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Leprosy Review

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

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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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CONTENTS

Lepr Rev (1991) **62,** 353–361

Editorial

ENVIRONMENTAL MYCOBACTERIA AND HUMAN DISEASE

in the latter part of the last century, the causative organisms of leprosy and tuberculosis were described, respectively, by Armauer Hansen in 1874 and Robert Koch in 1882. These bacteria were distinguished from all others known at that time by a characteristic acid-fast staining property by Paul Ehrlich in 1883. In 1898, when the generic name *Mycobacterium* was introduced, no other acid-fast bacillus had been formally described and named but from that time onwards many such organisms were isolated from environmental sources and from diseased mammals, birds and cold-blooded animals. A few were also isolated from patients, but their role as human pathogens was not seriously considered until the middle of this century when two new mycobacterial skin diseases, swimming pool granuloma[1] and *M. ulcerans* infection,[2] later termed Buruli ulcer, were described and when Runyon published his classical description of the four groups of mycobacteria causing pulmonary disease.[3]

Many unsatisfactory collective names including 'atypical', 'anonymous', 'tuberculoid' and 'MOTT (mycobacteria other than typical tubercle) bacilli' have been given to these mycobacteria but when it became apparent that these species were not primarily pathogenic but widely distributed in nature, the name 'environmental mycobacteria' (EM) was generally adopted. At present there are about 60 known mycobacterial species: 41 are included in the Approved Lists of Bacterial Names[4] published in 1980 and the others have been described subsequently.[5] Cultivable mycobacteria are divisible into two main groups: the slow and rapid growers, which, by antigenic analysis and DNA homology, appear to belong to two quite distinct subgenera.

The ecology of the environmental mycobacteria

It is not generally appreciated just how common the EM are in nature. Sphagnum marshes contain very large numbers[6] and they are also readily isolated from mud, compost, wet soil, surface water, rivers and estuaries.[7] Some species colonize piped water supplies and have been isolated from taps and showerheads. There is also evidence that mycobacteria are washed into estuaries, taken up into aerosols generated by breaking waves and wafted inland by sea breezes and thereby sensitize people who inhale them.[8] Some species or strains are more hydrophobic than others and thus more readily enter

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aerosols.[9] There is also some evidence of an association between hydrophobicity and virulence[10] so that strains entering aerosols may be more likely to cause disease than other environmental strains.

The population of EM varies quantitatively and qualitatively from region to region, being affected by temperature, dryness, pH and mineral content of the environment and possibly by the availability of nutrients derived from decomposing vegetable material. Thus, for example, slowly growing species are particularly prevalent in Burma while rapid growers predominate in Uganda. The EM present in a given region may be determined directly by culturing soil and water samples and indirectly by skin testing surveys based on use of sensitins prepared from a range of mycobacteria.[11]

Immunologically effective contact with mycobacteria

In view of the widespread distribution of EM in nature, exposure of man to them is a regular occurrence in most parts of the world. Thus EM may be consumed in drinking water, inhaled in aerosols or enter the skin through cuts and abrasions. Despite this repeated exposure, overt human disease due to them is very uncommon. On the other hand, there is increasing evidence that overt disease is just one of a complex range of interactions occurring between these commonly encountered micro-organisms and man. These interactions include transient or long term colonization of the intestinal and upper respiratory tracts and there is evidence that they may cross the pharyngeal or intestinal wall (translocation) and persist in the tonsils or gut-associated lymphatic tissue.[12] Exposure may also lead to 'immunologically effective contact' manifesting as reactions or cross-reactions on skin testing with tuberculin and other mycobacterial antigens.[11] More importantly, such contact early in life may affect the pattern of immune responses elicited by subsequent exposure to mycobacteria—a concept picturesquely termed 'Original Mycobacterial Sin'.[13]

In this context, there has, in recent years, been considerable interest in the possible effect of immunologically effective contact with EM on the way in which the host subsequently responds to challenge by BCG vaccination or by infection with *M. leprae* or *M. tuberculosis*. Much of this interest resulted from attempts to explain why an extensive BCG trial conducted in South India failed to reveal any protective efficacy of this vaccine.[14] This led to the restatement of the hypothesis, originally formulated in 1966, that contact with EM provided a form of natural vaccination.[15] If this is the case, a human population repeatedly exposed to EM might become so immune that administration of BCG could not add to this and would therefore appear ineffective in a clinical trial. The alternative hypothesis is that exposure to mycobacterial antigens can prime the host for a range of different immune responses—protective immunity, tissue destroying hypersensitivity and autoimmunity—and that the actual response is, in part at least, determined by the extent of the exposure to EM and the species to which the population is exposed.[16] This hypothesis has two important consequences. First, it may be important to give BCG vaccination before the 'wrong' antigens have been encountered, i.e. neonatally. Secondly, the judicious administration of mycobacterial antigens may lead to the enhancement of protective responses and the suppression of harmful ones. There have been some encouraging preliminary studies on this approach to immunotherapy.[17]

Species of EM causing human disease

Most of the species of slowly growing EM are able to cause opportunist disease in man but, with very rare exceptions, only two rapid growing species, *M. chelonae* and *M. fortuitum*, cause such disease. These two species were once called the 'cold blooded tubercle bacilli' as they were originally isolated from, respectively, turtles and frogs.

By far the most prevalent causes of human disease among the slowly growing EM are the closely related species *M. avium* (the avian tubercle bacillus) and *M. intracellulare*. Being closely related, they are not easily distinguished outside specialist reference centres and are therefore usually grouped together as the *M. avium-intracellulare* (MAI) complex.[18] Other commonly encountered slowly growing opportunist pathogens include *M. kansasii*, *M. xenopi* and *M. scrofulaceum*. Less common members of this group include *M. szulgai*, *M. simiae* and *M. malmoense*, with infections due to the latter showing a considerable, but unexplained, increase in frequency over the last few years. A few other species very rarely cause disease and others may eventually be added to their number.[19]

Epidemiology of human disease due to EM

The incidence and nature of human disease due to EM in a given region is dependant upon the number and species of mycobacteria in that region, the opportunities for contact with potential hosts and the susceptibility of those hosts to disease. As the source of the causative organisms is almost invariably the environment, control measures against tuberculosis, which are designed to break the chain of person to person infection, have no impact on the incidence of disease due to EM. Consequently, as tuberculosis declines in a given country, a relatively greater proportion of mycobacterial disease is due to EM. Also, as a result of an increase in the number of individuals with natural or iatrogenic immunosuppression, the absolute incidence of the latter is also increasing. As mentioned above, the two main opportunities for infection are inoculation through the skin and inhalation of aerosols. Thus, an important group of diseases due to EM, including the two named diseases Swimming pool granuloma and Buruli ulcer, are the result of inoculation.[20] Inhalation of aerosols as a cause of pulmonary disease is less easy to demonstrate but there is strong evidence that a cluster of cases of disease due to *M. kansasii* in pneumoconiotic coal miners in Czechoslovakia was related to the presence of this organism in the water supplying the shower houses used by the miners.[21]

Types of human disease due to EM

Overt disease is divisible into four main types: Inoculation mycobacteriosis, localized lymphadenopathy, pulmonary and disseminated disease.

INOCULATION MYCOBACTERIOSIS

This is usually caused by the rapid growers *M. chelonae* and *M. fortuitum*.[20] result from the use of contaminated needles or injectable materials—many so-called 'sterile' postinjection abscesses are caused by these mycobacteria. Such abscess may be

very chronic and reach very large sizes but they tend to remain localized and respond to surgical drainage, curettage or excision. There have been a number of 'mini-epidemics' of postinjection abscesses resulting from the use of contaminated vaccines and other injectable materials. Multiple abscesses or spreading cellulitis may occur in diabetics and these lesions usually require chemotherapy.

Other examples of inoculation mycobacterioses include posttraumatic corneal ulcers and lesions resulting from the accidental implantation of mycobacteria during operative surgery, particularly cardiac valve replacement.[22] These more serious forms of inoculation mycobacterioses require therapy as well as surgical debridement. Owing to the sporadic nature of these infections, there have been no formal comparisons of drug regimens but success has been reported with various combinations of erythromycin, trimethoprim, sulphonamides, gentamicin, amikacin, fluroquinolones and third generation cephalosporins. In the author's experience, erythromycin with trimethoprim, with the addition of amikacin in more serious cases, is often effective. Corneal infections are usually treated with topical amikacin and erythromycin but in many cases, especially in those caused by *M. chelonae*, relapses follow initial resolution or dense scarring develops. Hence, corneal grafting is often required.

The inoculation mycobacterioses include two named diseases: Swimming Pool Granuloma[1,23] (also known as Fish Tank Granuloma or Fish Fancier's Finger) and Buruli Ulcer.[2,24]

Swimming Pool Granuloma is caused by *M. marinum*, and manifests as warty lesions on trauma-prone parts of the skin, particularly the elbows and knees of swimming pool users and the hands of tropical fish enthusiasts. The lesions are usually localized, although 'sporotrichoid' secondary lesions may occur along the draining lymphatics. The disease is usually benign and self-limiting although excision and/or antibacterial chemotherapy is sometimes required.

Buruli ulcer is a much more serious disease which was first described in Australia[2] but mostly occurs in various limited localities throughout the tropics. The causative organism is *M. ulcerans* which is unique among the mycobacteria by having a very narrow temperature range of growth *in vitro*—32–34°C—and it is the only pathogenic mycobacterium known to produce a cytotoxin.[25] Although it has not yet been isolated from the environment, there is epidemiological evidence that *M. ulcerans* is a free-living mycobacterium that enters the skin by traumatic inoculation by, in most cases, spiky grasses and other vegetation.[26] Following such inoculation into the skin, the toxin released by the organism causes necrosis of the subcutaneous tissues and, eventually, the overlying skin, thereby forming deeply undermined skin ulcers which may reach enormous size. During the progressive phase of the disease, the lesion contains numerous acid-fast bacilli but there is no detectable immune response to them. At this stage, the patient fails to react to tuberculin and to Burulin[27]—a specific skin test reagent prepared from *M. ulcerans*.

A peculiar characteristic of Buruli ulcer is that a point is invariably reached when immune responsiveness develops, the patient reacts to tuberculin and Burulin, the organism disappears and the lesion heals, although often with severe residual scarring and deformity. Even more peculiarly, anergic and reactive lesions may be seen simultaneously in the same patient. The reason why there is a shift from an anergic, multibacillary state, analogous in some respects to lepromatous leprosy, to an abacillary healing stage is

unknown but an unravelling of this mystery could perhaps have profound significance for the development of immunotherapy for leprosy and other mycobacterial diseases.

Treatment of Buruli ulcer is not easy.[24] Although rifampicin and clofazimine are effective *in vitro* and in the mouse model, clinical experience has been rather disappointing. Treatment therefore usually involves excision, often requiring very major surgery with skin grafting. Radical excision is particularly important in the progressive stage in order to remove all infected tissue. For this reason, community education in the importance of presenting with early lesions is of great benefit. As *M. ulcerans* has a very restricted temperature range of growth—32–34°C, resolution of infection has been obtained by applying external heat to lesions for prolonged periods of time but the practical problems associated with this therapy greatly limit its usefulness.

LOCALIZED LYMPHADENOPATHY

This is caused by many species although the great majority of cases are caused by *M. avium-intracellulare*.[2] solitary lymph node in the neck is involved, although other nodes and age groups may also be affected. Although some cases are associated with congenital or acquired immunodeficiency, including AIDS, most such infections, particularly those affecting children, occur in otherwise healthy individuals. Treatment by excision of the affected node is usually curative and chemotherapy is not usually required. Drainage, rather than excision, should not be attempted as this may lead to chronic sinus formation.

PULMONARY DISEASE

This is usually due to the slowly growing species *M. avium-intracellulare*, *M. kansasii* and, in some countries, *M. xenopi*. Less common causes include *M. malmoense*, *M. scrofulaceum*, *M. simiae* and the rapid grower *M. chelonae*. Most cases occur in persons with local or systemic predisposing causes such as industrial dust-associated lung disease, old tuberculosis cavities, rheumatoid lung, cystic fibrosis, malignant disease and any form of congenital or acquired immunosuppression.[29] Some cases, however, occur in the absence of detectable predisposing conditions. Such disease is indistinguishable clinically and radiologically from tuberculosis and diagnosis depends on isolation and identification of the causative mycobacterium. The species of EM causing pulmonary disease may also occur as transient saprophytes in abnormal lung tissue. Great care must therefore be made to distinguish such colonization from actual disease. As a general rule, an EM should not be considered as the primary cause of lung disease unless it is repeatedly isolated from patients with compatible signs and symptoms and in whom all other possible causes of such signs and symptoms, including tuberculosis, have been rigorously excluded.

The causative organisms are usually resistant to most anti-tuberculosis drugs *in vitro*. Nevertheless, good results have been obtained in disease due to the slowly growing species mentioned above by use of first line antituberculosis drugs rifampicin, ethambutol and isoniazid.[30,31] Although infection due to *M. kansasii* has been shown to respond to 9 months therapy, disease due to other slowly growing species requires treatment of 1 year or 18 months duration. In contrast to tuberculosis, ethambutol appears to be a more

effective drug than isoniazid and should therefore be continued throughout the duration of therapy, with due attention to possible ocular side-effects. There are no well-tried regimens for pulmonary disease due to rapid growers but there are anecdotal reports of success with the various drug combinations used for the treatment of inoculation mycobacterioses due to these species (see above).

DISSEMINATED DISEASE

As in tuberculosis, disease due to EM may disseminate from the primary site of infection to other organs. Cases of solitary lesions due to EM in the genitourinary tract, bones and central nervous system have been described but they are very rare. Until the early 1980s, widely disseminated disease due to EM was very uncommon and the few described cases mostly occurred in children or young adults with congenital immune deficiencies, people with leukaemia and other malignancies and renal transplant recipients.

In recent years, however, there has been an increasing number of such infections associated with AIDS. For reasons that are not clear, such AIDS-related disease is mostly, though not exclusively, due to *M. avium-intracellulare* (MAI).[18] Furthermore, there is evidence that the population of strains of MAI involved in AIDS-related disease differs from those causing disease in HIV-negative patients. Thus, in one study, 73% of MAI from AIDS patients were of a particular genotype, compared with only 39% from non-AIDS patients and none of 8 strains from faeces of healthy persons.[32] The significance of this finding is unknown. The source of infection is uncertain: one possibility is that it is the result of activation of dormant MAI in the gut-associated lymphatic tissue (see above) rather than direct acquisition of the bacilli from the environment.[12]

Unlike tuberculosis, which often occurs early in the course of HIV infection, opportunist disease due to MAI usually occurs in patients with fully developed AIDS. Bacteria are often found throughout all internal organs and in the blood. Involvement of the intestinal wall leads to debilitating diarrhoea. The incidence of AIDS-related MAI disease varies from country to country, being uncommon in Africa but occurring in up to 50% of those dying of AIDS in the USA.[33]

There has been some controversy as to whether AIDS patients die of or with MAI infection and whether such infection reduces life expectancy. Although more information is required, therapy does appear to prolong life and enhance its quality. The most effective drug regimens currently available are based on rifabutin and clofazimine, sometimes with the addition of isoniazid and ethambutol but, even with this powerful combination, relapses are common.[34]

EM as possible causes of other diseases in man

There have been several claims during the last few decades that mycobacteria are responsible for a number of human diseases of unknown aetiology, notably sarcoidosis and Crohn's disease. In most studies, acid-fast bacilli have neither been seen in, nor cultured from, the lesions of patients with these diseases. Nevertheless, by analogy with tuberculoid leprosy, the failure to observe acid-fast bacilli in, or to culture them from, diseased tissue does not necessarily exclude them as the prime cause of that disease. There

have, however, been a few isolations of *M. paratuberculosis*, the causative agent of hypertrophic enteritis in cattle, from Crohn's disease tissue.[35] Clearly, these few isolations do not prove that this mycobacterium is a cause of Crohn's disease: the tissue changes may merely promote secondary saprophytic colonization by certain bacteria that are present in small numbers in the healthy bowel.

Several authors have postulated that mycobacteria associated with Crohn's disease and sarcoidosis exist in cell wall-free forms and, as such, are very difficult to detect and isolate.[36] For this reason, attention has turned to the detection of specific components of mycobacteria by sensitive chemical or molecular biological techniques but the limited data yielded so far have been somewhat conflicting and the aetiological significance of detected components remains unknown.

Tuberculostearic acid, a long-chain fatty acid specific to the genus *Mycobacterium*, has been detected in lymph nodes from patients with sarcoidosis.[37] By use of suitable DNA probes, DNA compatible with *M. paratuberculosis* has been detected in Crohn's disease tissue but it was also detected in tissue from cases of ulcerative colitis and non-inflammatory bowel disease.[38] More recently, use of a DNA–RNA hybridization technique showed that bowel tissue from Crohn's disease contained much more (almost five times as much) RNA binding to a non-species-specific mycobacterial DNA probe than normal bowel tissue. Likewise spleens from patients with sarcoidosis contained an equally increased amount of such RNA.[39] Not all attempts to detect mycobacteria in such tissues have, however, been successful. One group of workers failed to detect mycobacterial DNA in Crohn's disease tissue, even though they used the very sensitive polymerase chain reaction to amplify any such DNA.[40]

Thus, at present, the topic is a challenging yet controversial one but, with the increasing sophistication of the techniques available to the microbiologist of today, there can be little doubt that this subject will generate a large amount of work and, probably, even more controversy. In order to avoid drawing false conclusions, it is crucial that workers in this field should interpret their data with great caution, always bearing in mind that the well-established criteria for determining the causative role of micro-organisms in disease, namely Koch's postulates, are as relevant now as they were when introduced over a century ago.

Prevention of human disease due to EM

As EM are so common in nature, prevention of infection of man by them is virtually impossible. Any measures to control, treat or prevent predisposing lung damage, especially pneumoconiosis, and natural or iatrogenic causes of immunosuppression will limit the subsequent development of overt disease. Likewise, strict attention to the sterility of injectable materials, needles and syringes will have an impact on the incidence of inoculation mycobacterioses.

The effect of previous BCG vaccination on the incidence of disease due to EM is poorly understood. The effect on Buruli ulcer in Uganda was transient and limited. On the other hand, termination of neonatal BCG vaccination in Sweden was followed by an increased incidence of mycobacterial lymphadenitis in young children, providing indirect evidence that BCG afforded protection against that disease.[41] The effect of previous BCG vaccination on AIDS-associated disease due to EM, particularly *M. avium-intracellulare*,

remains to be established. If such disease is due to recent and direct infection from the environment, then any protective effect of BCG would probably be abrogated by the immunosuppression. If, on the other hand, disease is due to reactivation of dormant bacilli in lymphatic tissue, then BCG given early in life could well have a beneficial effect by preventing the establishment of such dormant foci of infection. It would be interesting to know whether the high incidence of AIDS-related disease due to EM in the USA is due to the fact that BCG vaccination was abandoned many years ago in that country.

Conclusions

Once regarded as a mere curiosity, overt disease due to EM is now recognized as being a serious cause of human illness. Once regarded as a rarity, the tragedy of the AIDS pandemic has assured the increasing prevalence of such disease. Future studies may well confirm the long-suggested causal link between EM and certain chronic diseases of at present unknown aetiology. Despite these actual and postulated associations with overt human disease, the main cause of interest in future may well relate to their ability to predetermine the nature of immune responses on subsequent encounters with the tubercle or leprosy bacilli. Detailed studies of the immunological consequences of the interactions between environmental mycobacteria and man, and the development of ways of manipulating these interactions, may enable 'Original Mycobacterial Sin' to be changed to Original Blessing!

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Lepr Rev (1991) **62,** 362–373

Comparison of polymerase chain reaction technique with other methods for detection of *Mycobacterium leprae* in tissues of wild nine-banded armadillos

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Summary Thirty, nine-banded armadillos weighing between 3 and 5 kilograms trapped from an area endemic for armadillo leprosy were collected at random; killed, autopsied and examined histopathologically. Also, one of the right inguinal lymph nodes was removed under sterile precautions and examined using PCR, direct smear examination, mouse footpad study, culture in laboratory media and histopathology with a view to detecting *Mycobacterium leprae*. Blood was collected at death and tested for IgM antibodies to PGL-1.

According to the PCR study of the inguinal lymph nodes 16 of 30 armadillos (53·3%) had evidence of *M. leprae*. Significant levels of IgM antibodies to PGL-1 and identifiable lepromatous granuloma in inguinal lymph nodes were found in 2 animals (6·7%) with advanced disseminated disease. The prevalence of generalized leprosy according to autopsy study was 13·3% and according to histopathological examination of ear tissue 3·3%. The presence of *M. leprae* in the tissues evoked no special tissue reaction in the early stages. The pattern of spread of the disease in 2 animals closely resembled that found in experimental animals infected intracutaneously. Initiation of infection by inoculation of *M. leprae* through thorn pricks remains a distinct possibility.

Introduction

Leprosy in the wild nine-banded armadillos of Louisiana was first reported in 1975.[1] The rate of infection as determined by histopathological examination at autopsy in animals caught from various regions in Louisiana varied from 4% to 29·6%.[2] Smith *et al.* confirmed the occurrence of naturally-acquired leprosy in wild armadillos and according to their studies the prevalence rate in different areas in the Texas Gulf Coast and in Louisiana varied from 1% to 15·4%.[3–5] Since the discovery of phenolic glycolipid-1 (PGL-1), a substance specific to *M. leprae*,[6] the presence of IgM antibodies to PGL-1 (AbPGL-1) in leprosy patients and their contacts has been reported.[7,8] The presence of

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AbPGL-1 in wild armadillos was investigated and it was found that up to 20% of Louisiana armadillos were positive for these antibodies.[9]

Recently it was reported that using a specific polymerase chain reaction (PCR), based on DNA sequences present in the 18 kDA protein gene, as few as 100 *M. leprae* could be detected in tissues.[10] This method is a valuable addition to other methods available to study the prevalence of infection, mode of transmission, and the pathogenesis of leprosy in armadillos in nature and perhaps helps us to further clarify our understanding of human leprosy.

Materials and methods

Nine-banded armadillos trapped from different parts of Iberville Parish, Louisiana are regularly used for experimental studies in the laboratory. Invariably, on routine screening some among them are found to have naturally occurring leprosy. We used 30 consecutive animals weighing between 3 and 5 kg collected from the area for this study.

The armadillos were killed under anesthesia by exsanguination and a thorough autopsy was done within a week of their being received in the laboratory. Plasma was separated from blood obtained at autopsy for antibody studies.

AUTOPSY STUDIES

In the earlier autopsy study of experimentally-infected lepromatous armadillos it was found that the inguinal and axillary lymph nodes were more frequently colonized by *M. leprae* than any other organs studied.[11] Therefore, it was planned to use the right inguinal nodes to investigate in detail the presence of acid-fast organisms (AFB) in all 30 animals using several different techniques. Ordinarily 2 to 3 enlarged lymph nodes were found in the inguinal region. They were removed under strict sterile conditions. The skin over the inguinal region was shaved and cleansed twice for 5 min using ACUdyne (containing a mixture of iodine compounds and detergents) skin cleanser (ACME United Corporation) dried with sterile gauze and twice more cleansed with 70% alcohol and dried. The lymph nodes were dissected out using another set of sterile instruments. One of the lymph nodes excised was divided into 3 portions; one was used for PCR studies, another for histology and the third for microbiological studies. Only histopathological studies were done on the remaining nodes. During autopsy, tissue pieces were removed from liver, spleen, left inguinal lymph nodes, left and right axillary and mesenteric lymph nodes, left and right sciatic nerves, heart, lungs, adrenals, kidneys, testes or ovaries and uterus, nose, ears and tongue. All the 4 footpads were dissected out and were divided longitudinally into several pieces so that the footpads in their entirety could be examined. Tissues were fixed in 10% buffered formalin and were processed for paraffin sections. Five micron sections were cut and stained with hematoxylin-eosin and a modified Fite stain for AFB. The bacterial load was assessed according to Ridley's scale from 0 to 6+.[12]

PCR STUDIES

Lymph nodes (200 mg) were prepared by mincing with scissors, followed by homogenization in 2 ml of Hanks balanced salt solution using a Mickle homogenizer (Mickle

Laboratory Engineering, Surrey, UK) with 25, 3-mm diameter sterile glass beads for 1 min at 25°C. Tissue debris was allowed to settle at 1 g for 5 min and the supernate was decanted and saved. One hundred microlitres of digestion buffer containing 250 μg proteinase K(10) were added to 0·4 ml of lymph node homogenate and the mixture was held at 60°C for 30 min. Inactivation of proteinase K was accomplished by shifting the temperature of the mixture to 94°C for 8 min. The homogenates were cooled to room temperature and 500 μg of lysozyme in 50 μl (Sigma Chemical Company, St Louis, MO) were added and the samples were held at 37°C for 30 min. Proteinase K (250 μg) was added again and samples were held at 60°C for 30 min. The enzyme-digested homogenates were extracted with an equal volume of phenol/chloroform isoamyl alcohol (1 : 1) and the resultant aqueous phase was extracted with an equal volume of chloroform/ isoamyl alcohol (1 : 1). The DNA in the aqueous phase was precipitated with 2 volumes of ethanol at −20°C for 2 hr and the precipitate was resuspended in 30 μl of sterile distilled water. Two mock buffer samples were processed identically and served as negative controls to monitor possible contamination of samples with *M. leprae* DNA during processing. We have reported earlier that uninfected armadillo tissue homogenates and purified armadillo DNA test negative in PCR.[10]

Ten microlitres of the resuspended material was added to the PCR reaction tube containing oligonucleotide primers which have been shown to amplify an *M. leprae*-specific 360 base pair (bp) DNA fragment.[10] Thermocycling parameters and buffer conditions for optimal production of this fragment have been described.[10] Detection of the 360 bp PCR product was by gel electrophoresis and DNA hybridization analysis using a ^{32}p-labelled 212 bp probe specific for the 360 bp PCR product.

MICROBIOLOGICAL STUDIES

A piece of the lymph node weighing approximately 0·2 g was ground up in a sterile mortar and pestle. To the homogenized tissue 2 ml of Hanks balanced salt solution was added and mixed. Approximately 1 ml of this homogenate was used to inoculate 3 Lowenstein–Jensen slants (LJ) and 3 Middlebrook's 7H11 agar plates. One of each was incubated at 25°C, 33°C and 37°C for 8 weeks. They were checked for growth at 24 hr, 48 hr, and every week for 8 weeks, and the organisms grown were subjected to standard identification procedures.[13] The remainder of the homogenate was put into a Mickle cup with glass beads, homogenized for 2 min, and was allowed to settle for 5 min. The supernatant fluid was aspirated, smears were made and were stained for AFB. The AFB in the supernatant were counted according to the method described by Shepard.[14] The suspension was then diluted so as to contain 5000 AFB in 0·03 ml. Both hind footpads of 5 BALB/c mice were inoculated with 5000 AFB in 0·03 ml of the suspension. If no organisms were seen in the smear 0·03 ml of the supernate from the homogenate was used for inoculating each hind footpad of 5 mice. Harvesting of the footpads for AFB was carried out at 6 and 9 months and the number of bacilli obtained at the earliest period of positivity are given in Table 1.

IgM ANTIBODIES TO PHENOLIC GLYCOLIPID-1

Plasma samples were tested in an ELISA for IgM antibodies to the phenolic glycolipid-1 (PGL-1) antigen of *M. leprae* using the method described previously.[9] The PGL-1 antigen was prepared by Dr Patrick Brennan (Colorado State University, Fort Collins) and

provided through contract with the National Institutes of Allergy and Infectious Diseases (Dr Darrell Gwinn, Leprosy Project Officer). The resulting ELISA absorbances were judged for positive and negative reaction using the earlier definitions.[9] Values from 0 to 580 $(OD \times 10)^3$ were considered negative, and from 580 to 720 were equivocal and 721 and above were positive. Specificity of the reactions were confirmed by adsorbing presumed positive plasmas with whole *M. leprae* and other mycobacterial species. The ELISA absorbency of a true positive was significantly reduced by absorption with *M. leprae* but not altered by absorption with the other mycobacterial species.[9]

Results

The inguinal lymph nodes were enlarged on both sides in all animals as compared to animals housed in captivity. There were 2 to 3 of them on each side and together they weighed 1 to 2 g. One lymph node from the right side removed under strict sterile

Table 1. Armadillos (21) with AFB in the right inguinal node in one or more tests and IgM antibody values to PGL-1

Serial No.	PCR	Smear from homogenate and AFB count per gramme of tissue	Growth of AFB in footpads. Count per footpad	Culture of AFB in 7H11 LJ medium at 25°C, 33°C & 37°C	Histopath. exam.	IgM antibodies to PGL-1 ELISA absorbance $OD \times 10^3$
1	–	$4{\cdot}58 \times 10^5$	Not done	–	1+	447
3	+	$5{\cdot}24 \times 10^5$	$6{\cdot}60 \times 10^5$*	–	1+	620 (equivocal)
5	+	—	—	—	—	363
6	+	—	Failed	—	1+	412
10	+	—	$3{\cdot}60 \times 10^4$†	—	—	405
11	+	—	—	—	—	205
12	+	$1{\cdot}31 \times 10^5$	$1{\cdot}88 \times 10^4$†	—	—	398
13	+	$1{\cdot}31 \times 10^5$	$2{\cdot}95 \times 10^4$*	—	—	293
14	+	$1{\cdot}02 \times 10^7$	$1{\cdot}97 \times 10^4$*	—	3+	370
15	+	$1{\cdot}31 \times 10^5$	$6{\cdot}26 \times 10^5$*	—	—	316
18	–	—	$1{\cdot}64 \times 10^5$†	—	—	409
19	+	—	—	—	—	432
21	–	—	$9{\cdot}48 \times 10^4$*	+(LJ‡) *M. gordonae*	3+	396
22	+	—	—	—	—	307
23	+	—	—	—	—	270
25	+	$9{\cdot}24 \times 10^9$	$4{\cdot}59 \times 10^4$*	—	6+	1160 (positive)
26	–	—	—	—	1+	240
27	+	—	—	—	—	323
28	+	—	$3{\cdot}08 \times 10^5$*	—	—	235
29	–	—	$1{\cdot}31 \times 10^4$*	+ (LJ & 7H11‡) *M. scro.*	4+	603 (equivocal)
30	+	$2{\cdot}00 \times 10^9$	$3{\cdot}14 \times 10^5$*	—	5+	907 (positive)
Total number	16	8	12	2	9	

* 6 months; † 12 months; ‡ at 37°C.

precautions was studied using 5 different methods, namely (a) PCR; (b) examination of direct smear; (c) mouse footpad study; (d) culture in laboratory media; and (e) histopathology. AFB were discovered in 21 of the 30 specimens studied (70%) (Table 1).

PCR STUDIES (Table 1)

Detection of the *M. leprae*-specific 360 bp fragment by PCR indicating the presence of *M. leprae* were obtained in 16 specimens (53·3%). In 5 among them, only PCR signals were positive for *M. leprae* and all other tests were negative. There were 5 which were AFB positive according to one or more of the other methods, but were PCR negative. Samples testing negative by PCR, but containing noncultivable AFB were spiked with 1 pg of *M. leprae* DNA and retested by PCR. All samples spiked with *M. leprae* DNA in this manner tested positive for the 360 bp PCR product indicating the samples were not inherently inhibiting in the PCR test. Of the 16 positive specimens, 8 were positive by both agarose gel electrophoresis and hybridization (Nos 3, 10, 12, 13, 14, 15, 25 and 30) while the other specimens were positive by hybridization only:

MICROBIOLOGICAL STUDIES

Smear from homogenates of lymph nodes (Table 1)

Direct smear from homogenates of lymph nodes from 8 animals showed AFB. Except one (No. 1), all recorded positive PCR signals and were found to grow in footpads of mice.

Mouse footpad studies (Table 1)

From 12 specimens growth was registered in the footpads of mice. Nine of them had positive PCR signals and 2 were culturable in laboratory media. In one, all other tests to identify the presence of mycobacteria were negative (No. 18).

Culture in laboratory media (LJ & 7H11)

The homogenate from the lymph node was cultured in both LJ and 7H11 media at 25°C, 33°C, and 37°C. From 2 specimens (Nos 21 and 29) AFB were grown at 37°C in LJ medium and from one (No. 29), in both LJ and 7H11 media at 37°C. No growth was detected at 25°C and 33°C with either medium up to 8 weeks. Both positive specimens had negative PCR signals. However, both registered growth in the footpads of mice and were present in histopathology sections stained for AFB. They were identified as *M. gordonae* (No. 21) and *M. scrofulaceum* (No. 29). The organisms obtained from the mouse footpads were also subjected to PCR tests for *M. leprae* and were found negative. They were again identified as *M. gordonae* and *M. scrofulaceum* according to standard identification procedures.[13]

HISTOPATHOLOGICAL STUDIES

The right inguinal node (Table 1)

Histopathological examination of the right inguinal lymph node showed marked reticuloendothelial hyperplasia and prominent germinal centres. The sinusoids in some lymph nodes were packed with large collections of macrophages and occasional

neutrophils. There were small and large clumps of mast cells distributed irregularly both in the cortex and in the medulla. There were no granulomas or any identifiable difference in the lymph nodes of 7 animals which showed AFB up to 3+ load (1 to 10 bacilli per oil immersion field). However, in one animal there were a few focal areas of epithelioid cells with poorly formed giant cells, and the granuloma lacked organization. Only 2 animals (Nos 25 and 30) showed macrophages characteristic of lepromatous disease with abundant pink granular cytoplasm replacing large areas of normal lymph node tissue. Foamy degeneration, though present, was scarce. In the 2 animals (Nos 21 and 29) infected with *M. gordonae* and *M. scrofulaceum* there was no evidence of granuloma.

Acid-fast stain showed intracellular AFB mainly in the macrophages infiltrating the subcapsular region, and the sinusoids of lymph nodes of animals with less than 3+ load. In 2 specimens (Nos 21 and 29) AFB were confined to certain localized spots and large areas of the lymph nodes did not show any bacilli. However, in animals with large loads of AFB (Nos 25 and 30) there was diffuse infiltration of the lymph nodes with AFB packed macrophages. Some of the mast cells also contained AFB. Morphologically atypical AFB not identifiable as *M. leprae* were seen in 3 animals (Nos 1, 21 and 29) in the right inguinal node (Table 1). Two of these were grown in laboratory media and mouse footpads (Nos 21 and 29). In one the mouse footpad inoculation test was not done, and it did not grow in laboratory media.

HISTOPATHOLOGY OF OTHER ORGANS

Changes in organs with AFB (Table 2)

AFB were present in one or more tissues in 14 of the 30 armadillos. Four of these animals (Nos 3, 14, 25 and 30) had lepromatous granulomas in the liver, spleen, axillary and inguinal nodes as evidence of disseminated leprosy. One or more footpads were also infiltrated with lepromatous granulomas. The nose was infected in 3, the sciatic nerve in 2, the tongue in 2, the ears and other organs in only one with advanced disease. Skin nodules were present in 3 of them. The lepromatous granulomas in all organs were composed of mostly macrophages with clumps of intracellular AFB. In one animal (No. 3), there was a single large skin nodule measuring 2·0 cm in diameter in the left inguinal region and histologically it consisted of a large collection of bacilli-filled macrophages and scattered lymphocytes. There were also a few areas of necrosis.

Where the bacillary load was less than 3+ the presence of AFB did not evoke any specially identifiable cellular reaction.

AFB associated with thorns were seen in the footpads of 5 animals and in the noses of 3 animals. AFB were found only in association with a thorn in the nose of one animal (No. 11) and in the left hind footpad of another animal (No. 19).

Other lesions

Of the 30 animals autopsied 15 showed thorns in all 4 feet, and 14 more had thorns in at least one foot. Thorns were present in the noses of 9 and in the ears of 14 armadillos. The thorns were invariably surrounded by a foreign body granulomas. Occasionally they were enveloped in dense hyalinized fibrous tissue. Sarcocystis was present in the tongue muscles in 22 animals and in the cardiac muscle in one and the striated muscles of the foot

Table 2. Armadillos (13) with histopathological evidence of AFB

Serial No.	Liver	Spleen	Right inguinal lymph node	Left inguinal lymph node	Other lymph nodes	Footpads	Ears	Nose	Other organs	Remarks
1	—	—	1+	1+	1+ Left axillary	—	—	—	—	Morphologically atypical
3	1+	1+	1+	4+	—	2+ Right hind	—	2+	Skin nodule left inguinal region, 6+	AFB associated with a thorn in the nose
6	—	—	1+	—	—	—	—	—	—	None
9	—	—	—	2+	—	—	—	—	—	None
11	—	—	—	—	—	—	—	1+	—	AFB associated with a thorn
14	2+	1+	3+	2+	2+ Both axillary	4+ Right hind	—	—	—	AFB associated with a thorn in the right hind footpad
19	—	—	—	—	—	1+ Left hind	—	—	—	AFB associated with a thorn
20	—	—	—	—	1+ Left axillary	1+ Right hind	—	—	—	Morphologically atypical. AFB present around thorn.
21	—	—	3+	—	—	—	—	—	—	Morphologically atypical
23	—	—	—	—	1+ Right axillary	—	—	—	—	None
25	4+	5+	6+	6+	6+ Both axillary and mesenteric	6+ All four feet	5+ Both	6+	Skin nodule 6+; lungs 5+; tongue 6+; kidneys 3+; adrenals 4+; testes 3+; thymus 2+; pancreas 2+; sciatic nerve epineurium 6+	AFB associated with thorn in the left hind foot and right fore footpad
26	1+	3+	1+	—	—	—	—	—	—	None
29	—	—	3+	2+	—	—	—	—	—	Morphologically atypical AFB
30	3+	3+	5+	5+	4+ Both axillary	4+ All four feet	—	5+	Skin nodule 6+; sciatic nerve 4+; tongue 5+	AFB associated with thorn in the nose, right hind foot, and right fore footpad
Total	5	5	9	7	6	6	1	4	3	

Table 3. Armadillos (9) with all 5 tests negative for AFB in the right inguinal lymph node and IgM antibodies to PGL-1 ELISA absorbance OD × 10^3

Serial No.	IgM antibodies to PGL-1 ELISA absorbances (OD × 10^3)
2	654 (equivocal)
4	482
7	579
8	585 (equivocal)
9	403
16	730 (false positive)
17	306
20	381
24	293

in one. Fragments of adult schistosomes with granulomatous reaction around them were found in liver, lung, and lymph nodes in the axillae, inguinal region and the mesentery in 19 animals.

IgM antibodies to PGL-1(Tables 1 and 3)

The values were positive in 3 animals (Nos 16, 25 and 30). Two of them (Nos 25 and 30) had disseminated disease with high bacterial load in many organs. One animal with a positive value did not show evidence of AFB in any of the other tests. The ELISA absorbances of 2 of the animals (Nos 25 and 30) were significantly reduced when their plasmas were adsorbed with whole *M. leprae*. Absorbances were not altered when they are adsorbed with other mycobacterial antigens. The ELISA absorbance of animal 16 was significantly reduced when its plasma was adsorbed with both *M. leprae* and *M. kansasii* and, therefore, was considered false positive.

Discussion

Using direct smear, laboratory culture, mouse footpad studies, histopathological examination and PCR techniques, AFB were found in the right inguinal lymph nodes of 21 of the 30 wild nine-banded armadillos investigated (70)% (Table 1). Of these, 16 animals (53·3%) had positive PCR for *M. leprae*. Experimental studies have shown that the PCR method used in this investigation is highly specific for *M. leprae*.[10] Therefore, it is reasonable to conclude that 53·3% of the armadillos were infected with *M. leprae*. Of the other 5 animals with AFB in their right inguinal nodes, 2 had culturable AFB using Lowenstein–Jensen and 7H11 media. The AFB in the other 3 may by the highly fastidious, armadillo-derived mycobacteria (ADM).[15,16]

There is much interest in the study of the effects of previous exposure of humans to environmental and pathogenic mycobacteria on susceptibility to *M. leprae* infection.[17,18] No other associated mycobacteria were isolated from any of the 16 animals which had *M. leprae* infection by PCR, although 5 from the other 14 animals had evidence of another mycobacterial infection.

IgM antibodies to PGL-1 were detected in 2 of the 30 animals (6·7%). Both had advanced disseminated lepromatous disease with high bacterial loads. With the present cut-off values, the screening test for IgM antibodies to PGL-1 was not sensitive enough to detect early disease. Nevertheless, the test is highly specific and virtually always positive in lepromatous leprosy with high bacterial load. This finding is in keeping with our earlier reports.[11,19]

During histopathologic examination, although AFB were seen in different organs in 14 animals, only 4 (13·3%) had macrophage granulomas characteristic of lepromatous leprosy as described in earlier studies.[20–22] If the histopathological study was limited to the inguinal lymph nodes only 2 armadillos (6·7%) could be diagnosed as lepromatous animals. Biopsy study of ears in armadillos is considered a very useful, reliable and feasible method of detecting lepromatous disease. Only one animal (3·3%) showed lepromatous granuloma in the ears (Figure 1). When the bacterial load was less than 3+ there was no specific tissue reaction to the presence of AFB. Until the disease was well established, it appeared to be a 'quiet invasion' by *M. leprae*.

Of the 4 animals which had acquired histologically identifiable lepromatous disease, 2 had such advanced lesions in many organs that it was not possible to trace the route of entry or the mode of spread of the disease. In the other 2 the disease was sufficiently early to derive some conclusions. In armadillo No. 3 there was a large single skin nodule in the left inguinal region composed of largely macrophages with a bacterial load of 6+. The left inguinal nodes were infiltrated with macrophages having a bacterial load of 4+. In the liver, spleen, and the right inguinal nodes there was a bacterial load of 1+. It is highly likely that the skin nodule was the primary lesion following a local entry of *M. leprae*. Then there was a lymphatic spread to inguinal nodes followed by bacteraemia and dissemination of *M. leprae* to other sites. In animal 14, it seems reasonable to state that the organisms entered the right hind footpad, produced locally an extensive lepromatous granuloma with a bacterial load of 4+ followed by a lymphatic spread to the regional

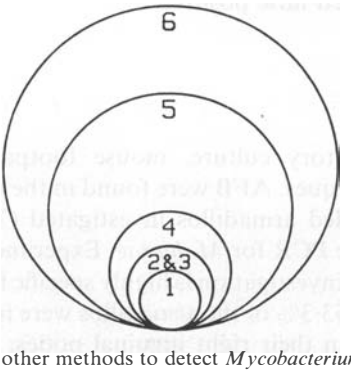

Figure 1. Comparison of PCR with other methods to detect *Mycobacterium leprae*. 1, Ear biopsy; 2, inguinal node biopsy; 3, IgM antibodies to PGL-1; 4, autopsy; 5, PCR study of inguinal lymph nodes; 6, total number of animals examined (30).

lymph nodes with a bacterial load of 3+ and later a bacteraemic spread to other organs of the reticuloendothelial system. The nature of the initial lesion and the pattern of spread of the disease in these 2 animals were very similar to what was found in intracutaneously infected experimental armadillos.[11]

There is sufficient evidence in this study to infer that at least in a few animals *M. leprae* entered the body through the skin. Penetrating injuries by thorns had been associated with entry of *M. leprae* into the skin.[23] In the present investigation one or more thorns were found in the footpad of all but one of the 30 armadillos studied. In 7 instances the thorns were associated with AFB in the tissues. In animal No. 11, AFB were present only in the nose, in animal No. 19 only in the left hind footpad, and in both armadillos the organisms were present in associations with thorns. Therefore, thorn pricks as a mode of entry of *M. leprae* into the skin of the armadillos is a clear possibility, if not probability.

In this study, 16 of the wild armadillos had evidence of infection with *M. leprae* in their right inguinal nodes. In an earlier report when armadillos were experimentally-infected subcutaneously in the footpads with *M. leprae*, 17 of the 18 showed *M. leprae* in the regional lymph nodes but only 10 had lesions at the site of inoculation. The lower the dose of infection the less likely it was to have a local lesion at the site of entry.[11] A thorough microbiological and pathological study including PCR for *M. leprae* of superficial lymph nodes of normal contacts of leprosy patients with a high level of IgM antibodies to PGL-1 may yield very valuable data and add to our understanding of the pathogenesis of leprosy.

In 5 of the PCR positive animals there was no evidence of *M. leprae* in any of the other tests including histopathological examination. In patients with indeterminate leprosy, with polar tuberculoid disease and with lesions highly suspicious of leprosy, detection of *M. leprae* in biopsies can be crucial in confirming the diagnosis. Search for *M. leprae* in histopathologic sections is often unproductive. The use of PCR as a specific and sensitive tool to detect *M. leprae* in such cases should be further investigated.

Two animals as mentioned earlier had cultivable mycobacteria and they were identified as *M. gordonae* and *M. scrofulaceum*. AFB found in these animals grew in the footpads of mice. The footpad isolates were further tested and were found to be *M. leprae*-PCR negative and were again identified as *M. gordonae* and *M. scrofulaceum* using standard identification procedures.[13] It is possible to obtain multiplication in mouse footpads which is similar to that of *M. leprae* with other mycobacteria also.

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Comparaison de la methode de la polymerase chain reaction avec celle du depistage du *Mycobacterium leprae* chez 30 tatous chez qui un marquage en bandes sequentielles du chromosome 9 à été effectué

C K Job, V Drain, D L Williams, T P Gillis, R W Truman, R M Sanchez, A T Deming et R C Hastings

Résumé Trente tatous furent choisis au hasard dont le chromosome 9 avait été marqué en bandes séquentielles, pesant entre 3 et 5 kilos et pris au piège dans une région où la lèpre des tatous est endémique; ils furent tués, une autopsie fut faite ainsi qu'un examen histopathologique. Un des ganglions inguinaux droits fut également enlevé dans des conditions stériles et examiné par la méthode de la polymérase chain reaction, du frottis direct, par l'étude de sensibilité sur le coussinet plantaire de la souris, par culture dans un milieu de laboratoire et par examen histopathologique afin de dépister le *Mycobacterium leprae*. Le sang fut prélevé à la mort et examiné pour déterminer les anticorps IgM dirigés contre PGL-1.

D'après l'étude de polymérase chain reaction des ganglions inguinaux, des preuves de *M. leprae* existaient chez 16 des 30 tatous (53,3%). Des taux importants d'anticorps IgM dirigés contre PGL-1 et des granulomes lépromateux identifiables dans les ganglions inguinaux furent trouvés chez 2 animaux (6,7%) présentant un stade avancé de dissémination de la maladie. D'après l'autopsie, la prévalence de la lèpre généralisée était de 13,3% et d'après l'examen histopathologique des tissues de l'oreille de 3,3%. La présence de *M. leprae* dans les tissues ne donna lieu à aucune réaction tissulaire spéciale aux premiers stages. Le schéma de la propagation de la maladie chez 2 animaux resemblait fort à celui des animaux expérimentaux infectés intracutanément. Il est très probable que l'infection par inoculation de *M. leprae* avait été causée par des piqûres d'épines.

Comparacion de la tecnica de reaccion en cadena por polimerasa con otros metodos de deteccion de *Mycobacterium leprae* en los tejidos de armadillos salvajes, de nueve bandas

C K Job, V Drain, D L Williams, T P Gillis, R W Truman, R M Sanchez, A T Deming y R C Hastings

Resumen Se atraparon al azar treinta armadillos de nueve bandas, con pesos entre 3 y 5 kilogramos, en una zona que era endémica para la lepra en armadillos; después de matarlos, y realizar una autopsia, se les hizo un estudio histopatológico. Además, se hizo una extracción de los nodos linfáticos inguinales derechos tomando precauciones de esterilidad, y se les examinó utilizando PCR, estudio director de frote, examen de pata de ratón, cultivo en medios de laboratorio e histopatología con la intención de detectar *Mycobacterium leprae*. Se recogió sangre al momento de muerte y se hicieron pruebas para anticuerpos IgM según PGL-1.

Según el estudio PCR (Reacción en Cadena por Polimerasa) de los nodos linfáticos inguinales, 16 de los 30 armadillos (53,3%) indicaban la presencia de *M. leprae*. Se encontraron niveles significativos de anticuerpos IgM según PGL-1, y en 2 animales (6,7%), se encontraron granulomas lepromatosas identificables con un estada avanzado de enfermedad diseminada. Según el estudio por autopsia, la presencia generalizada de lepra era un 13,3%, y según un examen histo-patológico del tejido del oído un 3,3%. La presencia de *M. leprae* en los tejidos no provocó una reacción tisular especial en las primeras etapas. La forma en que se diseminó la enfermedad en los animales se parecía mucho a la que se encuentra en los animales de laboratorio infectados por vía intracutánea. Es muy posible que la iniciación de la infección por inoculación de *M. leprae* resulte de pinchazos causados por espinas.

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Lipid-laden macrophages in bone marrow of leprosy patients

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Summary While conducting a study to observe bone marrow cytomorphological changes in multibacillary leprosy, lipid laden macrophages as seen in sphingolipidoses were noted. The present study was planned to observe the occurrence and morphological characterization of these macrophages in various types of leprosy. Bone marrow records from 48 cases of paucibacillary and 72 cases of multibacillary leprosy were analysed. The macrophages accounting at the most for 3·5% of marrow cells were observed in 5 cases of paucibacillary and 43 cases of multibacillary leprosy with a maximum incidence being observed in patients with ENL (16/17). The lipid present in the cytoplasm of these cells could be derived from the lipid of the cell wall of *Mycobacterium leprae*. To the best of our knowledge, these cells have not been reported in leprosy so far.

Introduction

A variety of cytomorphological changes have been described in bone marrow (BM) of leprosy patients. These include megaloblastic erythropoiesis, increased percentage of plasma cells, large reticulum cells and epitheloid granulomas and histiocytes with lepra bacilli in ghost areas.[1–4] We observed large sudanophilic macrophages which showed on Romanowsky stains ample sky blue cytoplasm and small central nuclei in the bone marrow of these patients. While collections of lipid containing macrophages are seen in sphingolipidoses (Gaucher's disease, Niemann–Pick's and Sea-blue histiocyte syndrome), cells with similar morphology have been described in many other conditions including chronic granulocytic leukemia (CML), thalassaemia major, vitamin E deficiency, idiopathic thrombocytopenic purpura (ITP), hyperlipoproteinemia and sickle cell anemia.[5] To the best of our knowledge, so far, their presence has not been described in leprosy. The present study was planned to observe the occurrence of these macrophages in various types of leprosy and their morphological characterization.

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Material and methods

We studied 120 cases of leprosy in patients attending the leprosy clinic, irrespective of age and sex. While 48 patients had paucibacillary leprosy (PB), 72 patients had multibacillary (MB). In the former group 15 patients were new and in the latter, 17. All the other patients were receiving multidrug therapy (MDT) for a variable period. Erythema nodosum leprosum (ENL) was observed in 17 out of 55 MB patients receiving MDT. These patients were also receiving steroids to control the reactional state. The bone marrow (BM) was aspirated from the sternum/posterior superior iliac spine taking precaution to avoid contamination by the lepra bacilli present in the overlying skin and several smears were prepared. The BM smears were stained with Ramanowsky's stains including May–Grunwald–Giemsa (MGG), and Leishman, Ziehl–Neelsen's, Sudan black B, Prussian blue and periodic acid Schiff reaction (PAS).

Observations

Lipid containing macrophages were observed in the BM smears of 48 patients out of the 120 patients investigated. The percentage varied from occasional to 3·5% of all the marrow cells. The size of these cells varied from 20 to 50 μ. The nuclei were vesicular and central in location. The cytoplasm was ample and sky blue to deep blue in colour on MGG staining. Cytoplasmic granularity and foamy appearance as observed in sea-blue histiocytes[5] were noted in some of these cells. Cytoplasm was strongly positive for Sudan black B staining and a variable, generally weak positivity was observed for Prussian blue and PAS stains. Ziehl–Neelsen's staining revealed a diffuse faint pink coloration of the

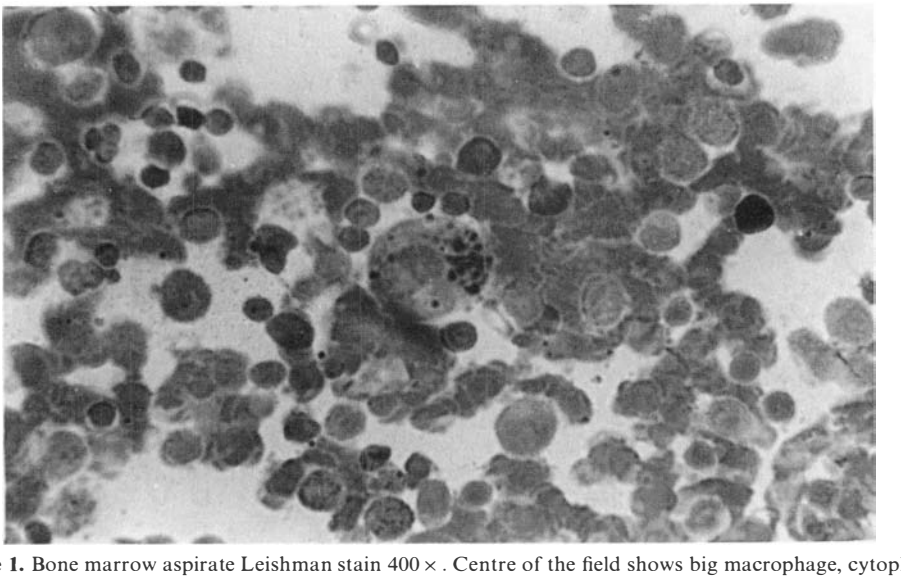

Figure 1. Bone marrow aspirate Leishman stain 400 × . Centre of the field shows big macrophage, cytoplasm shows coarse granularity.

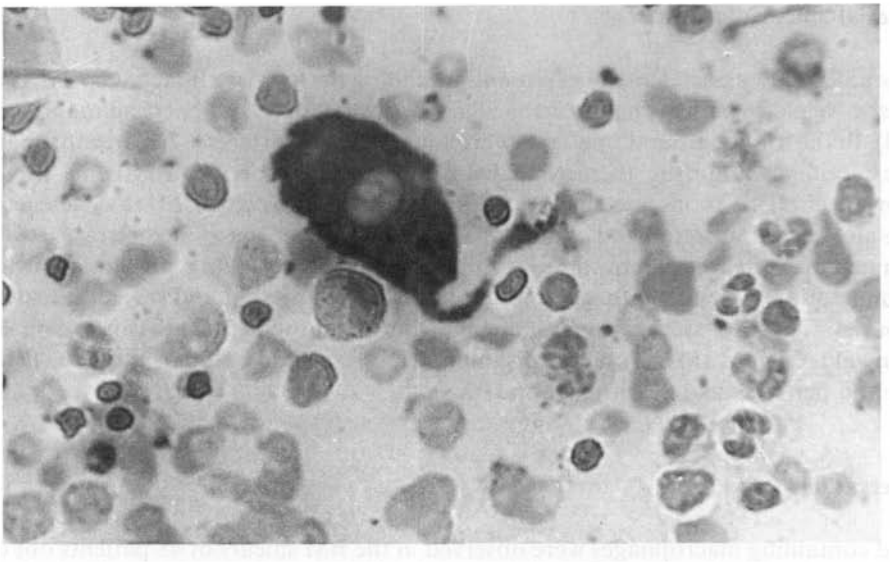

Figure 2. Bone marrow aspirate PAS stain 400×. The macrophage shows PAS positivity.

cytoplasm in some of the macrophages. However, definite structures identified as lepra bacilli were not observed in any of these macrophages. In this regard, it is interesting to note that such faint diffuse acid fastness may also have been seen with lipofuscin, the age pigment which is also derived from lipids.[6]

These macrophages could be differentiated from the foamy macrophages on the basis of their distinct sky blue to deep blue, and at times granular, ample amount of cytoplasm

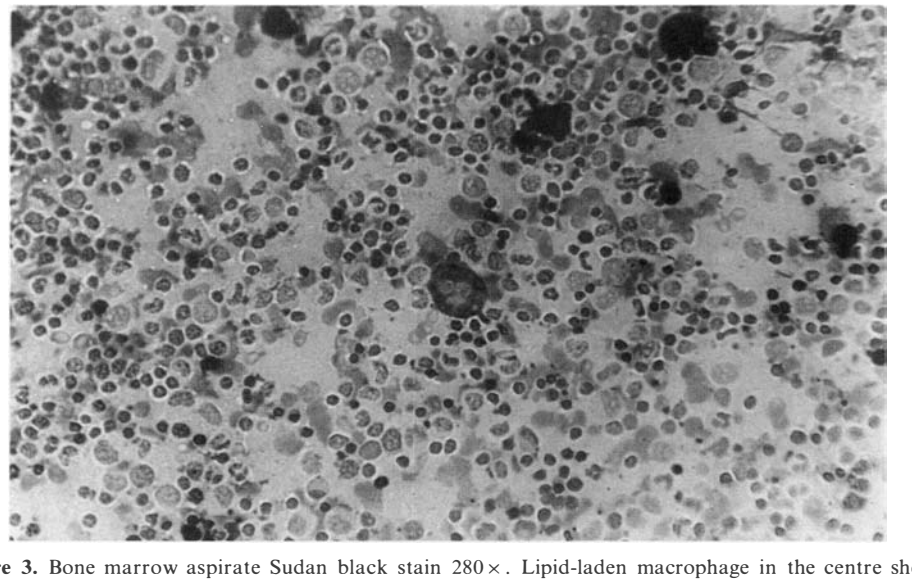

Figure 3. Bone marrow aspirate Sudan black stain 280×. Lipid-laden macrophage in the centre shows cytoplasmic positivity for Sudan black.

in Romanowsky stains that showed prominent bluish-black granularity on Sudan black staining, whereas the foamy macrophages did not show Sudan black positive granules and the foamy appearance was imparted by the presence of lepra bacilli with all of its morphological features demonstrated on Z–N staining. Similarly, the histiocytes with lepra bacilli in ghost areas may be considered a variant of foamy macrophages and can be differentiated from lipid-laden macrophages.[4]

As shown in Table 1 these macrophages were observed with a greater frequency in MB leprosy than PB. In both groups a higher frequency was noted in those receiving treatment compared with new patients, while 94% of 17 patients with ENL had these macrophages in bone marrow. Table 2 depicts the relationship of these macrophages with the bacillary load in bone marrow. It was observed that with an increasing bacillary load, an increasing percentage of patients had macrophages in the bone marrow.

Associated cytomorphological changes in bone marrow are shown in Table 3. The marrow with lipid-laden macrophages revealed a higher incidence of acid-fast bacilli, megaloblastic erythropoiesis, collections of foamy macrophages, collections of epithelioid cells and collections of plasma cells compared with the marrow which did not reveal lipid-laden macrophages.

Table 1. Incidence of lipid-containing macrophages in bone marrow

	No.	No. of marrow smears showing macrophages
Paucibacillary		
Total	48	5 (10·4%)
New cases	15	1 (6·6%)
Cases on treatment	33	4 (12·1%)
Multibacillary		
Total	72	43 (59·7%)
New cases	17	6 (35·2%)
Cases on treatment	55	37 (67·2%)
Cases with ENL	17	16 (94·1%)

Table 2. Relationship of lipid containing macrophages with bacillary load in bone marrow

	Paucibacillary		Multibacillary	
Bacillary load in bone marrow	No. of patients	No. of patients showing lipid macrophages in bone marrow	No. of patients	No. of patients showing lipid macrophages in bone marrow
Negative	40	1 (2·5%)	—	—
1–2+	8	4 (50%)	12	2 (16·6%)
3–4+	—	—	46	28 (60·8%)
5–6+	—	—	14	13 (92·8%)
Total	48	5 (10·4%)	72	43 (59·7%)

Table 3. Associated changes in bone marrow

	Bone marrow with lipid macrophages (48)	Bone marrow without lipid macrophages (72)
AFB	45 (93·7%)	13 (18%)
Megaloblastic erythropoiesis	38 (79·1%)	5 (6·9%)
Collection of foamy macrophages	12 (25%)	2 (2·7%)
Collection of epithelioid cells	4 (8·3%)	6 (8·3%)
Collection of plasma cells	21 (43·7%)	8 (11·1%)

Discussion

Inherited enzymatic deficiencies seen in sphingolipidoses (Gaucher's disease, Niemann–Pick's disease and sea-blue histiocyte syndrome) result in storage of lipids in macrophages and their accumulation in reticuloendothelial (RE) organs.[7] However, the appearance of these cells is nonspecific and similar histiocytes in smaller numbers have been described in the spleen or BM in many different hereditary and acquired conditions without any primary defect in enzymes.[8,9] These conditions include CML, thalassaemia, major ITP, hyperlipoproteinemia and sickle cell anaemia.[5] Such cells have been referred to as Gaucher-like cells and if the cytoplasm is blue, granular and foamy appearing on a Giemsa stain, as sea-blue histiocytes.[8,9] The lipids which accumulate in these cells are sphingolipids that have major structural functions in many cells and are found in cell membranes, including those of erythrocytes, leukocytes and platelets amongst others.[7] The blue–black staining of granules on Sudan black B suggests the presence of phosphatide or cerebroside.[10] In the hereditary lipoidoses, clear-cut deficiencies in specific catabolic enzymes have been well documented.[11] On the other hand, in the acquired conditions, overloading of normal lipid catabolic mechanisms seems likely, however, the mechanism of presence of these cells in secondary conditions is not precisely defined. In CML and thalassemia major, increased catabolism of myeloid and erythroid cells giving rise to glucocerebroside accumulation may be responsible.[7] In ITP, the accumulation of these cells may be related to the therapeutic use of steroids or the breakdown of platelets in macrophages.[12] Steroids facilitate the effect of adipokinetic agents in eliciting lipolysis of triglycerides of the adipose tissues.[13]

We observed these cells in all types of leprosy patients. The incidence was higher in MB leprosy compared with PB. In both groups the macrophages were discovered in a higher proportion of patients who were receiving treatment compared with new patients. The incidence was highest in patients with ENL who were receiving steroids as well. The percentage of such cells was in a range which indicated that these cells did not cause a significant reticuloendothelial overload. The associated findings in bone marrow included a higher incidence of demonstration of lepra bacilli, megaloblastic changes, collections of foamy macrophages, and collections of plasma cells in the marrow that showed these macrophages compared with negative marrow smears of such cells.

The observations suggest that lipid-laden macrophages in the bone marrow of leprosy patients may appear as a result of one or more of the following mechanisms:

1 Incomplete metabolism and degradation of lipids, phosphatides and lipopolysaccharides which are present in the cell wall of lepra bacilli.[14]
2 Treatment with steroids for a long period in patients having ENL.
3 Rapid cell turnover associated with megaloblastic erythropoiesis.

A high incidence of megaloblastic erythropoiesis in lepromatous leprosy has been documented.[15] Also, in the present study megaloblastic erythropoiesis was observed in association with these macrophages in most of the marrow samples.

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Les macrophages chargés en lipides dans la moelle osseuse des lépromateux

R Sen, P K Sehgal, V Dixit, Uma Singh, S D Chaudhary, R Sikka y V K Jain

Résumé Au cours d'une étude des changements cytomorphologiques de la moelle osseuse dans le cas de la lèpre multibacillaire, on observa des macrophages chargés en lipides semblables à ceux qui avaient été notés dans les sphingolipidoses. La présente étude fut réalisée pour observer l'apparition et les caractéristiques morphologiques de ces macrophages dans différents types de lèpre. Les résultats de l'examen de la moelle osseuse de 48 lépreux paucibacillaires et de 72 lépreux multibacillaire furent analysés. Les macrophages représentant tout au plus 3,5% des cellules de la moelle osseuse, furent obsevés chez 5 lépreux paucibacillaires et chez 43 lépreux multibacillaires. La plus forte incidence fut observée chez les patients souffrant d'ENL (16/17). Les lipides dans le cytoplasme de ces cellules pourraient provenir des lipides de la paroi du *Mycobacterium leprae*. Pour autant que nous le sachions, jusqu'à présent, ces cellules n'ont pas été rapportées dans le cas de la lèpre.

Los macrofagos cargados con lipidos en la medula osea de los pacientes leprosos

R Sen, P K Sehgal, V Dixit, Uma Singh, S D Chaudhary, R Sikka y V K Jain

Resumen Durante un estudio en la que se observaban cambios citomorfológicos de la médula ósea, se notaron macrófagos cargados con lípidos como las que se observan en casos de esfingolipidosis. El estudio actual fue planificado para observar la occurencia y caracterización morfológica de estos macrófagos en various tipos de lepra. Se analizó la información sobre las médulas óseas de 48 casos de lepra paucibacilar y 72 casos de lepra multibacilar. Los macrófagos, que representaban un máximo del 3,5% de las células óseas, fueron observados en 5 casos de lepra paucibacilar y en 43 casos de lepra multibacilar, con una incidencia máxima en los pacientes con ENL (16/17). Es posible que el lípido presente en el citoplasma de estas células derive del lípido de la pared celular de *Mycobacterium leprae*. Somos del parecer que hasta ahora no se ha informado este hecho en conexión con la lepra.

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Squamous cell carcinoma in chronic ulcers in leprosy: a review of 38 consecutive cases

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Summary The histories of 38 consecutive cases of squamous cell carcinoma (SCC) arising in chronic ulcers of leprosy patients treated between 1981 and 1990 at the McKean Rehabilitation Centre, Northern Thailand were analysed retrospectively. The study included 37 individual patients; 29 males and 8 females. The average age was 60 years, the average duration of leprosy was 34 years and the average duration of ulcers was 12 years. Most patients (76%) came from leprosy settlements. Patients with borderline–tuberculoid (BT) leprosy were most commonly affected (63%), followed by lepromatous (LL) leprosy (21%) and borderline–lepromatous (BL) leprosy (16%). Four patients (11%) had histories of SCC on other extremities. Metastatic spread was observed in 2 cases (5%), both instances leading to death. The commonest site of involvement of SCC was the foot, but it was seen on the knee in 1 patient and on the hand in 2 others.

The incidence rate of SCC in the group at risk (leprosy patients with disability grading 1 and 2) is calculated as being 0·79 : 1000 per year. SCC was seen in 1·8% of all cases admitted for ulcer care at the Centre. Treatment is by radical amputation.

SCC in chronic ulcers in leprosy patients cannot be considered rare and emphasizes the need for an active policy of disability prevention in leprosy programmes.

Introduction

Squamous cell carcinoma (SCC) developing in chronic ulcers of leprosy patients was first described in 1942.[1] Only in 1964 was it mentioned again explicitly, in an article reporting on the case histories of 4 patients in India.[2] Since then several articles have appeared on the subject, mostly from India and mainly they are accounts of individual cases.[3–24] Only three articles have dealt with a larger series of patients, 13, 16 and 12 cases respectively.[5,9,18] At the present time (1991) about 76 instances of SCC in leprosy have been reported. It would appear from the evidence of published case reports that the incidence of SCC in leprosy is very low. It has been mentioned by several authors that the complication is perhaps commoner than the literature suggests, but there are no epidemiological studies available to shed more light on this matter. In this paper we report

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on 38 consecutive cases of SCC in chronic ulcers of leprosy patients seen at our centre between 1981 and 1990. It is a retrospective study primarily aimed to elicit some of the epidemiological circumstances concerning SCC in patients with leprosy.

Patients

The McKean Rehabilitation Centre in Chiang Mai, Northern Thailand, has been a (church-related) treatment institute for leprosy patients since 1908. It serves patients from the Northern Thailand area (population approximately 10 million). The case histories of all leprosy patients admitted to the Centre from 1981 to 1990 and diagnosed with squamous cell carcinoma in a chronic ulcer were reviewed. The diagnosis was made clinically and usually confirmed histologically by the Pathology Department of Chiang Mai University Hospital. SCC arising from other skin conditions in leprosy patients (such as Bowen's disease, as seen in 2 cases during the study period), were not included.

Results

A total of 38 cases of SCC in chronic ulcers were seen during the 10-year period, involving 37 individual patients (Table 1). All patients came from Northern Thailand. Of the 37 patients, 29 (78%) were males and 8 (22%) females. The average age (male and female) at time of diagnosis was 60 years (ranging from 36 to 82 years); the average age of males was 61 years (ranging from 44 to 82 years), the average age of females was 56 years (ranging from 36 to 61 years). Of all patients, 28 (76%) came from special leprosy settlements, the others lived independently. The distribution of the leprosy classification (Ridley–Jopling) was as follows (see also Table 4): borderline–tuberculoid (BT): 24 (63%); borderline–lepromatous (BL): 6 (16%) and lepromatous (LL): 8 (21%). The average duration of leprosy at the time of diagnosis was 34 years, ranging from 10 to 60 years. The average duration of the ulcer was 12 years, ranging from 1 to 40 years. All but 2 patients had been treated with dapsone at some stage and all were skin-smear negative.

Four patients (11%) had a history of SCC in a chronic ulcer on another extremity: 3 were diagnosed in the decade preceding our investigation period; 1 patient (a male with BT leprosy) was diagnosed with SCC twice during the 10-year period—in 1985 on the left hand and in 1988 on the right foot. In 35 cases (92%) the SCC was localized on the foot

Table 1. Instances, per year, of squamous cell carcinoma in chronic ulcers diagnosed at the McKean Rehabilitation Centre

	Year									
	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990
Male	2	3	4	3	4	1	1	5	4	3
Female	0	0	0	0	1	5	0	1	0	1
Total	2	3	4	3	5	6	1	6	4	4

(right foot: 12, left foot: 23). The tumour was explicitly described as being on the forefoot in 15 cases and in 5 cases on the heel. In the remaining cases the tumour was either localized elsewhere on the foot (mid-sole, dorsum or ankle) or it was not possible to determine the origin of the tumour exactly due to its extent. In 1 case the SCC was localized on the extensor side of the left knee and in 2 cases on the palm of the left hand.

The appearance of the ulcer was described as 'fungating' or 'cauliflower growth' in 20 patients. Other, less explicit, descriptions were used in the remaining cases such as: 'nonhealing ulcer', 'suspicious ulcer' etc. Secondary spread of the cancer was seen in 2 patients (5%); in both cases it lead to death.

The first patient was a 62-year-old male from a leprosy colony classified with borderline–tuberculoid (BT) leprosy of 40 years duration. Ulcers on the right foot had existed for at least 20 years. In 1981 he was admitted and diagnosed on clinical grounds with a squamous cell carcinoma on the right sole. No mention was made of enlarged inguinal nodes. A below knee amputation was performed and the patient was discharged after a normal recovery. He was seen again 4 years post-operative with a large ulcer in the popliteal fossa of the right leg and large, hard inguinal glands, also on the right side. Biopsy of the ulcer revealed a squamous cell carcinoma, moderately differentiated. An above knee amputation was done, but soon after multiple hard subcutaneous nodules appeared between the suture line and the groin. The general condition of the patient deteriorated rapidly and he died 4 weeks after surgery. The cause of death was registered as metastasis of squamous cell carcinoma primarily located in the right foot.

The second patient was a 58-year-old male, classified with lepromatous (LL) leprosy of 25 years duration. He had had ulcers on the left foot for at least 17 years. When he was seen by us his left foot had almost ulcerated away and only a foul-smelling mass was visible. He had large, painful inguinal nodes on the left side. A below knee amputation was done and the stump recovered well. The inguinal nodes, however, continued to grow. Three months post-operative they were described as hard, irregular, lobulated and some with fluctulent centres. The tumour grew slowly over the next year and started to ulcerate and become more painful. His general condition remained stable and the patient refused all medical assistance. Sixteen months after the operation his condition deteriorated; he started to lose weight and a persistent cough developed. He died 2 months later. Death was registered as being caused by secondary metastatic spread of squamous cell carcinoma of the left foot. No autopsy was carried out.

By 1991 none of the other patients had died from reasons related to the SCC for which they were treated.

Histological confirmation of the diagnosis was obtained in 28 (74%) cases. In all cases the pathologist reported squamous cell carcinoma, in 23 cases described as being well differentiated. In 1 case it was characterized as 'infiltrating', in 1 case as 'moderately differentiated' and in the remaining 3 reports no further specification was given.

Discussion

This study confirms previous observations that SCC in leprosy patients arise in ulcers of long duration. The average duration of the ulcer was 12 years. In reality this average duration was probably higher, because in order to establish the duration of an ulcer, only figures relating to ulcers observed and reliably recorded in the clinical notes were

considered. In fact, many ulcers may have existed longer. On the other hand, ulcers often healed for some time only to break down again. Thus the 'duration of ulcer' refers to the period during which there was definite ulceration at the site involved. It was not possible to determine accurately the time when malignant transformation occurred. Usually the patients were not aware of any particular change apart from the fact that the ulcer gradually became worse. The average age of the patients was 60 years and the average duration of leprosy 34 years. More males were affected than females.

The 'pool' of leprosy patients serviced by the Centre was 6190 at the beginning of 1981 and had increased to 6862 by the end of 1990. This increase (11%) takes into account both the number of new registrations and the number of deaths reported to us. The percentage with disability in this group (grade 1 or 2 as defined by the WHO[25]) is 78%. This figure did not change between 1981 and 1990. The group at risk (at the beginning of 1981) of developing or having ulcers can therefore be put at 4834. The number of instances of SCC diagnosed during the 10-year period was 38 or an average of 3·8 per year. The incidence rate of SCC amongst the population at risk is therefore 0·79:1000 per year (Table 2). The incidence rate in females is only slightly less than in males, the difference not being significant. The age group specific rates are given in Table 3. The highest incidence rate is in the age group 60–69 years: 1·93:1000 per year. SCC occurred most frequently in

Table 2. Incidence rate of squamous cell carcinoma in the group at risk (leprosy patients with disability grading 1 and 2)

	Total no. of patients	Disability grading 0	Disability grading 1 and 2 (risk group)	Instances of SCC	Incidence rate per 1000 per year
Male	4439	907	3532	30	0·85
Female	1751	449	1302	8	0·61
Total	6190	1356	4834	38	0·79

Table 3. Incidence rate of squamous cell carcinoma in the group at risk (leprosy patients with disability grading 1 and 2)

Age group (years)	Total no. of patients	Disability grading 0	Disability grading 1 and 2 (risk group)	Instances of SCC	Incidence rate per 1000 per year
0–9	21	15	6	0	0
10–19	232	145	87	0	0
20–29	680	262	418	0	0
30–39	1119	266	853	1	0·12
40–49	1526	273	1253	4	0·32
50–59	1301	220	1081	15	1·39
60–69	775	100	675	13	1·93
70–79	403	64	339	4	1·18
>80	133	11	122	1	0·82
Total	6190	1356	4834	38	0·79

Table 4. Incidence rate of squamous cell carcinoma in the group at risk (leprosy patients with disability grading 1 and 2), using the Ridley–Jopling leprosy classification

Classification	Total no. of patients	Disability grading 0	Disability grading 1 and 2 (risk group)	Instances of SCC	Incidence rate per 1000 per year
TT	1137	346	791	0	0
BT	1394	208	1186	24	2·02
BB	270	83	187	0	0
BL	1025	228	797	6	0·75
LL	2122	422	1700	8	0·47
U*	242	69	173	0	0
Total	6190	1356	4834	38	0·79

* Unknown, other (indeterminate, pure neural).

borderline–tuberculoid (BT) patients (Table 4). The incidence rate in the BT group was 2·02:1000 per year. Borderline–lepromatous (BL) was less commonly involved with an incidence rate of 0·75:1000 per year, and lepromatous leprosy (LL) patients showed an incidence rate of only 0·47:1000 per year. The finding of high involvement of patients in the total borderline group (BT and BL) is in accordance with previous reports and most likely reflects the degree of nerve damage (anaesthesia) as frequently found in borderline cases. During the 10-year study period there were 2129 admissions in the Centre for ulcer care. The percentage of admissions for treatment of ulcers being malignant was 38 out of 2129 or 1·8%. There was no significant change in frequency during the 10-year study period.

Of all patients diagnosed with SCC, 28 (76%) came from special leprosy settlements or colonies. In Northern Thailand both the Thai government and non-governmental organizations have settlements. The total number of patients living in these settlements is approximately 1100. Virtually all the patients have disabilities because this was often the reason for them entering the settlement. Most members of these settlements would be referred to the McKean Rehabilitation Centre for treatment requiring hospitalization, especially in the case of ulcers. The incidence rate of SCC amongst this group is 2·55:1000 per year.

The tumours were usually localized on the foot, the most common site of neuropathic ulcers in leprosy patients. In contrast to the report of Fleury & Opromolla,[9] the proximal third of the foot was not the commonest site of involvement in our group; the heel was identified as the origin of the tumour in only 5 cases, while the forefoot was affected in 15 cases. Interestingly, the left foot was involved nearly twice as often as the right foot. In 2 cases, the tumour was on the palm, a feature only reported once before.[12]

Another noteworthy finding was that 4 patients had SCC on different (unrelated) sites, diagnosed either before or during the 10-year study period. One wonders if, apart from the time factor, genetic or environmental factors are involved in the pathogenesis of these cancers in chronic ulcers.

The prognosis after treatment of SCC, usually by amputation, is very good. However, 2 patients in our series (5%) died from metastatic spread of the cancer, highlighting the potential danger of this complication. On the other hand, secondaries only seem to occur

after several years and early, radical treatment should be able to avoid this happening. Regional lymph nodes are often enlarged due to the infected tumour on the extremity. These septic lymph nodes settle down after the primary focus of infection is removed. It is not routine in the Centre to take biopsies from these nodes, following the advice of Andersen[8] to leave these 'severely alone' in order to prevent chronic, fistulating lesions. Only when regional lymph nodes fail to resolve after amputation, is further histological investigation indicated.

Pathohistological examination, done in 74% of our cases, was usually reported as squamous cell carcinoma, well differentiated. In the remaining 26% no biopsy was taken because the clinical diagnosis seemed adequate and treatment (amputation) would not have been influenced by the pathology report because of the size and extent of the tumour. It has been argued that so-called malignant growths arising in chronic ulcers in some cases are really instances of pseudoepitheliomatous hyperplasia.[5,21] This is considered benign and therefore would justify a more conservative approach in treatment such as local excision or repeated curettage. But Fleury & Opromolla[9] remark that the distinction between a hyperplastic pseudoepitheliomatous reactivity and a well-differentiated carcinoma is very difficult in preoperative biopsies. They analysed their cases on the infiltrative features of the epithelial projections of the tumours and considered the lesions malignant by analogy with other human neoplasms such as the giant condyloma acuminatum and the epithelioma cuniculatum pedis. We encountered this problem of distinction in one case where the initial biopsy as reported was, 'chronic and acute inflammation with pseudoepitheliomatous hyperplasia'. A second biopsy, taken only 1 month afterwards, was reported as showing a well-differentiated squamous cell carcinoma. In another biopsy report it was explicitly noted that 'most areas have the appearance of pseudocarcinomatous hyperplasia, with differentiated cells and inflammatory infiltration. However, small foci of true squamous cell carcinoma are present, which are poorly demarcated from the surrounding stroma. These cells show individual keratization and atypia of nuclei'. It is clear that biopsy reports cannot be conclusive in deciding on therapeutical measures. Biopsies are not always from the right location or not taken deep enough into the tumour mass, and pathological features can be difficult to interpret. Clinical features such as the extent of the ulcerous fungating process and radiological evidence of bone involvement must be taken into consideration. We are in favour of radical amputation, either of the forefoot (if possible) or otherwise below the knee. With the availability of a good prosthesis workshop, disability can be kept to a minimum.

In summary one could say that the profile of our 'typical' leprosy patient with SCC is a 60-year-old male with borderline–tuberculoid (BT) leprosy of 34 years duration, living in a leprosy colony. There have been (plantar) ulcer problems for at least 12 years before presenting with SCC.

The incidence rate among the risk group (leprosy patients with disability grading 1 and 2) is 0·79:1000 per year. Of all patients with ulcers admitted to the Centre, 1·8% were diagnosed as having a malignant ulcer. SCC in chronic ulcers of leprosy patients cannot be considered rare and should be recognized in time. They lead to considerable disability (amputation, often below the knee) and even to death in 5% of the cases due to metastatic spread. The occurrence of SCC in chronic ulcers emphasizes once again the need for an active policy of disability prevention in leprosy programmes.

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Epithelioma spino-cellulaire accompagnant des ulceres chroniques chex les lepreux: un examen de 38 cas consecutifs

J H Richardus et T C Smith

Résumé Une analyse fut faite respectivement des antécédents de 38 cas consécutifs d'épithélioma spino-cellulaire (SCC) accompagnant des ulcères chroniques chez des lépreux traites entre 1981 et 1990 au centre de réadaptation McKean en Thaïlande du Nord. L'etude incluait 37 patients: 29 hommes et 8 femmes. La moyenne d'âge était de 60 ans, la durée moyenne de la lèpre était de 34 ans et la durée moyenne des ulcères était de 12 ans. La plupart des patients (76%) venaient de colonies de lépreux. Les patients de type borderline-tuberculoïde (BT) étaient le plus fréquemment affectés (63%), suivi de ceux souffrant de lèpre lépromateuse (LL) et de lèpre borderline-lépromateuse (BL) (16%). Quatre patients (11%) avaient des antécédents de SCC à d'autres extrémités. La présence de métastases à distance fut observée dans 2 cas (5%), causant dans les deux cas le décès du patient. Le pied était l'endroit où le SCC se manifestait le plus fréquemment mais chez un patient, c'était le genou qui était atteint et dans deux autres cas, c'était la main qui était atteinte.

Le taux d'incidence de SCC dans le groupe à risque (patients lépromateux avec une invalidité de 1 et 2) est de 0,79 pour 1000 par an. Le SCC fut noté dans 1,8% de tous les cas admis à notre dispensaire suite à un ulcère. Le traitement est l'amputation radicale.

Le SCC dans le cas des ulcères chroniques chez les lépreux ne peut être considéré comme rare et c'est pourquoi une politique de prévention active de l'invalidité dans le cadre du programme de la lèpre est nécessaire.

Carcinoma escamocelular en las ulceras cronicas de la lepra: un estudio de 38 casos consecutivos

J H Richardus y T C Smith

Resumen Se analizaron los antecedentes de 38 casos consecutivos de Carcinoma Escamocelular (SCC) que resultaron de las úlceras crónicas de pacientes leprosos tratados entre 1981 y 1990 en el McKean Rehabilitation Centre, Tailandia del Norte. El estudio comprendió 37 pacientes individuales; 29 hombres y 8 mujeres. El promedio de edad era 60 años, el promedio de duración de la lepra era 34 años y el promedio de duración de las úlceras era 12 años. La mayoría de pacientes (76%) eran de colonias leprosas. Los pacientes con lepra tuberculoide (BT) marginal dudosa eran los que más eran afectados, seguidos por los con lepra lepromatosa (LL) (21%) y los con lepra lepromatosa marginal (BL) (16%). Cuatro pacientes (11%) tenían antecedentes de SCC en otras extremidades. Se observó la diseminación metastática en dos casos (5%), ambos casos culminando en la muerte. El sitio más común para la SCC fue el pie, pero se observó en la rodilla en un paciente y en la mano en dos otros.

La incidencia de la SCC en el grupo de más riesgo (pacientes leprosos con incapacidad de 1 y 2) se calcula en 0,79 por 1000 por año. Se observó la SCC en 1,8% de todos los casos que se recibieron para el tratamiento de úlceras en neustro centro. El tratamiento es por amputación radical.

No se debe considerar rara la SCC en los pacientes con úlceras crónicas ye esto hace resaltar la necesidad para una política activa para la prevención de incapacidad en el programa de la lepra.

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Nasal myiasis in leprosy

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Summary Infestation of the nose with larvae of certain files can occur in leprosy patients. This results in severe distress and agony and can cause extensive tissue damage. The predisposing factors, clinical presentation and treatment is described.

Introduction

The term myiasis is derived from the Greek word 'Myia' meaning a fly. Myiasis is infestation of living tissues by larvae of flies.[1]

A proportion of leprosy patients having open ulcers and wounds get infested with larvae at some time or other. The larvae of certain flies (maggots), are seen frequently in nose and plantar ulcers; sometimes wounds in hands are also infested.[2]

We got interested in the problem for the following reasons: The nasal fistulae in leprosy patients, an outcome of neglected nasal myiasis, when presented at one of the clinical meetings surprised many. The number of patients that we see, their suffering and scant literature about the problem in leprosy patients, were other compelling reasons. Here we report our experience with nasal myiasis in leprosy patients and its management.

Materials and methods

The patients with nasal myiasis usually presented with facial cellulitis. They described a feeling of gnawing, crawling and irritation inside the nose and forehead, headache and nasal obstruction (Figure 1).

Blood mixed with mucus was seen dripping from the nose. Frank epistaxis was also seen, though rarely. Patients were disinterested and apathetic but in severe agony. At times a history of larvae dropping out of the nose was also obtained.

Some of the cases presented only with complaints of blood mixed with a thin mucus

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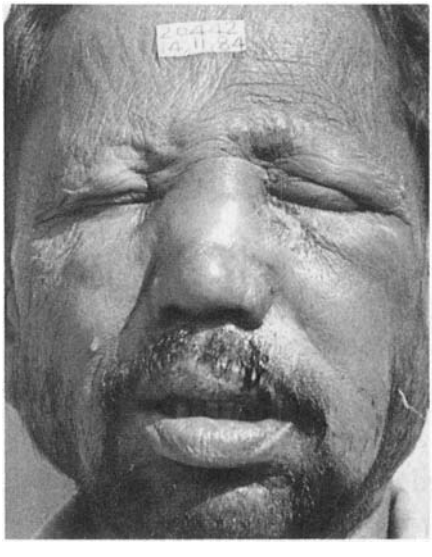

Figure 1. Cellulitis face.

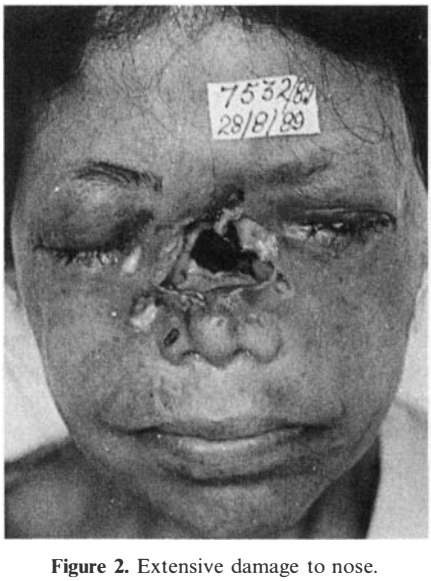

Figure 2. Extensive damage to nose.

discharge from the nose. Rarely they presented at an acute stage with extensive damage to the nasal tissues (Figure 2). Recurrent infestation was also seen.

The cases were hospitalized and their nasal cavity was irrigated with a turpentine: water mixture (1:10) twice daily, asking the patient to blow his nose immediately after irrigation. The nostrils were lightly plugged with a ribbon gauze soaked in a turpentine: water mixture after instilling a few drops of liquid paraffin. The procedure was continued till the nasal discharge subsided.

In addition, the patients were given systemic antibiotics, Aspirin and diazepam orally till the cellulitis settled down. At the time of discharge from the hospital, patients were advised about routine nasal care.

Observations

The patients of lepromatous and borderline lepromatous leprosy were involved in this problem and the majority of them were seen between September and the early part of December when the mean temperatures were around 25°C and the humidity 80–90%. Most of the cases were from the poor strata of society, middle-aged and usually males suffering from leprosy for 3 years or more.

The nasal cavity was completely free of maggots in 48–72 hr after starting treatment. However, local cellulitis lasted for about 7–10 days.

Discussion

Nasal myiasis in leprosy has been reported by Rao[5] and Bose[6]. Maggot infestation indicates a chronic debilitated condition of the patients. The patients were unhygienic, unhealthy and had foul smelling discharge from the nose.

Nasal involvement in leprosy is almost always seen in BL and LL types.[3,4] In untreated cases, the nasal mucosa ulcerates and soon gets covered with a mucopurulent exudate which on secondary infection gives a foul odour and attracts flies. In due course, exudates dry up and adhere to mucosa forming a plug and giving a feeling of nasal obstruction. As a result, patients pick their nose to remove this plug, further injuring the nasal mucosa in the process. Atrophic rhinitis seen in lepromatous leprosy patients also predisposes to nasal myiasis. It is likely that patients contaminate their noses while picking or wiping with dirty clothes. The possibility of flies entering the nose during sleep and laying eggs, as suggested by Rao,[5] seems unlikely because the flies are quite large.

To begin with the larvae, at least some of them if not all, live on putrid discharges and necrotic mucosa. Later as they grow, they burrow deeply, firmly anchoring themselves to the surrounding living tissues, the end result being tissue destruction.

Severe infestation, if neglected, can lead to extensive tissue destruction. Full thickness of the nasal wall when eaten away results in a nasal fistula (Figure 3). Occasionally the larvae burrow deep into the floor of the nasal cavity and eat away the bony palate to produce a palatal fistula (Figure 4). These fistulae are difficult to treat because of intense scarring. Nasal myiasis can prove fatal if cavernous sinus thrombosis sets in or the floor of the cranium is invaded.

It was observed that the number of live maggots removed from the nose is much less than from plantar ulcers. Probably the maggots are deeply embedded posteriorly in the nose. The dead maggots are coughed out mixed with discharges or else patients suffering from nasal myiasis present late when maggots start dropping off. Deep posterior burrowing of maggots makes their manual removal difficult.

Myiasis is common between September and December (postmonsoon season) in this part of the country though a few scattered cases can be seen throughout the year. The reason for this appears to be climatic with the prevalence of flies being high during that

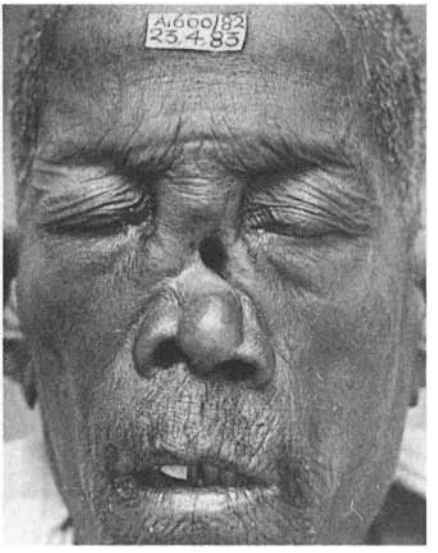

Figure 3. Nasal fistula.

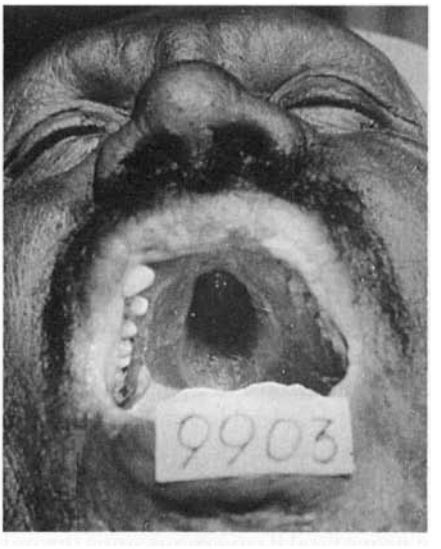

Figure 4. Palatal fistula.

time. Flesh-eating flies *Chrysomia bezziana* and *Sarcophaga ruficornis* of the order diptera were found to infest the cases of this study (Figures 5 and 6).

The aim of treatment is to remove the maggots, kill them to prevent maturation, promote wound healing and prevent secondary complications.[7] Numerous medications have been used to clear the infestation. Some of these are: chloroform, ether, phenol, camphor, mercurous chloride, turpentine oil and eucalyptus oil.

The use of oily substances makes the surface slippery and interferes with the anchoring

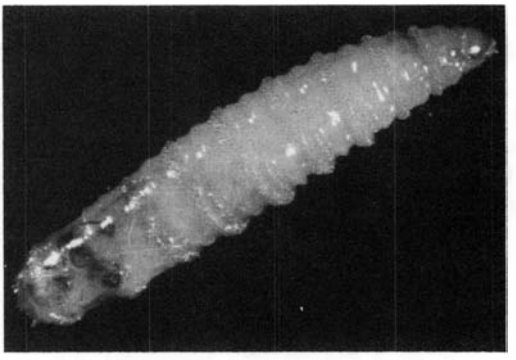

Figure 5. Maggot (larvae—*C. bezziana*).

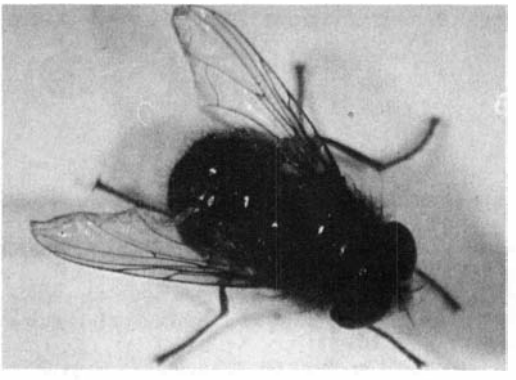

Figure 6. Fully grown fly (*C. bezziana*).

of larvae. An oily film prevents the larvae from breathing so that they come to the surface and fall off. Liquid paraffin is a nonirritating agent which serves the purpose well but in addition some larvicide like chloroform or a repellant like turpentine oil is also required. Irrigation with chloroform and/or a turpentine: water mixture followed by light packing with the same solution rapidly clears the nasal cavity. Instillation of a few drops of liquid paraffin in the nose prevents crust formation and helps healing.

These cases require systemic antibiotics and Aspirin to prevent further complications. Anxiolytics are needed to reduce restlessness. These drugs are continued till facial cellulitis subsides.

As stated earlier, sometimes an extensive invasion by maggots can lead to loss of the full thickness of nasal tissues producing defects—nasal fistulae.

These fistulae can vary greatly in size and are difficult to repair because of scarring in the surrounding tissues and persistent nasal ulcers. Other associated abnormalities like palatal perforation, collapse of nasal architecture, partial absorption of nasal bones and deformities like deviation of nasal columella might exist along with nasal fistulae.

Once the surrounding inflammation and oedema subsides and the tissues settle down, these fistulae can be repaired using standard techniques with suitable modifications. We preferred to use the locally available skin for such repairs because it was a better colour

match and healed better. The results were satisfying to the patients, improving their appearance. Bone grafting was not done because the disease was active and there was risk of graft absorption.

To prevent nasal myiasis patients need to be educated about routine nasal care and hygiene. Instillation of oily nasal drops (liquid paraffin with eucalyptus oil) prevents crust formation and nasal obstruction. Partial closure of nostrils using local mucosal flaps (Young's procedure)[8] has been tried by us successfully in a few cases to prevent recurrence.

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Myiase de la muqueuse nasale chez les lépreux

S Husain, G N Malaviya, A Girdhar, Sreevatsa et B K Girdhar

Résumé Les larves de certaines mouches peuvent être la cause d'une infestation des muqueuses nasales chez les lépreux qui résultent en des douleurs graves et intenses et peut causer d'importantes lésions tissulaires. Les facteurs de prédisposition, le tableau clinique et le traitement sont décrits.

Miasis nasal en la lepra

S Husain, G N Malaviya, A Girdhar, Sreevatsa y B K Girdhar

Resumen La infestación de la nariz con larvas de ciertas moscas puede ser observada en pacientes con lepra. Esto resulta en gran dolor y agonía y puede causar un extenso daño al tejido. Se describen los factores de predisposición, la presentación clínica y el tratamiento.

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An educational approach to leprosy control: an evaluation of knowledge, attitudes and practice in two poor localities in Bombay, India

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Summary Based on the hypothesis that a systematic, carefully planned educational approach to leprosy would yield results in terms of knowledge, attitudes and case presentation superior to those of the established and traditional mass survey method, ALERT-India launched a programme in S ward of Bombay in February 1985, to compare the two. An intensive programme of health education, using trained teams, was carried out in one zone of this ward over a period of 12 months. Eight months later, mass survey work (as used routinely in previous years and on a country-wide basis) was carried out in an adjacent zone. In 1987, the Centre for Social and Technological Change in Bombay, in association with the School of Oriental and African Studies, University of London, was requested to evaluate the effect of the above educational approach in terms of knowledge, attitudes and practice in both the trial and control zones. Other aspects of this experimental approach, including its cost and effectiveness in identifying cases of leprosy, will be published separately. The design of the 'KAP' evaluation and the social and environmental controls introduced in the statistical analysis are described. The results pointed to a considerable degree of ignorance about leprosy as a disease (and its treatment) in both the study and the control zones. Knowledge about early symptoms was particularly weak and on all aspects scores for women were invariably lower than men. General education enhanced the absorption of specific knowledge, and the education of children compensated adequately for lack of parental education in this respect. Overall the evaluation indicated that the intensive educational approach was superior to the survey approach in terms of improving knowledge, attitudes and practice.

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Introduction

ALERT-India is a voluntary organization committed to the control of leprosy in the eastern suburbs of Bombay, by identifying and treating early cases of leprosy, and by enlightening the public on various aspects of the disease.[1] The prevalence rate for leprosy in Bombay is believed to be between 10 and 15 cases per 1000 population,[2–4] and the city is listed as a hyperendemic district by the National Leprosy Eradication Programme.[5] The neighbourhoods covered by ALERT consist mainly of slum settlements, with an aggregate population of some 400,000. For case detection the main tool has been the door-to-door survey, during which some educational material is disseminated, mainly in the form of leaflets. The educational component is backed up by slide or film shows at local schools, factories, and community meeting places.

A major drawback of the mass survey method is that it is time consuming. Further, as the approach is one of 'seeking out' the patient, and following him or her up to ensure completion of the required treatment, patient conviction and motivation are sometimes lacking. Finally, as an educational tool, the method has disadvantages. Whatever education is imparted mainly reaches the patients as a result of treatment and follow-up. Non-patients receive only perfunctory information at the time of the initial door-to-door examination, and the community-level programmes are spread too thinly over the population, whose attendance at these events is sometimes meagre.

Methodology

In 1985 ALERT launched an experimental approach designed to eliminate these drawbacks. Over a 12-month period a well-defined slum community (referred to as L zone) was visited by a health education team, which held a film or slide show at the end of every road or lane. Leaflets were distributed door-to-door. Posters and stickers were widely displayed and talks and exhibitions held at the community level. In short, the approach was one of intensive education, rather than mass survey and more peripheral education.

This paper reports the results of a subsequent evaluation of knowledge, attitudes and practice carried out in 1987 in L zone by the Centre for Social and Technological Change.[6] A questionnaire was presented to 200 residents; they were selected so that there should be 100 patients and 100 nonpatients. Similarly, in another community (referred to as M zone), where a mass survey had been conducted in 1985 8 months after the experiment in L zone, a further sample of 200, similarly selected, was used as a control. The questionnaire was designed to test the public's basic knowledge about, attitudes towards, and behavioural practice of relevance to the disease. Items for the test of knowledge consisted of a range of symptoms, the bacteriological origin of the disease, the transmission mechanism, and the curability and methods involved. Knowledge of symptoms was graded from basic knowledge (the existence of a skin patch), through an intermediate level (for example, absence of sensation on the patch) to a higher level (for example absence of hair or sweating on the patch). Use of a questionnaire to elicit responses on questions such as these may not be fully reliable in a semi-literate population. However, in Bombay the illiterate are more familiar with the ways of the modern world than they would be in a remote rural village, and in our experience are

unusually articulate. Furthermore, the investigators were paramedics working for ALERT, who would have some familiarity with testing opinions and knowledge in this population.

Results

In both zones the amount of knowledge absorbed was distressingly low: only 30% of respondents could recall the symptom classified as basic, roughly the same proportion recalled symptoms at the intermediate level, and 17% at the higher level. However, the difference between the experimental and control zones was brought out fairly clearly, with the experimental zone yielding a higher proportion of respondents with pertinent knowledge at all levels (a statistically significant difference at the two higher levels, as illustrated for the medium level in Table 1).

As the sample design was not stratified by social factors it would seem desirable to control for these statistically. Doing so reveals that, for example, in households where fewer than half of the adult members have achieved the middle school level of education, basic knowledge of symptoms is still further enhanced by the intensive education programme (though the effect in the better-educated households is unclear); medium level knowledge is also better in the experimental zone after general education controls are made. Similar findings are made regarding the knowledge that leprosy is caused by a 'germ': the differences between the zones are large, and statistically significant in the case of the less educated households (Table 2). This pattern of the superiority of the experimental zone over the control tends to repeat itself for most items of knowledge and is robust against the effect of general education differentials.

Respondents were canvassed on their attitude to different aspects of the disease: here responses from the patients proved most conclusive, with their willingness to accept the diagnosis and their confidence in the cure both being significantly enhanced by the intensive educational programme in comparison with the survey method (Table 3). This is a clear indicator of the better motivation achieved when patients have been identified by themselves (or their peers) rather than by visiting paramedics. Again the observation remains valid when controls for general educational attainment are introduced. However, some care in interpretation is needed here, in that a small proportion of patients will have

Table 1. Medium-level perception of symptoms by zone

	Zone		
	M	L	Total
Knowledge	46 (23·0)	77 (38·5)	123 (30·7)
Rest	154 (77·0)	123 (61·5)	277 (69·3)
Total	200 (100·0)	200 (100·0)	400 (100·0)

Difference between zones is significant at 5% level.

Table 2. Knowledge of germ according to educational composition of household

	Zone		
	M	L	Total
Less than 50% of educated adults in household			
Knowledge of germ	14 (11·2)	15 (22·7)	29 (15·2)
No knowledge	111 (88·8)	51 (77·3)	162 (84·8)
Total	125 (100)	66 (100)	191 (100)
More than 50% of educated adults in household			
Knowledge of germ	18 (25·0)	47 (36·4)	65 (32·3)
No knowledge	54 (75·0)	82 (63·6)	136 (67·7)
Total	72 (100)	129 (100)	201 (100)

Difference between zones is significant at 5% level in the lesser educated group. Difference between educational levels is also significant at 5% level.

already suffered some deformity, so that the concept of cure will have had some ambiguity for them since chemotherapy cannot repair the damage already done.

As far as practice is concerned, our questions were confined to eliciting information on how far people looked for symptoms in each other and motivated clinic attendance in suspected patients. Here the superiority of the experimental zone failed to emerge. However, 30% of patients in that zone claimed to have been motivated in that way

Table 3. Confidence of patients in cure

	Zone		
	M	L	Total
Confident of cure	71 (72·4)	84 (88·4)	155 (80·3)
Not confident	27 (27·6)	11 (11·6)	38 (19·7)
Total	98 (100·0)	95 (100·0)	193 (100·0)

Difference between zones is significant at 5% level.

(against only 11% in the control zone). It is possible that those motivating, though no greater in number, were more active and successful in L zone.

In some cases the superiority of the intensive education method was enhanced or diminished by other characteristics of the individuals surveyed (besides zonal residence). For example, overall educational attainment by adult members of the household nearly always strengthened the effect of the experimental method in imparting knowledge and in improving attitudes (see, for example, Table 2). More strikingly, relevant knowledge was increased by the presence of school-attendant children in the household, often compensating for the effect of lack of parental education. The sex of the respondent was another important differentiating characteristic. Women were in possession of less of the relevant knowledge than were men, even in the experimental zone.

Discussion

It should be stressed that this evaluation was not intended to test the superiority of case-detection in the experimental zone. Its purpose was purely to see whether the same levels of public awareness would be achieved by the cost-saving experiment of an intensive community-level educational approach in place of the laborious door-to-door survey technique. In fact both patients and non-patients who were subjected to the educational experiment showed superior awareness of important facts relevant to the prevention, cure and social understanding of the nature of the disease. This should constitute a step on the road towards the ultimate removal of stigma. Furthermore, since a higher proportion of those in the experimental zone claimed they were convinced that treatment would be effective, there is some reason to expect that non-compliance would be reduced. Some of the recent literature has linked compliance to the quality of information that is provided to the patient.[7] The outcome of our study has prompted ALERT-India to enhance the educational component in its existing survey programme.

The question may be raised, however, as to whether appropriate personnel would be readily available to replace the survey technique comprehensively with an intensive educational programme. The ALERT experiment drew on the existing skills of its health educators, and simply used more intensively the educational materials they already possessed. Our view (which in essence is shared by others)[8] is that at least the more experienced members of the existing paramedical corps could be adopted as health educators in the programme; they would need to be equipped with additional educational materials which would add to the resource cost, but only as a one-off expenditure. This would create a two-tier structure of paramedics, which would have the added advantage of offering promotional prospects as an incentive for the greater involvement of new recruits in the wider aims of the organization: by developing their understanding of and ability to interact with the community, rather than simply acquiring skills in case detection and delivery of curative services, they would be securing a career for themselves as a valuable cadre of health educators. At the same time, this awareness would ensure some much needed variety in the activities and career structure of paramedics, for whom the repeated combing of vast urban slums for new and recalcitrant patients is a tedious chore, as detrimental to the motivation of paramedics as to the compliance of their patients.[9]

Finally our study brings out the importance of seeking to involve specifically both

women and children in any health education programme. The less informed responses of women in both our zones underlines how any programme of information that relies upon the spontaneous attendance of women is likely in most cultures effectively to discriminate against women: special programmes for women's groups and appropriate timings for women to attend would seem to be the solution. At the same time, the fact that better informed respondents came from households where school-attending children were present suggests the value of carrying out leprosy education work in schools, especially in urban settings where attendance is high.

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Le contrôle de la lèpre grâce à l'éducation: une évaluation des connaissances, des attitudes et des habitudes dans deux localités pauvres de Bombay en Inde

N. Crook, R Ramasubban, A Samy et B Singh

Résumé Estimant qu'un programme éducatif bien conçu sur la lèpre donnerait des meilleures informations en matière de connaissances, d'attitudes et de dépistage des cas de lèpre que celles obtenues par les enquêtes traditionnelles à grande échelle, ALERT-India a lancé en février 1985 un programme de comparaison des deux méthodes dans le quartier S de Bombay. Un programme intensif de 12 mois d'éducation sanitaire faisant appel à des équipes entraînées fut organisé dans une zone du quartier. Huit mois plus tard, une étude à grande échelle (faite régulièrement dans tout le pays les années précédentes) fut menée dans une zone voisine. En 1987, le Centre pour le Changement social et technologique à Bombay en association avec la faculté des études orientales et africaines de l'Université de Londres fut prié d'évaluer l'effet du programme éducatif en matière de connaissances, d'attitudes et d'habitudes dans les zones d'essai et de contrôle. Les autres aspects de cette expérience y compris son coût et son efficacité en matière de dépistage des cas de lèpre, seront publiés séparément. Le rapport décrit la méthode d'évaluation des connaissances, des attitudes et habitudes ainsi que les contrôles sociaux et environnementaux inclus dans l'analyse statistique. Les résultats révèlent une ignorance profonde de la lèpre et de son traitement dans les zones faisant l'objet de l'étude et dans les zones de contrôle. La connaissance des premiers symptômes était particulièrement faible et à tout égard, les scores des femmes étaient constamment inférieurs à ceux des hommes. L'éducation générale favorisait l'assimilation de connaissances spécifiques et l'éducation des enfants compensait le manque d'éducation des parents dans ce domaine. Dans l'ensemble, l'évaluation indiquait que les résultats du programme intensif d'éducation étaient supérieurs à ceux de l'étude à grande échelle en matière d'élargissement des connaissances, d'attitudes et d'habitudes.

Un enfoque educacional del control de la lepra; una evaluación del conocimiento, actitudes y práctica en dos localidades pobres de Bombay, India

N Crook, R Ramasubban, A Samy y B Singh

Resumen Basándose en la hipótesis de que un enfoque educacional sistemático y cuidadosamente planeado de la lepra podria producir resultados superiores, en términos de conocimiento, actitudes y presentación de casos, a aquellos de los métodos de estudios en masa tradicionales y ya establecidos, ALERT-India lanzó un programa en el distrito S de Bombay en febrero de 1985, para comparar los dos métodos. Se llevó a cabo un programa intensivo de educación en la salud, usando grupos entrenados en una zona de este distrito durante un periodo de 12 meses. Ocho meses más tarde, se llevó a cabo un estudio en masa en una zona adyacente (como se usó en forma rutinaria en los años previos y basado en todo el país). En 1987, se le solicitó al Centro para Cambio Social y Tecnológico de Bombay, en conjunto con la Escuela de Estudios Africanos y Orientales, Universidad de Londres, que evaluaran el efecto del enfoque educacional mencionado arriba en términos de conocimiento, actitudes y práctica en las dos zonas, en la de control y en la en estudio. Otros aspectos de este enfoque experimental, incluyendo su costo y eficacia en identificar casos de lepra será publicado separadamente. Se describe el diseño de la evaluación 'KAP' y los controles sociales y medio ambientales introducidos en el análisis estadistico. Los resultados indican un considerable grado de ignorancia acerca de la lepra como una enfermedad (y su tratamiento) en ambas zonas, en la en estudio y en la control. El conocimiento acerca de los primeros síntomas fue particularmente pobre y en todos los aspectos las mujeres consiguieron invariablemente menos puntos que los hombres. La educación general mejoró la absorción de conocimiento específico, y la educación de los niños compensó en forma adecuada por la falta de educación de los padres en este aspecto. La evaluación, en forma completa, indicó que el enfoque educacional intensivo fue superior al enfoque de estudio en masa en términos de un conocimiento, actitudes y práctica mejoradas.

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Psychosocial aspects of deformed leprosy patients undergoing surgical correction

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Summary A psychosocial study was conducted on 25 randomly selected leprosy patients undergoing corrective surgical procedures for their deformities. High anxiety and depression levels found preoperatively, reduced significantly after operation. Psychiatric assistance is needed for these patients in order to clear their psychic aberrations, create awareness, boost morale and to give self-confidence.

Only 50–75% of preoperative expectations were satisfied but that was only in 40% of patients. This calls for a preoperative counselling session with the patients to help them reach the realistic goals that they can achieve. They should be told what benefits surgery can offer them and be made aware of the problems which will persist after operation, such as anaesthesia and analgesia.

Introduction

Leprosy predominantly affects the skin and peripheral nerves, which if damaged result in deformities of the face and extremities. It has been estimated that approximately 25% of leprosy patients are deformed. Patients with leprosy are very self-conscious of any deformity they have which they feel may advertise to others that they have or have had leprosy. The majority of these patients can benefit from surgery, and surgery is important in the overall rehabilitation of the patient.

Depression is the main psychological feature of patients with leprosy. A specific alteration in mood, sadness, loneliness, apathy and a negative self-concept is found. This may be associated with feelings of self-blame, self-disgrace or shame, self-punishing wishes and a desire to run away from everyday problems.

Anxiety is a common feature of many clinical states and it is reported to be significantly higher in leprosy patients. It is suggested that it creates worries, tension and irritation.[2]

Previous social and economic status are important factors in the rehabilitation of leprosy patients.[3] One study[4] concluded that reconstructive surgery helps leprosy

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patients, at least to some extent, to regain their cosmetic, functional, occupational and economic status in society.

The best results of surgery are obtained in patients with a positive outlook and having a favourable social and family environment, which aids resettlement and rehabilitation after surgery.

Various psychological aspects of leprosy are being investigated but there are few reports on deformed patients and even less on deformed patients undergoing surgery. This prompted us to undertake this preliminary study in order to find out the psychosocial status of the patients with deformities before and after surgical correction and also to assess:

1 The sociodemographic characteristics of leprosy cases who opted for surgical correction for the deformities.
2 The intelligence and personality make-up of these patients.
3 The depression and anxiety levels of these patients before and after surgical correction.
4 The expectations from surgery and its fulfilment after operation.

Materials and methods

The study was conducted at the Central JALMA Institute for Leprosy, Agra. The cases were selected at random from the group opting for corrective surgery and a final sample of 25 patients has been included in the study. The cases were hospitalized for 1 or 2 days as many of them had travelled long distances. This was done to eliminate the effects of travel and exertion. The patients were assessed a week prior to surgery and then every 3 months for 3 successive visits.

The tools for collection and analysis of data are:

The examination, which aims to ascertain from the patients information regarding their sociodemographic characteristics and details of leprosy, duration, type of deformity etc., and also their expectations of surgery.

Psychological evaluation using:[5]

Beck's depression inventory; Taylor's manifest anxiety scale test; Thematic apperception test (TAT); and Wechsler adult intelligence scale test as modified and adapted to Indian situations by Ramlingaswamy (1972).[6]

Beck's depression inventory

The inventory consists of 21 categories of symptoms and attitudes. Each category describes a specific manifestation of depression in a graded series of four to five self-evaluative statements. Numerical values of 0 to 3 are given to each statement reflecting neutrality to maximum severity. The tester reads the statements in each category while the patient follows from his own answer sheet and he is asked to circle the number of the statement which best describes him at that particular moment. The total score is obtained by summing up the scores of the individual's symptom categories. The inventory has been shown to be reliable, consistent and valid in several studies.

Taylor's Manifest Anxiety Scale

This scale provides scores for anxiety. The scale has a list of forty items. It is a self-administering scale and gives better results with individual testing rather than group testing. In a group situation the tester can also get quite appropriate results after establishing a good rapport with the testee. If the subject was illiterate, he was asked to hear and follow the statement. If the subject was literate, he was asked to read the instructions. So everyone could be included. Subjects were asked to tick 'true' or 'false' to whichever they agree. The testee should go through each item carefully. At the end of the procedure, a score is given for each correct answer and totalled. This scale is valid and reliable.

Thematic Apperception Test (TAT)

The TAT consists of a series of pictures with people and objects in ambiguous situations. The person is asked to describe what he thinks were the events that led up to the situation in the picture and what he thinks will be the outcome.

Wechsler Adult Intelligence Scales (WAIS)

The test presented here is an adaptation of the Wechsler Adult Intelligence Scales to suit Indian situations. It consists of eleven sub-tests, namely, information, comprehension, arithmetic, similarities, digit span, vocabulary, digit symbol, picture completion, block design, picture arrangement and object assembly. Of these the first six form the verbal scale and the last five the performance scale. Picture completion and picture arrangement tests have been modified. Digit symbol, block design and object assembly remain the same as in the original WAIS. The age range for the scale is 15 years and above. The items for each of these tests were scored and the points summed up to give the 'raw score' for each test. The 'raw scores' were then transformed into weighted scores according to the manual.

Observations

The general sociodemographic information is given in Table 1. Of the 25 patients studied 18 were in the 15–35 year age group and 23 had suffered from leprosy for 1–5 years. Twenty-three patients had tuberculoid or borderline–tuberculoid leprosy and 2 had lepromatous leprosy. Twenty patients came from rural or semi-urban settings. Only half of the patients had received primary or higher education, others were totally illiterate. Eleven patients were farmers and labourers; 6 (24%) were without work. Fourteen of the patients were married. Family size was medium (4 to 6 members) in 15 cases. Ten patients had an average socioeconomic status. Family atmosphere was congenial in 18 (72%), manageable in 3 and hostile in 4. Eighteen patients came from nuclear families and 7 from joint families.

Of the deformities operated on, 19 patients had claw hands, 4 had foot drop and two had collapse of the nose. In 11 cases multiple deformities were present which were

Table 1. Sociodemographic data of the cases

Item	Data
Age	15 to 30 years, 15 31 to 50 years, 8 Above 50 years, 2
Sex	Male, 20 Female, 5
Type of disease	T/BT, 23 LL, 2
Duration of disease	1 to 10 years, 21 Above 10 years, 4
Type of deformity	Claw hand, 19 Drop foot, 4 Collapsed nose, 2
Extent of deformity	Single, 14 Multiple, 11
Religion	Hindu, 18 Muslim, 7
Cultural status	Rural, 14 Semiurban, 6 Urban, 5
Education	Illiterate, 12 Primary, 5 Above primary, 8
Occupation	Farmer/Labourer, 11 Housewife, 4 Nil, 6 Others, 4
Marital status	Married, 14 Single, 9 Separated, 2
Family size	Small (1 to 3), 2 Medium (4 to 6), 15 Large (above 6), 8
Nature of family	Nuclear, 18 Joint, 7
Family atmosphere	Congenial, 18 Manageable, 3 Hostile, 4
Socioeconomic status	Low, 15 Average, 10 High, 0

subsequently operated on but have not been included in this study. The psychological characteristics of these cases are shown in Table 2.

As revealed by the psychological projection tests (TAT), these patients had a tendency to blame their surroundings—family and outside, for their shortcomings, indecisiveness and failures. However, these patients were realistic, conforming and had a creative nature. Most of the patients accepted their social set up and evaluated themselves to be good and

Table 2. Psychological features of cases

IQ	15 Below normal	8 Average	2 Above average
Anxiety	11 High	9 Moderate	5 Nil
Depression	9 High	9 Moderate	7 Nil

Table 3. Anxiety and depression levels before and after operation

	Anxiety		Depression	
Level	Before operation	After* operation	Before operation	After operation
Nil	5	15	7	15
Moderate	9	5	9	7
High	11	5	9	3

*9 months postoperatively.

Table 4. Clinical expectations before and after operation

Level of Expectations (%)	Before operation	After operation*
76 to 100	14	3
51 to 75	6	10
26 to 50	4	9
0 to 25	1	3

*9 months postoperatively.

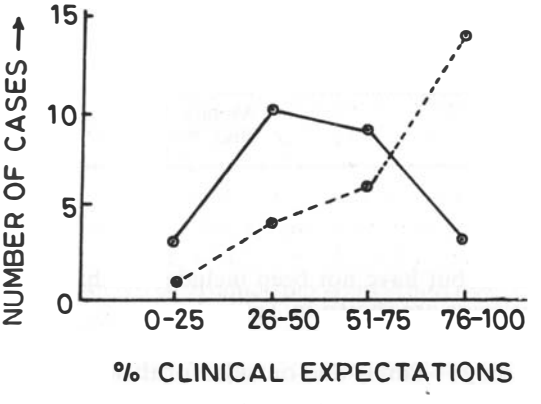

Figure 1. 'Expectations' before operation and the fulfilment after surgical correction. – – –, preoperative; ——, postoperative.

ambitious. They were frustrated with life and were in an unhappy and hostile mood. They preferred to withdraw themselves to avoid unfavourable or hostile situations.

Table 3 shows that before surgery 11 (44%) of the patients had high anxiety levels, the number came down to 5 (20%) postoperatively. Depression also cleared up in 32% and in 24% the high levels of depression disappeared.

Table 4 shows the expectations for improvement (before operation) and the expectations fulfilled after operation. Fifty-six per cent expected miraculous results and presumed that all their expectations were going to be fulfilled. However, after a third follow-up interview, it was found that only 50 to 75% of the pre-operative expectations were fulfilled and that was in only 10 (40%) of the patients.

Discussion

Leprosy deformities act as an advertisement proclaiming the presence of the disease and failure of treatment. The clinical cure is different from a bacteriological cure or clearance. In addition to producing physical disfigurement and functional incapabilities, the deformities are usually associated by the public with infection which is often not true; in fact many of the deformed patients are not infectious. Surgery is important in the overall care of such patients and is part of the rehabilitation programme.

From the series reported here, some interesting observations have been made:

1 A male predominance in the series probably suggests that being an earning member and also male means patients get better attention within the family. This may also be due to the sex ratio seen for leprosy itself where males have been found to be more affected than females.

2 Patients with borderline–tuberculoid leprosy comprised 92% in contrast to 8% lepromatous. This is due to the fact that borderline leprosy patients get paralytic deformities more often. There were more claw hands because ulnar nerve involvement is more common.

3 Patients with a shorter duration of the disease were much more interested in getting rid of the deformity compared with cases of long-standing disease.

4 Sixty per cent came from the low socioeconomic strata. It was not clear whether it was because of deformity that the social status was low or because this reflected the general trend of the patients attending the hospital.

5 There were more married patients (56%), mostly from medium-sized families. These patients appear to be better motivated and well supported. In 72% (18 cases) family atmosphere was congenial which was a positive factor towards their rehabilitation.

6 It is often stated that leprosy causes psychological problems which manifest as symptoms. In our series we found that 20 patients (80%) had moderate to high anxiety levels preoperatively. This may be a sum total of the effects of deformity and the anticipation of surgical operation. A surgical operation stands as a major threat to anyone who has to undergo one. This is particularly so in leprosy because of its chronicity and the social stigma attached to it. The lack of awareness about these operations also contributes because they are not routinely performed in a general hospital.

Postoperatively anxiety disappeared in about half the patients and in others the level was reduced. As anxiety affects the personality and life style of the patients, it would be

worth evaluating anxiety levels well in advance of surgery to establish the true levels of anxiety without the additional effects of anxiety-reaction developing in anticipation of surgical operation. The high levels of depression were also reduced after operation, as shown in Table 3. These are the two psychological benefits the patient gets, in addition to the correction of deformity and restoration of functional abilities.

The study confirms the findings of Dean (1983),[7] that surgical procedures may well result in even less psychiatric morbidity. Therefore true rehabilitation including reconstructive surgery must be a part of the leprosy control programme; it is also essential that, in addition to medical and surgical care, these patients get some form of psychiatric counselling in order to dispel their psychic fears, boost their morale and bring self-confidence to them. For many of the patients, surgery will help to contain the psychological problems, by replacing a stigmatizing lesion with a socially acceptable one. Patients think that if they are questioned about the lesion, they can say they have had an operation or an accident and show the scar as proof.[8]

After corrective surgery only 50 to 75% preoperative expectations are fulfilled and that in only 40% of patients. This needs researching. The surgical procedure can result in the correction of deformities and restoration of some functions. The operations have their own limitations and not all delicate functions can be brought back by available techniques. Moreover the presence of anaesthesia in extremities or the lack of olfactory sensibility in the nose persists, which is frustrating for many patients. Our results reflect the importance of preoperative counselling to develop realistic postoperative expectations and therefore better psychological adjustment.

It is suggested that before corrective surgery is undertaken, a proper discussion should take place with the patients about their problems, and the benefits and limitations of surgery. This will help to improve patient cooperation and motivation and also reduce the frustrations of either side. The postoperative goals should be more realistic for the patients and this should be explained to them like any other cosmetic surgical procedure.

Well-motivated patients for surgery will improve overall results and increase the number of satisfied patients. Health education should be part of such a programme so that anaesthetic extremities are prevented from injuries and mutilation. Sensory functions are restored in a number of cases after operation when the operated extremity is put into use, but it can take several years and is influenced by many factors.

It therefore seems essential to include surgical reconstruction in a programme of rehabilitation designed to assist these patients to return to society as useful members. The surgical correction of deformities in leprosy is most rewarding and indispensable for the rehabilitation of the patients who have been deformed due to the disease.

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Aspects psychologiques des lepreux difformes subissant une reparation chirurgicale correctionnelle

U RAMANATHAN, G N MALAVIYA, NOOTAN JAIN ET S HUSAIN

Résumé Une étude psychologique de 25 lépreux choisis au hasard qui devaient subir des réparations chirurgicales correctionnelles de leurs difformités fut entreprise. Avant l'intervention, les taux d'anxiété et de dépression étaient élevés et après l'intervention, ils avaient baissé de manière significative. Ces patients ont besoin d'une aide psychiatrique pour soigner leurs aberrations psychiques, pour provoquer une prise de conscience, améliorer leur moral et leur donner confiance en eux-même.

50 à 75% des espérances pré-opératoires furent satisfaites mais uniquement chez 40% des patients. Une consultation avec les patients avant l'intervention s'avère donc nécessaire pour les aider à atteindre des objectifs réalisables. Ils doivent prendre connaissance des effets positifs d'une intervention chirurgicale et des problèmes qui persistent après l'intervention comme par exemple l'anesthésie et l'analgésie.

Aspectos psiquico-sociales de los pacientes leprosos deformados sometidos a correcciones quirurgicas

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Resumen Se realizó un estudio psíquico-social en 25 pacientes leprosos seleccionados al azar sometidos a intervenciones quirúrgicas para la corrección de sus deformaciones. Se encontraron elevados niveles preoperativas de ansiedad y depresión que bajaron de modo significativo después de la intervención. Es necesaria la ayuda psiquiátrica para tales pacientes para despejar sus aberraciones psíquicas, despertar la consciencia, estimular el ánimo y para que recuperen la confianza en si mismo.

Solamente se satisficieron entre 50% y 75% de las expectaciones preoperativias, pero esto fue en solamente el 40% de los pacientes. Esto indica la necesidad para una sesión preoperativa de asesoramiento para ayudar a los pacientes que establezcan metas realistas de que sean capaces realizar. Se les debe informar los beneficios que ofrece la cirugía, y se les puede alertar de los problemas que persistirán después de la intervención, como la anestesia y la analgesia.

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The private GP and leprosy: a study

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Summary In urban and rural areas alike, people in India tend to prefer private medical care to the existing government health services. Nevertheless, the large private health care sector has hitherto been virtually alienated from activities of public health importance including priority disease control programmes. This study of 106 private general practitioners (GPs), practising in low socioeconomic areas of Bombay, shows a gross lack of knowledge and awareness among private doctors about leprosy and also about the National Leprosy Control Programme. The possible reasons are discussed. Effective involvement of GPs in the National Leprosy Control Programme should facilitate both integration and better implementation of leprosy control activities. The study also highlights some areas for future interventions at both primary and secondary health care levels and the need for a strategy, based on larger studies, to train and make private doctors participate in controlling diseases of major public health concern like leprosy.

Introduction

According to WHO, leprosy prevalence is currently estimated at 10–12 million cases in the world.[1] India has an estimated 4 million cases.[2,3] The prevalence rate for the state of Maharashtra in Western India is estimated to be 6.7 per thousand.[3] In the low socioeconomic areas of Bombay city, the prevalence rate of leprosy is about 12 per thousand.[4,5] Health care in Bombay is organized by a mixture of public and private health providers. It is believed that about 60% of the population of Bombay city is cared for by private medical practitioners, modern and traditional, and that the remainder are dependent on municipal and government health services.[6] This is no different from other parts of Maharashtra. In rural and urban areas alike, only 40% of the people utilize government health services.[7] However, few attempts have been made so far in India to involve GPs into any of the national disease control programmes.

Leprosy deserves a special place because of the social stigma attached not only to the

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patients suffering from the disease but also to the health care services and personnel working in the field of leprosy.[8] The present study examines the knowledge and awareness of leprosy among private doctors—usually the first contact of a patient—practicing in the slums of Bombay. An assessment of their knowledge, attitudes, practices and beliefs about leprosy is expected to help identify the areas of investigation and intervention for their active cooperation and participation in leprosy control.

Materials and methods

Urban slums in metropolitan cities like Bombay, where about half the population lives in slums, provides a unique situation where both diseases and doctors are in abundance. Table 1 summarizes the major characteristics of the areas providing varying exposures to leprosy control activities to the GPs selected for the study.

SELECTION OF AREAS

With a view to including practising private doctors, who have had varying exposures to leprosy control activities, three areas in the slums of Bombay were selected for the study, each having different characteristics. Area A has a municipal leprosy clinic, no voluntary agency working in the field of leprosy is operating in this area. GPs practising here have not received any formal training in leprosy. Area B has two peripheral leprosy clinics, both run by a voluntary agency active in the field of leprosy, also no GP in this area has received any formal training in leprosy. Area C also has two leprosy clinics, one run by the municipality and the other by another voluntary organization, this voluntary organization (Bombay Leprosy Project) had offered an intensive orientation and training programme in leprosy to GPs practising in the area in 1981–1982. The GPs were then followed up for about 18 months by the project staff to encourage them to diagnose and treat leprosy patients in their own clinics and reduce referrals to specialist centres.

SELECTION OF SAMPLES

One-hundred and six private practising doctors (GPs) were included in the study. From areas A and B, a list of practising doctors was made and a simple random sample was drawn from all practising GPs irrespective of their age, years of practise and professional qualifications. In area C, 2 doctors who had not participated in the training programme

Table 1. Characteristics of the areas and GPs

Area	A	B	C
Practising doctors	148	80	71
Doctors interviewed	52	29	25
Municipal leprosy clinic	One	None	One
PVO leprosy (clinics)	None	Two	One
Past training in leprosy (in practice)	No	No	Yes (5 years before)

Table 2. The questionnaire

1	Do you come across leprosy patients in your clinic?
2	Do you treat leprosy patients in your clinic?
3	What are the classified types of leprosy?
4	When do you suspect leprosy? How do you confirm diagnosis?
5	How do you treat tuberculoid leprosy?
6	How do you treat lepromatous leprosy?
7	When do you stop treatment in the above types of leprosy?
8	Should leprosy patients be referred to specialists? Why?
9	Do you suggest isolation of a leprosy patient on treatment?
10	What causes leprosy? Could you name the causative organism?
11	Should a cured leprosy person be allowed to work in public places?
12	What do you know about the National Leprosy Control Programme?

were not included in the list. A random sample was drawn from the remaining doctors who had undergone training in leprosy then provided by the Bombay Leprosy Project.

DATA COLLECTION AND ANALYSIS

Doctors were interviewed individually, face-to-face, in their clinics. Responses to an open ended, structured questionnaire (Table 2) were recorded on the spot. Doctors were not obliged to answer any questions they chose not to. The responses were then compiled and analysed.

Results

Table 3 illustrates classification of replies and performance of doctors in the three areas in response to basic questions on leprosy. The response rate was 100%.

LEPROSY PATIENTS IN PRIVATE CLINICS

All except 2 of the 106 doctors interviewed had met leprosy patients in their clinics. However only 38% from area A, 21% from area B and 20% from area C were treating them in their own clinics, while the rest preferred to refer them to private or government specialists. The 2 doctors who had never met leprosy patients in their clinics were from area A. They did not answer many of the further questions posted to them.

CLASSIFIED TYPES OF LEPROSY

For control programmes, WHO has classified leprosy into two major types—'multibacillary' if the slit-skin smears of a case show the presence of acid-fast bacilli and 'paucibacillary' if they do not.[2] These two broad types include various types for which different classifications exist. The most recent and generally accepted classification includes 5 subtypes—tuberculoid, borderline–tuberculoid, midborderline, borderline–lepromatous and lepromatous. The only doctor who gave a correct answer was from area A. Partially correct replies were recorded by 68% of doctors from area A, 55% from area

Table 3. Performance of GPs in three areas on key questions about leprosy

Questions and Answers		Performance by area (%) A	B	C
Q	**Classified types of leprosy**			
A	*Correct*: Any answer mentioning two broad types of leprosy (tuberculoid and lepromatous; or paucibacillary and multibacillary; or smear positive and smear negative) with or without a mention of any intermediate types.	2	0	0
	Partially correct: A correct mention of any one of the major types or subtypes.	68	55	36
	Incorrect: Other than above	0	0	0
	No response:	30	45	64
Q	**Diagnosis of leprosy**			
A	*Correct*: Clinical examination and slit-skin smears for AFB and skin biopsy if necessary.	88	76	80
	Partially correct: Mention of any one of the investigative procedures. (skin smears/skin biopsy)	0	0	0
	Incorrect: Other than above.	2	0	0
	No response:	10	24	20
Q	**Treatment of tuberculoid leprosy**			
A	*Correct*: (WHO recommendation); Dapsone 100 mg per day and rifampicin 600 mg once a month for 6 months at least.	0	0	0
	Partially correct: Correct mention of drugs with or without correct dosages or correct duration.	13	24	8
	Incorrect: Other than above.	23	7	12
	No response:	64	69	80
Q	**Treatment of lepromatous leprosy**			
A	*Correct*: (WHO recommendation); Dapsone 100 mg per day; rifampicin 600 mg once a month and clofazimine 300 mg once a month followed by 50 mg per day for 2 years at least.	0	0	0
	Partially correct: Correct mention of drugs with or without correct dosages and duration.	0	3	4
	Incorrect: Other than above	17	17	16
	No response:	83	80	80
Q	**Name of the causative agent of leprosy**			
A	*Correct*: *Mycobacterium leprae.*	0	0	0
	Partially correct: Mycobacteria.	0	0	0
	Incorrect: Other than above	27	52	28
	No response:	73	48	72
Q	**Knowledge of National Leprosy Control Programme**			
A	*Correct*: A programme run by the central government for control of leprosy. The programme conducts, through existing and special health centres, survey, education, treatment and other services for leprosy patients, free of cost.	2	7	8
	Partially correct: Any answer partly suggesting the above.	0	0	0
	Incorrect: Other than above.	40	34	92
	No response:	58	59	0

B and 36% from area C. Thirty per cent of the GPs from area A, 45% from area B and 64% from area C chose not to reply.

DIAGNOSIS OF LEPROSY

Presence of one or more anaesthetic skin patches is diagnostic of leprosy. In lepromatous variety, there may be other skin lesions. Peripheral nerves are involved in most types. The diagnosis and classification is confirmed by slit-skin smears or skin biopsy if necessary, to judge the quantity and to some extent viability of the organisms. Ten per cent of the doctors from area A, 24% from area B and 20% from area C did not reply to this question. The replies of 88% from area A, 76% area B and 80% from area C were almost correct while only one doctor from area A gave an incorrect reply.

Questions 5–7, inquiring about treatment of leprosy were not answered by those doctors who did not treat leprosy patients in their clinics. Those who responded included 38% from area A, 21% from area B and 20% from area C.

TREATMENT OF LEPROSY

Only 3 drugs are used in the treatment of leprosy and WHO recommendations about drug regimens to be used are unchanged since 1982. Thirteen per cent of GPs from area A, 24% from area B and 8% from area C were using correct drugs for the treatment of tuberculoid leprosy but not in correct dosages. The rest were employing less or more than adequate drug regimes. None of the doctors followed the recommended regime correctly in all respects with regard to drugs used, dosage and duration. Fifty-three per cent from area A, 44% from area B and 20% from area C had never treated a case of lepromatous leprosy. Of those who did, only two, one each from areas B and C had used correct drugs but in haphazard dosages.

CESSATION OF TREATMENT

None of the doctors interviewed had a clear idea of when to stop treatment. A very wide range of responses were noted, from less than 6 months treatment to life-long treatment, without knowledge of the rationale behind it.

REFERRAL OF PATIENTS

Thirty-eight per cent from area A, 21% from area B and 20% from area C felt that patients need to be referred to specialists only if they fail to respond or complications like exacerbations occur during the course of treatment. Twenty per cent from area A, 24% from area B and 16% from area C were concerned that by treating leprosy patients in the clinics they may adversely affect their practice, while the remaining were convinced that leprosy patients always need specialist care.

ISOLATION OF PATIENTS

An expected reply was obtained from only two doctors, one each from areas B and C, who were emphatic in saying that there is no need for isolation if a patient is on regular

treatment. Seventy-eight per cent of doctors from area A, 76% from area B and 24% from area C favoured isolation of patients if possible while the remaining felt that isolation should be compulsory.

CAUSE OF LEPROSY

When asked what causes leprosy, 73% of doctors from area A, 48% from area B and 72% from area C chose not to reply. The remaining mentioned various causes such as germs, infection, and close contact with a leprosy patient. One doctor from area A still believed that leprosy is hereditary. When asked to name the causative organism of leprosy, none of the doctors from any of the three areas could do so.

REHABILITATION

In reply to the question, whether a person cured from leprosy should be allowed to work in public places, 36% of doctors from area A, 59% from area B and 88% from area C answered in the affirmative; 40% from area A and 7% from area B replied in the negative while 34% from area A, 34% from area B and 12% from area C refused to reply.

AWARENESS ABOUT NATIONAL CONTROL PROGRAMME

Most doctors were unaware of any activity being carried out under the banner of such a programme. All doctors from areas B and C and a majority (80%) from area A knew of the many groups (non-governmental organizations) engaged in antileprosy work. Most doctors felt that nothing special was being done for leprosy. Free treatment is given in public hospitals for leprosy as it is for any other disease, there are a couple of leprosy hospitals just as there are hospitals for tuberculosis or other infectious diseases.

Discussion

It is reasonable to expect a GP practising in an area endemic for leprosy with a prevalence rate of over 10 per thousand to know basic facts about the disease. Despite the fact that most GPs did come across leprosy patients in their clinics, their response to simple questions on leprosy exhibit a gross lack of knowledge and awareness about leprosy. Ramanathan & Ramu, in their study of the attitudes of doctors engaged in antileprosy work under the National Leprosy Eradication Programme found that 33% had inadequate knowledge about the disease.[9] They observed that this could be a result of disinterest among the 'leprosy doctors' caused by fears of being socially stigmatized and facing poor job prospects. According to Duggal *et al.* leprosy is considered a 'punishment posting' and leprosy workers, especially physicians are not only most disinterested in their work but also exhibit stigma towards the disease.[10] These and other studies maintain that the status accorded to a leprosy programme and as a consequence to those who work in it is very low.[8,11] The observations on doctors working full-time in leprosy highlights the concern of doctors about their image with regard to society and work prospects. Would these observations also apply to doctors engaged in private medical practice?

No direct questions were posed to GPs about 'stigma', but only a minority of doctors (about 20%) from all three areas felt worried about their practice being affected adversely

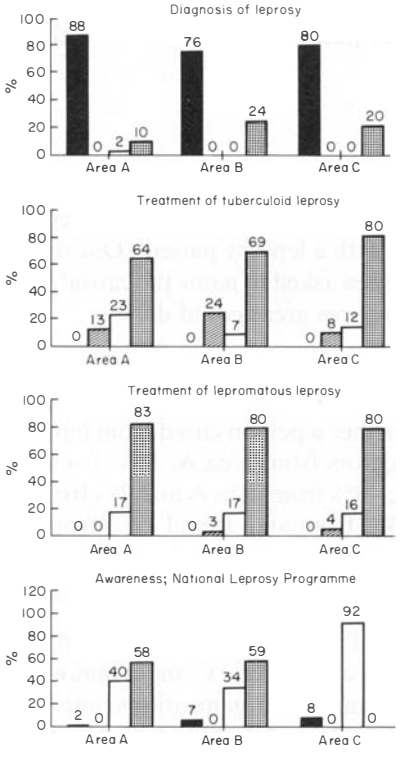

Figure 1. Performance of doctors. See Table 2 for details. Responses of doctors: ■, correct; ▨, partially correct; □, incorrect; ▧, no response.

by treating leprosy patients in their clinics. This is understandable, since for doctors who would be willing to treat them, leprosy patients would form only a small part of their general medical practice.

Although the private doctors practising in area C had received formal training in leprosy offered by a nongovernmental organization many years before, the performance of doctors in all three areas appeared consistent. Figure 1 illustrates the comparative performance of private doctors in the three areas on key questions about leprosy.

The voluntary agency that conducted short-term training and provided the services of a leprosy technician to the GPs had found, during their 18 months follow-up, that there was a significant increase in the number of patients being properly treated by GPs in their own clinics.[6] It seems that the effect of training had diminished and disappeared over the years emphasizing the need for the regular follow-up of training activities and continuing education. Also, since the clinic run by the voluntary agency in the area continued to function after conclusion of the training activity, GPs preferred to refer their cases to the clinic rather than treat them in their own clinics. The effect of training was seen only in the responses obtained for the questions regarding isolation of leprosy cases and rehabilitation of cured leprosy patients. Unlike doctors in areas A and B, a large majority of doctors in area C thought it safe not to isolate leprosy cases while on treatment and to let cured leprosy patients work in public places.

The choice given to responders to be able not to answer a question was done essentially to prevent embarrassment to the doctor being interviewed. While these are maintained as nonresponses, it may not be unfair to conclude retrospectively, taking into consideration the overall findings of the study, that the most probable reason for the nonresponse was a lack of knowledge.

Clearly, far too many doctors from all three areas performed poorly. In fact, health planners already expect little if anything from private doctors that might benefit public health problems like leprosy. Early detection, prompt reporting, optimal treatment, sound advice to the patient about the importance of regular treatment and to his contacts about the infectiousness of the disease, and facilitating rehabilitation constitute services private doctors should provide routinely.

Doctors in all the three areas performed best when asked about diagnosis of leprosy. However, they did not do as well when it came to treatment (Figure 1). One of the reasons for this, besides of course lack of training, could result from a proliferation of, and confusion about, contradictory drug regimes advocated by private medical consultants, educational institutions and voluntary agencies. Until recently the recommendations for treatment by the Indian Association of Leprologists were different from those by WHO. Even today, senior specialists continue to prescribe regimes which vary from one patient to another. The resultant confusion might mystify simple guidelines about treatment of leprosy deterring GPs from treating patients. This also highlights the role of specialists at secondary and tertiary care levels in public health. While their freedom and competence of treating a case may not be questioned, in dealing with diseases of public health importance like tuberculosis or leprosy, the senior specialists should try and stick to one rule so that those at the periphery could follow their actions. If they must deviate, they should clarify the rationale behind their actions to the referring GPs, junior doctors or students, their patients and others who need to know. Better communication would prevent confusion about the choice of drugs, duration of treatment, need for isolation and opportunities for rehabilitation.

It is both surprising and sad that the priority national control programmes exert so little influence on private doctors. It is unlikely that doctors would intentionally prescribe incorrectly if they knew what they should prescribe. When the pharmaceutical industry can successfully promote any number of irrational and non-essential products, why cannot the government promote its own programmes to GPs, who have to depend on the pharmaceutical industry to update their knowledge? Unfortunately no national disease control programme has, as one of its integral components, the continuing education of medical personnel at all levels.

The nongovernment organizations may also play a vital role, with the help of their motivated work force, in carrying control programmes to private clinics. Like the organization in this study, it could be worthwhile for similar organizations to facilitate integration of leprosy into general health services by encouraging private doctors to treat leprosy patients in their clinics. Doctors may be willing to participate if facilities like laboratory services for skin-smear examinations and the right type of drugs are provided for the convenience of their patients. The general notion that private doctors are interested in nothing but profits derived from their practice and are incapable of providing any inputs for implementation of disease control activities is certainly not based on the results of any kind of attempts or experiments to involve them.

Conclusions

The private doctors serving the urban poor in the slums of Bombay, with or without exposure to the existing leprosy control activities, have a grossly inadequate knowledge of a major, highly prevalent disease like leprosy although many people first seek their services. This could be due to the lack of adequate basic and continuing education of private doctors on major diseases of public health importance. Stigma attached to leprosy and general apathy among private doctors about national disease control programmes could be other contributory factors.

Most private doctors practising in urban slums identify leprosy patients in their clinics, and they know how to diagnose leprosy. Many however prefer to refer these cases to specialists for treatment. Those who treat them are confused about which drugs to prescribe and for how long. This could be a result of inconsistencies in recommendations and practices observed by specialists in the leprosy control programmes, educational institutions and those in private practice. Those responsible for giving out leprosy information could improve the implementation of leprosy control by GPs, e.g. by providing laboratory services, giving adequate information about the National Control Programme and updating the GPs knowledge by frequent communications.

Further research on the role of private doctors in public health considering deficiencies in basic medical education and continuing medical education would make it possible to remedy the problems our study has identified. The communicable diseases for which no truly effective vaccines exist, adequate treatment and cure of a case constitute the most important measures of control and these are the primary functions of a practising doctor. Appropriate incentives and sanctions may be provided by the government to encourage private doctors to actively participate in implementation of major disease control programmes.

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Le médecin généraliste privé et la lèpre: une étude

M W Uplekar et R A Cash

Résumé Dans des zones rurales aussi qu'urbaines, les gens de l'Inde préfèrent normalement avoir des soins médicaux privés au lieu de se soummetre aux services d'hygiène de l'etat déjà existents. Néanmoins, le secteur privé des soins médicaux, bien qu'il est important, a été jusqu'ici presqu'aliéné de toute activité d'importance pour la salubrité publique, y compris les programmes prioritaires pour le contrôle des maladies. Cette étude de 106 médecins généralistes privés exerçant dans des zones de bas niveau socio-économique à Bombay, découvre entre ces médecins une manque crasse de connaisance et de sensitivité sur la lèpre et aussi sur le Programme National pour le Contrôle de la Lèpre. On discute les possibles raisons à la base de cette situation. Une participation éffective des médecins généralistes devrait aider l'intégration et aussi la meilleure mise en exécution des activités pour le contrôle de la lèpre. L'étude souligne aussi quelques secteurs pour intervention à l'avenir au niveau primaire autant que sécondaire de soins médicaux et le besoin d'avoir une stratégie, basée sur des études à plus grande échelle, pour former les médecins privés et leur obliger à participer dans le contrôle des maladies de grande importance pour la salubrité publique comme, par exemple, la lèpre.

El médico general privado y la lepra: un estudio

M W Uplekar y R A Cash

Resumen En zonas rurales tanto como urbanas, la gente en la India suele preferir recibir asistencia médica privada en vez de someterse a los servicios sanitarios del estado ya establecidos. Aún así, hasta ahora el importante sector privado de asistencia sanitaria ha permanecido casi completamente al margen de las actividades relativas a la salud pública inclusive los programas prioritarios para el control de enfermedades. Este estudio de 106 médicos generales privados, ejerciendo en zonas de bajo nivel socio-económico de Bombay, muestra una gravecarencia de conocimientos y de entendimiento entre los médicos privados acerca de la lepra y también acerca del Programa Nacional para el Control de la Lepra. Se discuten las posibles razones de esta situación. La participación eficaz de los médicos generales en el Programa Nacional para el Control de la Lepra debiera de facilitar tanto la integración como una puesta en práctica más eficaz de las actividades para el control de la lepra. También subraya el estudio algunos sectores para futuras intervenciones a niveles primarios y secundarios de asistencia sanitaria y la necesidad de desarrollar una estratégia, a base de estudios más amplios, para que la formación de los médicos privados les imponga a participar en el control de enfermedades de importancia máxima para la salud pública como, por ejemplo, le lepra.

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SPECIAL ARTICLE

Pattern of leprosy in Queensland, Australia, 1855–1990

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Summary Leprosy was first diagnosed in Queensland in 1855. From then until 1990, 929 patients with the disease were notified. The pattern of notification has varied with the passage of time, and with the changing pattern of migration into Queensland. In the early days, Chinese, Melanesians and Caucasians featured prominently. The first Aboriginal notification was in 1892. In the latter part of this century, significant numbers of Torres Strait Islanders and migrants from South East Asia have been recorded. Among Caucasians, the incidence peaked in the decade 1931–1940, although the prevalence rate in this population remains much higher than in Caucasians. The control of leprosy is at a high level in Queensland today, but there is a continuing low level of new case reporting, many of them imported.

Introduction

The origins of leprosy in Queensland are obscure. Ashburton Thompson,[1] in 1897, listed all the cases recorded in the state from 1855 to 1895; he concluded that Chinese immigrants were responsible for the introduction of the disease. He also noted that many Melanesian-indentured labourers were suffering from the disease (but were not recorded as such) but did not attribute any epidemiologic role to this population. This early period also coincided with mass movements of other racial groups into Australia and Queensland. Significantly, the Chinese appeared to bear the brunt of responsibility for leprosy not only in Australia but also in other Western societies.[2] Queensland responded to the perceived threat to public health with its own leprosy regulations in 1890, followed by the Leprosy Act of 1892, which allowed for the compulsory notification and segregation of persons afflicted with the disease.

Some of the difficulties inherent in making a diagnosis of leprosy, and thus in defining the epidemiology of the condition, have been outlined previously.[3,4] Traditionally, epidemiologic studies have tended to segregate migrants from analyses of endemic diseases. The State of Queensland was founded on migration, and migrants have played an important role in its development. Between 1873 and 1976, approximately 20,000 Chinese entered the State, largely to work in the gold fields. Starting in 1863, indentured labourers from neighbouring Melanesian Islands were imported to work in coastal sugar

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cane plantations. By 1883, an estimated 13,000 such labourers were working in Queensland. White settlers came in three great waves, between 1871 and 1890, between 1906 and 1930, and after the Second World War. The early white settlers were mainly from the British Isles, later they came from all over Europe. In the past 15 years, there has been increasing migration from South East Asia. All of these groups have contributed to the pattern of leprosy as seen in Queensland, and need to be considered in assessing epidemiologic trends.

Epidemiology is also concerned with the geographical distribution of disease. Studies in Norway,[5] Portugal[6] and Louisiana[7] (among some western countries), have described the limited geographical distribution of leprosy in these countries. Various explanations for this phenomenon have been offered. This area of study is particularly difficult for Queensland, and especially for the Aboriginal population. In 1897, a policy of 'removal' was instituted which encouraged the development of settlements—run either by religious organizations or Government agencies—in various parts of the State.[8] While most numerous in the northern half of Queensland, where white population pressure was less extreme, the settlements did not necessarily reflect either the original pattern of population distribution, or its original tribal constitution.

The Torres Straits Islands are a group of islands lying between the northern tip of continental Australia and the island of New Guinea. Most of these islands are part of Australia, and are politically and administratively an integral part of the state of Queensland. There exist rights of passage from New Guinea to some of the islands without administrative control; this is likely to have an impact on the epidemiology of leprosy within that area. The population of the Islands is genetically heterogeneous, the original inhabitants having intermingled with Aboriginal people from Australia, Melanesians from New Guinea, Japanese pearl fishermen, Indonesian bêche de mer cullers and Europeans.

These confounding factors complicate any epidemiologic study, and allowance has to be made for these problems. This paper attempts to describe the situation in Queensland over the past one hundred and fifty years.

Materials and methods

For the period 1855 to 1890, the cases recorded by Ashburton Thompson were accepted as they stand. These cases were not included in the analysis. From 1890 onwards, leprosy was a notifiable disease. Basic demographic data usually included sex, age, race, country of origin, marital status and clinical type. Data from 1890 were entered into and manipulated on a custom PC database programmed in R base language. Analysis and graphic output were via the Microsoft chart package.

Queensland population figures and other demographic details were obtained from standard texts. Average annual incidence rates were calculated for each decade as the number of new cases occurring in that decade $\times 100{,}000$ divided by the mid-decade population $\times 10$ (for years of observation): and an average incidence rate for the whole period of observation was derived from the mean population through the study period.

Aboriginal populations were not officially numbered until the census of 1967. Rates for this population were derived from Queensland statistical texts and extrapolated backwards. The results of bacteriological investigations are included in some notifica-

tions. Because of difficulties in comparing clinical classifications from the distant past with the more modern Ridley–Jopling classifications (see Irgens[5] for a discussion of this), when possible, patients have been classified as multibacillary or paucibacillary, based on the presence of *Mycobacterium leprae* in material from the patients. Clearly in the early stages of the epidemic, many patients were not smeared, and classification for these patients is difficult. Statistical analysis included standard χ^2 tests, tests for coefficients of correlation, and Student '*t*' tests for differences between means.

Results

Between 1855 and 1890, 30 cases of leprosy were recorded. From 1891 to 1990, a further 899 patients were notified; these comprised 375 Aborigines, 293 Caucasians (of whom 179 were born in Queensland) and 231 others. The change in ethnic origin of the patients, 1851–1990, is shown in Figure 1. For 43 patients, the data of diagnosis were not recorded.

CAUCASIANS

The case detection rate for Caucasians peaked in the decade 1901 to 1910 and has declined ever since. The pattern is similar for both males and females (Figure 2). The sex ratio shows a male preponderance in all decades except the last. The excess of males is not

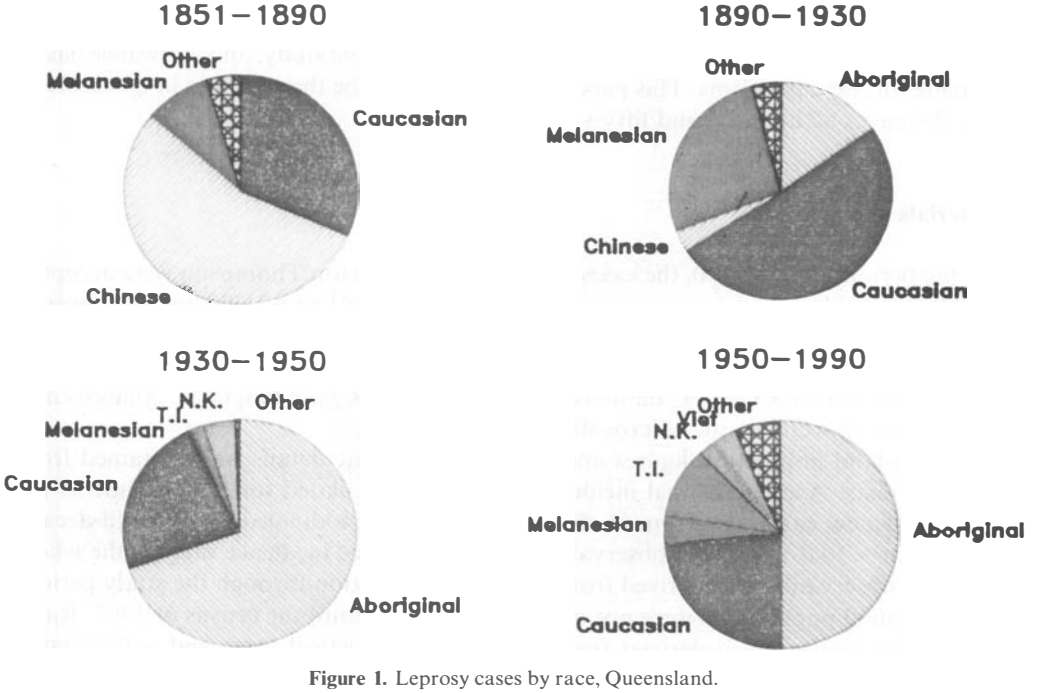

Figure 1. Leprosy cases by race, Queensland.

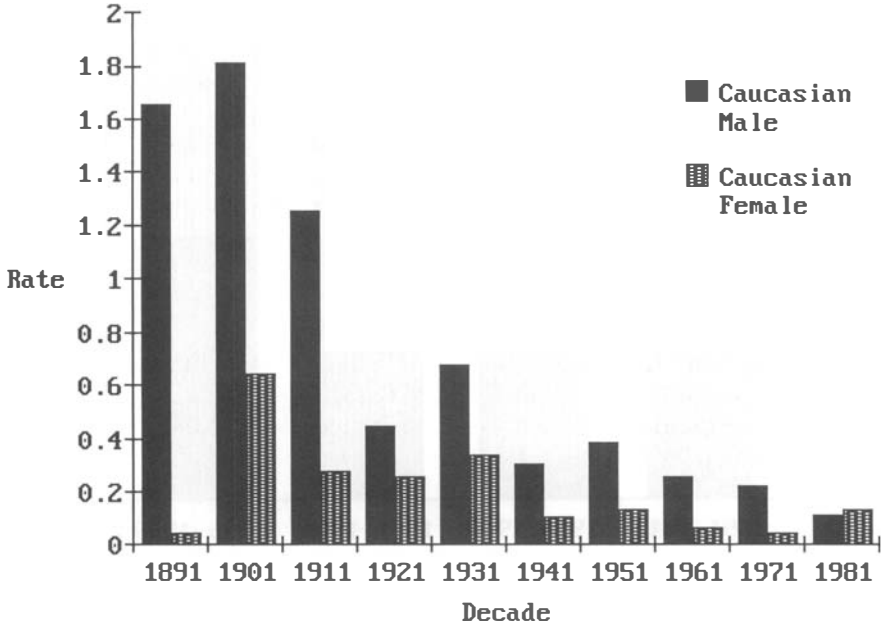

Figure 2. Caucasian annual leprosy rate per 100,000 by decade.

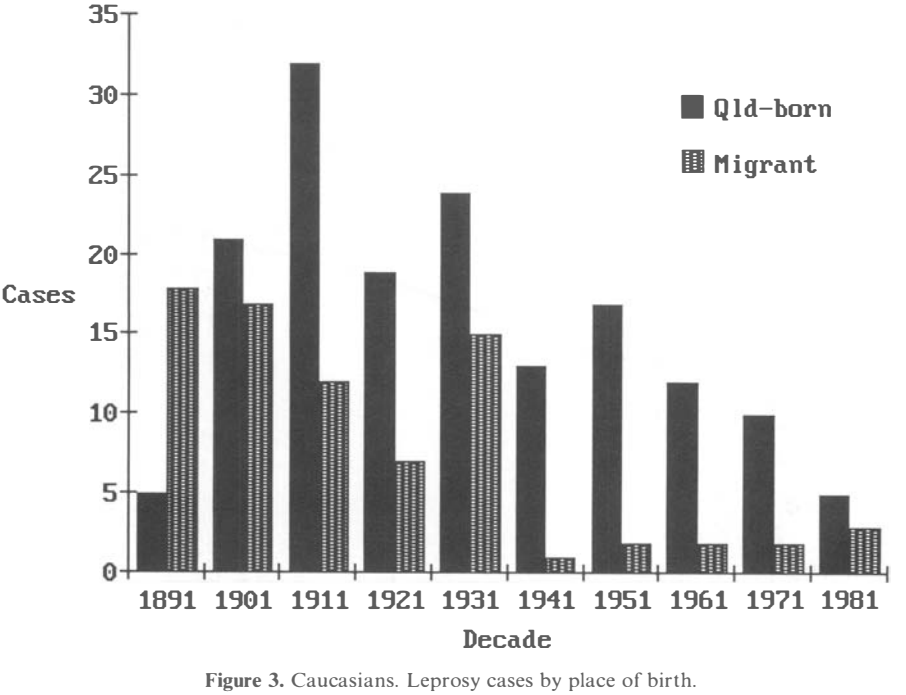

Figure 3. Caucasians. Leprosy cases by place of birth.

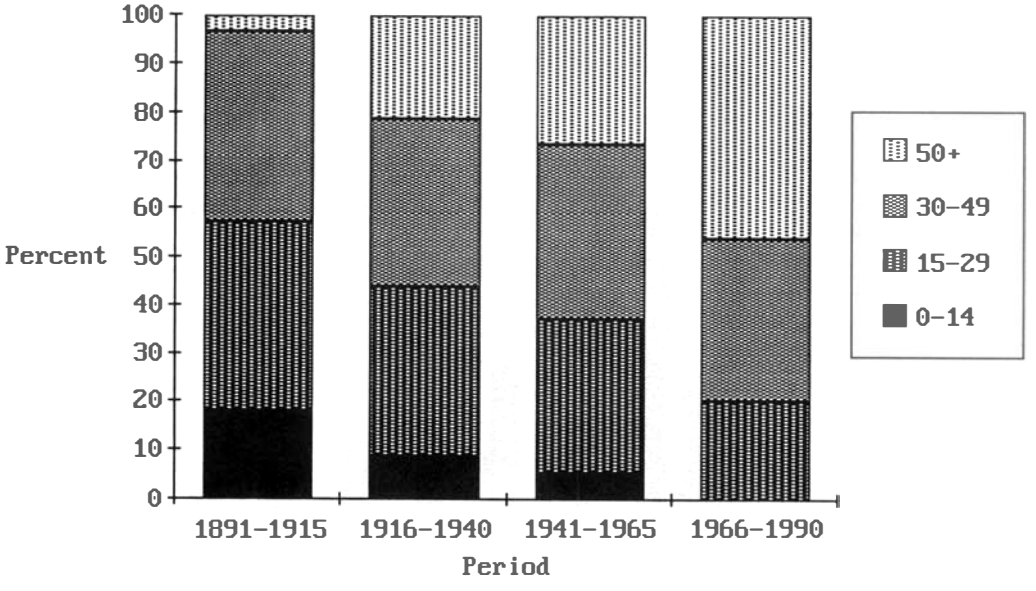

Figure 5. Age distribution of native male Caucasians by year of diagnosis.

related to an excess in male migrants, since the sex ratio is not significantly different between migrants and Queensland-born Caucasians.

In the decades 1891 to 1920, many of the Caucasians were migrants (Figure 3), 61 % of whom originated in the British Isles. The average age of the migrants at the time of diagnosis was significantly greater than that of the Queensland-born Caucasians

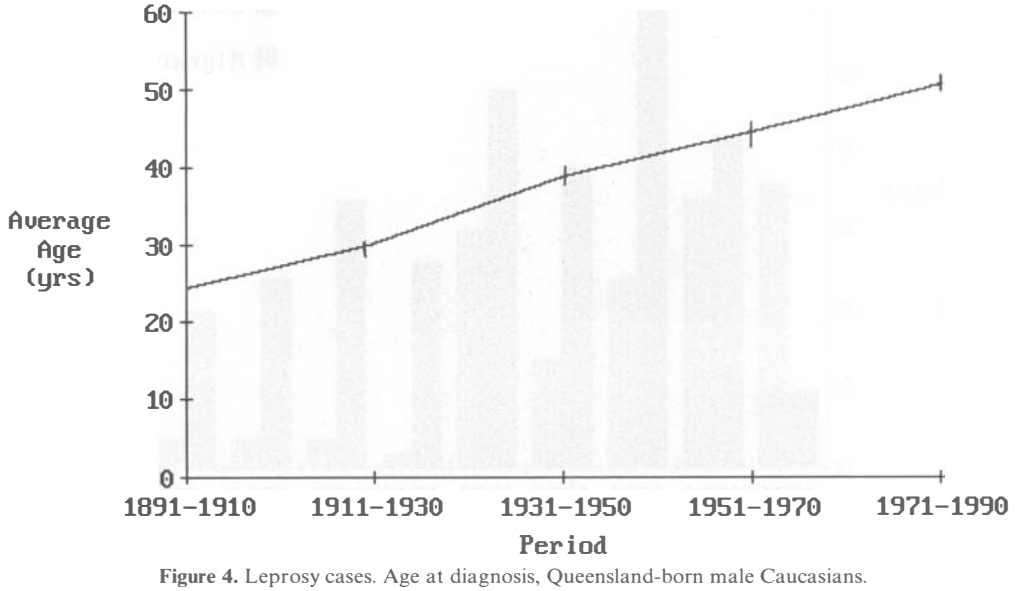

Figure 4. Leprosy cases. Age at diagnosis, Queensland-born male Caucasians.

(52·2 ± 13·3 years *vs* 28·2 ± 14·1 years (mean ± SD), $P < 0{\cdot}001$). The migrants were, on average, 21·3 ± 10·8 years of age on arrival in Queensland. Excluding Caucasian migrants from the analysis, the mean age at the time of diagnosis has gradually increased with time, a trend which is highly significant ($r = 0{\cdot}998$, $P < 0{\cdot}001$) (Figure 4). This change is caused by a fall in the number of young people, and an increase in the number of older persons being diagnosed with the disease (Figure 5). Over the past one hundred years, the burden of leprosy has fallen on the age group 30–39, with the lowest average incidence in the age group 0–19 (Figure 5).

The average incidence is highest in the coastal, wet areas of Queensland (Figure 6). The dry, western areas of the state are less affected, but this may reflect not only total population in those divisions (which are small), but also relative population density: there is a significant correlation between population density/square-kilometre in the various divisions and the average case detection rate ($r = 0{\cdot}67$, $P < 0{\cdot}05$).

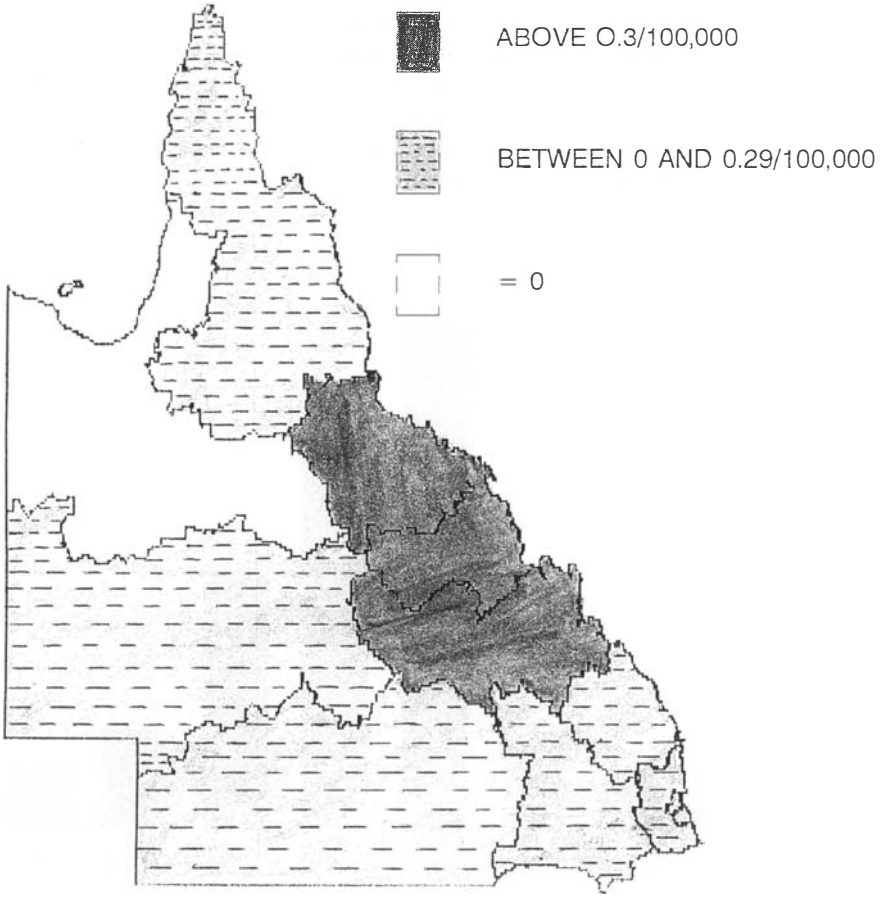

Figure 6. Queensland Statistical Divisions average incidence rate, Caucasians.

TORRES STRAIT ISLANDERS

The Islanders are a genetically heterogeneous group of people living on small, scattered islands between the northern tip of continental Australia and the island of New Guinea. Thirty-two cases of leprosy were recorded in this population between 1931 and 1990, of whom more than half were diagnosed in the past 15 years.

The population of the Torres Strait Islands in 1971 was 7508 (of whom 3607 were male). The average incidence rate for the past 40 years (which includes all but 4 patients) was, therefore, 9·3/100,000 (11·8 for males, and 6·4 for females, giving a sex ratio of 173:100).

ABORIGINES

The first recorded case of leprosy in a Queensland Aborigine was in 1892. A gradual increase in incidence rates led to a peak in the decade 1931 to 1940, followed by a sustained fall since then (Figure 7).

The sex ratio, based on notification numbers and not incidence rates, has varied widely from decade to decade, and averages at 171·4 males to 100 females. The ages for the Aboriginal patients were unreliable. For 74 (19·8%) no ages were recorded. For the remainder, an excess of ages ending in 0 or 5 was recorded. There were 19 (5·1%) patients for whom the geographical origin was not recorded, of the remaining 355, 129 (36·3%) were from settlements, the others from non-settlement areas.

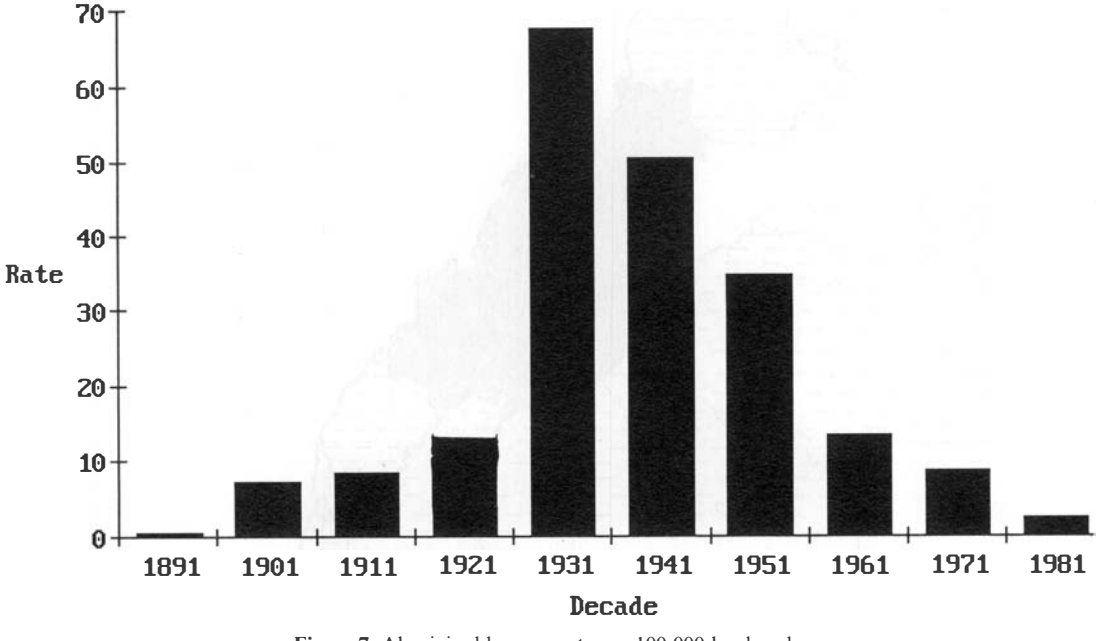

Figure 7. Aboriginal leprosy rate per 100,000 by decade.

MIGRANTS

Only 11 Chinese patients were recorded after the introduction of the Leprosy Regulations, 9 of whom were diagnosed between 1897 and 1912. The remaining 2 were recent migrants. 92 Melanesians were registered, 77 of whom were indentured labourers diagnosed between 1892 and 1923. Of the 114 Caucasian migrants, 47 were from other Australian States, of the 67 from outside the continent, 43 (64·2%) were from the British Isles, 79% of whom were diagnosed prior to 1930. Of the 24 migrants from other

Table 1. Bacteriologic classification within different periods of time (No. (%))

Period	1891–1920	1921–40	1941–90	Total
Paucibacillary	5 (1·8)	7 (3·6)	101 (3·6)	113
Multibacillary	30 (10·9)	128 (66·8)	226 (58·4)	385
Not done/reported	239 (87·2)	57 (29·5)	60 (15·1)	356
	274	193	387	854*

* There were 43 patients for whom no clinical data are given.

Table 2

	I	TT	BT	BB	BL	LL	PN	Total
Causasian								
M	—	7	1	4	1	28	4	45
F	1	4	—	2	1	5	2	15
Aborigine								
M	—	13	1	2	5	36	4	61
F	—	9	—	6	1	21	—	7
Torres St.								
M	—	2	1	2	3	—	1	9
F	—	4	—	1	—	1	2	8
Vietnamese								
M	—	2	1	1	—	—	1	5
F	—	1	1	1	2		—	5
PNG								
M	—	1	—	—	1	2	—	4
F	—	—	1	1	—	1	—	3
Others*								
M	—	1	1	1	—	2	—	5
F	1	4	1	—	—	—	—	6
Total								
M	—	25	5	10	10	68	10	131
F	2	22	2	11	2	28	4	72
Grand total	2	47	7	21	12	96	14	203

*Includes: Indians, Indonesians, Chinese, Fijians, Laotian, Filipinos, El Salvadorans, Thai.

European countries, 50% were diagnosed before 1930. Between 1976 and the end of 1990, 15 patients from South East Asia were notified. During the last decade, migrants from South East Asia represented 22% of the notifications.

BACTERIOLOGY

The first recorded bacteriological notification was made in 1892, a Melanesian male with nodular disease. For the first 30 years the majority of patients of all racial groups did not have bacteriology performed, or, if it was performed, the results were not recorded. That situation changed subsequently (Table 1).

THE PRESENT SITUATION

There are at present 203 patients on the leprosy register; all but 9 (2 Torres Strait Islanders, 2 Vietnamese and 5 Aboriginal patients) are considered to be inactive. The distribution of these 203 cases by ethnic origin and clinical type is shown in Table 2.

Discussion

In historical studies, it is likely that many cases of leprosy (and especially minor tuberculoid cases) are either missed, not diagnosed, or not notified. The notifications therefore are often biased towards patients with more severe disease, or those with smear positivity who represent a public health danger. That this occurred in Queensland is suggested by the very high numbers of patients with bacteriologically positive lesions. Most authors emphasize the year of onset rather than the year of diagnosis, as there are often significant delays in reaching a diagnosis—especially where the disease is rare because it is newly introduced, or declining. However, this was not possible for this study as the information was not available.

It seems likely from the pattern of leprosy in Aboriginal people that the disease was introduced into Queensland—what the ethnic origin or origins of those responsible was is impossible to tell at this stage—what is clear however, is that in both Caucasians and Aborigines, leprosy came, peaked, and has been in decline now for a number of decades; whether this decline was the result of forced isolation into leprosaria (legislated by the Leprosy Act of 1892), or of socioeconomic change, or a combination of these effects, or other effects, is uncertain. Enforced isolation for Caucasians ceased in 1963, and clearly there has been no resurgence of disease since that date. Antimycobacterial treatment may have hastened the decline, but did not start it. The trend for an increasing age at onset with declining incidence has been noted in previous studies.[5,6] Whether this represents an increase in incubation periods, or a postponement of infection to a higher age, is uncertain.

Comparing clinical types of disease over relatively long periods of time is hazardous—definitions and classifications change with time, and it is impossible to state whether a patient diagnosed as having 'mixed leprosy' in 1890 is the same as a person with borderline today.[5] The bacteriologic status is perhaps more instructive—in the period 1921–40, when bacteriological investigation was (almost) routinely performed, the majority of notified patients were multibacillary—in the last 50 years however, that

situation has changed, with a third of notified patients in whom bascteriology was performed being paucibacillary. Most authors agree that paucibacillary disease is more common than multibacillary; in the remarkable epidemic in Nauru,[9] the majority of cases were described as maculo–anaesthetic in whom bacteriologic examinations were usually negative. Clearly in Queensland, large numbers of patients with paucibacillary disease were either misdiagnosed, not notified, or ignored as of no epidemiologic significance.

Migration has played an important role in the development of the State: it is, however, unlikely that new migrants from leprosy-endemic areas will be able to re-introduce the disease into the autochthonous population. Studies in Britain and other countries have shown that secondary cases are exceedingly rare after the disease has spontaneously declined.

There is a pronounced male preponderance in this study for both Caucasian and Aboriginal patients. The sex ratio is often higher in lepromatous patients, who are probably over-represented, and there are remarkably few children (in whom the sex ratio tends to be more equal). There is no definite trend to a decline in the sex ratio with the decline in the endemicity of the disease, as has been reported in some studies.

The situation in Queensland has been unusual from the large ethnic variations which have contributed to the epidemiology of the disease; that there has been a significant decline is indisputable, and it is hoped that continuing surveillance will ensure that no resurgence occurs.

Acknowledgments

I am grateful to the Director-General, Health and Medical Services, for permission to publish this paper; to Dr A M Patel for helpful comments; to Ms L Hansson for endless patience in preparing the manuscript; and to Mr M Kanowski for the graphics.

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Evolution de la lèpre dans le Queensland, en Australie, de 1855 à 1990

G H Ree

Résumé C'est en 1855 que la lèpre fut diagnostiquée pour la première fois au Queensland. Depuis cette date jusqu'à 1990, 929 cas de lépreux furent déclarés. Le profil de la déclaration s'est modifié avec le temps et avec l'évolution de la migration au Queensland. Au début, il y avait un grand nombre de Chinois, Mélanésiens et d'hommes de race blanche. La première déclaration parmi les Aborigènes date de 1892. Au vingtième siècle, au cours des dernières années, un grand nombre de cas ont été rapportés chez les habitants des Iles Torres Strait et chez les émigrants du Sud-Est asiatique. Parmi les blancs, l'incidence a atteint son maximum au cours des années 1930 à 1940 bien que le taux de prévalence dans la population du Sud Est asiatique reste beaucoup plus élevé que celui de la race blanche. Le contrôle actuel de la lèpre est très stricte au Queensland mais on continue à rapporter un petit nombre de nouveux cas, en particulier parmi les immigrants.

La distribucion de la lepra en Queensland, Australia, 1855–1990

G H Ree

Resumen La lepra fue diagnosticado por primera vez en Queensland en 1855. Desde entonces hasta 1990, han sido notificados 929 pacientes. La distribución de la notificación ha variado con el paso del tiempo, y según el cambio de migración en Queensland. En los primeros días, se destacaban los Chinos, Melanesios y Caucásicos. La primera notificación de un aborigen fue en 1892. A fines de este siglo se han registrado números significativos de isleños de Torres Strait e inmigrantes del sudeste de Asia. Entre los Caucásicos, la incidencia alcanzó un pico en la década 1931–40, aunque el nivel que prevalece en esta población continúa más elevada que la de los Caucásicos. Se mantiene un nivel muy elevado de control de la lepra en Queensland hoy en dia, pero persiste un nivel bajo de registraciones de casos nuevos, muchos de ellos importados.

Lepr Rev (1991) **62,** 431–437

Letters to the Editor

TYPE II (ENL) REACTION IN HISTOID LEPROSY IN A CHILD

Sir,

SR, a 15-year-old male from eastern India, reported with asymptomatic, nodular eruptions of 2 years' duration, which were distributed over the face, buttocks and extremities. Accompanying this was the impairment of sensation of the hands and feet. These symptoms had been present for 2 years. A few days after admission the patient developed fever, malaise, loss of appetite, arthralgia and myalgia with ulceration of the nodules. On questioning the patient disclosed that he had had dapsone monotherapy for 6 months without any amelioration in the symptoms, on the contrary he developed fresh lesions during the course of therapy. He also revealed that his mother was a known case of borderline–lepromatous leprosy and had had dapsone monotherapy 9 years ago for a period of 6 months. However, she had taken the treatment irregularly and had discontinued it after 6 months.

Cutaneous examination revealed skin coloured, translucent, dome-shaped nodules, 1–3 mm, regular in contour with shiny and stretched overlying skin. They were present over an apparently normal skin. Some of the nodules were ulcerated and tender (Figure 1). These were distributed over the face, buttocks, thighs, legs and arms. Earlobes and eyebrows were infiltrated. There was impairment of sensation to temperature, touch and pain confined to the glove and stocking areas. The lateral popliteal, posterior tibial, superficial branch of radial and ulnar nerves were bilaterally thickened.

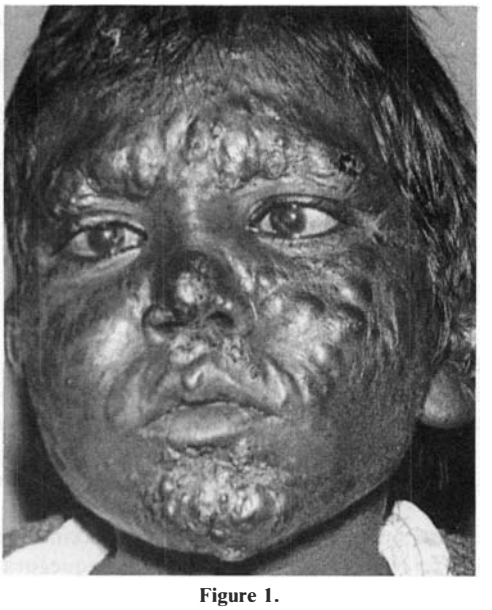

Figure 1.

Slit-skin smear examination of the patient revealed a marked discrepancy in the bacillary index from the nodule and the surrounding skin. The former being 6+ and the latter 3+. The bacilli were granular and fragmented. There was also an infiltration with neutrophils in smear from the nodules. An hematoxylin eosin section revealed the presence of numerous, thin, spindle-shaped histiocytes arranged either in an intertwining, criss-cross or whorled fashion. The conspicuous absence of appendages within the nodules was another feature. An abundance of acid-fast bacilli identified by Fite's stain were distributed all over. They were uniformly stained and measured longer than the ordinary lepra bacilli and were arranged in groups along the long axis of the cell. Globii were seen occasionally.

Taking cognisance of history, clinical examination, slit-skin smear examination and histopathology, a diagnosis of histoid leprosy with Type II (ENL) reaction was made, caused presumably by a primary dapsone-resistant strain of *Mycobacterium leprae*. The child had been in intimate contact with his mother, and was infected by the strain of *M. leprae* rendered resistant as a result of the inadequate, irregular monotherapy with dapsone which had been taken by her. Histoid leprosy is a distinct expression of multibacillary leprosy[1,2] and may occur as a result of irregular and inadequate treatment with dapsone, which may be responsible for the emergence and selective proliferation of drug-resistant bacilli in these patients.[3–5] This case is probably due to primary dapsone-resistant bacilli.

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SUGGESTED NEW TECHNIQUE FOR SKIN BIOPSY UNDER FIELD CONDITIONS

Sir,

Most lesions of indeterminate leprosy regress,[1] but some may progress to multibacillary leprosy.[2] Therefore histopathology may be considered vital for the classification and determination of the prognosis of all types, especially indeterminate leprosy. Skin biopsies are not done routinely because of administrative reasons and operational constraints under the field conditions. The old technique of punch biopsy may crush the tissue and may delay healing and leave a bad scar at the site.

For assessing the immunotherapeutic efficacy of the ICRC vaccine, where histopathology is one of the parameters for assessment, we have used a modified technique for taking skin biopsies under field conditions. The selected site (usually the periphery of a lesion, adjoining normal skin) is

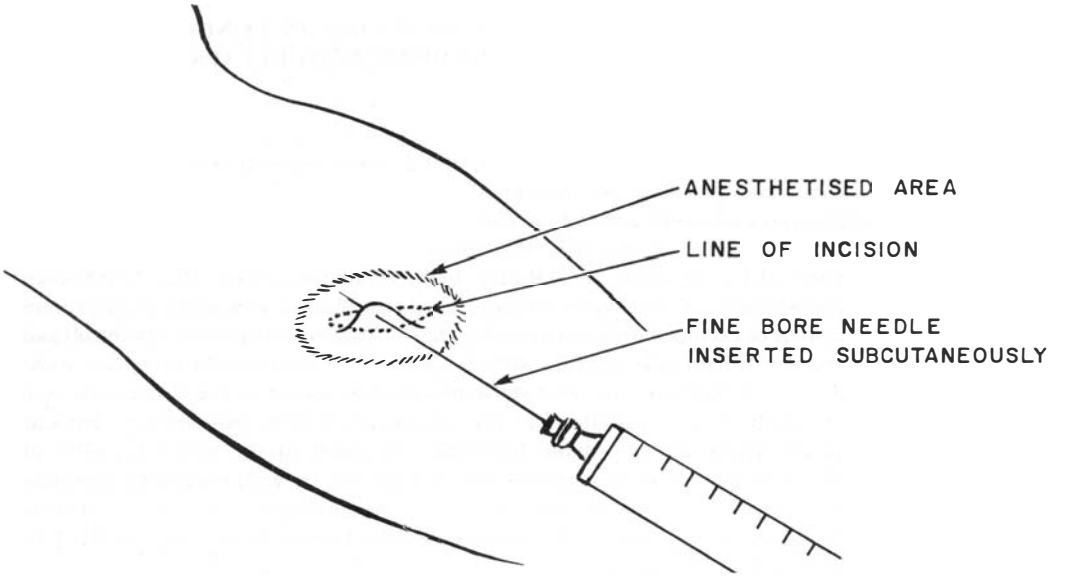

Figure 1.

infiltrated with 2% Lignocaine (plain) using a fine bore (26 G) needle after the area has been cleaned with antiseptic. The same needle is inserted subcutaneously to lift up the skin. An elliptical scalpel incision of about 10 mm length is made around the needle, the tissue is cut and transferred to a vial containing fixative. The incision is closed with a single suture made of absorbable material (removing the need for suture removal later) using a thin eyeless needle. A readymade medicated adhesive pad (available under various brand names) is applied to the site to prevent secondary infection. Alternatively, Tincture Benzoin seal may be used. The specimen is transported in vials containing the fixative, which are sealed with a portable capping machine.

Besides being quick, this technique ensures that subcutaneous tissue is included in the specimen. The procedure can be performed at the patient's residence. All the necessary material can be carried in a portable bag. This modified technique is so simple that skin biopsies can be done routinely under field conditions.

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COMMENT: POSITIVE MITSUDA LEPROMIN REACTION IN LONG-TERM TREATED LEPROMATOUS LEPROSY AND TUBERCULOID RELAPSE IN LEPROMATOUS LEPROSY

Sir,

Regarding the apparent conversion of the late lepromin reaction following long-term therapy as described by Waters, Ridley & Lucas[1] and Waters & Ridley[2] it appears that perhaps owing to the long period of observation, some 30 years or over at the time of diagnoses and first classification, no lepromin readings were reported. Particularly, this refers to patients of group 1[1] classified before 1966 as lepromatous (LL), the year that Ridley–Jopling published their now well-known classification.[3] Therefore some doubt remains on the original classification and on the first lepromin readings. Thus it cannot be excluded with certainty that those 13 patients with 3 mm (doubtful) and 4 mm (one plus positive)[4] lepromin readings already at the time of infection possessed some immunological competence. Still, assuming that at the time of onset of disease these 13 patients were either lepromin negative (0–2 mm) or doubtful (3 mm), experience with the postlepromin test scar (PLS)[5–7] has also shown that negative or smaller lepromin indurations, up to 5 mm, may in 30% of such cases give rise to scar formation, i.e. a patient with a 'negative' or 'weakly positive' lepromin reaction, when assessed by his PLS formation, may have immunological competence.[7] This is regardless of his clinical classification, as can be expected, in most T forms but also in some BL, LLs or even in a few LL forms of the disease.

Once a leprosy patient[7] or a healthy non-leprosy individual[6] has developed a PLS, normally his *immunocompetence* or in its absence, his *immunoincompetence*, will not change unless it can be demonstrated that by means of chemotherapy or immunotherapy the initial PLS absence truly converts into positivity. In this context it would be important to know which of these lepromin converted patients have developed a PLS reading which can never be doubted and remains so for life.

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Paraguay

J WALTER

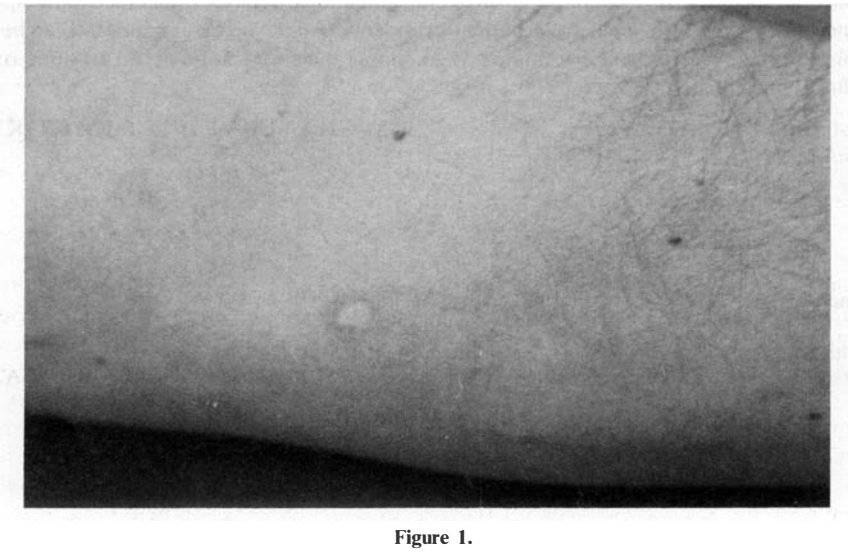

Figure 1.

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REPLY: POSITIVE MITSUDA LEPROMIN REACTION IN LONG-TERM TREATED LEPROMATOUS LEPROSY AND TUBERCULOID RELAPSE IN LEPROMATOUS LEPROSY

Sir,

We are very grateful for the interest shown by Dr Walter, whose work with the World Health Organization, and in particular whose studies on the post-lepromin scar (PLS), from the WHO BCG Immunoprophylaxis Study in the Singu area of central Myanmar (Burma), is well known.

In our studies on tuberculoid relapse in lepromatous leprosy,[1] the original London biopsies of patients 3–6 were all reviewed and all were classified as subpolar lepromatous (LLs). Pretreatment biopsies were not available for patients 1 and 2, but their clinical histories (patient 1 was becoming blind from lepromatous infiltrate in the anterior part of the eye, and patient 2 had developed lepromatous laryngitis, before they commenced treatment with dapsone), clinical findings and smear results all confirmed the diagnosis of LLs. In our study of positive Mitsuda lepromin reactions in long-term treated lepromatous leprosy,[2] the original London biopsies of all patients in group 1 were reviewed and were classified as LLs. In some cases, Mitsuda results from 22 or more years ago were available and all had been negative. Clinical findings and past smear records also confirmed that all patients in group 1 had suffered from lepromatous disease.

In our studies, we used standard lepromin containing 4×10^7 leprosy bacilli/ml, prepared from human lepromas, and kindly supplied by Dr M J Colston. No special attempt was made to look for the PLS; however, the majority were retested at 6 months and at 1 year, when the forearm was carefully inspected, and no postlepromin scar was seen. But it must be remembered that a number of the Mitsuda reactions were biopsied. On biopsy, an epithelioid granuloma was found, confirming the positive Mitsuda status of the patients. Incidentally, in Dr Walter's original paper,[3] a 3-mm Mitsuda reaction was graded 1+ positive, not 'doubtful', as in his letter. Our finding of epithelioid granulomata confirms that these 3-mm tests were indeed positive. We agree that the development of a 3–4 mm positive Mitsuda reaction does not necessarily imply subsequent lifelong immunity, but it would suggest that on relapse, should it ever occur after 2 years of multidrug therapy which almost all group 1 patients had received, the initial relapse would be borderline–tuberculoid in character.

We have observed a small number of PLS in patients who have had strongly positive (3+) Mitsuda reaction, but do not recall having seen a PLS after a weak positive (1+) Mitsuda response. It is difficult to picture the mechanism of scar formation in the latter type of response, although Dr Walter (who was using lepromin containing $1{\cdot}6 \times 10^8$ leprosy bacilli per ml) has reported that it can occur infrequently after 3–5 mm (1+) and 6–9 mm (2+) reactions without necrosis or ulceration.[3] Perhaps Dr Walter might like to suggest a hypothesis, other than that such patients might have scratched their Mitsuda papules after the readings of their reactions had been performed.

We would like to add a postscript to our original report on these patients. Further review of the

voluminous old notes of the patient in Group 1 who was known to have taken treatment irregularly for many years, confirms that he did in fact relapse in 1968. Therefore only 3 patients with completely negative Mitsuda reactions in this group had no history of relapse, and Table 1[2] should be appropriately amended.

We would also like to record that patient 5 in our study of tuberculoid relapse in lepromatous leprosy[1] developed a second tuberculoid relapse, or rather a late reversal reaction, at the end of December. His dry erythematous plaques were exactly similar, clinically and histologically, to those which developed in June 1984, although some of the sites were different. It must be noted that he was still receiving rifampicin monthly. His lepromin test had remained negative both in 1984 and in 1989; when retested in January 1991, he developed a 2-mm tiny nodule at the site of the lepromin injection, which on biopsy, revealed a focus of loose granulomatous inflammation indicating a weakly positive response.

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COMMENT: CARVABLE SILICONE RUBBER PROSTHETIC IMPLANT FOR ATROPHY OF THE FIRST WEB IN THE HAND

Sir,

I have the following comments to make on the paper by Duerksen & Virmond (*Lepr Rev*, 1990; **61:** 267–72). The authors must be congratulated on their work, particularly for their concentration on the aesthetic value of the implant. The feel of the implant is also equally as important.

For instance, in cultures where hand shaking is the form of greeting, a palpable hard substance in the first web space of the right hand is a stigmatizing sign. Once I had the experience of unwarily shaking hands with a patient who had a similar implant. I can still recollect the unpleasant feeling of touching an unusual palpable bulk in his hand. The reaction in such a situation is to want to know 'What is wrong with his hand?' often in such a situation the patient ends up answering questions about his/her prosthetic implant. A few more specific comments are as follows:

1 As per the authors, the implant material (Silastic Dow Corning) has a consistency of that slightly harder than the normal muscle tissues of the first web. The manufacturers of such an implant should be instructed to produce the material to mimic exactly the tissue consistency of the first web.
2 Its movement within the deep fascia, as much as possible, should be similar to that of the original attachment of first dorsal interosseous and the abductor pollicis muscle.

3 The authors used external evaluators to grade the cosmetic appearance of the pre- and post-operative photographs. Besides this, I would consider another parameter to evaluate the results, namely, 'the feel test'. This test will elicit the specific perception and attitude of the patient regarding the implant palpability. But such a test must be carefully planned, otherwise the results may not be accurate. This can be avoided by having the reliability and the internal consistency of the test items within a satisfactory level.

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R PREM KUMAR

Lepr Rev (1991) **62,** 438

Book Review

***Tropical medicine*. Kevin M Cahill and William O'Brien**

Ever since the demise of the tropical supplement to Davidson's *Principles and Practice of Medicine* there has been a need for a concise, yet adequate, and authoritative text on tropical medicine. Does this little book fulfil that need satisfactorily?

Certainly the book is the right size at 250 pages, neatly produced, clearly printed and easy to read. I like particularly the interesting, semi-historical introductions to many of the chapters, with their cameos, quotes and informal style of writing, although at times this leads to lack of precision.

Sections on the classical infectious and parasitic diseases of the tropics are supplemented by others on diarrhoeal disease, malnutrition, hereditary anaemias, tumours, snake bite, eye disease and heart disease. This provides a fair coverage but sections on drugs and imunization would greatly enhance the book and there are some idiosyncratic omissions such as fasciola hepatica from the flukes.

Unfortunately, the text is riddled with mistakes and inaccuracies, which range from the merely annoying to the dangerously misleading, and there are numerous 'infelicities of expression' as the late Dr S G Brown would have called them. The treatment sections recommend drugs for use but sometimes only give the trade name and hardly ever the dose, thus reducing the usefulness of the book. The majority of the 33 black and white plates are of such poor quality as to be valueless. The excellent list of references, which are in fact suggestions for further reading, does not compensate for the book's other inadequacies. Sadly, I doubt if this little book will fulfil the need.

Heinemann Medical Books, Jordan Hill, Oxford. 250 pp; £14.95.

Lepr Rev (1991) **62,** 439–441

Teaching Materials and Services

Library services for primary health care

The above paper by Rolf Weitzel, Information Services Consultant, 4 Oche-Marchand, 1291 Commugny, Switzerland (*Soc Sci Med*, 1991; **32:** 51–7) highlights the inadequate provision of library and literature information services for health care staff in the developing countries. It identifies the different types of information needs—current awareness, clinical inquiries—and makes suggestions on how these could be met by simple and inexpensive means. The various administrative, organizational and financial problems that may have to be overcome are discussed. Hope is expressed that in the future more sophisticated services will become feasible through the application of information technologies.

TOOL: Reference Centre Services

The aim of TOOL, Technologie Overdracht Ontwikkelings Landen, which is based in the Netherlands is to further the transfer of technology for development to developing countries. TOOL offers three main services: 1, selling publications; 2, a library and library training; and 3, an inquiry service.

The TOOL Catalogue, 1990–1, contains some 600 titles of which 100 are new. Topics covered are general development issues and background issues.

The Library has one of the world's largest collections of literature on small scale technologies and development—9000 titles and 250 magazine subscriptions. The library also offers training in establishing and maintaining small technical libraries, as well as a Selected Articles Services. Issued quarterly this gives access to recent practical and technical articles derived from 250 technical, medical and agricultural development magazines.

The Inquiry Service is able to deal with specific questions in the field of technology. TOOL has a pool of 400 plus contacts, both group and individuals, who will provide a detailed answer as quickly as possible. This may be in the form of a letter, related documentation or the result of a short research and development project, e.g. prototype development.

For further details on any of the above services write to: TOOL Reference Centre, Entrepotdok 68a/69a, 1018 AD Amsterdam, The Netherlands.

Christoffel Blindenmission/Lepra Ophthalmic Course, Karigiri, India, 1991

The sixth annual 5-day ophthalmic teaching module was held at the Schieffelin Leprosy Research and Training Centre, Karigiri from 25 February to 2 March 1991. This course, which was again sponsored jointly by the Christoffel Blindenmission and LEPRA, was designed to give instruction to leprologists on the detection, prevention and management of the ocular complications of leprosy by means of a series of lectures, clinical and surgical demonstrations, videos and slide-tapes.

Teaching included presentations on basic anatomy, physiology and pathology of the eye with special emphasis on leprosy: in addition there were lectures on the clinical signs and management of lagophthalmos, corneal ulcers, intra-ocular inflammation and infiltrative lesions, together with discussions on 'high risk eyes', ocular manifestations of relapsed disease, rehabilitation and the global aspects of blindness in leprosy.

The course, which was attended by 13 participants, was run by Dr Margaret Brand of The Leprosy Mission and Mr Timothy ffytch from St Thomas's Hospital, London, together with contributions from Dr Ebenezer Daniel and Dr Mary Jacob of Karigiri.

The Director and staff of Karigiri and The Leprosy Mission are to be congratulated on their continued support for this important and popular contribution to teaching.

Health workers and blindness prevention in leprosy. Video

This 19-minute video, produced by P Courtright and S Lewallen, sets out to provide basic information and advice on the management of some of the ocular complications of leprosy. It is designed primarily for health care workers and trainers and concentrates mainly on the three main causes of blindness in the disease—lagophthalmos, iritis and cataract. The importance of early diagnosis and prevention is emphasized, and it is clear that a mechanism for swift referral for ophthalmic treatment at a secondary level is essential in the management of leprosy patients.

It is encouraging to see how the activities of Project Orbis have expanded into primary care in blinding conditions such as leprosy, and the authors are to be congratulated on their contribution to the subject.

Further information: Project Orbis, 330 West 42nd Street, Suite 1900, New York, NY 10036, USA.

J J ffytche, FRCS, FCOphth

International Foundation of Dermatology

Following a workshop held in Arusha, Tanzania, in January 1991 the International Foundation of Dermatology in association with the Ministry of Health, Tanzania has developed a training curriculum for a dermatology officers' course. Extracts from the introduction, philosophy, rationale and justification sections include the following.

The setting up of a Regional Dermatology Training Centre (RDTC) at the Kilimanjaro Christian Medical Centre in Moshi Tanzania is the culmination of deliberations by the International Foundation for Dermatology (IFD) to help alleviating skin problems for the needy. The Foundation found it necessary to set up an objective which aims at improving Dermatological Health in developing countries through promotion of services, training and science.

The Regional Workshop on Curriculum Development for Training of Dermatologists at all levels was held in Nairobi, Kenya from 27–31 August 1990 to follow up the IFD objectives. Participants who came from all member states of the Commonwealth East, Central and Southern Africa Region, reviewed the subject of Dermatological training at all levels, and agreed on an action oriented Regional syllabus for a Dermatology Officers' course scheduled to start at KCMC Moshi, Tanzania in September 1991 with an implementation time table.

The Primary Health Care approach has recently evolved into emphasizing District Health systems in order to accelerate the achievement of Health for All by the year 2000. Manpower planning and development has been identified as one of the priority areas in the implementation of District Health Systems. The choice and development of manpower in the delivery of Health Care has to be carefully done in order to utilize the health services efficiently and effectively.

The following is the elaboration of the need of training Dermatology Officers in this Region:

- Reduction of morbidity of common skin disorders, STD/HIV/AIDS and leprosy at Primary Health Care level which can be done by using locally available resources and appropriate technology.
- Promotion of dermatological services in the country can be achieved if the community is properly educated on the causes and preventive measures of common skin diseases.

Surgery and anaesthesia at the district hospital, WHO

Patient care in small hospitals has long suffered from the lack of a capacity to perform essential surgical operations. Whether a patient presents with trauma, obstructed labour, or acute appendicitis, lives are all too often lost when emergencies arise.

To improve the situation, the World Health Organization took a pragmatic approach: if small hospitals are not staffed with surgeons, then general duty doctors must be trained to perform essential operations. With this goal in mind, WHO collaborated with several specialist societies to develop a repertoire of standard surgical and anaesthetic techniques simple enough to be mastered by doctors during supervised training.

Now described and illustrated in a series of three handbooks, these standardized surgical procedures define the safest line of action to take in hospitals with limited resources. Procedures were selected for inclusion on the basis of their capacity to save lives, alleviate pain, prevent the development of serious complications, or stabilize a patient's condition pending referral.

The books cover many, though not all, of the operations most commonly required in district hospitals. Operations that cannot be performed safely without highly specialized training or equipment are not included. WHO also anticipates that this basic repertoire will provide a foundation for adding on other operations specific to locally important diseases and emergencies.

For the doctor working at a remote post, the handbooks will mean a head start—based on a world's worth of experience and expertise—when learning to perform safe, life-saving surgical operations.

Further information is available from: WHO Publications, 1211 Geneva 27, Switzerland.

Prevention of blindness in leprosy

The above, edited by Paul Courtright and Gordon J Johnson, is a 39-pp booklet covering the prevention of blindness under the following headings: ocular leprosy as a global cause of blindness; programme development for the prevention of blindness in leprosy; training personnel in ocular leprosy; and research needs in ocular leprosy. The booklet also contains many good quality colour plates and is available from: International Centre for Eye Health, 27–29 Cayton Street, London EC1V 9EJ.

Health learning materials for developing countries, WHO

The following is extracted from information produced by the WHO Health Learning Materials Programme.

The WHO Interregional Health Learning Materials (HLM) Programme is operating at country level in nearly thirty developing countries, of which 14 are on the African continent. It is helping to build up a self-sustaining national institution in each country which can produce the required numbers of training and information materials for all categories of health staff and the community, relevant to the country's priorities for primary health care delivery.

These country projects are coordinated and supported by intercountry HLM networks which promote the pooling of scarce resources such as training and information materials, training facilities and staff skills.

Relevant materials—from text to television—play a vital role in building and maintaining the competence of health workers, and thus improving the quality of health care. In the same way, materials which educate the general public in the elements of primary health care help to promote individual and family self-care. These two processes together lead to an improvement in the health of populations.

A serious defect in the health systems of many developing countries is the almost total lack of a competent work force to deliver primary health care. So there is a vital need for basic training and continuing education of health staff.

To achieve any lasting effect, training must be supported by high quality teaching, learning and promotional materials, developed specifically for each target group (e.g. medical assitants, nurses, technicians, community health workers). Such materials simply do not exist in most developing countries.

Lepr Rev (1991) **62,** 442–449

News and Notes

Towards elimination of leprosy, WHO

The above WHO publication (12 pp.) describes the present state of leprosy in the world, with particular attention to what is happening, and what has already been achieved, by the use of multiple drug therapy. Page 2 includes the following: 'Commitment from non-government and other agencies has also increased, as reflected in increased extra-budgetary funding available to WHO, now totalling US$6·4 million for the 1990–1 period and in an increase in public funds—currently US$60 million—raised annually by the International Federation of Anti-Leprosy Associations through its 22 autonomous member associations. WHO estimates that if the current rate of progress can be maintained, the prevalence of leprosy worldwide could fall over the next decade to a tenth of its 1986 level, bringing known cases to less than 500,000, compared with the 1990 figures of 3·7 million.'

Forty-fourth World Health Assembly—elimination of leprosy by the year 2000, WHO

'The Forty-fourth World Health Assembly has called on World Health Organization (WHO) Member States in which leprosy is endemic to take action to eliminate the disease as a public health problem by the year 2000. A resolution adopted by the Health Assembly at its annual meeting in Geneva, Switzerland defined eliminating the disease as a public health problem as "reduction of the prevalence of leprosy to a level below one case per 10,000 population".

Further, Member States in which leprosy is endemic are urged to: (1) to further inrease or maintain their political commitment and give high priority to leprosy control so that the global elimination of leprosy as a public health problem is achieved by the year 2000; (2) to strengthen managerial capabilities within leprosy programmes, particularly at the intermediate level, and to improve training in leprosy for health workers at all levels, including medical students and student nurses; (3) to ensure that coverage of multidrug therapy is maintained at the highest level possible and that patients comply with treatment; (4) to strengthen case-finding activities through various approaches, including health education, community participation and training of health workers.

This marks the first time the Organization has committed itself to the elimination of leprosy, according to Dr S K Noordeen, Chief of the leprosy programme of the WHO, reflecting the significant progress achieved during the past five years in treating people with leprosy through the application of multidrug therapy (MDT).'

National Leprosy Eradication Programme, India, 1990

A recent document, *Guidelines for a modified multidrug therapy in selected districts*, is now available from the Leprosy Division, Directorate General of Health Services, Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi 110011, India. The Foreword by Professor G K Vishwakarma, Director General of Health Services records an important decision regarding the implementation of multiple drug therapy and the primary health services: 'it is important to recognize that MDT could and should be implemented through existing general health care systems. Though 130 out of 196 endemic districts have been brought under MDT, the major concern is how to bring quickly the remaining 66 problem districts under MDT. . . . It is time to

involve primary health care for MDT delivery.' Appendix 8 (Section 2) refers to efforts which will be made to supply blister–calendar packs (all three medicines in 1 pack for 1 month) to facilitate the dispensing of drugs for self-administration, to ensure better compliance and to avoid misuse.

TDR News, December 1990

The following is extracted from *TDR News,* No. 34, published by the UNDP/World Bank/Special Programme for Research and Training in Topical Diseases, WHO, 27 Geneva 1211, Switzerland:

'A resolution adopted at the end of October 1990 (Washington, DC) by the Pan American Health Organization could be the first step towards the disappearance of onchocerciasis, leprosy and Chagas disease from the Americas by the year 2000—or at least their elimination as public health problems. Governments of the region, the resolution states, should now determine whether eradication or elimination of these diseases is feasible, and if so, draw up "appropriate plans of action . . ." Leprosy in Latin America with 295,000 officially registered cases presents nothing like the problem it does in South-East Asia (over 3 million). Brasil, with 240,000 cases accounts for the bulk of the Latin American cases, followed at a distance by Mexico (17,000), Argentina (10,000), Colombia (9000), Cuba (4000) and Venezuela (4000).'

Third World Guide 1991–92, OXFAM, England

Now in its sixth English language edition, the *Third World Guide* is a biennial compendium of information and analysis of the state of the world from a unique Third World perspective. This edition includes articles on global environment, trade, health, culture, aid, and many other issues vital to an understanding of world development in the 1990s. In addition, there are 217 country profiles from Afghanistan to Zimbabwe (with maps and key economic, social and political indicators), country-by-country statistical information, and a full bibliography of reference sources. The *Third World Guide* is now recognized as one of the most comprehensive resources for anyone interested in Third World development. Order from: OXFAM Publications, PO Box 120, Oxford OX2 7FA, England. Price £18.50; 616 pp.

Heiser Program for Research in Leprosy—First Decade

The following is abstracted from the most recent report of the Heiser Program:

'The Heiser Program for Research on Leprosy was initiated in 1974 and made its first grants for research in 1975. The present report includes all of the research awards from 1975 to 1986 that had terminated by the time the review was initiated in 1988. Thus, it covers slightly more than a decade but provides a coherent picture of the activity during the formative period of the program.

The guidelines that were established for the program at the beginning have been maintained without major change, placing the primary emphasis on training of young investigators in leprosy-related research. To provide flexibility in the identification and selection of promising candidates, applications for postdoctoral fellowships were accepted either directly from the candidate or from the head of a laboratory engaged in leprosy research. A second type of award, the small research grant, was included, since it was recognized that many useful projects might be promoted by this mechanism. In a third area, visiting research awards were established to provide travel funds for collaborative studies and for studies involving clinical leprosy.

The 103 research awards represented in this report include all three of these areas. There were a total of 53 postdoctoral fellowships: 19 by direct application and 34 by application of a head of laboratory. Research grants numbered 38, awarded to 30 different investigators, and there were 12 visiting research awards.'

Further information is available from: The Director, Heiser Program for Research in Leprosy, 450 East 63rd Street, New York, NY 10021, USA.

Health Action International (HAI)

Health Action International (HAI) is an informal network of some 100 consumer, health, development action and other public interest groups involved in health and pharmaceutical issues in 60 countries around the world. HAI has participants in Africa, Asia, Europe, Latin America, North America and the Pacific region. HAI believes that all drugs marketed should meet a real medical need; have therapeutic advantages; be acceptably safe; and offer value for money.

In 1988 the World Health Organization (WHO) calculated that of the 5 billion people in the world, between 1·3 and 2·5 billion have little or no regular access to essential drugs. At the same time it is estimated that as many as 70% of the drugs on the global market are inessential and/or undesirable products. HAI supports the Essential Drugs Policy of the WHO which concentrates on the supply and use of some 250 drugs considered to be the most essential. HAI also believes that the problem of the enormous numbers of inappropriate and ineffective products must be tackled.

HAI recognizes that access to appropriate medicines is only one element of health care and that a significant improvement in world health will only be achieved if the problems of poverty, poor sanitation, and malnutrition are addressed.

HAI works at many different levels: with health workers in many countries; with academics and trainers; with government officials and national health associations; with regional decision making bodies such as the Commission of the European Community (EEC); with the pharmaceutical industry; and at international level. HAI participants have taken part in many consultations and discussions organized by the WHO as part of its Revised Drug Strategy and have been active in mobilizing support for the WHO Action Programme on Essential Drugs and Vaccines.

In 1988 HAI groups in Europe set up the independent HAI Europe Foundation whose principal objective is 'to raise and distribute funds . . . to support worthwhile initiatives which reflect HAI ideals and objectives—and in doing so, to extend and strengthen the HAI network'.

The Board of Trustees and the Advisory Board is comprised of health workers, development workers and academics, and includes pharmacologists, who give advice and support to the coordinating team and help to guarantee the standard of project work. Further information can be obtained from the following addresses: HAI Europe, J van Lennepkade 334-T, 1053 NJ Amsterdam, The Netherlands; HAI Asia/Pacific, c/o IOCU, PO Box 1045, 10830 Penang, Malaysia; HAI Latin America, c/o IOCU, Casilla 10993, Sucursal 2, Montevideo, Uruguay.

The continuing spread of AIDS

The following is extracted from *The Guardian*, 18 June 1991:

The future spread of the global AIDS epidemic in the heterosexual population will make drug addict and homosexual cases almost irrelevant in numerical terms, the chief AIDS statistician of the World Heath Organization said yesterday.

Dr James Chin, head of AIDS surveillance and forecasting, said that by the year 2000 around 90% of global AIDS cases would be among heterosexuals.

He told the seventh international AIDS conference in Florence that there may be 'anything from a quarter to a half billion' heterosexuals at very high risk of a sexually transmitted disease, because of multiple sexual partners.

'There may be only 10–20 million homosexual men throughout the world with multiple sexual partners, and 5–10 million injecting drug users throughout the world who share needles on a regular basis.

'The point is to say that the future of the HIV and AIDS pandemic is in the heterosexual population.

'Because of the relative size, even if we were to infect all homosexuals and all injecting drug users, the future really rests with the large number of susceptible heterosexuals.'

Dr Chin said that AIDS cases were likely to peak in Europe and North America in the mid-1990s

if the spread of the HIV virus did not increase. This was because most infections occurred in the early 1980s and would have progressed to the full disease by then.

But he said there would be no decrease in the developing countries of Africa, Latin America and Asia.

'Although all projections must be interpreted cautiously, there can be no doubt that during the next several decades, AIDS in most developing countries will become the leading cause of death among adults in their most productive years, and will also be one of the leading causes of infant and child mortality in many regions.'

Dr Chin warned there were disturbing signs that Asia, which contains more than 50% of the world's population but currently has only 8% of the AIDS cases, was about to see an explosion of the virus.

Figures from Thailand taken among 20,000 military recruits in June last year suggested an infection rate of 2%. Similar tests on the next group of recruits in December showed an infection rate of 6%.

Dr Chin said that in sub-Saharan Africa it was now estimated that one in 40 men and one in 40 women carried the virus.

The Arkleton Trust, UK

The Arkleton Trust seeks applications for a Rural Communications Fellowship in 1992, to be awarded from the Bernard Conyers Fund. An award, or awards of up to a total of £5000 will be offered in the current year. The purpose of the award is to encourage an individual or small organization to disseminate information, findings or ideas related to rural development. Priority will be given to material relating to the Third World, the links between Europe and the Third World, or the lessons which Europe can learn from Third World experience.

The Selection Committee is especially interested in helping to disseminate material which might otherwise remain unpublished or unavailable, relating to unconventional or new and novel approaches to rural development, or to the strengthening of links between small scale projects and programmes to improve the possibilities of self-learning amongst those working at field level who would not normally have access to conventional means of communicating their ideas or findings. However, the work which is the subject of the proposal should already have reached the dissemination state, as it is not the intention that this particular fund should be used to support research.

The means by which information or experience may be disseminated and/or shared may also be unconventional or novel. Whilst it could include a book, monograph or series of information leaflets or a newsletter it might also involve a film, video or digital communications system or a workshop or meeting at which ideas and experience can be exchanged. The Committee will be anxious to encourage the use of new media where relevant and useful.

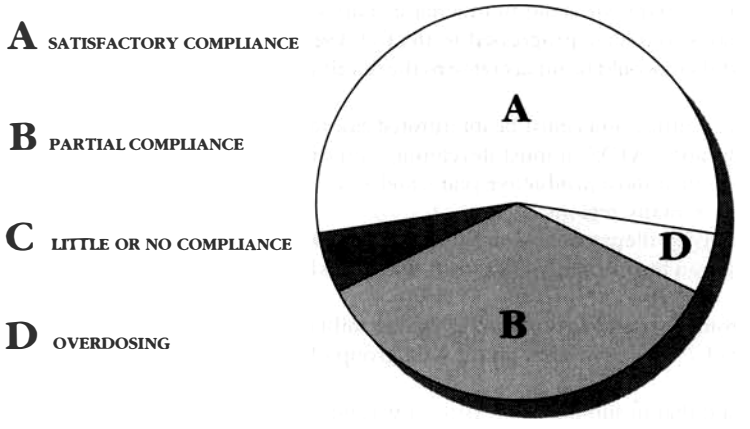
Applicants may be of any nationality or origin, although preference will be given to suitable applicants from individuals or groups working in the Third World, or from under-privileged regions or groups in Europe. The Committee would also welcome enquiries from anyone who is acting on behalf of an individual or group who would not be in a position to see this advertisement and/or submit a conventional application. The closing date for applications for the 1992 award(s) is 14 May 1992 and details of how to apply are available from:

The Administrator, The Arkleton Trust, Enstone, Oxford OX7 4HU, UK.

Compliance and medication monitoring, APREX

The following, headed 'Cutting the compliance pie', is extracted from a recent circular from APREX, European Operations, Postfach 4358, Bundesstrasse 3, CH-6304 Zug, Switzerland:

This pie chart is a reflection of the range of compliance that usually prevails in long-term trials where there are neither unusual incentives for good compliance (e.g., vivid symptom relief, frequent



patient visits to the investigator or use of special compliance-enhancement techniques) nor unusual incentives for poor compliance (i.e. unpleasant side-effects, inconvenient regimen, or large or otherwise difficult to administer dosage forms).

Rule of thumb figures for asymptomatic, chronic treatment are: satisfactory compliance (55%), partial compliance (35%), little or no compliance (5%), overdosing (5%). The definition of 'partial' compliance is: two-fifths to four-fifths of prescribed doses taken. The pattern of gaps between doses taken by partially compliant patients varies widely, often with 2, 3 or even 4 days of consecutively missed doses. Among patients who do take all of nearly all doses, however, dose timing is often poor and quite different from what is assumed by those who design and regulate drug regimens.

Tuberculosis in the Sudan

Professor D A Enarson, Director of Scientific Activities, International Union Against Tuberculosis and Lung Diseases, 68 Boulevard Saint-Michel, 75006 Paris, recently visited the Sudan to advise the Ministry of Health on the further development of the National Tuberculosis Control Programme, with the emphasis of training. The problem is widespread; by no means under control; and has shown no decline in the past decade. Despite the current security and other problems in the Sudan, it was considered entirely feasible to set up a national programme. Particularly in view of recent evidence suggesting that HIV positivity and AIDS are spreading, the necessary steps should be taken as soon as possible, including the provision of chemotherapy for all cases in need.

Neurological disorders in Ethiopia by Redda Tekle-Haimanot

The above, 185 pp plus hundreds of references, is a dissertation from the Department of Neurology, University of Umea, Umea, Sweden. The abstract reads as follows:

There exists only scanty information on the epidemiology of neurological disorders in Africa at large, and Ethiopia in particular. This thesis is the product of epidemiological studies aimed at providing an overview of the pattern and prevalence of neurological disorders in Ethiopia with special emphasis on two rare but important endemic neurological disorders of neuro-fluorosis and neuro-lathyrism. A community-based study was undertaken in the rural sub-district of Meskan and Mareko in central Ethiopia involving a population of 60,820. Epilepsy, poliomyelitis, mental retardation and peripheral neuropathy were found to be the most prevalent disorders (Papers I, II). In the study of 316 identified persons with epilepsy, the highest age-specific prevalence was in ages 10–19 years, with generalized tonic-clonic seizures as the most common type. Ninety-eight per cent of the cases had never been on treatment (Paper III). Concerning attitudes of the community toward epilepsy, traditional views on the association of evil spirits and superstitions were prevalent. Persons

with epilepsy still faced social deprivations and rejection (Paper IV). The results of survey in the fluorosis-endemic area of the Ethiopian Rift Valley for crippling osteofluorosis and its neurological complications (myelo-radiculopathies) revealed that the disorder will in the future be a serious public health problem. The Rift Valley, where artesian wells supply high-fluoride water to the inhabitants, continues to attract many agroindustrial development projects, thus exposing large populations susceptible to the disease (Paper V), Lathyrism, an epidemic neurotoxic disorder induced by heavy consumption of the grass-pea, *Lathyrus sativus*, extensively cultivated in northwestern Ethiopia, was found to have a prevalence rate of 6/1000 in the Dembia and Fogera region, with some villages having rates as high as 2·9% (Paper VI). The changing pattern in the epidemiology of leprosy, the most common cause of peripheral neuropathy in Ethiopia, was evaluated, using the 13 years' records of the Leprosy Control Programmes. A progressive decline in prevalence of the disease was observed, with a dramatic fall in prevalence starting in 1982, a year before the start of the Multiple Drug Therapy programme (Paper VII).

This is a comprehensive account of neurological disorders in Ethiopia including leprosy from a neurologist in Addis Ababa, who is closely connected with the All Africa Leprosy and Rehabilitation Training Centre (ALERT).

Integrated Rehabilitation Clinic for leprosy patients, Bombay

A joint venture between the Bombay Leprosy Project (BLP) and the Vocational Rehabilitation Centre for Handicapped (VRC) began 1 May 1991. The joint venture screens leprosy patients for integrated rehabilitation and is held fortnightly in the VRC premises. It is hoped that the integrated training and rehabilitation offered will help towards the elimination of stigma for leprosy patients.

Wall Journal, Bombay Leprosy Project

Another initiative of the Bombay Leprosy Project has been to start a 'Wall Journal' on leprosy in the Preventive and Social Medicine Campus of the Sion Hospital, Bombay. At the inauguration Dr R Ganapati, stated that the wall chart was intended to keep staff and students up to date on current developments in leprosy. He also reiterated that the fight against leprosy should be done from general medical institutions and not from leprosy hospitals. Mr P V Purandhare, Publications Officers for the BLP proposed that the 'Wall Journal' could become more broadbased if all the doctors from municipal and government hospitals shared their views with voluntary organizations like BLP.

Wellcome Medal for Medical Anthropology, 1990

Dr Zachary Gussow has received the above award for 'Leprosy, racism and public health: social policy in chronic disease control'. It is awarded biennually by the Royal Anthropological Institute of Great Britain and Ireland and in association with the Wellcome Trust. The book is published by Westview Press, San Francisco & London, 1989. A review of the book was printed in *Lep Rev*, 1990; **61,** 196.

Multiple drug therapy manual for Pakistan and Azad Kashmir

Dr Shaukat Ali, Director of Training, Marie Adelaide Leprosy Centre, 'Mariam Manzil', A.M. 21, off Shahrah-e-Liaquat (Frere Road), P O Box 8666, Karachi 03, Pakistan has kindly supplied a copy of this maual which fully describes all aspects of the implementation of multiple drug therapy for leprosy in the above areas in practical terms. The manual should be consulted by those intending to implement MDT, especially in South-East Asia. Amongst many, one item of particular interest concerns the criteria for giving the paucibacillary (PB) regimen, which are as follows: 1, typical TT lesions with clear-cut margin and central anaesthesia: 2, number of lesions: 1–5, including skin AND nerve lesions; and 3, BI (bacteriological index): negative.

UK Training Institutions: Third World and Tropical Health

The following are extracted from a list supplied by the Tropical Child Health Unit at the Institute of Child Health, University of London, 30 Guildford Street, London WC1N 1EH, England:

The Overseas Unit
Health Services Management Centre
Birmingham University
Park House
40 Edgbaston Road
Birmingham B15 2RT
Tel: 021 455 7511

BOMS
Bureau for Overseas Medical Service
Africa Centre
38 King Street
London WC2E 8JT
Tel: 01 836 5833

Christian Medical Fellowship
157 Waterloo Road
London SE1 8XN
Tel: 01 928 4694

Christian Nurses Fellowship
277a Ewell Road
Surbiton
Surrey KT6 7AX
Tel: 01 390 2626

Health Unlimited
3 Stamford Street
London SE1 9NT
Tel: 01 928 8105

HEARU
City of London Polytechnic
Walburgh House
56 Bigland Street
London E1 2NG
Tel: 01 283 1030

Alison Butcher
Hospital for Tropical Diseases
4 St Pancras Way
London NW1 0PE
Tel: 01 387 4411

ICRC
International Committee of the Red Cross
HELP 89
17 Av. de la Paix
1202 Geneva
Switzerland
Tel: 022 346001

IDEA
International Disability Education & Awareness
William House
101 Eden Vale Road
Westbury
Wiltshire BA13 3QF
Tel: 0373 827 635

Teaching Area
IDS
Institute of Development Studies
University of Sussex
Brighton BN1 9RE
Tel: 0273 606201

DICE
Institute of Education
University of London
20 Bedford Way
London WC1H 0AL
Tel: 01 636 1500

Institute of Ophthalmology
Woolfson Building
27/29 Cayton Street
London EC1V 9EJ
Tel: 01 253 3411 Ext. 480

The Course Secretary
Dept. of International Community Health
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool L3 5QA
Tel: 051 708 9393

Administration Department
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool L3 5QA
Tel: 051 708 9393

The Registrar
LSHTM
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT
Tel: 01 636 8636

Medicins Sans Frontieres (Belgium)
24–26 Rue Deschampheleer
1080 Bruxelles
Belgium
Tel: (2)425 03 00

Medicins Sans Frontieres (France)
8 rue Saint-Sabin
75011 Paris
France
Tel: (1)40 21 29 29

Medicins Sans Frontieres (Holland)
Reguliersbreestraat 12
PO Box 10014, 1001 E A Amsterdam
Holland
Tel: (020) 251272

The Open University
PO Box 48
Milton Keynes
MK7 6AB
Tel: 0908 74066

Department of International Health and Tropical Medicine
Royal College of Surgeons in Ireland
St Stephen's Green
Dublin 2
Tel: 0001 780200

Dept. of International Training
Royal Tropical Institute
Mauritskade 63
1092 AD Amsterdam
The Netherlands
Tel: (020) 5688711

The Short Course Coordinator
Overseas Development Group
University of East Anglia
Norwich
Norfolk NR4 7TJ
Tel: 0603 57880

Institute of Health Care Studies
University College of Swansea
Singleton Park
Swansea SA2 8PP
Tel: 0792 295314

Population Centre
UWCC
University of Wales
College of Cardiff
51 Park Place
Cardiff CF1 3AT
Tel: 0222 874 833

WHO regional offices

The following is an up-to-date list of all the Regional Offices of the World Health Organization:

Africa: WHO, Regional Office for Africa, PO Box 6, Brazzaville, Congo. Tel: 83 38 60-65. Telex: Unisante Brazzaville 5217/5364.

Americas: WHO, Regional Office for the Americas, Pan American Sanitary Bureau, 525 23rd Street N.W., Washington, D.C. 20037, United States of America. Tel: 861-3200. Telex: Ofsanpan Washington 248338. Fax: (202) 223-5971.

Eastern Mediterranean: WHO, Regional Office for the Eastern Mediterranean, PO Box 1517, Alexandria-21511, Egypt. Tel: 483 00 90. Telex: Unisante Alexandria 54028. Fax: 483-89-16.

Europe: WHO, Regional Office for Europe, 8 Scherfigsvej, DK-2100 Copenhagen 0, Denmark. Tel: 29 01 11. Telex: Unisante Copenhagen 15348. Fax: (451) 18-11-20.

South-East Asia: WHO, Regional Office for South-East Asia, World Health House, Indraprastha Estate, Mahatma Gandhi Road, New Delhi-110002, India. Tel: 331 7804. Telex: WHO New Delhi 3165095. Fax: (91) 331.8607.

Western Pacific: WHO, Regional Office for the Western Pacific, PO Box 2932, 1099 Manila, Philippines. Tel: 521 84 21. Telex: Unisante Manila 27652. Fax: 632/52-11-036.

WHO Liaison Office with the United Nations: 2, United Nations Plaza, DC-2 Building, Rooms 0956 to 0976, New York, N.Y. 10017, United States of America. Tel: 963-6004/5. Telex: Unisante New York 234292. Fax: (212) 223-2920.

Leprosy Review Index

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Instructions to Authors

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

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