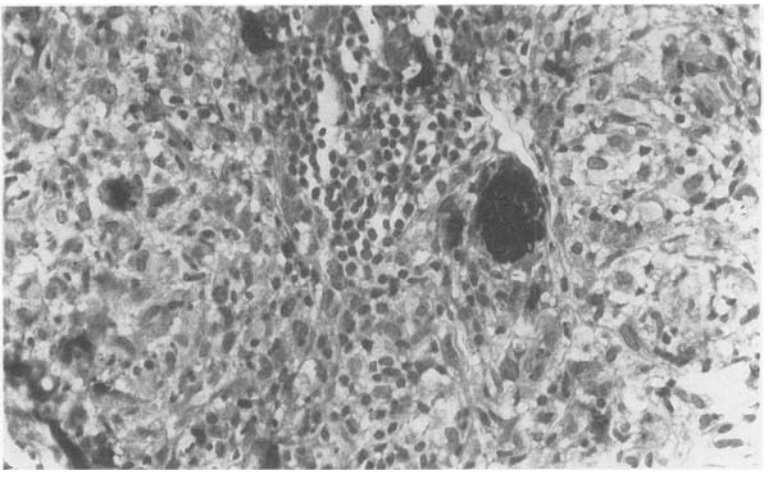


Figure 4. Dermal granuloma surrounding an uninvolved nerve (arrow) (S-100 ×400).

in the sections. Of these, 169 (30%) showed perineuritis and only 5 (0·9%) presented endoneuritis; 86 unaffected nerves were found inside the granulomas (15%) and 161 (29%) at the periphery of the granulomas; 54 nerves (10%), although related to the granulomas, were difficult to classify due to artifacts or to blurring of their perineural areas. Considering together all types of nerves, affected or related to the granulomas, the total count was 475 (85%). Normal distant nerves not related to the granulomatous reaction accounted for only 82 (15%) of the total (Table 1).

In perineuritis and endoneuritis the penetrating cells were basically lymphocytes ($UCHL_1$+ and CD_{45}+). No granulomas were observed inside the nerves.

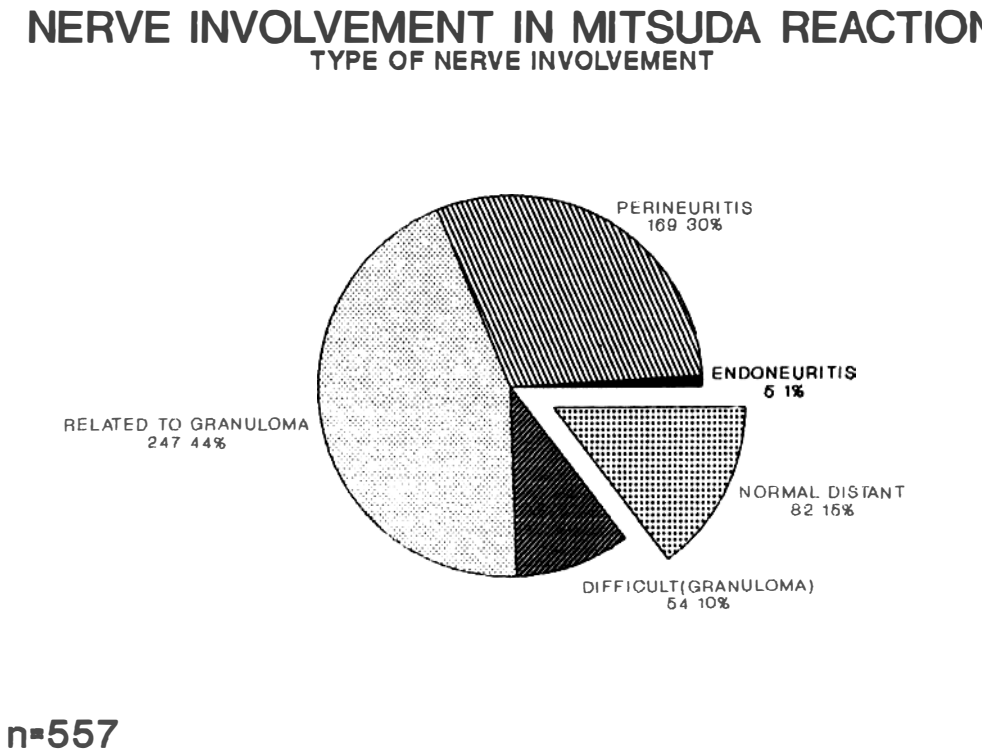
Acid-fast bacilli (AFB) were identified in 53% of the biopsies. When present, the granular or fragmented bacilli were found isolated or in small clumps inside the macrophages or more infrequently, isolated between collagen bundles. They formed groups or large clumps in areas of the necrosis and even more intensely in those of suppuration. No AFB were found in dermal nerves.

AntiBCG stain was very sensitive to detect mycobacterial antigen, being positive in 98% of the biopsies, and negative in only one case, a strongly positive lepromin reaction of a tuberculoid patient. The antigen could be detected within macrophages, in multinucleated giant cells, in necrotic areas and even between collagen bundles, with varied intensity. The antigen reached the neighbouring area of the nerves, without normally penetrating the perineural areas. Five hundred and fifty-five nerves (97%) did not show any mycobacterial antigen. Only two nerves with perineuritis showed 1+ deposit of antigen. In one nerve the antigen was located in the inflamed perineurium. In the other, obtained from a BL case having undergone long-term treatment, a small deposit of BCG-positive material was present within a Schwann cell (Figure 5).

In all cases of endoneuritis we were not able to demonstrate any antigen inside the nerves.

Sometimes nerves were difficult to identify in the PAP/BCG sections, making impossible the precise counting and the distance between them and the antigen deposits. Very frequently, however, especially in 1+ and in some 2+ deposits, we could see nerves

Table 1. Type of nerve involvement and its position regarding the granuloma. Only 15% of all nerves were unaffected and not related to the granuloma.



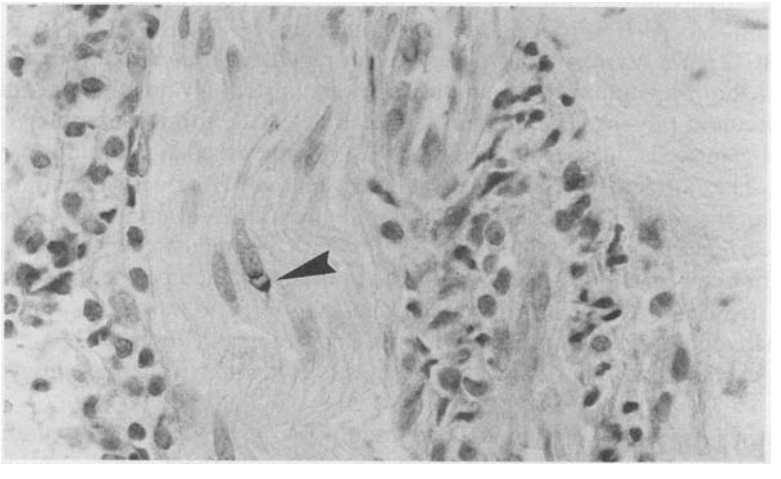


Figure 5. BCG-positive material within a Schwann cell (arrow) (BCG ×1000).

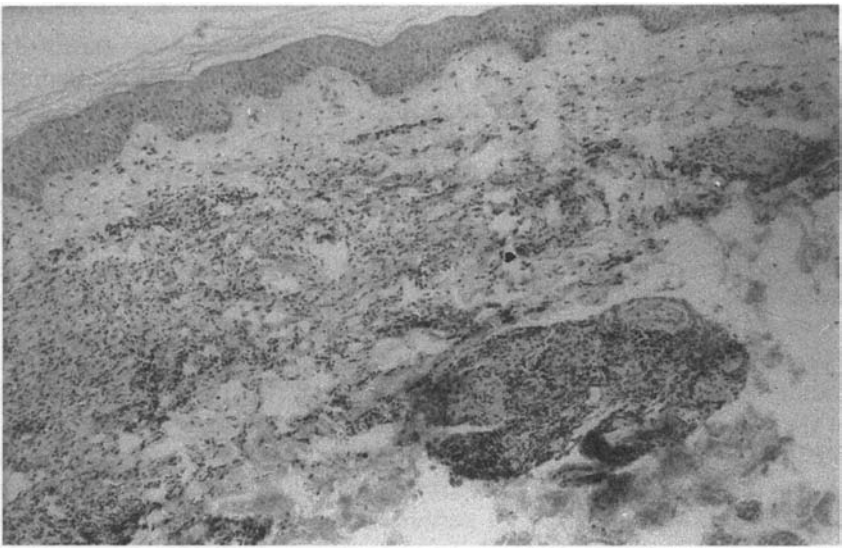


Figure 6. Low power micrograph of a lepromin reaction showing preference of the inflammatory infiltrate to concentrate around nerve bundles and blood vessels (right bottom corner), far from the granuloma produced by the antigen (left). (BCG ×100).

surrounded by the inflammatory infiltrate, at times distant from the brown granules of the antigens and from the granuloma produced by these antigens (Figure 6).

Blood vessels were also seen within the infiltrate, normally at the side of a nerve bundle.

Discussion

Büngeler & Fernandez[12] were the first to report the frequency of altered nerves in the granuloma of the Mitsuda reaction. Serial,[15] studying 56 biopsies of lepromin reactions, encountered nerve alterations in 44 cases (78%), described as consisting of infiltration of the epineural connective tissue, infiltration of the epineurium and partial, sometimes total, endoneuritis of some areas in the fine nerves. Desikan *et al.*[7] described a tendency for the lymphocytes to cluster around nerve twigs in TT and BT cases, as soon as 24 hours after lepromin inoculation. In the 39 of their 77 cases in which nerves could be seen, exsudate cells were found to surround them, without actually infiltrating or destroying them.

Mistry *et al.*,[20] also in a sequential study of lepromin in 5 patients, detected no changes in most of the dermal nerves, but nevertheless found some of them to be surrounded by infiltrate. In one tuberculoid and in two borderline patients they found minimal perineural cell activity on 10th/21st post-injection days of Dharmendra lepromin. They were not able to demonstrate mycobacterial antigens in the sections on the 21st day with BCG and PAP method.

In our study, 85% of nerves showed some degree of contact with the granuloma, or

involvement by the granuloma. Involvement was much greater than that expected by chance, as measured by the frequency of involved nerves versus that expected (on the basis of areas of the slides having nerves and areas of the slides having inflammation). Of all nerves, only 15% were not in contact with the inflammatory infiltrate.

This makes quite likely the existence of some sort of relationship between the neural tissue and the immunological response to the lepromin, as suggested by Desikan *et al.*[7] The absence of intraneural antigen in practically all cases and the low incidence of endoneuritis (less than 1% of all nerves) observed in our study, makes it very unlikely that the hypothesis of nerve damage in lepromin reaction was caused by a selective predilection of the inactivated bacillus and its antigens for a dermal nerve, or some 'affinity' for Schwann cells, as described in the actual disease.[5,21,27,28]

On the other hand, the finding of 85% of nerves being closely related to the inflammatory infiltrate, with 30% presenting perineuritis, suggests that a relationship between the granuloma and the perineural area could exist.

Positive *lepromin-like* reactions have been obtained in the past by injecting normal skin extracts in humans,[30,31] and also tuberculoid granulomas were demonstrated in rabbits inoculated with an extract of peripheral nerves, devoid of any mycobacterial antigen.

That *lepromin-like* reactions can be produced by skin and nerve extracts supports the hypothesis of some antigenic similarity between *M. leprae* and peripheral nerves, with possible cross-reactivity of antigens. This hypothetical possibility certainly needs further research for confirmation.

Ghaswala *et al.*[32] has demonstrated identical binding of serum antibodies in leprosy patients and in normals, to a sonicate of normal human peripheral nerves. *In vitro*, Benjamins *et al.*[33] observed cross-reactivity of sera from leprosy patients between a 35-kDa neural antigen and a synthetic analogue of the terminal dissacharide portion of phenolic glycolipid-I. Naafs *et al.*[35] showed that anti-*M. leprae* monoclonal antibodies cross-react with dermal antigenic determinants. Some of these determinants may be associated with small nerve fibres, as was observed using MoAb F116-21, which cross-reacted with the peripheral axons.

The absence of mycobacterial antigen within the nerves is strong evidence that nerve involvement in lepromin reaction is not caused by direct action of the inoculated substance. The finding of BCG-reactive deposits in one case, without producing endoneuritis, could perhaps be explained by the fact that, to be recognized and to produce local inflammation, bacterial antigen has first to be externalized by Schwann cell destruction,[27] and in this particular case the stained antigen was placed inside an apparently intact Schwann cell cytoplasm. Moreover, as that particular patient was a previously multibacillary case, this antigen could be a residual of his former multibacillary period, and not the lepromin antigen.

Further studies should be done for a better understanding of the significance of the neurotrophic tendency of the granuloma in lepromin reaction, which appears to be caused not by the simple presence of the antigen in the nerves (as suggested by Serial[15]) nor by simple chance, as there is a clear preference for the infiltrate to locate around nerve structures in more than 85% of all detectable dermal nerves, even distant from the antigen deposits.

The type and intensity of the histological reaction to the Mitsuda antigen has been graded by several authors,[3,17,29] mirroring the clinical spectrum of the disease.[6,14,18]

There is a general agreement that the absence of scarcity of bacilli in the sections of the positive cases is important to measure the resistance of the patient to the disease or to *M. leprae*. The higher sensitivity of BCG in demonstrating the presence of *M. leprae* or its antigens, in comparison with bacillary stainings like the Wade–Fite method, is well demonstrated in our study, as BCG-reactive deposits were found in 98% of cases, compared with only 53% of AFB detection. Therefore, the anti-BCG method could be of much more value in classifying the cases, when associated with spectral histological criteria of lepromin reaction. The clearance of the antigen in the tissue could evaluate, with more accuracy, the capability of the host to respond to mycobacterial stimulus, and thus to measure its resistance, especially in weak reactors or in clinically doubtful Mitsuda reactions.

This study reinforces the hypothesis of the existence of an antigenic link between *M. leprae* and peripheral neural tissue,[7] which could explain the neurotropic tendency of the granuloma in the Mitsuda reaction and the *Mitsuda-like* granulomas produced experimentally with normal tissue antigens. If the possibility of an antigenic link is confirmed in the future, the positivity of lepromin reaction should be re-evaluated, as the size of the granuloma could result from a reaction to antigens other than that of *M. leprae*, thus complicating its interpretation as a measurement of the host response to *M. leprae* and, consequently, providing a theoretical basis to question its validity when used to characterize the epidemiology of leprosy.

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Extended studies on the viability of *Mycobacterium leprae* outside the human body

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Summary Very little is known in leprosy regarding the transmission of the infection from the source to the susceptible host. One of the important factors which governs the transmission of the disease is the viability of *Mycobacterium leprae* outside the human body. In this study *M. leprae* obtained from untreated patients have been subjected to several adverse conditions. Their viability was verified by their multiplication in the footpads of normal mice. After drying in the shade the organisms were viable up to 5 months. On wet soil, they remained alive for 46 days. Kept in saline at room temperature, the organisms lived for 60 days. Surprisingly on exposure to direct sunlight for 3 hours a day the bacteria survived for 7 days. On refrigeration at 4°C, the bacteria could be preserved for 60 days. On the other hand, keeping at −70°C, the bacteria could be maintained in a living condition for only 28 days. On exposure to antiseptics like Savlon (R) and alcohol, the bacteria were rapidly killed. These results indicate the survival outside the human body of *M. leprae* under different environmental conditions in India where the disease is endemic. Transmission of infection by indirect contact and occurrence of new cases in the absences of any known source, are consistent with *M. leprae* being viable outside the human body for varying periods of time. The findings could also be pointers to understand the epidemiology of leprosy.

Introduction

The only known source of infection in leprosy is from the patient with the infectious type of disease. Bacilli are discharged in very large numbers through nasal secretions, from breaking down of nodules and from abraded skin over bacillated lesions. Very little is known regarding the transmission of the infection from the source to the susceptible host. One of the important factors which governs the transmission of the disease is the viability of *M. leprae* outside the human body. This was for many years difficult to assess since the organisms are not cultivable *in vitro*. However with the advent of the mouse footpad model it has been possible to grow the organisms in experimental animals to verify their state of viability. The results of earlier work have indicated that the

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organisms are viable for at least 9 days in a dried state.[1,2] Our present work is an extension of the studies carried out earlier.

Materials and methods

The suspension of *M. leprae* was prepared by homogenization of skin biopsy material obtained from cases of untreated lepromatous leprosy. A piece of skin obtained at the biopsy was minced with scissors, homogenized and suspended in Hanks' Balanced Salt Solution (BSS); all procedures were carried out aseptically at low temperature over ice. The large particles were allowed to settle by standing the suspension for 3 min. The supernatant fluid was collected and the bacterial suspensions thus prepared was processed as follows:

(a) A part of the suspension was used for immediate inoculation. Enumeration of bacilli was carried out on this aliquot by standard procedures followed in this laboratory. The suspension was diluted with Hanks' BSS so that 0·03 ml contained 10^4 bacilli. A batch of 6 mice were inoculated with the specimen, each animal receiving 0·03 ml into each hind footpad. These animals served as positive controls.
(b) The diluted suspension was autoclaved to 20 min at 15 lbs inch^2 pressure. The autoclaved material was inoculated into a second batch of 6 mice, each animal receiving 0·03 ml into each hind footpad. These animals served as negative controls.
(c) The original suspension was subjected to several procedures and left outside for different periods of time under varying conditions. These experiments had to be carried out at different parts of the year to provide for seasonal variations in temperature and humidity. For all these experiments, positive and negative controls described above were provided with the same material and the material was put up for culture on Lowenstein–Jensen (LJ) medium to exclude any cultivable mycobacteria. The following procedures were carried out with the specimen obtained:

(i) *Drying in shade*. The bacillary suspension was distributed in a number of sterile Petri dishes, covered and allowed to evaporate at room temperature. The Petri dishes were kept in a cardboard box in the shade in the laboratory. On days 3, 7, 14, 21 and 28, the dried material from each Petri dish was scraped and suspended in Hanks' BSS. The bacilli in each suspension were enumerated. A batch of 6 mice was inoculated so that the animal received a maximum of 10^4 bacilli per footpad. The actual number inoculated into footpad in each batch was recorded. The first experiment was conducted in the hot, dry summer season in the months of March and April when the temperatures ranged from 24 to 33°C and atmospheric humidity ranged from 28 to 44%. The second experiment was conducted in the hot, wet monsoon season in the months of August and September, when temperatures ranged from 29 to 33°C and atmospheric humidity from 72 to 80%. In an extended study, a third experiment was conducted in which the material was left in the shade for a full year during which time the material scraped from the Petri dishes was inoculated into the mice at the end of 1·5, 2, 3, 3·5, 4, 4·5, and 5 months and subsequently at monthly intervals.
(ii) *Maintaining in wet soil*. A sample of local soil was obtained. The soil was autoclaved for 20 min at 15 lbs/inch^2 pressure. The autoclaved soil sample was aseptically transferred to sterile test tubes. About 1·0 g of soil was added to each test tube. 0·5 ml

of the bacillary suspension was then added to each test tube, mixed with the soil and kept at room temperature. Each day, the specimen was inspected to check that it remained moist. Otherwise, a few drops of sterile distilled water were added to the specimen. On days 7, 14, 21, 28, 35 and 46, the bacilli from the soil were retrieved by shaking it in Hanks' BSS and collecting the supernatant. The bacilli in the retrieved samples were counted. The material was inoculated into mice, each mouse receiving a maximum of 10^4 bacilli per hind footpad. This experiment was carried out in the months of September and October when the temperature ranged from 25 to 32°C and atmospheric humidity ranged from 44 to 66%.

A sample of the soil used for the experiment was put for culture on LJ medium to exclude any cultivable mycobacteria. In an extended study the experiment was conducted all through the year when bacilli retrieved from the soil samples were inoculated into the mice at monthly intervals.

(iii) *Maintaining in saline.* Bacterial suspension prepared in Hanks' BSS was distributed into a number of sterile test tubes and left at room temperature. On days 3, 7, 14, 21, 28, 35 and 43, the material was inoculated into mice after enumerating the bacilli and taking care to see that the mice received 10^4 bacilli per footpad. This experiment was carried out in the months of October and November, when the temperature ranged from 22 to 30°C and atmospheric humidity ranged from 46 to 50%. This experiment was later continued for a period of 3 months, and samples were inoculated into the mice at the end of 1·5, 2·5, and 3 months.

(iv) *Exposure to direct sunlight.* The bacillary suspension was poured into a number of sterile Petri dishes, covered and allowed to evaporate. Each day, in the morning from 09.30–12.30 h the samples were exposed to direct sunlight, the Petri dishes were opened and material directly exposed to sunlight. In order to prevent excessive heating of the glassware exposed to sunlight in the hot summer mornings, the Petri dishes were kept in sand moistened with cold water. The exposure to sunlight was carried out on the terrace of a screened area so as to lessen the chances of contamination to dust from the ground. After exposure to direct sunlight the Petri dishes were covered and kept in the laboratory. On days 1, 2, 3, 4, 5 and 7 the dried material was scraped off and suspended in Hanks' BSS. The bacilli in each suspension was counted and inoculated into mice so that each mouse received a maximum of 10^4 bacilli per footpad. The experiment was performed in the month of May when the temperature ranged from 38 to 43°C in sunlight and humidity in the laboratory ranged from 30 to 40%.

(v) *Preservation at low temperatures.* Bacterial suspension prepared in Hanks' BSS was distributed to a number of sterile test tubes and preserved at 4°C, −20°C and −70°C for one year. At different intervals, a test tube from the refrigerator and the deep freezer was taken out and thawed. The bacilli in the suspension were inoculated, so that the animals received 10^4 bacilli into the footpad.

(vi) *Study of the effect of Savlon (ICI) and ethyl alcohol.* To the original bacterial suspension, Savlon (chlorhexidine with cetrimide) and absolute alcohol were added to make concentrations of 1% and 7% respectively. The material was distributed in several test tubes and kept up to 48 h. At different intervals, namely 0·5, 1, 2, 4, 24 and 48 h, one test tube from each of the batches was centrifuged, washed, resuspended in Hanks' BSS. The bacilli were enumerated and the suspension diluted as required. Batches of 6 mice were inoculated to give 10^4 bacilli per footpad. All the experiments were carried out in Agra, located in the northern part of central India at a latitude of 27°N.

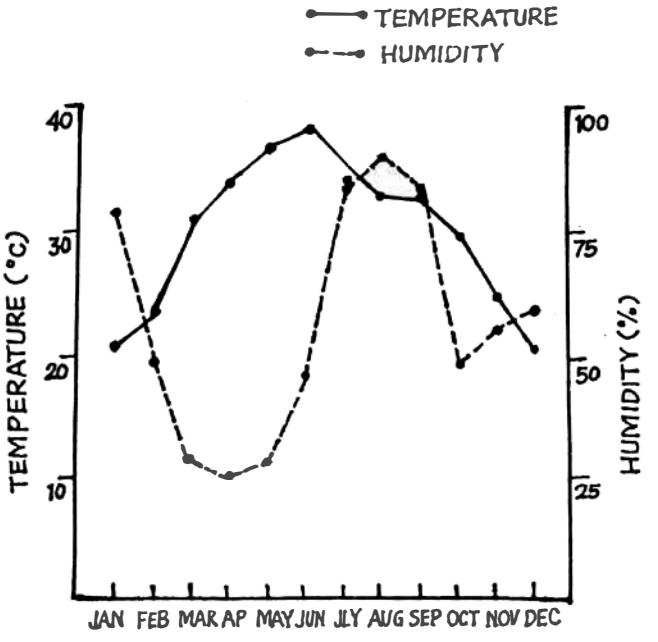

Figure 1. Mean midday temperature and humidity as taken in the shade, monthly.

The weather is generally dry except in the monsoon season. There are extremes of temperature in summer and winter with wide diurnal variations. The mean midday temperature and the mean humidity are shown in Figure 1. The inoculated animals (control and experimental groups) were housed in an air-conditioned room at a temperature ranging from 22 to 33°C. After 6 months, the mice were killed one at a time at monthly intervals. Harvests from both the hind footpads were pooled together for enumeration. Method of harvesting, enumeration of bacilli and inoculation were according to those described by Desikan and Venkataramanaiah.[3] All observations were double blind. The smears of harvested material were examined along with smears of harvested material from other routine experiments by a different person who was not aware of the type of experiments. Out of the results at different monthly intervals, the highest yield of any single harvest is the one given in the results.

Results

Tables 1 and 2 show the multiplication of *M. leprae* in footpads of mice after being inoculated with material dried in the shade for varying periods. In the first experiment carried out in March and April, material dried up to 14 days was found to contain viable bacilli but not material dried up to 21 or 28 days. The diurnal room temperature at the time of the experiments ranged from 24 to 33°C. Since it was approaching the summer season, the humidity dropped from 44% to 28%.

The second experiment was carried out in the months of August and September which happened to be the latter half of the monsoon season. The temperature was quite

Table 1. Viability of *M. leprae* after drying in the shade (March–April, temperature, 24–33°C; humidity, 44–28%)

Multiplication of *M. leprae* in footpads of mice					
Fresh sample (0 day)	Days of drying before inoculation				Autoclaved sample (Control)
	7	14	21	28	
5×10^5	$3{\cdot}7 \times 10^4$	$2{\cdot}5 \times 10^4$	N	N	N

Inoculum-up to 10^4 bacilli per footpad. N-negative.

Table 2. Viability of *M. leprae* after drying in the shade (August–September, temperature 29–33°C; humidity, 80–72%)

Multiplication of *M. leprae* in footpads of mice						
Fresh sample (0 day)	Days of drying before inoculation					Autoclaved sample (Control)
	3	7	14	21	28	
$1{\cdot}5 \times 10^6$	N	$3{\cdot}7 \times 10^4$	$1{\cdot}8 \times 10^4$	D	$8{\cdot}2 \times 10^5$	N

Inoculum-up to 10^4 bacilli per footpad. D-mice died and discarded, N-negative.

high, varying from 29–33°C. The humidity was also quite high, between 72 and 80%. Dried material maintained at these atmospheric conditions of very high humidity showed bacilli viable even at the end of 28 days, the end point not having been reached.

In another study on dried *M. leprae* followed for a year, the bacilli remained viable for 5 months (Table 3). These experiments were initiated in June. Table 4 shows that the viability of *M. leprae* in wet soil was retained for 46 days. When the study was extended for a year (Table 5), it was found that bacilli in wet soil were viable after 1·5 months. Tables 6 and 7 confirm these findings when the bacilli were kept in saline. The room temperature at the time of the above two experiments ranged between 22 and 32°C, but the humidity was irrelevant since the bacteria were kept moist.

Table 3. Viability of *M. leprae* after drying in the shade (throughout the year)

Multiplication of *M. leprae* in footpads of mice														
Fresh sample (0 day)	Months of drying before inoculation													Autoclaved sample (Control)
	1·5	2	3	3·5	4	4·5	5	6	7	8	9	10	11	12	
1×10^6	$1{\cdot}7 \times 10^5$	5×10^4	1×10^4	8×10^4	2×10^4	4×10^4	9×10^4	N	N	N	N	N	N	N	N

Inoculum-up to 10^4 bacilli per footpad. N-negative.

Table 4. Viability of *M. leprae* in wet soil (Sept–Oct, temperature, 25–32°C: humidity, 66–44%)

Multiplication of *M. leprae* in footpads of mice							
Fresh sample (0 day)	Days maintained in soil before inoculation						Autoclaved sample (Control)
	7	14	21	28	35	46	
$1{\cdot}2 \times 10^6$	N	$1{\cdot}6 \times 10^5$	$1{\cdot}3 \times 10^5$	$5{\cdot}6 \times 10^4$	N	$1{\cdot}8 \times 10^5$	N

Inoculum-upto 10^4 bacilli per footpad. N-negative.

Table 5. Viability of *M. leprae* in wet soil (all through the year)

Multiplication of *M. leprae* in footpads of mice						
Fresh sample (0 day)	Months maintained in soil before inoculation					Autoclaves sample (Control)
	2	3	6	9	12	
$4{\cdot}8 \times 10^5$	N	N	N	N	N	N

Inoculum-up to 10^4 bacilli per footpad. N-negative

It can be seen from Table 8 that after exposure to direct sunlight for 3 h daily for a period of 7 days, *M. leprae* still remained viable for at least 7 days. In the two specimens collected on the 3rd and 4th day, the results were negative. However, these results can be ignored since bacilli were found to be viable on the 5th and 7th day specimens.

Preservation at low temperatures gave somewhat unexpected results. For example while *M. leprae* were viable under refrigeration at 4°C and −20°C for a period of 60 days (Tables 9, 10), when preserved at −70°C, the organisms remained viable for only 28 days (Table 11).

It was also surprising to find that bacilli exposed to 1% Savlon were still viable up to 24 h, while exposure to 70% alcohol killed the organisms within 30 min (Table 12).

In these experiments all the fresh strains of *M. leprae* used multiplied in the footpads of mice, whereas no growth of these autoclaved strains was detected in the mouse footpad. Moreover, none of the fresh strains used multiplied on LJ medium.

Table 6. Viability of *M. leprae* in saline (Oct–Nov, temperature, 30°–22°C: humidity, 50–46%)

Multiplication of *M. leprae* in footpads of mice								
Fresh sample (0 day)	Days maintained in saline before inoculation							Autoclaved sample (Control)
	3	7	14	21	28	35	43	
$3{\cdot}1 \times 10^5$	$1{\cdot}1 \times 10^5$	$5{\cdot}6 \times 10^4$	$7{\cdot}5 \times 10^4$	$5{\cdot}6 \times 10^4$	$2{\cdot}7 \times 10^5$	$3{\cdot}7 \times 10^4$	$5{\cdot}6 \times 10^4$	N

Inoculum-up to 10^4 bacilli per footpad. N-negative.

Table 7. Viability of *M. leprae* in saline

Multiplication of *M. leprae* in footpads of mice					
	Months maintained in saline before inoculation				
Fresh sample (0 day)	1·5	2	2·5	3	Autoclaved sample (Control)
$8{\cdot}5 \times 10^5$	4×10^4	3×10^4	N	N	N

Inoculum-up to 10^4 bacilli per footpad. N-negative.

Table 8. Viability of *M. leprae* under direct sunlight (May, temperature, 38–40°C; humidity, 30–40%, exposure to sun daily for 3 h, from 9.30 am to 12.30 pm)

Multiplication of *M. leprae* in footpads of mice							
Fresh sample (0 day)	Days of drying in sun and shade before inoculation						Autoclaved sample (Control)
	1	2	3	4	5	7	
$6{\cdot}7 \times 10^5$	$1{\cdot}2 \times 10^5$	5×10^4	N	N	$3{\cdot}5 \times 10^5$	5×10^4	N

Inoculum-up to 10^4 bacilli per footpad. N-negative.

Discussion

In an earlier published work, nose blow material and skin homogenate were dried in the shade in Petri dishes. The material when inoculated into the mice contained viable bacilli, even after 9 days of drying. However, these earlier experiments did not establish the end point of viability of the organisms outside the body. The work therefore, needed to be extended. It was also thought to be useful to conduct the experiment under different atmospheric conditions of temperature and humidity. The earlier experiments were conducted in Chingleput, a coastal town in South India with a warm humid climate. In contrast Agra, in Central North India, presented an arid climate with

Table 9. Viability of *M. leprae* under refrigeration at 4°C

Multiplication of *M. leprae* in footpads of mice												
Fresh sample (0 day)	Days maintained at 4°C before inoculation											Autoclaved sample (Control)
	1	2	3	4	5	6	7	14	60	120	360	
1×10^6	$1{\cdot}8 \times 10^5$	$1{\cdot}2 \times 10^5$	$1{\cdot}1 \times 10^5$	$1{\cdot}6 \times 10^5$	$2{\cdot}1 \times 10^5$	1×10^5	$2{\cdot}6 \times 10^5$	$1{\cdot}4 \times 10^6$	5×10^4	N	N	N

Inoculum-10^4 bacilli per footpad. N-negative.

Table 10. Viability of *M. leprae* under refrigeration at −20°C

Multiplication of *M. leprae* in footpads of mice									
Fresh sample (0 day)	Days maintained at −20°C before inoculation								Autoclaved sample (Control)
	7	14	21	28	60	120	180	360	
1×10^6	$4{\cdot}8 \times 10^5$	$4{\cdot}6 \times 10^5$	$1{\cdot}8 \times 10^5$	4×10^5	$3{\cdot}5 \times 10^5$	N	N	N	N

Inoculum-up to 10^4 bacilli per footpad. N-negative.

Table 11. Viability of *M. leprae* under refrigeration at −70°C

Multiplication of *M. leprae* in footpads of mice											
Fresh sample (0 day)	Days maintained at −70°C before inoculation										Autoclaved sample (Control)
	5	7	14	21	28	45	60	129	180	240	360	
6×10^5	4×10^4	3×10^4	$2{\cdot}6 \times 10^4$	4×10^4	8×10^4	N	N	N	N	N	N	N

Inoculum-up to 10^4 bacilli per footpad. N-negative.

extremes of temperatures. It was therefore possible to conduct the experiments at conditions of widely varying temperature and humidity.

Experiments of Davey & Rees[2] showed the bacilli to be viable for 3 days or more and in one instance even for 7 days. This was in London where the humidity was 43·7% compared to 77·6% in Chingleput. It was felt, therefore, that a higher atmospheric humidity might favour bacillary survival. In the present study, two experiments have been conducted on the effects of drying on the bacilli. In the first experiment, the material was subjected to drying in the months of March and April, when the atmospheric humidity fell from 44 to 28%. Such bacilli did not survive for more than 14 days. On the other hand, when the experiments were repeated during the monsoon season with the atmospheric humidity at 72–80%, the bacilli survived for at least 28 days. On extending the study it was found that *M. leprae*, when left to dry, remained viable for up to 5

Table 12. Viability of *M. leprae* exposed to 1% Savlon (ICI) and 70% alcohol

Multiplication of *M. leprae* in footpads of mice								
Fresh sample (0 day)	Hours maintained before inoculation							Autoclaved sample (Control)
		0·5	1	2	4	24	48	
$1{\cdot}8 \times 10^5$	Savlon 1%	2×10^5	$\mathbf{3 \times 10^4}$	N	N	$\mathbf{4 \times 10^4}$	N	N
	Alcohol 70%	N	**N**	N	N	**N**	N	N

Inoculum-up to 10^4 bacilli per footpad. N-negative.

months, particularly under humid conditions. It was therefore surprising that when kept in saline or in moist earth, such bacilli died earlier, i.e. by about 2 months. It is difficult to explain these contradictory findings, although it is possible that enzymes are destroyed faster when exposed to fluids, whereas in a slow desiccation under only humid conditions, the enzymes may remain intact for a longer time. The bacilli were kept in moist soil because several varieties of mycobacteria are found in the soil. However, to avoid contamination the soil has had first to be sterilized by heat, which might have disturbed the natural conditions. It also is very surprising that *M. leprae* survived exposure to direct sunlight for 3 h a day for 7 days. Possibly the ultra-violet rays are filtered out to a considerable extent by the atmospheric dust which is very heavy in North India in the summer.

In all the experiments it is obvious that *M. leprae* can withstand severe adverse environmental conditions, yet remain viable for a considerable time. It is surprising that an organism like *M. leprae* which is said to be fastidious and which can grow and multiply only *in vivo*, can remain viable outside the human body for such long intervals despite desiccation or even exposure to sunlight for example. Such an unusually long period of viability, despite desiccation, has also been reported with regard to the tubercle bacillus. Cornet[4] was of the opinion that tubercle bacilli remain alive and virulent in dust for 3–4 months.

If the bacilli can remain viable outside the body despite desiccation, the possibility of the transmission of the disease by indirect contact must be seriously considered. In clinical practice, there are instances where there is no known source of infection within the family, in the neighbourhood or among close associates. In such cases it is likely that individuals at large have acquired the infection by indirect contact with *M. leprae* through objects in the environment. Such a mode of infection should be considered before concluding the possible infectivity of closed cases, a view expressed by some leprologists.

The present study also throws some light on the usefulness and limitation of refrigeration for preserving the bacteria. While *M. leprae* remain viable stored at 40°C and −20°C for about 2 months, refrigeration at −70°C remain viable only for half that time. A possible explanation is that a sudden exposure to very low temperature causes water to form crystals which may be detrimental to the bacteria. It is also known that freezing and thawing may destroy the organisms.

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Detection of IgA anti-PGL-I specific antigen to *Mycobacterium leprae* in mangabey monkeys inoculated with *M. leprae*

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Summary Using sera from 4 pairs of mangabey monkeys inoculated with titrated doses of *Mycobacterium leprae* we demonstrated that IgA antibodies against *M. leprae* specific PGL-I antigen were present in 75% of inoculated monkeys' sera. High IgA antibody was detected in 50% (3/6) of infected animals and all three developed lepromatous leprosy (LL). Antibody titers correlated with PGL-I antigen in serum. The highest IgA peak appeared late and corresponded to the beginning of treatment, and in two of them appeared shortly after or corresponded with neurological damage. Low IgA response was found in the other 3 monkeys (50%—3/6), two of which developed indeterminate leprosy (I) and the other one LL. Low IgA levels appeared late after IgG and IgM, and shortly after neurologic signs. Both I monkeys were negative for PGL-I in serum. The remaining 2 monkeys (25%—2/8) did not show an IgA response; one of them developed LL but the disease regressed to I. IgM seemed to correspond to the appearance of PGL-I in serum. The other animal did not develop clinical symptoms of leprosy, and PGL-I in serum was negative.

Although there was no clear relation between the development of anti-PGL-I IgA and experimental leprosy, the finding of a high IgA response in some animals suggests that further studies are needed to evaluate the role of antigen-specific IgA in the disease process.

Introduction

Infectious diseases have had a big impact on human life. Among those diseases leprosy has presented and continues to present a significant problem in developing countries.

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Leprosy is a chronic disease caused by *Mycobacterium leprae*, which has tropism to peripheral nerves, skin and mucosa where bacilli are found in large numbers in lepromatous leprosy (LL) patients. Infection with micro-organisms through skin and mucosa generally elicits specific antibody predominantly of the IgA class. However, the IgA antibody response in leprosy patients has so far escaped attention.

Since phenolic glycolipid-I (PGL-I) species-specific antigen to *M. leprae* was discovered,[1] several studies have attempted to evaluate the humoral response of the host.[2,3] However, despite the tropism of *M. leprae* to skin and mucosa we do not know if PGL-I elicits IgA class antibodies and what significance they might have for disease development. The lack of knowledge about the development of immune response in leprosy patients is due to the long incubation period between infection and clinical disease, so by the time the diagnosis is made the individual has already been ill for a long period of time. That makes it impossible to study the immunological response immediately after primary infection with *M. leprae*.

The sooty mangabey monkey (*Cercocebus torquatus atys*) has been reported to be a good model to study the immune response to leprosy, because it has a course of infection similar to humans.[3]

The aim of this paper is to evaluate the immune response of IgA class antibodies to species-specific PGL-I antigen by ELISA in the sera of 8 mangabey monkeys inoculated with *M. leprae* suspension and to correlate it with anti-PGL-I IgG and IgM titers, PGL-I in serum, and clinical course of the disease.

Material and methods

The animals' conditions, methods of *Mycobacterium leprae* inoculation, the clinical evaluation before and after inoculation, and IgG and IgM results have been described previously.[3] Briefly, four pairs of mangabey monkeys were inoculated with *M. leprae* suspension by combined intravenous and intradermal routes. Monkeys number D171 and D172 received $4{\cdot}8 \times 10^{10}$ acid-fast bacilli (AFB), D173 and D174 were inoculated with $4{\cdot}8 \times 10^{9}$ AFB, D175 and D176 received $4{\cdot}8 \times 10^{8}$ AFB, D177 and D178 received $4{\cdot}8 \times 10^{7}$ AFB. Two hundred and four serum samples were obtained over a 95-month period. There were two samples from each monkey 3 months before *M. leprae* inoculation and an average of 25 samples from each animal over 90 months after inoculation.

ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA) FOR IGA

The disaccharide moiety of PGL-I coupled to bovine serum albumin (D-BSA, provided by WHO) was used to measure IgA antibody levels. The detection of antibody IgA anti-PGL-I by ELISA serological test was performed as briefly described.[4] Flat bottom, polystyrene microplates (Nunc) were coated with 50 μl/well of D-BSA and BSA, respectively, diluted 100 ng/ml in 0·05 M sodium carbonate buffer pH 9·6 for 2 h at 37°C.

The plate was blocked with 100 μl/well of 1% bovine albumin in phosphate-buffered saline containing 0·1% v/v Tween 20 (BSA-PBST). After incubation for 1 h at 37°C, 50 μl of test monkey serum diluted 1 : 10 in 1% BSA-PBST was added and incubated as

before. Then 50 μl/well of mouse monoclonal peroxidase labelled anti-human IgA antibody (Nordic) was added, diluted 1 : 300 in BSA-PBST. After incubation and washing 50 μl/well of substrate solution containing 18 mM 2-2′ azino (3-ethyl-benzthiazoline-6-sulphonic acid) (ABTS; Boehringer) and 2·9 mM H_2O_2 in citrate-phosphate buffer pH 5·0 were added. After incubation for 1 h at room temperature in the dark the reaction was stopped by the addition of 50 μl/well of 0·32% (w/v) NaF. Extinction (ΔE) was read with a double wavelength micro ELISA autoreader MR 580 (Dynatech) at 405 nm (versus 490 nm) against a blank made up of substrate and stop solution. Known positive and negative control reference sera were included on each tray. Blank antigen wells were assayed in parallel to ensure that positive readings were, in fact, due to specific interactions between antibodies and the antigen. Each serum was tested twice and in duplicate. A serum was considered positive when the OD exceeded by two standard deviations (SD) the mean of results obtained before monkeys' inoculation with *M. leprae* (cutoff = 0·17).

ELISA DETERMINATION OF IGG AND IGM ANTI PGL-I

The assays were performed as previously reported,[3,5] but with some modifications, described in detail below, to ensure maximum accuracy and reproducibility. Natural PGL-I was used as antigen and was provided by Dr Brennan (Fort Collins, CO, USA).

Briefly, 96-well plates were coated with antigen (Ag), washed and blocked with BSA, washed again and reacted with a previously determined optimal dilution of monkey serum. After incubation and washing, the plates were coated with peroxidase-labelled anti-human IgG or IgM Fc fragment gamma or μ-chain-specific antibody diluted according to prior titrations, incubated, washed, reacted with o-phenylenediamine plus H_2O_2, acidified and OD's were determined at 490 nm on an ELISA reader.[3] Final OD's represent the difference in absorbance between wells containing Ag minus wells lacking Ag. Each reagent in the ELISA was carefully titrated in a checkboard manner to determine dilutions that would give final OD values between 0·1 and 0·5 OD whenever possible to utilize the OD range most sensitive to small changes in OD. This way longitudinal changes also would be accurately reflected. All sera were assayed together at one time in given experiments to permit accurate relative comparisons. The same batch of peroxidase antibody was used throughout. All experiments were done at least twice. OD values obtained with these precautions were reproducible in a given sample from one assay to another to within $\pm$0·05. The mean + 2 SD, taken as the cutoff points, respectively, were 0·043 and 0·073 for IgG and IgM.

DETECTION OF PGL-I ANTIGEN IN SERA

The PGL-I antigen assay was performed as described previously.[6] Briefly, for serum lipid extraction, 100 μl of serum was added to filter paper discs (0·5" in diameter) and dried completely. Lipids were then extracted using 2–3 ml of chloroform : methanol (2 : 1) solution and dried under N_2. Serum lipids were dissolved in chloroform and applied to fluorosil packed in a Pasteur pipette, 60–100 mesch (Sigma Chemical Co. St Louis, MO., USA) and eluted with chloroform, followed by 5% methanol in chloroform. The lipid fraction eluted with 5% methanol was saved and dried under N_2 and

examined for the presence of PGL-I by a dot-ELISA method as previously reported.[6] The lipid fraction was dissolved in 100 μl of hexane and a 5-μl portion was applied to a tuffryn (polysulphone) membrane (HT-200) (Gelman Sciences Inc., Ann Arbor, MI, USA), followed by anti-PGL-I antibody. A high titer of rabbit anti-PGL-I antibody (a gift from Dr P. J. Brennan) was used for the primary antibody and peroxidase-conjugated goat anti-rabbit IgG (Cooper Biomedical Inc., Malvern, PA, USA) was used as the secondary antibody. For colour development, 4-chloro-1-naphthol (Biorad Laboratories, Richmond, CA, USA) was used and the results were read visually.

Results

We demonstrated that the majority of monkeys developed IgA antibody against PGL-I. In six animals (6/8, 75%) increasing IgA levels were detected after *M. leprae* inoculation (D171, D173, D174, D176, D177, D178).

Three monkeys (D174, D176 and D177—3/6, 50%) showed high anti-PGL-I IgA levels ($\Delta E > 0{\cdot}5$) (Figure 1). All three monkeys developed lepromatous leprosy (LL) disease. Mangabey D174 developed LL by 10 months post-inoculation (pi) but regressed at 14 months. However, a relapse occurred at 35 months pi and persisted, requiring chemotherapy at 59 months (Figure 1(b)). Neurologic deformities appeared at 50 months and became worse after initiation of chemotherapy with a combination of rifampicin and clofazimine.[3] Early (within 3 months pi) moderate IgG and low IgM levels were seen which coincided with the appearance of the PGL-I concentration in serum (Figure 1(a) and (b)). Low anti-PGL-I IgA level appeared later after inoculation and corresponded with clinical reactivation at 36 months pi, and a second higher peak coincided with the beginning of chemotherapy and after neurologic deformities.

Monkey D176 showed a much more rapid clinical evolution of disease than any of the other animals, LL clinical symptoms were noted at 4 months with progressive evolution, thereafter requiring treatment at 27 months with rifampicin, and the complete remission of the disease was observed at 35 months.[3] No neurological signs have been noted. A low IgA peak appeared at 10 months pi and a second higher peak was seen at 24 months pi. On the other hand, D177 showed a slow development of clinical leprosy (LLs) by 26 months pi. The treatment with rifampicin was started at 42 months pi. Nerve enlargement was detected at 47 months pi and persisted after chemotherapy.[15] IgA appeared shortly after IgG and IgM and the highest peak of IgA appeared shortly (at 47 months pi) after treatment and corresponded to the beginning of the neurologic damage.

In these three monkeys early (within 3 months pi) anti-PGL-I IgG antibody titers were observed: moderate in D174, high in D176 and low in D177. IgM level in the same period was lower. The initial IgG and IgM were followed by a second or third peak that corresponded to periods of progression of the disease and higher serum concentration of PGL-I antigen in serum (Figure 1(a) and (b)). PGL-I in serum, as expected, decreased quickly after treatment. Anti-PGL-I IgG and IgM decreased slowly after treatment, but anti-PGL-I IgA decreased slower in D174 and D177 (Figure 1(a)).

In the other three monkeys (3/6, 50%) a low IgA response was found (D171, D173 and D178) (Figure 2). D171 developed severe clinical symptoms of LL at 5 months pi requiring treatment with rifampicin at 38 months pi.[3] Neurologic deformities appeared at 75 months pi and persevered beyond 90 months pi. A low anti-PGL-I IgA antibody

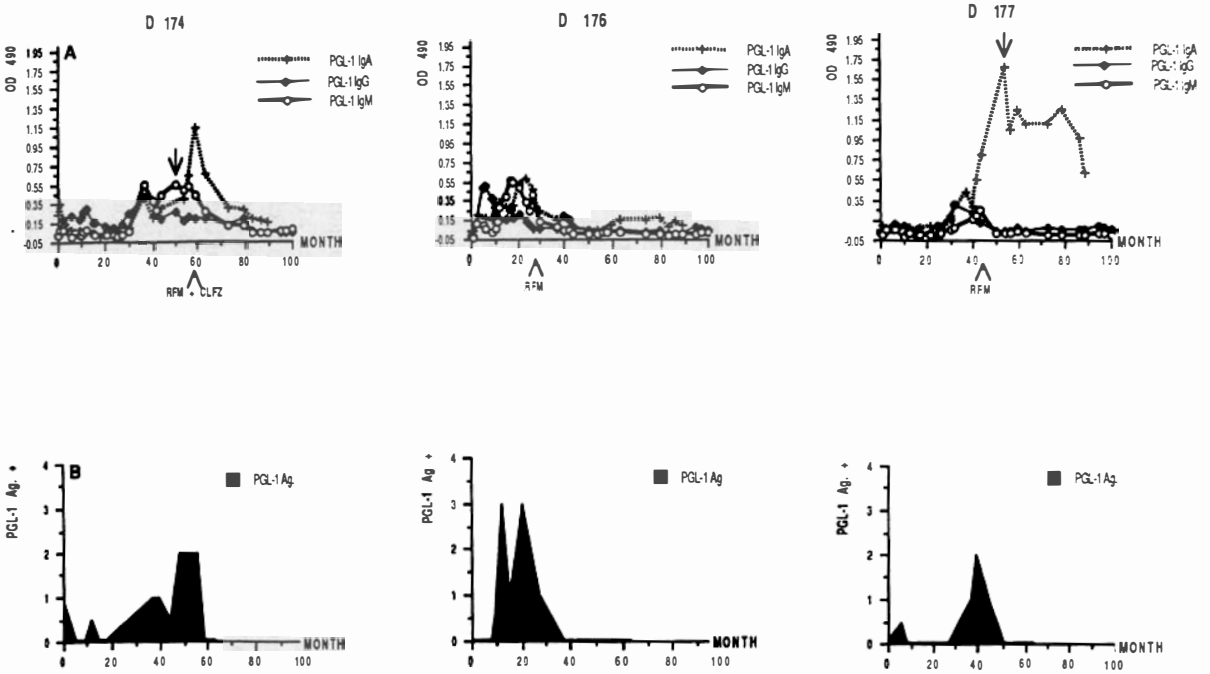

Figure 1. (A) Antibody responses (IgG, IgM and IgA) to PGL-I measured by ELISA in monkeys' sera. Mangabeys D174, D176 and D177 showed high anti-PGL-I IgA levels. ↓—development of neurologic signs. RFM—Rifampicin, CLFZ—clofazimine. (B) Detection of PGL-I antigen in monkeys' serum.

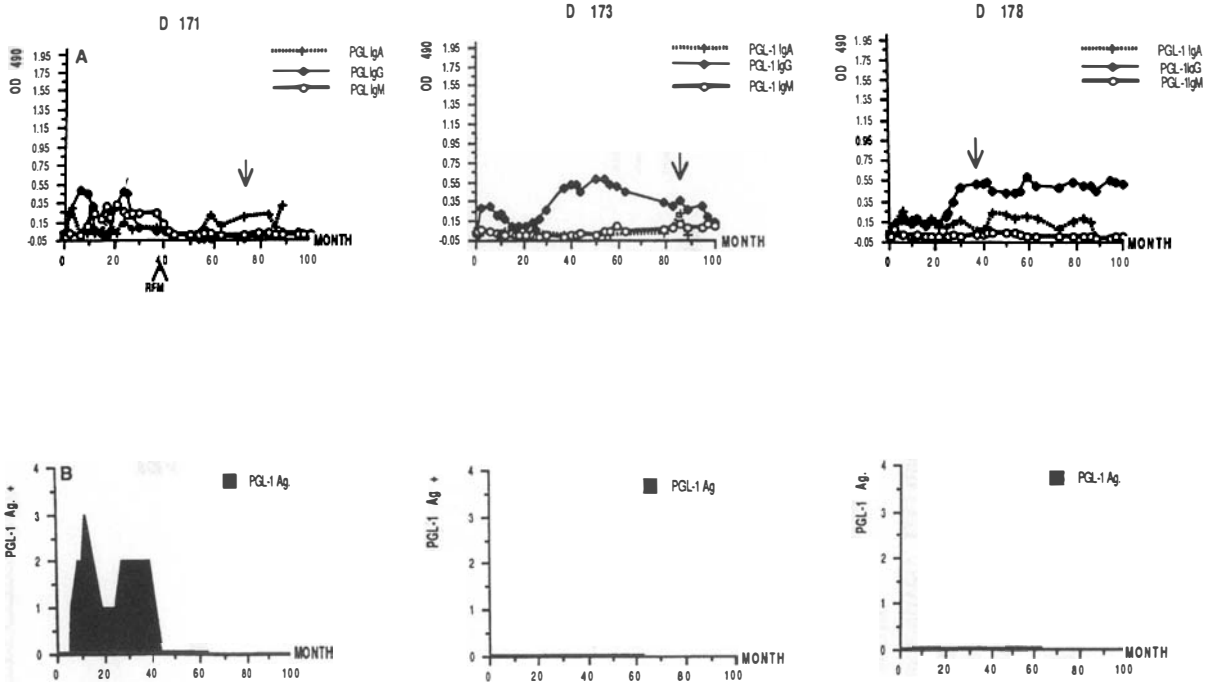

Figure 2. (A) Antibody responses (IgG, IgM and IgA) to PGL-I measured by ELISA in monkeys' sera. Monkeys D171, D173 and D178 showed low anti-PGL-I IgA levels. ↓—development of neurologic signs. RFM—Rifampicin. (B) Detection of PGL-I antigen in monkeys' serum.

titer was found late (at 60 months pi) after the appearance of IgG and IgM as well as after highest serum peak of PGL-I, and treatment. A second low IgA antibody peak, but higher than the first one, was detected at 90 months pi. Early (within 3 months pi), moderate IgG antibodies and very low IgM antibodies titers were found. IgG antibodies persisted and IgM antibodies rose corresponding with PGL-I concentration in serum and to the periods of clinical progression of disease. IgG and IgM antibodies and PGL-I antigen in serum decreased rapidly after chemotherapy, while IgA was still being elicited.

The animal D173 developed indeterminate leprosy (I) at 5 months pi but by 14 months the disease regressed.[3] Neurological signs appeared at 85 months pi, followed by progression to LL. Chemotherapy was given at 105 months pi.[15] Low IgA antibody titers appeared late after IgG and IgM and shortly (at 86 months pi) after aggravation of disease. Initial moderate IgG and very low IgM antibody levels were followed by a second high peak and low, respectively. IgG decreased slowly after 60 months pi. PGL-I antigen was not detected in serum.

D178 developed I leprosy by the 35th month pi. The indeterminate lesion of leprosy regressed spontaneously, however the nerve enlargement persisted.[3] A low early IgA peak appeared at the same time as IgG in the absence of disease, a second IgG peak

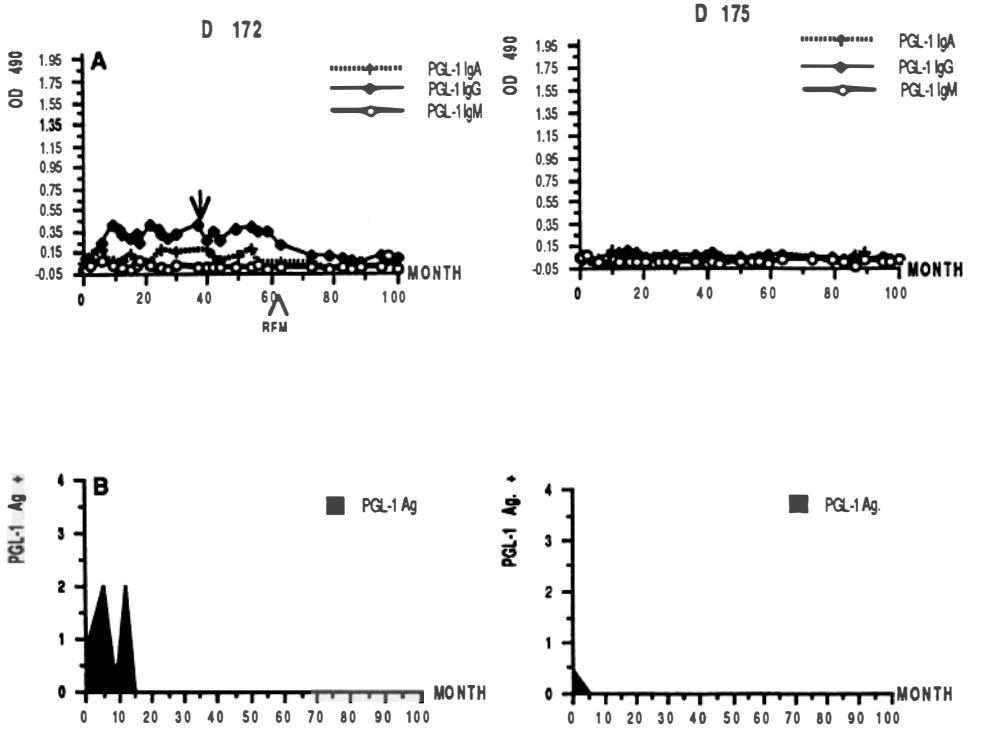

Figure 3. (A) Antibody responses (IgG, IgM and IgA) to PGL-I measured by ELISA in monkeys' sera. Monkeys D172 and D175 did not elicit IgA antibodies. ↓, development of neurologic signs; RFM, rifampicin. (B) Detection of PGL-I antigen in monkeys' serum.

appeared correlated with the clinical symptoms. Another slight increase of IgA was seen late (at 44 months pi) in the disease. IgM as well as PGL-I in serum were negative.

The remaining two monkeys (D172 and D175–2/8, 25%) did not show an IgA response (Figure 3). Monkey D172 developed LL at 9 months pi but the disease spontaneously regressed to I.[3] Relapse and regress of the disease happened several times during the follow-up (Figure 3(b)). It developed neurological signs at 39 months pi which persisted; chemotherapy was given at 65 months pi. IgG and IgM seemed to correspond to the appearance of PGL-I in serum and the development of the disease. PGL-I antigen disappeared much more rapidly in D172 than in any of the other monkeys. Mangabey D175 did not develop clinical symptoms of leprosy, mounted an early predominantly low IgG response and PGL-I was not detected in serum (Figure 3(b)).

Discussion

We report the detection of IgA to species-specific PGL-I antigen to *M. leprae* in serum of mangabey monkeys inoculated with *M. leprae* suspension over the entire course of the infection (over 90 months).

In this study the majority of animals presented increased levels of IgA after *M. leprae* inoculation (75%). An interesting finding was the presence of high levels of IgA after the appearance of clinical symptoms while the rise of IgG and IgM levels preceded the symptoms (D171, D173, D174, D176 and D177). It is already known that systemic immunization elicits preferentially IgM and IgG antibodies but a prolongated exposure to the antigens may induce high levels of serum IgA.[7]

It is commonly believed that human LL patients produce predominantly IgM anti-PGL-I, but our data show that in some monkeys anti-PGL-I IgG class is also elicited in significant quantities (4/7, 57%—D171, D172, D173, D178). One reason may be a difference between humans and monkeys, it may also be due to the inoculation routes or to the fact that our study looked at earlier time periods post-infection compared to most human leprosy studies.

It is not known whether IgG anti-PGL-I is elicited early in the disease, but IgM has been reported to be present before[8] and after disease symptoms. Our data show that IgG and IgM anti-PGL-I can be produced in significant levels early after the inoculation of monkeys with *M. leprae*. Gormus *et al.*[3,5,9] suggest that IgG antibody may correspond to resistance to clinical leprosy (D171, D172, D173 and D178) and that IgM antibody corresponds to susceptibility to LL forms of disease (D174, D176 and D177).

Five monkeys showed clinical evolution to lepromatous leprosy. In three of them (D174, D176 and D177) disease progression corresponded to the appearance of PGL-I in serum and high IgM anti-PGL-I, although the highest IgA peak came late after a serum PGL-I peak. In animals D171 (LL) and D172 (LL → I) only IgG and IgM corresponded to serum PGL-I antigen; IgA in D171 appeared late and was negative in D172. The monkeys D173 and D178 (both I) showed IgG and/or IgM and/or IgA in the absence of serum PGL-I antigen. These results suggest that mechanisms other than antigen load may be involved with IgA yield. Little is known about the production of IgA in leprosy but our data do not support the hypothesis that IgA would be useful for the detection of early leprosy infection,[10] since a significant anti-PGL-I IgA response in

the monkeys appeared later than IgG and IgM and most of the time corresponded to the beginning of treatment (D174, D176 and D177) or to the period shortly thereafter (D171). D172 had a different clinical evolution in comparison with the other monkeys. It seemed to be leprosy resistant (LL → I) and would probably not have developed clinical disease if it had received a low *M. leprae* dose.

It is established that a humoral response is dependent on the cooperation of B and T cells. On the other hand, the occurrence of lepromatous leprosy is due to a deficient cellular response to *M. leprae*, an obligate intracellular parasite. A high IgA response in animals with lepromatous leprosy, especially in those under treatment, then, seems to be a controversial finding. The existence of IgA titers may be explained by recent studies where it has been reported that the cytokine TGF-β (transforming growth factor beta) enhances the IgA production by LPS stimulated murine B cells even in the absence of T cells.[11] Bullock[12] links the high serum IgA concentration in LL patients under therapy to the persistence of killed *M. leprae* in the tissues but we believe that other mechanisms may also be activated. The association of TGF-β with immunosuppression was previously shown and increased production of this cytokine was reported in patients with the acquired immune deficiency syndrome (AIDS).[13] This suggests that TGF-β may play an important role in the spread of infection and/or disease progression.[13] This hypothesis may explain why a high IgA peak appears coincidently with the beginning of or shortly after treatment. Monkeys D171, D174, D176 and D177 received chemotherapy because the disease became severe. Perhaps high IgA peaks were elicited at this time by TGF-β action and not because of the chemotherapy effect. On the other hand, maybe an IgA response would be elicited to remove the circulating antigenic substances, incidentally this is the only function of IgA that is substantiated.

Another result of particular interest is that anti-PGL-I IgA antibodies were found shortly after or coincident with neurologic damage (D171, D173, D174, D177 and D178). Animals D174 and D177 produced IgA in excess of 1·0 OD. These monkeys seem to be more susceptible than the other animals. In D174 and D177, in which the clinical nerve symptoms persisted even after successful chemotherapy, the IgA antibodies remained at a high level for long periods of time (Figure 1). Mangabey monkeys D171, D173 and D178 seemed less susceptible to leprosy infection and produced low anti-PGL-I IgA antibody levels. Although D171 developed extensive disease in the beginning, it responded very well to chemotherapy and, as animal D173, developed neurologic signs later after regression of the disease. Mangabey D178 showed symptoms of leprosy nerve enlargement with indeterminate lesions of leprosy in the skin regressing spontaneously. Antibody responses to human nerve antigens have been reported in these monkeys, but it is not clear if these antibodies or anti-PGL-I IgA play some role in the pathogenesis of the disease.[15] If IgA antibodies were elevated only in the context of a wider humoral response against PGL-I of either IgG and IgM (as in D176), doubts may be cast on the possible significance of this immunoglobulin, but in some monkeys high IgA antibody levels were detected even when IgG or/and IgM were low or decreasing (D171, D173, D174 and D177). On the other hand, anti-PGL-I IgG and IgM have been elicited early pi and both immunoglobulins or one of them arose following the progression of the disease, so maybe the damage to peripheral nerves was originally caused by these two antibodies, and in this case the late increase of IgA may be involved in the amplification of the neurological damage. Or alternatively, anti PGL-I IgA may play a protective role from attack by humoral or cellular factors.

Several fluctuations in the antibody response and in the clinical evolution of disease between the monkeys studied were noted, which is perhaps influenced by intrinsic factors of the host, such as his cell-mediated immunity, environmental factors and the strain of *M. leprae*.

The interpretation of our data may not be simple. Leprosy seems to elicit a particular immune response. During the course of HIV induced-immunosuppression, tuberculosis, among other opportunistic infections, tends to appear. However, in a recent report no evidence of an association between the incidence of leprosy and HIV infection was found.[14] The authors suggest that leprosy may have a particular immune response mechanism. In our study the immunological events have been orchestrated since the monkeys were experimentally inoculated with *M. leprae*. Many cells and cytokines have played a role in the activation and suppression of the immune response and during this process the disease developed. The availability of an experimental model would be helpful in designing a longitudinal study to evaluate not only if IgA antibodies play a role in leprosy but also to study the interactions between lymphocyte subsets and cytokines produced and the humoral response in leprosy.

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Dapsone syndrome in a Filipino man

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Summary A case of dapsone syndrome occurring in a Filipino man under treatment for multibacillary (MB) leprosy is described. The patient manifested progressive fever, erythroderma and jaundice 4 weeks after initiation of multidrug therapy (MDT) with rifampicin, clofazimine and dapsone. The clinical symptoms conformed well to the dapsone syndrome first described in the 1950s and this report proves that the syndrome does still exist. There was recovery after dapsone was omitted and therapy with systemic corticosteroids was started.

In view of this potentially fatal hypersensitivity reaction, this case report emphasizes the need for caution when initiating MDT or dapsone therapy. It is also suggested that any patient on MDT or dapsone needs to be referred immediately to a dermatologist or internist if the patient develops a skin rash during the first 2 months of treatment.

Introduction

Dapsone or diaminodiphenylsulphone has been used for over 50 years in the treatment of a variety of dermatologic diseases but its prolonged and extensive use has been in the treatment of leprosy. While a variety of adverse and toxic effects are associated with dapsone, a distinct hypersensitivity reaction has been described.[1,2] This reaction, termed 'dapsone syndrome' is characterized by the sudden onset of a papular or exfoliative rash, accompanied by fever, malaise and weakness, and followed by jaundice, enlargement and tenderness of the liver, lymphadenopathy and mononucleosis after 2 to 8 weeks of dapsone therapy. However, not all symptoms are necessarily present.[1] The cutaneous manifestations of the syndrome show wide variations, including erythroderma, papular erythematous eruptions, erythema multiforme, toxic epidermal necrolysis and Stevens Johnson syndrome.[3]

Hypersensitivity reactions to dapsone which were common in the late 1940s and early

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50s, then virtually disappeared, were noted to become more frequent in the 1980s. Based on a postal survey by Smith[4] (1988), it was not possible to give an overall estimate of the frequency of the dapsone syndrome but it varied from 0 to 2% of new cases treated.

The fact that few additional cases have been reported since then, despite the millions of leprosy sufferers receiving the drug, is probably related to the lower dosages used and justifies the conclusion that the syndrome is a rare complication of dapsone therapy.[5]

In the Philippines, despite the widespread therapeutic application of dapsone, no case of dapsone syndrome has been reported in the literature. Although this could be a reflection of a true absence of such occurrence, the possible inability of the physicians to recognize the syndrome due to lack of awareness of its existence cannot be totally discounted. We report on the occurrence of this syndrome in a Filipino man who was given the WHO–MDT for MB leprosy.

Case report

An 18-year-old Filipino male who was seen at the dermatology department of the Jose R. Reyes Memorial Medical Center was diagnosed as having borderline lepromatous leprosy based on anaesthetic skin lesions, a bacteriologic index of 3+ and skin biopsy findings. He was one week into the WHO–MDT for MB leprosy consisting of rifampicin (600 mg once a month), clofazimine (300 mg once a month and 50 mg/day) and dapsone (100 mg/day) when he developed jaundice. Discontinuation of rifampicin and clofazimine was advised. However, the patient was maintained on dapsone.

Three weeks later, the patient developed fever, and maculopapular rashes on the face and chest. This was confirmed at a provincial hospital where laboratory studies revealed a normal full blood count but elevated liver function tests: SGPT, 874·0 IU/L (normal, 0–31 IU/L), direct bilirubin, 143 μmol/l (normal, 0–3·4 μmol/l), indirect bilirubin, 182 μmol/l (normal, 3·4–17·0 μmol/l) and alkaline phosphatase, 229 IU/L (normal, 9–45 IU/L). Liver ultrasonography showed diffuse parenchymal disease.

On the ensuing days, he developed mucopurulent eye discharge and blisters on the buccal mucosa, trunk and extremities. The maculopapular rash progressed into generalized scaling. At another hospital, a repeat haematologic study revealed anaemia: haemoglobin of 74 g/l, erythrocyte count of $2{\cdot}54 \times 10^{12}$/L, haematocrit of 25%.

The progression of the patient's condition prompted consultation and eventual admission to the medical centre.

On physical examination, the patient was acutely ill, jaundiced and febrile with a temperature of 38·8°C. In addition, he had mucopurulent eye discharge and erosions on the buccal mucosa and lips. He had generalized erythema and scaling with multiple tense and flaccid bullae located on the forearms, trunk and feet (Figures 1–4). Erosions and crusted lesions were likewise noted on the trunk and extremities. The liver was palpable but nontender. There was no lymphadenopathy. The rest of the examination was unremarkable.

A complete blood count revealed a haemoglobin of 8·0 g/l, a haematocrit of 25%, leukocyte count of $21{\cdot}45 \times 10^9$/L with lymphocytes of 48% and platelet count of $150 \times 10^3/\mu$L. Liver function tests were elevated at the following values: indirect bilirubin of 1033·6 μmol/l, direct bilirubin of 734·4 μmol/l, total bilirubin of 1768 μmol/l, alkaline phosphatase of 241·4 IU/L SGOT of 126·3 IU/L, SGPT of

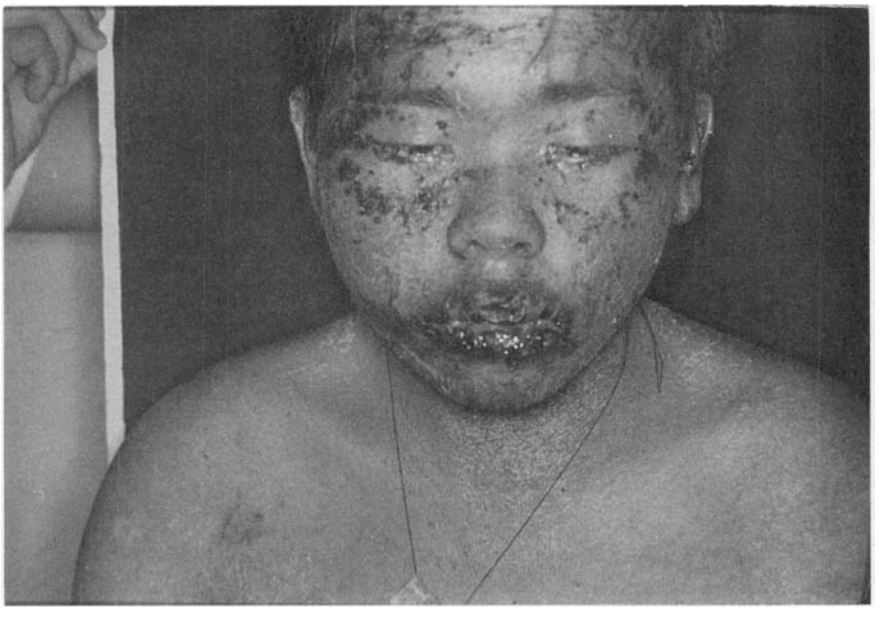

Figure 1. On admission, the patient had icteric sclerae, mucopurulent eye discharge and erosions on the buccal mucosa and lips.

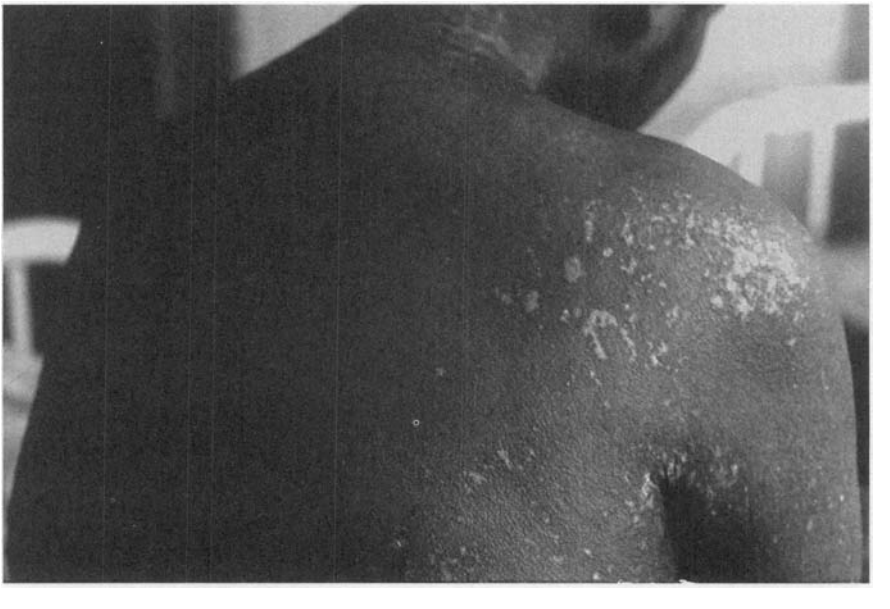

Figure 2. Diffuse scaling and erosions at the back of the patient.

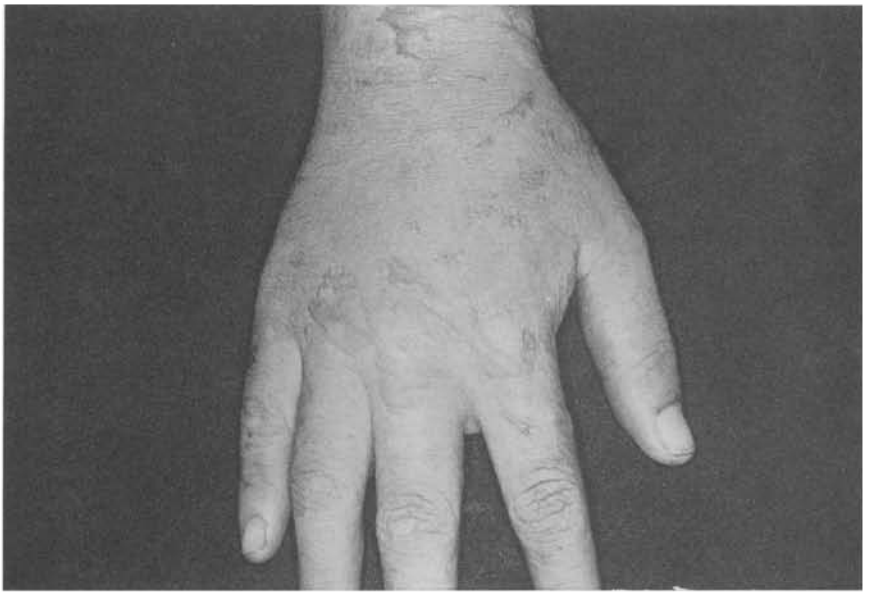

Figure 3. Flaccid bullae on the dorsum of the hand.

Figure 4. The patient on the 23rd hospital day, prior to discharge, with further clinical improvement.

196 IU/L, prolonged prothrombin time of 17 s (control, 12 s). A complete hepatitis profile was nonreactive for all antigens and antibodies. G6PD determination was over 120 min (normal, 30–60 min). Chest X-ray revealed normal findings. A skin biopsy done on a bulla was consistent with erythema multiforme.

An impression of a hypersensitivity reaction to dapsone was made. All previous medications were discontinued. He was started on intravenous steroid therapy with hydrocortisone at 240 mg/day. This was gradually tapered, then shifted to oral prednisone at 30 mg/day. Chlorpheniramine maleate was also given. Since all the drugs of the WHO–MDT regimen were withdrawn, ofloxacin, a fluoroquinolone with bactericidal properties against *Mycobacterium leprae*, was given at 400 mg/day. Packed RBC was transfused for the anaemia and vitamin K was given for the delayed prothrombin time. He was also given compresses, emollients, betamethasone lotion, tetracycline ointment, and betamethasone and fucidic acid cream.

The patient gradually improved and his skin eruptions cleared with residual hyperpigmentation within 3 weeks from the start of therapy. Upon discharge, haematologic studies and liver function tests were continually monitored and showed normal values within 1·5 months.

Rifampicin and clofazimine were reinstituted with no development of the earlier signs and symptoms observed. He was not challenged with dapsone because of the potential risk of recurrence and severity of his initial illness.

Discussion

The patient had fever, malaise, anaemia, exfoliative dermatitis and jaundice with gross hepatic dysfunction, all of which developed within 4 weeks after administration of dapsone.

The constellation of symptoms and results of all ancillary procedures favoured the possibility of an adverse drug reaction, most likely due to dapsone. Although rifampicin and clofazimine cannot be readily excluded as the precipitating agents, there have been no published reports attributing a reaction of this type to either drug. Moreover, despite the discontinuation of these two drugs, there was progression of the patient's illness, apparently because of the continuation of dapsone. Likewise there was no recurrence of lesions upon reinstitution of rifampicin and clofazimine.

The earliest report of a hypersensitivity reaction to dapsone was published in 1949. It was thought then that dapsone precipitated glandular fever. The adverse reaction occurred early during the course of treatment and was characterized by fever, lymphadenitis, splenomegaly, jaundice, abnormal liver function tests, mononucleosis and dermatitis, including generalized exfoliation. Diagnosis was confirmed by a positive Paul Bunell test and mononucleosis. Since this reaction was initially associated with high doses of dapsone, the authors suggested a gradual build-up of dapsone to 300 mg daily to avoid this complication.[4]

In 1950[6], Lowe reported three cases of hypersensitivity to the drug and advised early withdrawal of dapsone and the use of antihistamines followed by densensitization. Allday and Barnes in 1951 gave it the name 'dapsone syndrome' and were the first to put forward the view that it was a hypersensitivity reaction.[7] While the syndrome may appear in an incomplete form, as in this patient in whom lymphadenopathy was not appreciated, Tomecki & Catalano[1] have emphasized that dermatitis was always present.

In 1951, the frequency of hypersensitivity reaction to dapsone was 2%. Fatal outcomes associated with exfoliation were reported at a dose of 100 mg daily.[8] From 1956 until 1980, there were only two reports of the dapsone syndrome. Three distinct explanations were offered. Firstly, the reaction had continued to occur but had not been recognized; secondly, the reaction had been recognized but had not been reported; and finally, the reaction in fact virtually disappeared over this period. The first explanation seems unlikely due to its severity while the second is possible, having discussed the problem with mass users of dapsone, although the sudden reappearance of case reports from 1980 onwards emphasized that the hypersensitivity reaction is an unusual occurrence.[4]

One conclusion from these arguments is that the hypersensitivity reaction to dapsone did virtually disappear between 1956 and 1980. One explanation is that the incidence of the reaction is related to dose; in the 1950s, the recommended dose of dapsone was reduced from 300 to 100 mg daily. However, it has been argued that the hypersensitivity reaction to dapsone or to any other drug is not dose dependent. Explanations based on genetics cannot explain sudden changes. Factors related to the manufacture of dapsone have not been investigated.[4]

From 1980 to 1986, there were 27 published case reports suggesting a rise in the frequency of the reaction.[4] This was further demonstrated in a local study done in Thailand,[3] which showed an incidence of 3·6% for the period 1982–88, a tenfold increase compared with that of 0·3% for the previous period between 1970 and 1982. The following factors were mentioned as possibly contributing to the observed rise: increased awareness, low dose regimens before 1976, quality of dapsone and combination with other antileprosy drugs. This study showed an apparent increase in hypersensitivity reaction to dapsone after the introduction of MDT and raised the question of a possible drug interaction with rifampicin.

In 1993 in the Philippines, leprosy had a prevalence rate of 2·35/10,000 population as compared with a previous 7·2/10,000 in 1986.

Javier[10] in 1970 reported two cases of dapsone hypersensitivity which manifested as erythroderma with accompanying fever and chills followed by generalized coal black hyperpigmentation. To our knowledge, there has been no other documented case of dapsone syndrome as depicted by this case. Although this could be a reflection of a true absence of such an occurrence, the possible inability of the physicians to recognize the syndrome due to lack of awareness cannot be totally discounted.

The cause of the dapsone syndrome remains unknown. It has also been suggested[1,7,11] that the hypersensitivity reaction is probably not dose related as in the case of toxicity. Even a small dose may be dangerous in a previously sensitized person. Giving the drug by gradually increasing the dose may also not be of help.[11]

With the availability of alternative and effective antileprosy drugs, it is not necessary to desensitize these patients. Moreover, this practice may predispose to dapsone resistance.[11] The conditions of most patients improve after cessation of dapsone therapy. Indeed, the patient who has been reported in this present paper improved dramatically after cessation of dapsone and institution of systemic steroid therapy.

Conclusion

The partial or complete expression of the dapsone syndrome as a hypersensitivity

reaction may be more common than previously thought, and every physician should be familiar with this reaction pattern. Patients on dapsone treatment should be under close supervision and physicians should realize that with any drug-induced reaction, early recognition, prompt withdrawal of the drug and institution of systemic corticosteroids are the important life-saving measures.

Acknowledgments

I am grateful to the above patient who has been very cooperative. I would like to thank Dr Agnes Espinoza-Thaebtharm and Dr Gertrude P. Chan who were involved in the management of the case. Dr Elizabeth V. Tianco provided comments on the manuscript. Thanks are also due to Dr Antonio Chua for his help in preparing this paper and to Dr Jerry B. Rosario for his encouragement.

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Leprosy of the eustachian tube (nasopharyngoscopic study)

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Summary The technique of nasopharynogoscopy affords an accurate assessment of the lesions at the orifices of the eustachian tube. It was performed in 30 patients suffering from lepromatous leprosy in order to determine the type, nature and site of the lesion. Involvement of the eustachian tube in leprosy may begin with a localized area of erythema progressing to granuloma formation or ulceration. Leprous lesion at the eustachian tube orifices was related with subsequent changes in the tympanogram pattern. Nasopharyngoscopy is also found to be of therapeutic value in removing the crust, discharge and granulations at the eustachian tube orifices.

Introduction

Leprosy is a systemic disease which involves the upper respiratory tract, including the nasal mucosa as well as skin and peripheral nerves. In lepromatous leprosy, over 95% of patients have involvement of nasal mucosa.[1,2] The disease extends and involves the entire nasal cavity up to and including the posterior part and the nasopharynx. The orifice of the eustachian tube is situated on the lateral wall of the nasopharynx. Because of nasal and nasopharyngeal involvement there is a possibility of the spread of disease into the eustachian tube.

An extensive survey of the literature reveals no study of direct visualization of the eustachian tube in patients suffering from lepromatous leprosy.

Pure tone audiometry and tympanometry are of limited help in assessing whether middle-ear problems are due to actual involvement of the eustachian tubes with leprosy or to the secondary effects of nasal leprosy.

Nasopharyngoscopy is the only method which can give accurate information in respect to the type, nature and site of lepromatous lesions at the nasopharyngeal orifice of the eustachian tube. In view of the high incidence of nasal involvement associated with a highly infectious discharge and the possibility of the spread of leprosy into the

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Table 1. Showing clinical classification of stages in intranasal leprosy

Stage	Finding	No. of patients
Stage I (invasive)	Congestion, nasal discharge, early atrophic area.	5
Stage II (proliferative)	Polypoidal proliferation grey nodule, congestion oedema or early ulceration.	12
Stage III (destructive)	Ulcerative lesion septal perforation thick nasal discharge and crusting.	10
Stage IV (resolution)	Stage of resolution fibrosis and scarring.	3

eustachian tube, it was decided to investigate the eustachian tube by nasopharyngoscopy.

Material and methods

Thirty patients with bacillary positive untreated lepromatous leprosy were taken for the present study. Their ages ranged from 15 to 55 years. There were 19 males and 11 females.

Results

In each case, a complete ENT examination was performed. Intranasal examination was done and findings were recorded and categorized into different stages according to the classification used by Job *et al.*[3] as shown in Table 1.

Complete otoscopic examination was done in each case and wax removed if present and the findings were recorded. Seven patients (23%) showed clinical findings in one or both ears, of retracted tympanic membranes or secretory otitis media (Table 2). Similarly pharyngeal and laryngeal examinations were done in each case. The details have already been reported.[4] Pure tone audiometry was performed in each case. The details have been described elsewhere. Tympanometry was performed using an American Electromedics 86 AR tympanometer over a pressure range -400 to $+200\,\alpha$Pa. The details of the results have already been reported.[5–7]

X-rays of the nose and paranasal sinuses (Water's view) and lateral view of the nasopharynx were taken. The X-ray findings in the paranasal sinuses revealed that the

Table 2. Showing otoscopic finding in lepromatous leprosy

Finding	Number of patients
Retracted ear drum	4 patients: Both ear: 2 One ear: 2
Secretory otitis media	3 Patients: Both ear: 1 One ear: 2

Table 3. Various types of leprosy lesion seen in nasopharyngoscopy

Types of lesion	No. of cases
Normal	21
Superficial inflammation with or without ulcer	2
Ulcers of variable size and thick secretion deposit	3
Granulomatous lesion	3
Healed ulceration with scar	1
Total	30

maxillary antum was found to be affected more commonly, i.e. 60% more than the others (ethmoidal 33·33% and frontal sinuses 30%). There was evidence of diffuse mucosal thickening, patchy mucosal thickening to complete opacity of the sinuses. The details of the findings have already been reported elsewhere.[8]

All the cases underwent nasopharyngoscopy using a Storz 90° angled rigid nasopharyngoscope to study the eustachian tube orifices. The type, nature and site of the pathology observed was recorded. Biopsy was taken in 8 patients which revealed the typical picture of lepromatous leprosy with positive acid-fast bacilli (AFB).

Nine out of the 30 cases revealed pathological changes around the pharyngeal ends of the eustachian tubes while the remaining cases were normal in nasopharyngoscopy. The various types of pathology seen are shown in Table 3. The eustachian tube orifices are more commonly affected in stage III (ulcerative lesions, septal perforation with thick nasal discharge or crusting) and stage II (polypoidal proliferation greyish node, congestion, oedema or early ulceration) forms of intranasal leprosy (Table 4).

Discussion

Nasopharyngoscopy is the most appropriate technique for making an accurate diagnosis of lesions at the orifices of the eustachian tube. This technique has repeatedly been shown to provide information which is superior to that obtained by clinical or radiological investigations. Again, pure tone audiometry and tympanometry are of limited value in assessing whether middle-ear problems are due to actual involvement of the eustachian tubes with leprosy or to secondary affects of an extensive intranasal

Table 4. Relationship between clinical staging of intranasal leprosy and lesions at the eustachian tube orifices

Stage of nasal leprosy	Total No. of patients	Eustachian tube lesion	
		Normal	Positive
I Invasive	5	5	–
II Proliferative	12	**8**	4
III Destructive and ulceration	10	**6**	4
IV Resolution and fibrosis	3	2	1

leprosy. Nasopharyngoscopy not only allows direct visual assessment of the pathology but also allows biopsies to be taken from the lesion and thus confirms the lesion either to be actual leprosy or that the pathology is due to the secondary effects of nasal leprosy. Nasopharyngoscopy in leprosy is not only a diagnostic procedure but also has a therapeutic value. Collected secretions, crusting, and granulations can all be removed effectively from the orifice of the eustachian tube under direct vision with subsequent symptomatic improvement. It may also prove helpful in an accurate follow up of cases to assess the benefit of planned therapy.

The nasopharyngoscopy in the present 30 lepromatous leprosy patients revealed the presence of positive lesions at the orifices of the eustachian tube in 9 cases.

Similar to the intranasal lesion, different types of leprosy lesions were found at the pharyngeal orifice of the eustachian tube. Leprous involvement may begin with a localized area of erythma, progressing to ulceration or localized granuloma formation depending upon the immunity of the host and virulence of the organism. Scarring or evidence of healing may be seen in places.

The microscopic pathology of the lesions at the orifices of the eustachian tube is similar to other leprous lesion. Biopsy of the non-ulcerative form was not performed because of the risk of converting an early mucosal lesion into an ulcerative form and the chance of enhancing the disease by direct contact of the lesion with an infected discharge.

During nasopharyngoscopy cleaning of the eustachian tube orifices by removing the crust, discharge or granulations resulted in improvement in audiometric and tympanometric findings. Thus it is suggested that periodic cleaning of eustachian tube orifices along with prolonged antileprosy therapy may be more beneficial in preventing permanent disability of the eustachian tube by scaring or stenosis, especially in resistant cases.

The present study reveals that 30% of the patients have a subclinical involvement of the eustachian tube which may be diagnosed only on nasopharyngoscopy. This early diagnosis is of utmost importance to allow specific treatment before permanent damage to the eustachian tube has occurred.

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Leprosy in Croatia in the twentieth century

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Summary Even today, leprosy is a relatively frequently occurring disease, especially in tropical regions of the world. From the eleventh to thirteenth century, leprosy pandemics affected Europe, including Croatia. Probably as a consequence of such history, one can still find endemic foci of leprosy in present-day Croatia.

The aim of this study was to analyse all cases of leprosy registered in Croatia during the twentieth century; therefore, we studied thoroughly existing medical documentation and published reports on sporadic leprosy cases, and went on to collect the relevant data through on-site investigation in those parts of Croatia known as putative endemic foci of leprosy. In this way, we collected data concerning the number of leprosy cases, the probable sources of infection, and traced the possible paths of spread of the disease.

During the twentieth century, 17 cases of leprosy were registered in Croatia. However, due to the loss of medical documentation concerning the cases from Metković, the total number was obviously slightly greater. Concerning the 17 analysed cases, 4 patients were most probably infected during their visits (as sailors or immigrant workers) to the Middle East, South America or Africa; 3 patients developed leprosy after prolonged close contact with previously infected family members, while the exact source of infection remains unsettled for the remaining 10. However, 2 of these patients originated from the area of Cazin in Bosnia and Herzegovina, which is known to be an endemic focus of leprosy. Furthermore, the remaining 8 came from the small area of the village of Blizna in the Croatian municipality of Trogir, and therefore it seems reasonable to conclude that Blizna represents the endemic focus of leprosy in Croatia. The last case of leprosy in Blizna was registered back in 1956. Nevertheless, it is clear that sporadic cases of leprosy can reappear in Croatia, originating either from this endemic focus of Blizna, or as an infected person returning to Croatia from abroad. So, we can conclude that, even today, Croatian medical doctors (and especially dermatovenereologists) should still be acquainted with the clinical diagnosis of leprosy and basic principles of its treatment.

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Introduction

Taking into consideration social and psychological aspects of leprosy, one can expect that many cases go unnoticed and, therefore, that the real number of people presently affected is not always easy to estimate.[1,2] Leprosy occurs mostly in tropical regions, especially in equatorial and western Africa, southwest Asia, Oceania, Pacific islands, and Central and South America. It is generally believed that leprosy has occurred only sporadically in Europe since the First World War; however, the World Health Organization recorded 25,000 cases of leprosy in 1985, predominantly in Spain, Malta and Rumania.[3]

In Croatia, leprosy represents a less fortunate part of its historical heritage. It was already noted in Croatian regions (especially in Dalmatia) during the eleventh to thirteenth centuries as a consequence of the pandemic during the Crusades. Soon after that, leprosaria were established along the Croatian coast; the first in 1272 in Dubrovnik, followed by those in Zadar, Split, Čiovo and Kotor.[5] During the first half of the fourteenth century, the incidence of leprosy declined for the simple reason that most sufferers succumbed to plague (leprosy patients are especially vulnerable to secondary infections). The epidemic of leprosy reappeared significantly in Croatian regions after the Turkish conquest of the Balkan peninsula during the fifteenth and sixteenth centuries.[4,5] As a consequence, some endemic foci of leprosy can be found even today in the Republic of Bosnia and Herzegovina, and they were until recently observable even in some parts of the Republic of Croatia.[6]

The aim of this study is to analyse all leprosy cases registered in Croatia during the twentieth century, on the basis of available data as well as our own field research. We would like to stress the importance of clinical diagnosis in leprosy, because even today the disease can appear sporadically in 'hidden' foci within Croatia; furthermore, cases can come to Croatia from abroad.

Patients and methods

We have studied the number of leprosy cases as well as the sources and routes of spread of the infection in Croatia for the period from 1900 to 1994. We carefully collected and analysed all published sporadic cases of leprosy and then went on to collect information on leprosy patients within the former endemic foci in our country.

Results

The results of this study are summarized in Table 1 and Figure 1. In the following paragraphs, we offer a concise chronological description of registered cases of leprosy.

A small focus of leprosy was noted in 1924 in the village of Vidonja (the municipality of Metković), but unfortunately the complete documentation concerning these patients was subsequently lost. However, in 1904, the local governmental report from Zadar reports on the examination of one 64-year-old leprosy patient from the village of Vidonja, and thus indirectly confirms the existence of that endemic focus.[5]

The leprosy focus in the village of Blizna (the municipality of Trogir) was registered

Table 1. Leprosy cases in Croatia during twentieth century

Source and route of infection	Total No.	Year	Patients	Age (yr)	Place
Leprosy from foreign countries	6	1930	sailor	76	Brseć
		1939	mason	39	Krk
		1956	sailor	55	Gornji Okrug
		1963	student	22	Zagreb
		1984	housewife	63	Ogulin*
		1986	housewife	58	Zagreb*
Close contact with patients	3	1930	wife	68	Brseć
		1930	two sons	6, 14	Krk
Endemic area Blizna	8	1927	6 members of a family	7, 12, 17, 12, 21, ?	Blizna
		1956	man	46	Blizna
		1956	man	23	Blizna/Prgomet
Endemic area Metković	?	1924	medical records lost		Vidonja/Metković

* Two cases from endemic area Cazin in Republic of Bosnia and Herzegovina.

in 1927, and 10 years later those cases were described in an article published in a Croatian medical journal *Liječnički vjesnik*.[7] Leprosy was diagnosed in six members (3 boys and 3 girls) of the same family. The girls were aged 7, 12 and 17 years, respectively, and they were confined to the leprosarium in Sarajevo (Bosnia and Herzegovina) where they subsequently died; the fate of one boy was unknown, the other died at home at the age of 12, while the third died in the leprosarium in Sarajevo at the age of 21. The leprosarium in Sarajevo (Bosnia and Herzegovina) was the only one in former Yugoslavia. It was established in 1894 by Austrian dermatologists Glück & Fleger.[6] Even today, the village of Blizna is small and quite isolated which, together with our information collected on the spot, suggests that it was a real endemic focus of leprosy. It may be noted that, back in 1927, very strict measures were imposed by the local government, in an attempt to confine the infection to the village of Blizna, e.g. the police prevented anybody from leaving the village.

In 1930, leprosy was diagnosed in a 76-year-old fisherman and his 68-year-old wife in the village of Brseć (the municipality of Rijeka).[8] On questioning the patient disclosed that as a sailor he had visited Syria and Lebanon several times and then retired when he was aged 50. Although the first signs of leprosy appeared 20 years later, it was concluded that the patient was infected during his voyages as a sailor, and that his wife was infected through repeated close contact with him; however, no signs of leprosy were noted in other family members.[8]

In 1939, leprosy was also diagnosed in 3 members of one family (father and two sons) in the village of Županja on the island of Krk.[9] The man (aged 39) was formerly employed as a mason in South America, where he was engaged in building a leprosarium in Buenos Aires; he reported that on this occasion he was in close contact with local leprosy patients and that about 5 years after he returned to his home in Croatia he noted a loss of tactile sense and the appearance of 'bumps and nodules' on his hand and face.[9] Several years later, he died in the leprosium in Sarajevo. Leprosy was also diagnosed in his two sons, aged 6 and 14; however, their further fate is unknown. It has to be noted that their mother showed no signs of leprosy.

Figure 1. Leprosy in Croatia in 20th century.

The first case of leprosy in Croatia after the Second World War was diagnosed in Šibenik in 1956.[5] The patient, aged 23, was from the village of Prgomet (the municipality of Trogir); he noted polyps and ulcerations in his nose back in 1950, but at first he was treated as a typical case of tertiary syphilis. Two years later, he was admitted to hospital in Šibenik, and, interestingly enough, the first suspicion that he was suffering from leprosy was not raised by medical doctors but by a hospital guard who had previously seen some leprosy patients in Metković. Consequently, the diagnosis was soon established and the patient was transported to the leprosarium in Sarajevo, where he died several years later. As the village of Prgomet is situated in the close vicinity of the village of Blizna (mentioned above as an apparent endemic focus of leprosy), we believe that he was infected in the village of Blizna.

Because the case above alerted the local medical service, leprosy was successfully diagnosed in two other patients admitted to the hospitals in Šibenik and Split in 1956. The first patient, aged 46, was from the village of Blizna. The first signs of the disease appeared in 1943 in the form of ulcerations on his knees, hoarseness and chronic inflammation of the nasal mucosa. As the disease progressed, his nose became deformed and his toes mutilated, he suffered from partial alopecia and nodular-ulcerative changes developed on his forelegs. Therefore, his neighbours concluded that he was suffering from syphilis and he was excommunicated and expelled from his village.[5] After the diagnosis of leprosy was established, he was first treated for several years in the leprosarium in Sarajevo, and then returned to his home, where he was constantly under the supervision of the Public Health Service in Split. No sign of leprosy were found in other members of his family or his neighbours.

Another patient, aged 55, was a sailor from the village of Gornji Okrug (the municipality of Trogir). In the period from 1926 to 1947, he was sailing on the seas of the Middle East and South America. The first sign of the disease was wounds on his legs that he noted in 1953 and leprosy was diagnosed 3 years later. He was initially treated at the leprosary in Sarajevo, and then returned to his home. Although his village is also located near Blizna, we favour the conclusion that he was infected during his sea voyages.

In the period from 1956 to 1994, only 3 more cases of leprosy were registered in Croatia.[10,11] A 22-year-old student from Sudan (Africa) suffering from leprosy was admitted to the Clinics for Infectious Diseases in Zagreb in 1963. Another sporadic case was registered in 1984 in the municipality of Ogulin; this was a 63-year-old housewife, who had suffered from leprosy for 20 years and was formerly treated in the leprosary in Sarajevo. Her husband and her four children showed no signs of leprosy. Since that woman was born in the area of Cazin in Bosnia and Herzegovina, lived there for years and only later settled in Croatia, and since the area of Cazin is known as an endemic focus of leprosy, we may conclude that she was infected there during her youth. Finally, in 1986, another female patient from the area of Cazin (from the town of Velika Kladuša) was admitted and treated for leprosy in the Clinical Hospital for Infectious Diseases in Zagreb. Apparently, she represents another case of sporadic leprosy originating from the known endemic focus in Bosnia and Herzegovina.

Discussion

During the twentieth century, 17 cases of leprosy were diagnosed in Croatia. The exact number of cases from Metković is unknown, because their medical documentation was subsequently lost. Four patients were most probably infected by leprosy during their journeys or stays in the Middle East, South America or Africa. Three patients were infected due to prolonged and close contact with family members previously infected by leprosy in the above-mentioned parts of the world. For the remaining 10 patients, we were not able to determine the exact source of infection, and noted no suspicious contacts with other leprosy patients. Two of these patients originated from the area of Cazin, known as an endemic focus of leprosy in Bosnia and Herzegovina, while the remaining 8 patients all came from the area of the village of Blizna in the Croatian municipality of Trogir. Furthermore, clinically recognizable cases of leprosy in this area

appeared at widely separated time intervals (30 years or more). Therefore, we conclude that the area of Blizna may be designated as an endemic focus of leprosy in Croatia. Finally, both the presence of very few cases of leprosy at that endemic focus as well as the total lack of leprosy symptoms and signs in most members of their families, support the conclusion that the contagiousness of leprosy is quite low (3–6%), as already noted in the literature.[3]

Conclusion

The Department for Protection of Health of the Republic of Croatia has noted no cases of leprosy since 1986. However, our retrospective analysis of existing medical documentation as well as our in-field pilot epidemiological study clearly show that sporadic cases of leprosy can and do periodically appear in Croatia, either as a consequence of the arrival of infected patients from abroad or, more importantly, due to the existence of hidden endemic foci of leprosy within Croatia. Therefore, Croatian medical practitioners, and especially those in the field of dermatovenereology, should be acquainted with the clinical presentation of leprosy and the basic principles of its diagnosis and treatment.

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Letters to the Editor

INTERPRETATION OF DATA ON MONOLESION LEPROSY CASE VS TOTAL NEW CASE DETECTION RATE

Sir,

As a result of satisfactory implementation of multidrug therapy (MDT) in the National Leprosy Eradication Programme (NLEP) in India, the registered prevalence rate has shown an 87% reduction; and the new case detection rate (NCDR) or crude incidence rate has shown a 62% reduction after 11 years.[1] However it is observed that after 8 to 9 years NCDR remains more or less constant.[2] As emphasis has been laid on early case identification with a target set for case detection, more and more early single patch PB leprosy cases are recorded. Sometimes they are detected so early that it becomes difficult to demonstrate the cardinal signs, which may necessitate very careful examination. In a mass programme, over-diagnosis of such early monolesion cases at the peripheral level cannot be ruled out.

Generally it is believed that these monolesion PB leprosy cases have no transmission potential and are not of great significance from a public health point of view. Nearly 60–80% of such cases also show a tendency of self-healing.[3] NCDR is an indicator to assess the transmission of the disease in the community. It is a fact that among all the new cases detected, a large number of monolesion cases representing an exposure of population to a reservoir of infection contribute to the pool of new cases at present.

To look at this issue from a public health angle, we collected statistics on monolesions from seven MDT districts during the evaluation of NLEP–MDT programme assisted by Swedish International Development Authority (SIDA) in India. The analysis revealed the following findings:

1 The staff of these seven districts detected 19,210 new cases in one year—3509 (18%) were MB

Table 1.

Sl. No.	District	Population (1991 census)	Total new cases	Monolesion PB cases	Total NCDR/ 1000	NCDR of monolesion/ 1000	NCDR other than monolesion/ 1000
1	Baroda	31,94,692	1325	114	0·41	0·04	0·38
2	Belgaum	35,83,606	1181	467	0·33	0·13	0·20
3	Dharwar	35,03,150	1725	808	0·49	0·23	0·26
4	Amravati	20,08,568	3046	981	1·52	0·49	1·03
5	Ganjam	31,58,764	5518	2717	1·75	0·86	0·89
6	Puri	35,90,026	5146	1779	1·43	0·49	0·94
7	Varanasi	47,98,729	1269	90	0·26	0·02	0·25
		2,38,37,535	19,210	6956	0·81	0·29	0·52

and 15,701 (82%) were PB cases. 6956 (36%) out of the total detection were monolesion PB cases.

2 The monolesion PB case detection rate was 0·29/1000. This is 36% of the total case detection rate of 0·81/1000. Detection rate of cases other than monolesion PB cases was 0·52/1000. This reduced the total detection rate by 38%.

3 In view of factors like: i, negligible contribution of monolesion PB leprosy cases to the pool of infection; ii, their self-healing nature; and iii, difficulties in accurate diagnosis etc, programme managers may consider this 'monolesion phenomenon' as a 'clinical problem' and not as a 'public health problem' and calculate new case detection rates without including monolesion PB cases. This may reveal a more realistic picture of not only the transmission of leprosy, but also the quantum of the disease likely to pose a problem from the point of view of clinical management, such as reactions.

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PROPORTION OF BENEFICIARIES VS RELAPSE IN MDT PROGRAMME

Sir,

The recent review on the risk of relapse following WHO recommended multidrug therapy (MDT) revealed that this rate 9 years after stopping MDT[1] is very low, namely 0·77% for multibacillary (MB) and 1·07% for paucibacillary (PB). In comparison to dapsone monotherapy, this risk is lower by 10 times. This indicates that the rest of the patients without relapses had fully benefited from MDT.

In a time bound by a public health programme of a gigantic magnitude and carried out under constraints of limited resources with a target of the elimination of leprosy, it is important for the programme managers and clinicians, especially dermatologists managing leprosy, to consider first that a large number of patients benefited from MDT over a period of time rather than that a small number of patients are likely to pose a clinical problem such as relapse. Once the magnitude of the problem reduces to a nonpublic health level, these nonresponders to MDT could be considered as a special entity. Even the small numbers of relapses when they occur could be effectively controlled. During the smallpox eradication drive, even though vaccination in general population was marked by mortality due to encephalitis, the vaccination programme was continued even at the cost of a few deaths. The end result was global eradication of smallpox. A similar approach should be followed in a leprosy programme, if we want to achieve global elimination only with MDT. We present two tables which highlight the benefit offered to a large section of patient population belonging to MB and PB types.

To understand the net outcome from MDT intervention, which is a mass programme, the

Table 1. MB leprosy patients benefited from MDT

MB cases	100	1000	10,000	100,000
Relapses	0·7	7·7	77	770
Beneficiaries from MDT	99	992	9,923	99,230

Table 2. PB leprosy patients benefited from MDT.

PB cases	100	1000	10,000	100,000
Relapses	1·07	10·7	107	1070
Beneficiaries from MDT	99	989	9,893	98,930

following theoretical projections were made to demonstrate possible relapses as opposed to beneficiaries of the MDT based on the calculation of risk of relapse by WHO.[1]

The number of relapses calculated is over a period of 9 years as per the WHO calculation of relapse rate.[1]

These types of simple calculations in absolute numbers instead of percentages would be useful for training field workers.

It may be relevant in this context to point out that in view of negligible relapse risk rate after WHO–MDT, WHO considers that annual surveillance examination of patients after the end of treatment may not be required and patients are to be educated to report if they develop any clinical events.[1] This procedure, however, is not yet adopted by most control programmes.

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PROBLEMS DUE TO MIGRATION OF LEPROSY PATIENTS INTO URBAN AREAS

Sir,

The increasing migration of people into the fast-growing megacity of Delhi[1] is posing more problems with less time to tackle them. In addition to job opportunities, the Government of Delhi had been giving concessions to patients suffering from leprosy, namely allotment of land at highly subsidized rates, ration allowance for procuring food and other forms of financial help when

applicable. These privileges have over the years attracted a large number of people who have housed themselves in the outskirts of Delhi in separate colonies. Some of these colonies, who had demanded the concessional facilities, were rejected because the Government had considered their disease to be inactive and hence cured. However, they filed a law suit and the Honourable Supreme Court of India directed us to have them examined to assess the activity of the disease.

A total of 788 patients including 163 children were taken from six colonies in the periphery of Delhi. Of these 626 were available for examination which included, apart from a general health appraisal, a thorough cutaneous examination and slit-skin smear for acid-fast bacilli (AFB) from six sites for assessing bacteriological index (BI). Only two children had active disease. The total number of persons with active disease were 24 giving an overall activity rate of less than 4%. BI positivity ranged from 1+ to 3·4+. A total of 153 patients had various deformities (including anaesthetic hands and feet, claw hand and eye problems; ranging from exposure keratitis to corneal opacities) giving a total deformity rate of 24·44%. Among them those with eye complications alone accounted for 14·32%.

The continuous flow of migrants into cities, particularly Delhi, from other states in search of jobs has certainly created major problems for the already subsidized health care system.[2] This has to be tackled not only to help these sufferers but to check the spread of infection to the low endemic areas like Delhi. Though our survey revealed that in the majority of patients the disease was inactive and therefore did not qualify them for the concessions given to those suffering from leprosy, it brought to the fore the need for developing centres for rehabilitation and correction of deformities that would help the victim to lead a productive self-supporting life.

The main areas that need to be strengthened are:

1 Some patients discontinue the treatment for whom adequate case holding activities will be required till the completion of the surveillance period. Follow-up of the infected persons and their co-habiters will have to be ensured particularly for the children.
2 In some others who are more unfortunate, the crippling complications of the disease set in, such as ulcers and deformities. Adequate provision for their management should be provided in the city hospitals.
3. Some basic health care institutions such as Primary Health Centres or Rural Health Training Centres will have to be identified in the periphery of the city for delivering specialized care and follow-up of these patients. They should also be entrusted with the task of certifying the patients, both bacillary and multibacillary as either active or inactive and may take the help of urban leprosy centres if needed. To avoid further legal complications which can lead to misuse of the concessions granted to the victims of leprosy, a statutory body must specify these facilities for the truly deserving cases and not simply to all persons with active disease who can otherwise compete with a normal individual.
4. Reconstructive surgery though well developed elsewhere is still not available to the leprosy patients in Delhi. Specialized training in this area should be given to surgeons of the institutions and major hospitals where leprosy centres are located.
5. Health education with an emphasis on the early signs of leprosy may be disseminated so that apparently normal individuals know where to report when the need arises.

It has been pointed out that this situation has also arisen in other countries,[3] and so leprosy control activities in cities is intimately related to migration and steps to tackle this should definitely be considered in all effective programmes.

A similar situation would have perhaps been inevitable in Bombay which is another metropolis catering to a large migrant population in this country. However this has been remedied to a large extent owing to its good medical care provided by both governmental and non-governmental organizations and its being the capital of the endemic state of Maharashtra.

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THE RISK OF STANDARDIZED REGIMENS OF CORTICOSTEROIDS FOR THE TREATMENT OF LEPROSY REACTIONS IN THE FIELD

Sir,

Acute nerve damage due to leprosy reactions can often be treated successfully with corticosteroids. To make this treatment widely available under field conditions, standard steroid regimens are required. Courses of 12 weeks for paucibacillary (PB) patients and 20 weeks for multibacillary (MB) patients have been recommended.[1] The initial dose is 40 mg daily, given for 2 weeks and then tapered off. These kind of standard regimens are gradually being introduced into field programmes, but general introduction is delayed for fear of the complications of corticosteroid use. There is uncertainty about the frequency of occurrence of complications and anxiety that they might be overlooked by paramedical staff.

In this respect we would like to refer to an important article published recently titled "Corticosteroids and peptic ulcer: meta-analysis of adverse events during steroid therapy."[2]

The objective of this meta-analysis was to determine whether corticosteroid therapy induces the development of peptic ulcers and putative complications of steroid therapy. It was a retrospective investigation in which all (known) randomized, double blind, controlled trials in which steroids had been administered were analysed. The number of episodes of peptic ulcer, dermatological effects, sepsis, diabetes, hypertension, osteoporosis, psychosis and turberculosis reported in both the placebo and steroid groups were compared. Of 1857 articles, 93 satisfied the requirements of the authors and were analysed by means of meta-analytic techniques. A total of 6602 patients were included. The relative frequencies of each of the eight mentioned complications were compared in the placebo and steroid groups. Subgroups were studied of patients who received treatment for 1 to 7 days, 1 week to a month, 1 to 3 months and more than 3 months.

The results showed that 0·3% of patients in the placebo group and 0·4% in the steroid group were reported to develop peptic ulcer, the difference not being significant ($P > 0.05$). Dermatological side-effects occurred four times as frequently in the steroid patients (10·5%) as in the placebo-treated control group (2·6%). Diabetes was reported four times more frequently in the steroid-treated patients (1·2%) than in the placebo-treated patients (0·3%). Hypertension was noted four to five times more frequently in the steroid-treated patients (0·9%) than in the groups

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that received placebo (0·2%). Psychological side-effects occurred two times more frequently in the steroid-treated patients (0·5%) than in the placebo-treated patients (0·3%). The differences in these last 4 categories are statistically significant. Bacterial sepsis, osteoporosis and tuberculosis all occurred more frequently in the steroid than in the placebo group, but the differences are not statistically significant. The main conclusion of the article is that peptic ulcers are a rare complication of corticosteroid therapy that should not be considered a contraindication when steroid therapy is indicated.

Of all patients included in this meta-analysis, the mean daily dose of prednisone was 35 mg (or its equivalent) for a mean duration of 64 days and a mean total dose of 2·2 g. This means that the study is very relevant for the use of corticosteroids for the treatment of leprosy reactions in field conditions. The 20-week course recommended by Rose & Waters, for instance, consists of 2·7 g of prednisone. It is of particular interest that certain well-known (and dreaded!) complications do not occur significantly more frequently in patients treated with steroid compared to the placebo-treated patients, or are rare (app. 0·5–1% of all patients). Dermatological effects (Cushingoid syndrome of moon face, buffalo hump and trunkal obesity, and acne and hirsutism) do occur in 10% of patients. Fortunately these symptoms are usually not dangerous and reversible after cessation of treatment.

Two important considerations must be borne in mind. Firstly the trials in the meta-analysis are primarily from developed countries. The risk for tuberculosis in a highly endemic country would be greater than reported in the meta-analysis. Secondly, patients entering trials were screened for disease before starting corticosteroids. The problems might be different if patients who were already diabetic or had active pulmonary turberculosis were commenced on treatment as could be the case in medically less well-supervised circumstances in the developing world. It is important that at least relevant basic examinations are done before patients are started on corticosteroids. It is also important that clear and strong criteria are maintained for commencing patients with reaction or signs of acute nerve damage on corticosteroids so that the benefits outweigh the risks. The known frequency of reactions offers a check to see how many patients would be expected to be treated with corticosteroids.

With this knowledge in mind, there should be more confidence in implementing standard steroid regimens for the treatment of leprosy reactions in field conditions. The benefit of saving peripheral nerves and thus preventing disability far outweigh possible complications of treatment with corticosteroids.

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Teaching Materials and Services

'Worldaware' (formerly Centre for World Development Education)

Worldaware is a national independent education agency which promotes education in Britain about world development issues and Britain's interdependence with developing countries. A special concern, through the work of its education department, is to support teachers in teaching with a global development perspective. It does this in several ways.

1 *Resources*: Worldaware publishes a Resources Catalogue which is up-dated each year. It contains over 400 items—books, leaflets, packs, simulation games, computer software and audio-visual material (on world development themes), from a wide range of sources, to provide differing perspectives on the issues involved. Most of the material is designed for classroom use. The Resources Catalogue is available free on request.
2 *In-Service Training*: Worldaware offers a range of inputs to teacher in-service training courses throughout the UK—training days; workshops for Infant and Primary, 9–13, GCSE, Computers, and the global dimension in the National Curriculum. For details write to the Education Officer at Worldaware.
3 *Enquiry and Advisory Service*: for teachers and pupils. Worldaware has extensive files of up-to-date material on a range of development themes and on many developing countries, together with lists of useful addresses and contacts. This information is available to teachers planning courses, and to pupils for project or coursework. In addition, the education department offers advice to teachers on curriculum planning.

Their current list of useful addresses includes the following:

ActionAid, Hamlyn House, Archway, London N19 5PS. Tel: 0181–281 4101.

Catholic Fund for Overseas Development (CAFOD), 2 Romero Close, Stockwell Road, London SW9 9TY. Tel: 0171–733 7900.

Catholic Institute for International Relations (CIIR), Unit 3, Canonbury Yard, 190a New North Road, London N1 7BJ. Tel: 0171–354 0883.

Centre for Global Education, University of York, Department of Education, Heslington, York YO1 5DD. Tel: (01904) 413267.

Christian Aid, PO Box 100, London SE1 7RT. Tel: 0171–620 4444.

Comic Relief, 7 Great Russell Street, London WC1B 3NN. Tel: 0171–436 1122.

Commonwealth Institute, Kensington High Street, London W8 6NQ. Tel: 0181–603 4535.

Concord Films Council Ltd, 201 Felixstowe Road, Ipswich, Suffolk IP3 9BJ. Tel: (01473) 715754.

Council for Education in World Citizenship (CEWC), Seymour Mews House, Seymour Mews, London W1H 9PE. Tel: 0171–935 1752.

Development Education Centre, Gillet Centre, 998 Bristol Road, Selly Oak, Birmingham B29 6LE. Tel: 0121–472 3255.

Intermediate Technology Development Group (ITDG), 103–105 Southampton Row, London WC 1B 4HH. Tel: 0171–436 9761.

International Broadcasting Trust (IBT), 2 Ferdinand Place, London NW1 8EE. Tel: 0171–482 2847.

National Association of Development Centres (NADEC), 6 Endsleigh Street, London WC1H 0DX, Tel: 0171-388 2670.

One World Week, PO Box 100, London SW1 7RT. Tel: 0171–620 4444.

Overseas Development Administration (ODA), 94 Victoria Street, London SW1E 5JL. Tel: 0171-917 0950.

OXFAM, 274 Banbury Road, Oxford OX2 7DZ. Tel: (01865) 56777.

Population Concern, 231 Tottenham Court Road, London W1P 9AE. Tel: 0171–631 1546.

Save the Children Fund (SCF), Mary Datchelor House, 17 Grove Lane, London SE5 8RD. Tel: 0171-703 5400.

Schools Partnership Worldwide, 1 Catton Street, London WC1R 4AB. Tel: 0171-831 1603.

Scottish Catholic International Aid Fund (SCIAF), 5 Oswald Street, Glasgow G1 4QR. Tel: 0141-221 4447.

Scottish Education and Action for Development (SEAD), 29 Nicolson Square, Edinburgh EH8 9BX. Tel: 0131-667 0120.

Survival International, 310 Edgware Road, London W2 1DY. Tel: 0171-723 5535.

Tourism Concern, Freobel College, Roehampton Lane, London SW15 5PU. Tel: 0181-878 9053.

UNICEF, 55-56 Lincoln's Inn Fields, London WC2A 3NB. Tel: 0171-405 5592.

Voluntary Service Overseas (VSO), 317-325 Putney Bridge Road, London SW15 2PN. Tel: 0181-780 2266.

WaterAid, 1 Queen Anne's Gate, London SW1H 9BT. Tel: 0171-222 8111.

Welsh Centre for International Affairs, Temple of Peace, Cathays Park, Cardiff CF1 3AP. Tel: (01222) 228549.

World Development Movement (WDM), 25 Beehive Place, London SW9 7QR. Tel: 0171-737 6215.

World Wide Fund for Nature (WWF), Panda House, Weyside Park, Godalming, Surrey GU7 1XR. Tel: (01483) 426444.

Colour Atlas of Tropical Dermatology and Venerology. K. F. Schaller (Editor). Published by Springer-Verlag, 1994

This Atlas from Springer-Verlag has been produced by Professor K. F. Schaller and a small group of colleagues, mainly from Hamburg in Germany. There are 303 pages, with index, and no fewer than 601 figures in colour, illustrating a wide range of dermatological and venereological conditions found in the tropics, with a degree of clarity and colour quality which will be difficult to surpass. The aim of this Atlas, as the Preface emphasises, is '... to provide clear guidance and a source of quick and easy reference for all physicians dealing with patients suffering from exotic skin diseases and for medical staff working in tropical and sub-tropical regions. It is not designed to replace the numerous excellent textbooks on tropical diseases and dermatology, but rather to supplement and complement them in a practical way.'

The main chapter headings include—Viral Diseases of the Skin, Rickettsial Diseases, Bacterial Dermatoses, Endemic Treponematoses, Sexually Transmitted Diseases, Superficial Fungal Dermatoses, Deep Mycoses, Protozoan Dermatoses, Helminthic Dermatoses, Dermatoses due to Arthropods, Venomous Animals, Dermatoses due to Malnutrition, Maculopapulosquamous Dermatoses, Vesiculobulbous Eruptions, Connective Tissue Disorders, Urticaria, Erythema Multiforme and Drug Eruptions, Diseases of the Skin Appendages, Diseases due to Physical Agents, Naevoid Conditions, Benign Skin Tumours, Malignant Skin Tumours and Miscellaneous Dermatoses. The succinct descriptive text alongside each set of colour pictures will be valuable, but the great potential of this publication almost certainly lies in the unusually high quality and visual impact of the colour pictures (the vast majority of which are from Professor Schaller's own collection), and which will surely be of great practical value in the identification and diagnosis of diseases due to infectious organisms, parasites, venomous animals and genetic, nutritional, chemical and physical factors.

Price DM 198.00 Published by Springer-Verlag GmbH and Co. KG, Tiergartenstrasse 17, D-69121, Heidelberg, Germany.

University of British Columbia Centre for Epidemiologic and International Ophthalmology

The Department of Ophthalmology at the University of British Columbia recently established the British Columbia Centre for Epidemiologic & International Ophthalmology (BC-EIO).

The mission of the Centre is to assist in the reduction of blindness, vision loss, and ocular pathology in Canada and developing countries. The three approaches to prevention of blindness that the centre will foster are: promotion of appropriate eye care services, training, and research. As a unit within the Department of Ophthalmology of the University of British Columbia, it will be multidisciplinary, building on expertise within the Department of Ophthalmology as well as throughout the University of British Columbia and its affiliated health care institutions. The Centre will focus activities in:

outcome research related to ophthalmologic care, patient satisfaction, and improved quality of life; and development and evaluation of appropriate eye care programmes of all levels in developing countries

For more information, please contact
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Liverpool School of Tropical Medicine, UK: visiting fellowships

The Liverpool Epidemiology Programme (LEP) was set up in response to the World Health Assembly's call for greater use of epidemiology in monitoring strategies for health for all and for improved training in epidemiology, particularly to meet the needs of developing countries. The aim of the programme is to promote the methods of epidemiology towards the improvement of health in developing countries.

LEP is based in the Unit for Statistics and Epidemiology (USE) in the Liverpool School of Tropical Medicine (LSTM) and receives financial support from the Overseas Development Administration. Our team of experienced epidemiologists and statisticians work alongside health professionals to define the role of epidemiology in their work and to identify training needs. Activities include the provision of short courses in Liverpool, assistance in running courses overseas and the development of training material.

We are inviting colleagues with similar interests to join the programme as visiting fellows for periods of between 3 and 6 months. The most suitable people will be health professionals involved in training programmes in their own countries who would like to develop and share their ideas with us in Liverpool. Their activities might include the development of

Methodologies, for example, methods of needs assessment, alternative training strategies, techniques of evaluation.
Training material using various media, for example, case studies, computer based learning, reference material.
Syllabuses for short courses for groups of health staff, for example, working in maternal and child health, disease surveillance, district health management, refugee health care.

We are looking for people with innovative ideas for promoting epidemiology in health care.

Apply: Unit for Statistics & Epidemiology, LSTM, Pembroke Place, Liverpool L3 5QA

Social Aspects of Leprosy (A classified bibliography), 1994

The Centre for Social Science Research on Leprosy, Gandhi Memorial Leprosy Foundation, Wardha 442 103, Maharashtra, India, has produced a document of 237 pages, with appendices, covering the whole subject of the social aspects in great detail. The project team for this remarkable, and probably unique, contribution included Dr S. N. M. Kopparty (Senior Research Scientist), Dr A. M. Kurup, Shri R. Giridhar and Shri K. Velayudham. The main subject headings cover epidemiology, leprosy control programmes, survey education and treatment, compliance, deformities and disabilities, rehabilitation, knowledge and attitudes to leprosy, psychosocial aspects, social groups, genetics, leprosy organisations, health, leprosy and other diseases and research. The preparation of this bibliography was helped by contacts with the library of the Mahatma Gandhi Institute of Medical Sciences in Sevagram, the National Medical Library in new Delhi, the libraries of the Bombay Leprosy Project, the JJ Group of Hospitals in Bombay, the Jawaharlal Nehru Medical College and the Tropical Diseases Research Division of the World Health Organization. Enquiries to Dr S. N. M. Kopparty as above (the document is heavy and it is likely that some contribution to postage costs may be needed).

Essential Drugs Monitor, WHO

The Essential Drugs Monitor is produced and distributed by the WHO Action Programme on Essential Drugs. It is published in English, French and Spanish, and has a global readership of some 200,000 to whom it is free of charge. The Monitor carries news of developments in national drug policies, therapeutic guidelines, current pharmaceutical issues, educational strategies and operational research.

WHO's Action Programme on Essential Drugs was established in 1981 to provide operational support to countries in the development of national drug policies and to work towards the rational use of drugs. The Programme seeks to ensure that all people, wherever they may be, are able to obtain the drugs they need at the lowest possible price; that these drugs are safe and effective; and that they are prescribed and used rationally.

All correspondence should be addressed to: The Editor, Essential Drugs Monitor, World Health Organization, CH-1211 Geneva 27, Switzerland.

ECHO International Health Services Limited, UK

ECHO is a self-financing registered charity, launched over 25 years ago, offering a comprehensive medical supply service for the relief of sickness abroad, regardless of race, caste or creed. It provides low-cost medical supplies to mission, charity and government hospitals, as well as rural health care units in developing countries and medical relief and emergency programmes world-wide. Further information: ECHO, Ullswater Crescent, Coulsdon, Surrey CR5 2HR, England.

Elimination of leprosy. Questions and answers, WHO

This booklet produced by the Leprosy Unit of WHO, 1211 Geneva 27, Switzerland, presents in question and answer form the main issues that require explanation in the context of eliminating leprosy. The 22 questions raised include the rationale of the elimination policy, definition of elimination, definition of a case of leprosy, the likely situation after the year 2000 and the likely impact of the elimination strategy on disability.

Voluntary Health Association of India (VHAI)

The primary role of the VHAI resource centre is to provide information and documents for the use of VHAI staff in research and for training programmes. However, many people use both the resource centre and *Health for the Millions*, a bulletin which carries information on books, journals, training programmes and government programmes. The resource centre also conducts training programmes in documentation techniques for health and development groups. VHAI's book *Basics for Documentation* is a useful publication, particularly for India.

Address: VHAI, 40 Institutional Area, South of IIT, New Delhi 110 016, India.

Teaching Aids at Low Cost (TALC)

Although TALC has no resource centre of its own, it is associated with the Centre for International Child Health at the Institute of Child Health, University of London which has an excellent resource centre. TALC produces many publications as well as small 'library packages' of vital medical publications for district hospitals and district health workers.

For further information, write to: TALC, PO Box 49, St Albans, Herts AL1 4AX, UK.

Appropriate Health and Technologies Action Group (AHRTAG)

AHRTAG has a resource centre with a unique collection of more than 17,000 primary health care materials. The group runs specialist programmes on many primary health care issues and publishes many practical newsletters (*Dialogue on Diarrhoea, ARI News, AIDS Action and CBR News*) and other publications. AHRTAG offers an information and enquiry service and provides technical support and resources to organizations managing primary health care resource and information centres. A directory of newsletters which are free of charge is available on request.

Address: 1 London Bridge Street, London SE1 9SG, United Kingdom.

Lower limb prosthesis, Jaipur, India.

The remarkable 'Jaipur limb' was developed 20 years ago by Dr Sethi in Jaipur, Rajasthan, India and has proved extremely successful for lower limb amputees in many different parts of the world. Further information is available from The Jaipur Limb Campaign, 7th Floor, Windsor House, 83 Kingsway, London WC2 6SD.

Back issues of *Leprosy Review* – Do you have any?

Lepra Head Office would like to complete their set of *Leprosy Review*. If you have any spare issues between Volumes 1 and 25 (1954) then please write to Ms Irene Allen, Lepra, Fairfax House, Causton Road, Colchester CO1 1PU, England, stating which issues you have available. Wherever possible Lepra will pay the costs of postage.

Lepr Rev (1995) **66,** 335–347

News and Notes

Special Action Projects for the elimination of leprosy—SAPEL SC •

Identifying the areas that call for a rapid response

One of the key recommendations to emerge from the International Conference on the elimination of Leprosy, held in Hanoi, Viet Nam, last July, was to set up Special Action Projects which would ensure that Multidrug Therapy (MDT) truly reaches all under-served areas and populations. It was recognized that—despite the commendably high MDT coverage already attained—this represented the 'easiest' part of the task ahead. Reaching the three million leprosy patients who need MDT between now and year 2000 will be a much harder job.

The Leprosy Working Group (LWG)* which met immediately after the Conference recommended, inter alia, the creation of a Steering Committee on Special Action Projects for the Elimination of Leprosy (SAPEL SC). Seven members were elected to sit on this Committee, chosen for their expertise in dealing with both the operational and the technical problems likely to be faced by leprosy control programmes between now and the end of the century. The Committee will also include as co-opted members the chairpersons of the Leprosy Elimination Advisory Group (LEAG), the Task Force on Monitoring and Evaluation (MEE) and the Task Force on Capacity Building and Health Systems Research (CBH).

SAPEL is a new initiative, one of several mechanisms supported by WHO to bring about elimination. It is not a research programme, nor is it meant to be an exclusive initiative of WHO. International NGOs and other donor agencies will be invited to participate and to provide funding; the WHO Secretariat's role will be to coordinate and cooperate with similar activities being undertaken by other agencies.

SAPEL's objective is to identify special situations and areas requiring rapid action, and to develop and put into effect innovative and feasible strategies, mainly involving operational solutions. It hopes to become a trend-setter in accelerating MDT coverage in difficult areas. Once the special action project has been concluded, the national programme will be expected to sustain any further activities that may be required.

The Steering Committee will meet at least twice a year—it held its first meeting on 9–11 January 1995—to discuss ways of accelerating MDT coverage in special situations, and the overall progress being made towards the elimination goal. It will also review and fund proposals for special action projects submitted to it by national programme personnel.

These projects should be confined to exceptional situations where routine activities are non-existent or not proving practical, and they should complement national leprosy elimination efforts. The situations and populations that might merit special action will include:

- areas where there is no health infrastructure;
- areas where the existing health service is unable to deliver MDT;

*Now replaced by the Leprosy Elimination Advisory Group (LEAG).

- geographically difficult-to-access areas;
- temporary breakdown of services due to hostilities or natural disasters;
- where there is no scope for rapid improvement through strengthening management capability;
- urban and peri-urban slums;
- groups of patients living in isolated communities as a consequence of social stigma;
- nomads and other migrants;
- refugee populations.

Beside the obvious aims of solving priority problems and increasing MDT coverage, SAPEL hopes to motivate staff working in the field of leprosy and develop their skills, to improve the quality of services, and to make it easier to apply the new strategies that are developed to comparable situations elsewhere.

Reproduced from *LepNews*, **Volume 4,** No. 1 (1995), WHO, CH-1211 Geneva 27 Switzerland

Message from the President on the future of ILA. Yo Yuasa

Greetings! Time passes swiftly, and it has been nearly 2 years since I became President of the International Leprosy Association (ILA). Or, looking forward, it is only 3 years until the next ILA Congress, expected to be held in Beijing, China, in the summer of 1998. It is also nearly 1 year, by the time this issue reaches you, that the ILA FORUM, a new and a trial publication of our Association, has been in existence.

The world leprosy situation is changing rapidly. 'The elimination of leprosy as a public health problem by the year 2000,' proposed by the World Health Organization (WHO) and accepted by practically all of those involved in the control of the disease as shown by the Hanoi Declaration of 1994 following the World Health Assembly Resolution of 1991, has been successful in reducing the global caseload remarkably, perhaps down 2 million, including the estimated or unregistered cases, by the second half of this year. Whatever is one's conception of leprosy problems and whatever is one's interpretation of the above figure, it is a great achievement, indeed, a positive result for which no apology is necessary.

However, we are still far away from achieving our ultimate goal, which must be the 'eradication' of leprosy, although I am aware that some of my more cautious or, indeed, conscientious colleagues may flinch at the use of that term. In order to realize that goal three separate and different stages are necessary, each an elimination program of its own. The first stage we are currently undertaking, and hope to achieve by the year 2000, is the elimination of the disease as a public health problem, defining it as having a caseload of less than 1 in 10,000 population at a national level. The use of the prevalence rather than incidence figures, or setting the target figure of 1/10,000, has been controversial for some good reasons but, to me, they are not that important provided, and this is crucial, that we agree to go on to the second stage, which is the elimination of leprosy as a disease of individuals. Because of highly competitive demands from other health problems in public health sectors, such as tuberculosis, malaria or AIDS, to take the most obvious examples, the expected global caseload of leprosy beyond the year 2000 is unlikely to attract much attention, let alone resource allocation, from health authorities of leprosy-endemic countries, and perhaps even from WHO. But those who are seriously concerned with leprosy, which I hope include the majority of the current members of ILA, must go on extending necessary and adequate care to a not insignificant number of remaining as well as emerging patients, expected to be as many as half a million at the beginning of the next century, at a more intensive degree and individualized manner, which is not possible at present as long as the disease remains a serious public health concern. Judging from the pattern of some new cases who develop the disease much later in their lives, long after their probable exposure to the disease, seen in some countries like Japan, where leprosy is no longer a public health problem and its endemicity is coming to an

end, this second elimination stage may take much longer than some of us would like to contemplate.

The third elimination stage is that of *Mycobacterium leprae* themselves from the face of the earth. Without this, there is no 'eradication' of leprosy, which is not just a disappearance of the disease but a total removal of any possibility of future re-emergence of the disease. How long will that take? No one knows, but from the known longevity of *M.leprae* as persisters in the human body and the occurrence of natural infection with *M. leprae* in some animals, such as the nine-banded armadillo or some monkeys in Africa, we may have to wait until the second half of the coming century for the eradication of the disease.

This brings me to a main concern and the reason for this message on 'The Future of ILA'. I am not spelling out my personal view of what that should be. All I am trying to point out is that these are likely to be leprosy problems needing solutions for the next 50 years or more in medical aspects alone, and I have not even mentioned problems related to social aspects of the patients and their families, which are much larger in scope and much more difficult to solve.

As I mentioned, current roles played by the public health authorities of the leprosy-endemic countries as well as by the leprosy unit of WHO are likely to be diminished substantially, and even in danger of disappearing altogether. International nongovernmental organizations, often pioneers and certainly critical supporters of the current worldwide leprosy activities, may find it difficult to continue their activities at the current levels, because the reduced global caseload may act adversely to their fund-raising efforts. After the last ILA Congress, an international group called 'IDEA' (composed of ex-leprosy patients from various countries) emerged thanks to the dedicated efforts of a few forward-looking individuals, and is expected to play a significant role in the future, but that remains to be seen. All of them, no doubt, will try to find new roles in, or new ways to tackle, the future leprosy problems in the next century. In such a situation, in my personal view at least, ILA seems to be the only global international organization whose *raison d'être*—ever since its founding in 1932—is to take a leading role in searching and shaping the future activities toward the eradication of leprosy until it is accomplished.

I am convinced that the above view of mine is shared by not a small number of the fellow members of the Association. But I am far from certain or, indeed, rather doubtful if it gets even 51% of the current members' approval, a minimal and not really satisfactory majority to take any action. The publication of the ILA FORUM was initiated under the President's prerogative because that is what I promised in my acceptance speech in Orlando. I was fairly certain of your approval, but I am not prepared to go any further without more specific approval from the majority of the members. Any major decision could be taken only at the General Meeting of the members at the next Congress, but that is a far from satisfactory occasion, because available time is usually too short and not even half of the members are present. That means that any major issues needing the members' decision, such as restructuring or new activities of the Association, must be proposed and discussed as thoroughly as possible prior to the time of the next Congress. Hence, the publication of the ILA FORUM as a possible venue for such discussions.

I am most grateful for those who have contributed an article to its first four issues, including this one. Each one of them, in its own way, was a thoughtful, interesting and useful contribution, worthy of publication. However, I am somewhat disappointed on two accounts. With only one exception, all of them are in response to my personal solicitation and not of their own initiative. Perhaps a little more time is needed for those who are taking a 'wait and see' article. By now, I hope, the objective and general nature of the ILA FORUM is apparent to warrant spontaneous contributions from the members at large. The second disappointment of mine is related to the contents or, rather, to the manner of presenting the contents. With a few exceptions, they are not provocative or challenging enough, to my taste at least, to elicit active responses from the readers, a quality quite different from the regular contributions to IL but necessary for the objective of the ILA FORUM. In the future, there could be too many contributions which require selection but, at present, we need more spontaneous contributions and I would urge any members who have

anything important to say for the future of leprosy and/or the ILA, to put down that thought and send it to the Editor of IJL,, clearly indicating that it is for the ILA FORUM. This open invitation for contributions is being addressed not only to those who think some changes are necessary, as I do, but equally to those more conservative or traditional members who may think more or less a status quo is what we need. That view could be equally as valid and important to be expressed publicly, if shared by a large portion of the current members, as I suspect.

Finally, one more point. The next ILA Congress will come in 3 years' time, and we should start planning seriously about it soon. A general pattern of the Congress has been established by which the pre-Congress workshops on a dozen or more subjects preceding the main Congress will again be subdivided into a number of groups according to the different specialties within the science of leprosy and leprosy control. A successful introduction of the state-of-the-art lectures and training sessions made the Congress more attractive and worth while to the field workers, who are mostly nonmembers but outnumber the members of the Association as the participants of the Congress three or even four to one. Is that a sort of Congress we want again in Beijing? Is the Congress meant to meet the needs of the members or to address the larger issues of the current and future leprosy situation?

Let us think of the objective of the Congress in terms of for whom and for what. Let us be a bit more imaginative in planning. I would like to invite the members to express their ideas on this subject. In the case of too many contributions needing selection for publication, the views for the Congress will be given priority for the next four issues up to the summer of 1996. By then we should have a clearer idea of what sort of Congress it will be in Beijing, so that more formal and earnest effort on the organization could start.

I look forward to the members' response to my request. Meanwhile I send my best wishes to all of you for success in whatever leprosy work you are currently undertaking.

Reproduced from *ILA Forum*.

Dr Mukherjee applauds leprosy research in Bombay

The Director General of Health Services Dr A. K. Mukherjee and The Deputy General of Health Services (Leprosy) Dr B. N. Mittal stressed the need for leprosy research on the residual problems still met in the field to continue, in order to maximize the advantage of the steady decline in leprosy already achieved by the National Leprosy Eradication Programme (NLEP). A function was organized by the Bombay Leprosy Project (BLP) on 24 June 1995 to honour these dignitaries at the Leela Moolgaokar Leprosy Ward of Adams Wylie Memorial Hospital, which is the nucleus of BLP's research to assist NLEP over the past 16 years. The ward is gifted for leprosy research by the Indian Red Cross Society. Dr R. Ganapati, director, highlighted how BLP took advantage of this gift to carry out research on newer drugs and disability care and outlined the future short course chemotherapy trials proposed to be undertaken using the in-patient facilities of the hospital.

A document entitled 'Can NGOs effect savings for the Donor?' giving a cost analysis of an experiment by BLP in assisting NLEP over two decades was submitted to the visitors by Mr P. Narayanaswamy, Manager-Administration of the Project. Dr Mukherjee applauded the highly significant contributions achieved at low cost and stressed the need for the continuance of such research by BLP. Dr Mittal and Dr A. R. K Pillai, President, Indian Leprosy Foundation pointed out that NLPE still needs to be guided by such research till leprosy is eliminated.

A vote of thanks was proposed by Dr C. R. Revankar, Deputy Director, BLP.

16th Anniversary of leprosy research in a Red Cross Hospital, Bombay, India

The importance of research work in leprosy undertaken by the Bombay Leprosy Project (BLP) at the Leela Moolgaokar Leprosy Ward at Adams Wylie Memorial Hospital over the past 16 years was highlighted by Dr R. Ganapati, Director, BLP at a function held in the hospital premises on Saturday, 22 July 1995 to mark the 16th Anniversary of BLP's work. He expressed his confidence in continuing the research work based on hospitalized leprosy patients elsewhere in the city, though the team of research staff is likely to be deprived of this in-patient care facility shortly, in view of the proposed demolition of the ward. He also recalled the importance given to such research by Dr A. K. Mukherjee, Director General of Health Services during his recent visit to the ward on 24 June 1995.

Dr Ganapati thanked the Bombay Branch of Indian Red Cross Society for enabling BLP to carry out the research work for 16 years.

Dr J. A. Ponniah, Consultant, WHO/Govt of India/National Leprosy Eradication Programme (NLEP) and the Chief Guest of the occasion admired the academic spirit and dedication of the staff of BLP for their contributions to NLEP. He will help the project to see that their exemplary work is continued without any hindrance till the goal of elimination of leprosy from the country is reached.

Undergraduate prizes offered by the Royal Society of Tropical Medicine and Hygiene, London, UK

Undergraduate project prize

The Royal Society of Tropical Medicine and Hygiene offers an annual prize of £200 for an account of work carried out in a tropical or developing country by a non-medical student of any nationality. The work will add to the knowledge of human or veterinary health or hygiene in the broadest sense. Particular attention will be directed towards originality and quality in the award of the prize. It is anticipated that the prize will act as a stimulus for the pursuit of excellence in research carried out by undergraduates.

Medical student elective prize

The Royal Society of Tropical Medicine and Hygiene offers an annual prize of £200 for an account of work carried out by a British medical student during an elective period spent in a tropical or developing country. In awarding this prize emphasis will be laid on the originality of the work and on its contribution to knowledge or understanding of tropical diseases.

Rules

1 Two prizes of £200 may be awarded annually in recognition of outstanding projects which increase knowledge of tropical medicine and hygiene in the broadest sense.
2 Candidates shall be nominated by their head of department, supervisor or Dean, with a supporting statement of up to 500 words.
3 The closing date for receipt of project reports is 31 December. The project should have been done or completed in the previous 12 months.
4 A Committee of 3 shall choose the prize winners.
5 The announcement of the prize winners will be made at the March meeting of the Society.
6 The prizes will be presented by the President of the Society at the Annual General Meeting in June or July.

Please note that the Society cannot provide funds to cover students' elective travel expenses.

Apply: Secretary, Royal Society of Tropical Medicine & Hygiene, Manson House, 26 Portland Place, London W1N 4EY.

Proceedings of the International Agency for the Prevention of Blindness, 1994

The above are the Proceedings of the Fifth General Assembly held in Berlin, 1994. Its contents includes sections on the following topics: Affordable eye care; accessible eye care; appropriate eye care; and optional workshop reports on: Assessment of vision function and quality of life as perceived by the cataract patient; Trachoma control – opportunities and constraints for integration into existing primary eye care and health care delivery systems; Ophthalmic medical personnel in prevention of blindness programmes: their training and use; and ocular leprosy – why should it concern us.

Copies are available from: WHO Publications, 1211 Geneva 27, Switzerland.

Women with leprosy in 'double jeopardy'

The following is reproduced from TDR News (Special Programme for Research and Training in Tropical Diseases, UNDP/World Bank/WHO), No. 46, November 1994, page 3:

A multiple survey of women leprosy sufferers near Bombay, India, has raised disturbing questions about their access to effective diagnosis, care and treatment—and suggested they are in 'double jeopardy'—neglected as women and rejected because of their illness.

The survey—by Seemantinee Khot and Shoba Rao—was presented by Khot at the headquarters of the World Health Organization in Geneva during the June 1994 meeting of TDR's top management body, the Joint Coordinating Board. Khot said the survey showed that women tend to neglect leprosy for longer than men, and to develop severe deformities—particularly of the hands, exposed to injury in cooking and domestic work. In leprosy colonies visited by the researchers, 70% of women had hand deformities.

Indian women dress to cover most of their body, and the tell-tale pale, insensitive skin patches of early leprosy are often detected only during child-birth—when another woman traditionally bathes the mother's body after the birth. Nearly half (48%) of the women leprosy suffers first detected the patches at this time, Khot reported.

Greater illiteracy and ignorance of the symptoms of leprosy among women also leads to fewer women seeking immediate treatment. Replies to a structured questionnaire showed that on average it took 15 months from detection of the symptoms before women sought treatment. Even if women want to visit the clinic, they say they cannot go alone, unlike men, often have no money for the bus fare, or are not allowed by the family (or their sense of duty) to take time off.

Discrimination can be extreme. Some women had been served food in the family dog's dish, and many had been physically beaten. Women were more likely than men to be socially isolated. Women were forced more than men to sit alone, eat alone, sleep alone, work alone and to avoid touching other people (all results at statistical confidence levels above 95%).

Women said that when they were forced to stop cooking for the family they felt redundant. But the most difficult adjustment was to be forced not to touch and care for children. 'It was touch, more than anything, that women longed for, and the loss of this intimate female right symbolised isolation and rejection', Khot said.

The number of women separated from—or deserted by—their husbands was 'strikingly high'. Very few were aware of their legal rights under the Indian Marriage Act, which condemns separation or divorce due to leprosy, and gives the woman the right to alimony (a regular sum of money from the ex-husband for maintenance), Khot said.

Some of the women had been forced into prostitution. One reported that they formed the lowest class of prostitute, to whom other prostitutes referred clients suffering from sexually transmitted diseases. As a result they were paid only US$0.50 per client.

When women reach the leprosy clinic, they are faced with further problems. Only 3% of the leprosy workers are women, inhibiting the patients in showing body parts or sharing intimate problems in relationships. Furthermore 'the new multidrug therapy (MDT) regime is more complicated for illiterate, non-numerate women—simple calendars should be developed to improve compliance'. Moreover women worry more than men about the strawberry coloured urine the treatment creates.

Among many important recommendations, Khot suggested that if the prevalence target of one case per 10,000 by the year 2000 is to be met in India, and if disabled women are to be cared for, urgent improvements are needed in: gender sensitization of male leprosy workers; the number of women leprosy workers; clearer MDT dosing instructions for illiterates and non-numerates; counselling of women on their legal rights; family counselling; provision of safe cooking wares to women with nerve involvement, to reduce the rate of hand deformities; and care for women with deformities.

Further information: Dr Carol Vlassof, Special Programme for Research and Training in Tropical Diseases, WHO, 1211 Geneva 27, Switzerland.

Concern over India's leprosy rehabilitation

The following is reproduced from *The Lancet*, London, UK, Volume 343, 26 March, 1994:

The parliamentary standing committee on health has expressed dissatisfaction over rehabilitation of leprosy patients and has suggested more humane measures for its implementation under the leprosy control programme.

For many years the department of health has done almost nothing for the rehabilitation of leprosy patients; this 'virtually negates' the objective of the National Leprosy Eradication Programme (NLEP), the committee said. Critical of the department's approach in regarding long-term cases as being 'burnt out' with little scope for improvement, the committee said 'no case is a burnt out case and every patient deserves the best treatment and rehabilitation even if he/she can not be cured'. The committee recommends the adoption of a more humane approach to these people by extending hospital stay for as long as required. India, which has the world's largest number of leprosy patients, also runs the largest multiple-drug-therapy (MDT) programme. The country's National Leprosy Control Programme launched in 1955 was redesignated National Leprosy Eradication Programme in 1982 with the aim of reducing infection in the community through MDT and social and economic rehabilitation of leprosy patients. The success of NLEP is evident from the decline in the estimated number of leprosy patients from 5·5 million in 1985 to 3 million in 1992 (although 1·8 million leprosy cases were recorded in 1991). India has adopted the World Health Assembly 1991 resolution to eliminate leprosy as a public health problem by the year 2000, elimination having been defined as prevalence of leprosy to less than one case per 10,000 population, the level at which leprosy would be expected to die out.

Rehabilitation of leprosy patients received NLEP attention only recently, when a scheme was launched for establishment of district rehabilitation centres. There are 75 rehabilitation promotion units but their work is hampered by stigma against the disease. Community-based rehabilitation is still a long way off. A Union party minister some time back called for legislation to make 'discrimination' against leprosy-affected people a punishable offence, as was done with untouchability in 1955. The voluntary agency Hind Kusht Nivaran Singh has recommended inclusion of leprosy-cured people in the definition of 'handicapped' to benefit from positive discrimination. India's leprosy control programme has the participation of over 250 non-governmental

organisations, some of which have contributed to the evolution and development of NLEP. They can be a major instrument for rehabilitation programmes in India.

People with leprosy are not wanted by anybody—neither relatives nor society. It is commonplace to find them begging on streets or living in isolated places, and on the river banks of religious places. The parliamentary committee has recommended the formulation of a scheme to provide them with complete care—food, clothing, shelter, and medical care.

Zaka Imam

Report of the International Conference on the Elimination of Leprosy, Hanoi, Vietnam, July 1994

This meeting, co-sponsored by the Sasakawa Memorial Health Foundation, was attended by more than 100 participants from all parts of the world, including the 28 most endemic countries. The topics discussed included progress towards elimination, regional elimination plans, country presentations, technical issues relating to elimination and the role of non-government organizations and WHO. Under the heading 'New approaches and strategies closer to the elimination goal' (page 18):

'The Conference considered that, in order to sustain the quality of services and to minimize the resources that will be needed, the following activities are essential:

contact surveillance should be maintained as the priority of new case-detection, particularly in low endemic areas;
health education and related activities should be targeted to various health professions and policy-makers;
core expertise in leprosy and capability building should be maintained among related health professions, especially dermatologists, physiotherapists and supervisors;
to validate achievement of the elimination goal, reduction of prevalence at the beginning reflects success in decreasing the numbers of untreated cases or the size of the problem. However, when it becomes low endemic, incidence is more important in monitoring recent transmission of the disease and the efficiency of case-detection—for instance, the incidence of leprosy in children and the incidence of new cases with visible deformity;
integration of both case-detection and rehabilitation into private sectors, primary health care and general health services is the most cost-effective method;
certification of elimination is not appropriate.'

The summaries of the 28 reports by country representatives that follow are given in alphabetic order.

Bangladesh

In 1994, 22,334 leprosy patients were registered for treatment out of whom 67·5% were receiving MDT. Among new cases, 21% were already disabled at the time of detection. In November 1993, the government launched a combined tuberculosis and leprosy control programme supported by the World Bank and NGOs. The goal of this programme is to eliminate leprosy as a public health problem by the year 2000 by extending MDT coverage to all districts (thanas) by June 1997. Main difficulties faced by the programme include very high population density, poor accessibility to health services, inadequate drug supply and lack of trained personnel.

Brazil

With about 200,000 registered cases, Brazil is one of the highest endemic countries in the world.

Since 1989, the national plan has been aimed at increasing the quantitative and qualitative coverage of leprosy services and at implementing MDT gradually. Stratification of states according to epidemiological criteria was prepared in order to set priorities. The main difficulties in implementing strategy are the magnitude of the problem, the need for decentralization and the difficult-to-reach population. It is expected that all states will elaborate their plans for elimination and implement them in 1995 in order to each the highest possible MDT coverage.

Cambodia

MDT has been implemented in 16 provinces and about 2000 cases are registered for treatment. About 1000 cases are detected annually. The major difficulties in controlling leprosy are lack of health infrastructure and poor accessibility to leprosy services.

Chad

Leprosy is still an important public health problem, and the disease is under-reported. A national programme was initiated in 1992 aimed at implementing MDT in all districts. Currently about 7500 patients are registered for treatment, and 516 new cases were diagnosed in 1993. As a result of the programme, 53% of registered cases were treated with MDT and the geographic coverage increased significantly. However, accessibility to leprosy services and MDT is limited by a number of operational factors such as the lack of skilled personnel and the considerable nomad population. It is planned to implement special actions in order to reach the uncovered population and to increase MDT coverage to 100% by 1997.

China

While leprosy has been eliminated in most parts of China, there are endemic provinces where leprosy is still a public health problem. In those provinces, the strategy is to diagnose existing cases promptly and to treat them with MDT. It is expected that the prevalence will be reduced to less than 12,000 by 1995 and less than 6000 by the year 2000. Counties situated in mountainous areas and those populated by minority groups are underdeveloped and will need special action. It is also estimated that about 200,000 patients previously treated with dapsone may require further treatment with MDT in order to prevent relapses.

Colombia

The leprosy control programme is being reorganized in order to comply with the recently proposed National Plan for the elimination of leprosy as a public health problem. This plan aims at decentralizing activities and at delegating responsibilities to the departmental and municipal levels. Leprosy prevalence has decreased from 16,600 cases in 1986 to 6311 in 1993, and the number of new detected cases fell by 15% during the same period. the most endemic departments are Santander, North Santander, Cesar and Bolivar.

Côte d'Ivoire

A leprosy elimination programme was launched in 1993, and aims at implementing MDT in all health centres in order to diagnose at least 90% of the patients before they develop deformities. It

is estimated that 8% of the population has no access to health services and this will require special action. The national programme is technically and financially assisted by ILEP and WHO. Currently, about 8000 patients require treatment and 2200 new cases are detected annually.

Egypt

MDT was implemented in 1985 and currently 3338 patients are under treatment. However, leprosy could be under-reported and the diagnosis is still being made very late as evidenced by the high proportion of patients disabled at diagnosis (26%). The national programme aims at integrating leprosy services into PHC units. Main difficulties are related to high stigma, including among health staff, and the high proportion of patients defaulting before completion of treatment.

Ethiopia

Since the implementation of MDT in 1984, the leprosy prevalence has been reduced tremendously. However, more than 15,000 cases are still requiring treatment and about 4000 new cases are detected annually. It is expected that MDT coverage will reach 100% by 1995 despite the difficulties posed by geographical inaccessibility. Efforts are being made to decrease the defaulter rate and to improve early case-finding.

Guinea

Leprosy in Guinea is an important problem, with about 4000 new cases detected annually. The government, in collaboration with WHO and NGOs, initiated and implemented a national plan aiming at the elimination of leprosy. Since 1992, the MDT coverage has been close to 100%. The main components of the programme have been integrated into general health services. The prevalence and detection of leprosy remain very high and new difficulties have emerged with the influx of refugees in the eastern part of the country.

India

With about one million registered cases, India contributes 60% of the leprosy burden in the world. About half a million new cases are detected annually. MDT was implemented in 1982 and its nationwide expansion had a tremendous impact on the leprosy situation, with many states reporting a more than 50% decline in the number of new cases detected. However, considering the magnitude of the problem, the objectives of the national plan were revised in order to make MDT accessible to all patients. This plan has received financial support from the World Bank and by the end of 1994 it is expected to cover all districts with MDT.

Indonesia

All districts (303) are implementing MDT and about 70,000 patients are registered for treatment, out of whom 66% are treated with MDT. The number of newly detected cases increased from 9348 in 1990 to 17,693 in 1993 as a result of the expansion of the programme activities. Leprosy control activities are integrated into general health services. The national plan for elimination of leprosy aims at reaching 100% MDT coverage by 1995. The main difficulty is geographical inaccessibility (17,500 islands), making operational costs very high.

Iran

Leprosy is in the elimination phase in this country. No new cases have been reported from nine out of the 25 provinces. After detailed review of registers and patients, the current prevalence is 2346 and 147 new cases were detected in 1993. All patients are treated with MDT. During the elimination phase, it is planned to intensify case-finding activities in an integrated manner and to provide rehabilitative services to persons disabled because of leprosy.

Korea

Detailed statistics on leprosy in Korea show that leprosy has already been eliminated as a public health problem, therefore activities are now mainly focused on the rehabilitation of more than 22,000 persons registered as having a previous history of leprosy.

Madagascar

The National Plan for elimination of leprosy was elaborated in 1991 in collaboration with the WHO and NGOs. Since its implementation, case-detection and MDT coverage have increased significantly. Out of 9557 patients registered for treatment, 98% are being treated with MDT. One of the main difficulties in maintaining high MDT coverage is the geographical inaccessibility. However, the intensified programme has been able to organize leprosy control activities in 193 health districts. It is planned to further decentralize activities, and to strengthen the prevention of disabilities and the rehabilitation of already disabled cases.

Mali

The elimination programme is now a fully integrated one. Out of 11,000 registered cases, about 40% are treated with MDT. While MDT has been implemented in all eight regions, the coverage is still low in four of them. In order to reach the elimination goal, it is planned to intensify leprosy control activities. The main problems are poor health services coverage and difficult-to-access areas. It is expected that the case-detection rate will increase until 1996 as the programme is still expanding to previously uncovered areas.

Mexico

The programme for elimination of leprosy has recorded that, out of 9532 registered cases, 7052 are being treated with MDT. After implementation of MDT an increase in case-detection has been observed. However, the proportion of cases already disabled at detection is still very high, about 30%. The national plan for elimination was implemented in 1992 and aims at integrating leprosy control at the most peripheral level.

Mozambique

Fifteen years of civil war have had severe consequences for the health structures and organization in this country. Today, with the return of peace, about five million displaced people are returning to their original districts. In this context, leprosy is one of the major health problems and high priority is being given to the disease. A special elimination programme was initiated and, in 1990, leprosy and tuberculosis control programmes were merged. At the end of 1993, 13,119 patients

were registered and 2339 new cases were diagnosed. MDT coverage increased significantly during the last three years to reach 45·5%. However, MDT is not available for 36% of districts. It is planned to reach full coverage by the end of 1997. Since 1992, the Ministry of Health has been rehabilitating health facilities destroyed during the war and is taking special action regarding the five million displaced people returning to the country.

Myanmar

Leprosy continues to be an important health problem. Formerly, it was addressed through a vertical programme until 1991. Since then, the programme has been integrated into basic health services and, out of 40,254 patients, 46% are being treated with MDT; 9432 new cases were detected in 1993. It is planned to reach full MDT coverage by the end of 1996. The main difficulties are lack of trained personnel and inadequate drug supply. Standardized national guidelines are being developed in order to simplify diagnosis and treatment procedures at the peripheral level. Special actions will be required in some isolated provinces and townships.

Nepal

While leprosy is prevalent throughout the country, there are more cases in the areas of the plains. At the moment, out of 18,000 registered patients, 15,000 are under MDT in 70 districts. MDT is not available in five districts, mainly because of their geographic situation. It is planned to conduct a national evaluation of the programme in 1995 and to reorient activities towards elimination of the disease.

Niger

Leprosy continues to pose serious problems in this country. Because of the low density of population and lack of health infrastructure, only 30% of the leprosy patients have access to MDT. To date, about 6500 patients are registered for treatment and 800 new cases are diagnosed annually. In 1992, the national plan was revised in order to expand MDT coverage and to strengthen leprosy control activities. It is planned to reach 100% coverage by the end of 1995 by implementing MDT in all existing services and by using special action, including mobile teams, to reach difficult-to-access population.

Nigeria

The National Programme was launched in 1991 and, since its implementation, the registered cases have decreased from 200,000 to 28,500. In contrast, case-detection increased from 3000 to 6000 because of intensified activities. MDT coverage has increased from 11% to 72%. Leprosy services are now available in all local government areas of each state. While leprosy is being eliminated in some districts, some others will require intensified efforts.

Pakistan

Elimination of leprosy is well under way in Pakistan and, out of registered 7000 cases, more than 80% are treated with MDT. However, the disability rate among new cases is still very high, about 25%, and the proportion of MB cases is increasing. In this situation of low prevalence, it is becoming difficult to maintain regularity of treatment and tracing of defaulters. Intensified health education will be necessary to maintain community awareness.

Papua New Guinea

The health system has been decentralized since 1992, and the leprosy control programme has been combined with other disease control programmes at provincial level. About 600 new cases are detected annually. Although it is planned to expand MDT in all provinces, accessibility to MDT is still low and only 34% of cases benefited from it in 1993. Monitoring and control of MDT drug use, in conjunction with an improved information system, remain a continuing concern for the programme.

Philippines

Currently about 15,000 cases are registered, and 3442 new cases were detected in 1993. MDT coverage reaches close to 100%. It is expected that leprosy will be eliminated by the end of 1988. However, the programme is facing difficulties because of restructuring which has led to problems with supervision, monitoring and drug supply.

Thailand

Leprosy is close to the elimination target following 10 years of intense MDT implementation. Since 1990, the MDT coverage has been maintained at 95% or more. The challenge is to maintain high quality of services under low endemic circumstances. But 35 out of 75 provinces have been reporting a prevalence rate below 1 per 10,000 for the last three years and the case-detection rate is continuously declining.

Vietnam

Leprosy is conceived in this country as a social disease, with more than 8000 registered cases and 3200 new cases detected annually. Leprosy control services are integrated into dermatology services and general services. However, 26% of the districts are not covered by the programme. About 2000 high endemic villages are located in mountainous areas without proper leprosy services. MDT coverage has increased from 10% in 1983 to 92% in 1993. This has helped to improve the epidemiological situation and has favourably changed the community's outlook and attitudes towards the disease; it is planned to intensify activities in high endemic and difficult-to-access areas.

Zaire

Leprosy is a serious problem in Zaire, with more than 8000 registered cases and 3600 new cases a year. Leprosy control activities are difficult to organize in the current political and social context. The programme coverage has decreased from 62% of the population to 36%. The situation is becoming even more complicated because of the problem of refugees in the eastern part of the country. Considering the lack of resources, poor accessibility, shortage of drugs and political unrest, leprosy control activities are very difficult to organize. While MDT coverage is reasonably high in some health districts, the situation is far from satisfactory in others. Leprosy elimination will require increased collaboration and the implementation of special action in difficult areas.

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