Volume 69, Number 4, December 1998

LEPROSY REVIEW

Published Quarterly for Lepra: the British Leprosy Relief Association

ISSN 0305-7518

Leprosy Review

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

LEPRA

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Editorial Office: LEPRA, Fairfax House, Causton Road, Colchester CO1 1PU, England
Assistant Editor: Susan Boobis, 118 Malvern Avenue, South Harrow, Middlesex HA2 9EY, England

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Editor's Choice

This issue of *Leprosy Review* was being prepared for printing as we returned from the 15th International Leprosy Congress in Beijing, but we wanted to have some immediate coverage of this event for readers who could not attend. I am very grateful to Colin MacDougall for his speedy production of an eminently readable congress report, which gives a good feel for the diversity of issues discussed. We hope to have further coverage of the conference with conference workshop reports in the next issue of *Leprosy Review*.

The review on stigma in leprosy takes up one of the conference themes and gives an interesting frame work within which to consider stigma. I found that thinking about the cognitive dimensions of leprosy gave anew depth to my biomedical model of disease.

Eric Post's paper from Nigeria on health seeking behaviours gives some indication of the challenges that are ahead. A majority of patients used traditional beliefs to explain the cause of leprosy and consulted folk healers. Unfortunately, none of the folk healer consultations resulted in a referral to the leprosy services. This indicates the need to think widely when considering which health care providers should be included in leprosy awareness programmes.

The importance of the nasal mucosa in the transmission of leprosy continues to tantalize and important questions remain unanswered about the exact role of the nasal mucosa in the transmission and acquisition of leprosy. The paper by Sujay Suneetha is intriguing, showing that in a group of patients with pure neuritic leprosy over half had specific leprosy pathology in the nasal mucosa.

I am very sad to report the death of Dr Dick Rees, one of the greatest twentieth century leaders in leprosy. His obituary (p. 403) tells of his work and the huge personal contribution that he made to the lives of many people working in the field.

DIANA LOCKWOOD

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Editorial

INTERNATIONAL LEPROSY CONGRESS, BEIJING, 7–12 SEPTEMBER 1998: WORKING TOWARD A WORLD WITHOUT LEPROSY

The 15th International Congress in Beijing was attended by over 1000 people, 350 of them from the People's Republic of China, where so much progress has been made in recent years towards the aim of basic eradication as described in this journal by Ma Haide and Ye Ganyun in 1982.[1] International delegates came from virtually all countries where leprosy is still endemic, with an appropriately high representation from India and other parts of South-East Asia, which currently account for over 591,000 of the world total of 828,803 registered cases.[2]

The theme of 'Working Toward a World Without Leprosy' was adopted by the Organizing Committee of the International Leprosy Association at a meeting held 2 years ago and interpreted by the President, Dr Yo Yuasa, as meaning 'a world without leprosy-related problems, both medical and social, emphasizing the point that it is not the disease *per se* but its related problems, mostly social but some medical, which require attention'.[3] The 15th Congress introduced a radically changed format, with emphasis on the need to be forward-looking, action-oriented, integrated and participant-friendly. Pre-Congress workshops were replaced by workshops in the afternoons of the main meeting, and the previous 'state of the art' lectures were replaced by 'Presentation of Current Issues' on the second and fourth days, followed by 'Open Panel Discussion', thus making the morning sessions open to all delegates. Day 5, entitled 'Synthesis', was intended to provide each participant with a broad picture of current and future needs, challenges and possible solutions. One of the main objectives of the Congress and this new, experimental format was to come up with a series of practical recommendations, or even action plans, but to be regarded as 'take-home' lessons rather than official resolutions. In addition, there were, as in previous Congresses, a large number of oral presentations of accepted papers over a 3-day period, together with poster presentations in an exhibition hall, training sessions in the evenings and facilities for non-government organizations, drug companies and other agencies to set up posters and distribute information from booths. The Book of Abstracts listed 43 sessions in the Scientific Programme, covering training, epidemiology, control and eradication, psycho-social aspects, clinical aspects, disability control, rehabilitation, surgery, chemotherapy, experimental aspects, immunology, microbiology and pathology. Headings, authors and summaries of an impressive total of 730 abstracts are recorded in alphabetical order according to subject.

Apart from the exhibits put up by individuals each day, several 'permanent' exhibits were

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of outstandingly high quality and importance. One in the main hall of the conference centre was devoted to the story of leprosy control in China, brilliantly researched and illustrated and surely worthy of preservation for archive purposes as a tribute to the almost unbelievable success of control efforts in this vast country in the present century. The same may be said of 'Quest for Dignity. Victory Over Leprosy/Hansen's Disease', a large-scale photographic exhibition on the upper floor of the conference centre, originally shown in the United Nations Building in New York in October–November 1997. It shows, often in stark terms, the conditions in which many patients had to struggle in the second half of the last century, up to fairly recent times, in various parts of the world. A series of more recent photographs shows people affected by leprosy/Hansen's disease who have overcome difficulties and are obviously managing to live in peace and happiness as individual world citizens, some even finding ways to care for those less fortunate than themselves. The pictures of the children, separated from their families and confined to leprosaria in the last century, are unforgettably poignant. An interesting feature of this Congress was the number and range of subsidiary meetings held by various groups and agencies to discuss matters outside the official programme and agenda. One of particular importance was arranged for members of the International Leprosy Association to discuss its future in the light of falling membership figures and the expense of printing and distributing the *International Journal of Leprosy*. Dr Yo Yuasa was unanimously re-elected as President of the ILA, and in his acceptance speech indicated that he and his Officers would be giving serious attention to this worrying situation in the near future.

With regard to the overall outcome of such a large and expensive event, perhaps the main burden of analysis and summary fell on the shoulders of key speakers in the plenary session, 'Synthesis', on day 5. They addressed 'Disease and Disease Control' (Dr W. C. S. Smith, UK), 'Social Aspects of Rehabilitation' (Dr C. M. Walter, India) and 'Causative Organism and Host Responses' (Dr J. L. Krahenbuhl, USA). Their summaries, while revealing little that was startlingly new, nevertheless focused attention on (1) the highly significant progress which has been made in recent years, much of it due to the implementation of multiple drug therapy, (2) the vital importance of keeping up the pressure with regard to case detection and treatment until the goal of elimination has been achieved, at least at national levels, (3) the need to intensify our efforts with regard to social aspects, rehabilitation, self-care and the acceptance and integration of leprosy patients into all levels of society and (4) the importance of maintaining a research capability in leprosy, to include new molecular and immunological assays to aid diagnosis, improvements in chemotherapy, studies on the pathogenesis of reactions and nerve damage and vaccine research.

Meetings of this kind, bringing together people from so many different parts of the world with interests in almost every conceivable aspect of a complex disease such as leprosy, continue to present a challenge to any reviewer with regard to effectiveness (including cost-effectiveness), success or even failure. However, as a gathering of enthusiastic and highly motivated people who would not otherwise have the opportunity to meet, there can surely be little doubt that this Congress, like many before it, was outstandingly successful. At a critical point in the history of this disease, it brought together medical and non-medical people, learners and experts, field workers and scientists, and gave them the opportunity to find out what more needs to be done to reach the goal of elimination of leprosy as a public health problem as defined by the World Health Organisation, whilst at the same time paying even more attention to the social, psychological and physical needs of those with this disease.

The first congress was held in Berlin in 1897. Beijing marked the centennial. The next, early in the third millenium, will be in Brazil. Is it even conceivable that it may be the last?

Department of Dermatology
The Churchill Hospital
Headington
Oxford OX3 7LJ
United Kingdom

A. COLIN MCDOUGALL

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REVIEW ARTICLE

Dimensions and process of stigmatization in leprosy

KOBINA ATTA BAINSON* &
BART VAN DEN BORNE**
**Ghana Leprosy Service, PO Box A99, Cape Coast, Ghana*
***Department of Health Education and Health Promotion, University of Maastricht, PO Box 616, 6200 MD Maastricht, The Netherlands*

Accepted for publication 15 September 1998

Summary Leprosy is a disease which has struck fear into human beings for thousands of years. This is partly because it causes considerable deformities and disabilities. In 1991, the 44th World Health Assembly adopted a resolution to eliminate the disease as a public health problem by the year 2000. However, one of the major obstacles to achieving this objective is the stigma associated with the disease. Stigma against leprosy patients affects all aspects of leprosy control. This paper describes a model of the stigmatization process in leprosy. The process of stigmatization can be divided into two stages. The first stage describes how certain cognitive dimensions of leprosy lead to a variety of affective responses towards the disease. The second stage involves how these affective responses contribute to social devaluation of the leprosy patient and, consequently, the adoption of negative behaviours towards them.

Introduction

Leprosy has been described as a disease that destroys not only the body but the soul; it is a disease that slowly turns a person into a 'thing'.[1] The disease has afflicted humanity for a long time. It once affected every continent and it has left behind a terrifying image in history and human memory of multilation, rejection and exclusion from society.[2] Since ancient times leprosy has been regarded by many communities as contagious, mutilating and incurable.[2]

Following the successes achieved after the introduction of multi-drug therapy (MDT) in leprosy control, the 44th World Health Assembly adopted a resolution in 1991 to eliminate leprosy as a public health problem by the year 2000. One of the constraints to achieving this objective is the stigma associated with the disease. Stigma is a word that was originally used by the Greeks to refer to bodily signs used to expose something unusual and bad about the moral status of the signifier. Today, the term is widely used similarly to the original literal sense. The meaning of stigma has been extended to embrace any mark or sign of

Correspondence to: K. A. Bainson

0305-7518/98/069341+10 $1.00

perceived or inferred conditions of deviation from a prototype or norm.[3] Furthermore, stigma might be considered as representing a negative outcome or unwanted effect.[4] Goffman[5] describes three types of stigma: physical abomination, blemishes of individual character, and tribal stigma.

Stigma has adverse consequences for leprosy control. The degree of stigma against leprosy in a given community influences many aspects of leprosy control. Some patients would rather conceal their illness than suffer the social rejection which may accompany revelation of the diagnosis. In addition, for fear of being stigmatized, some patients may discontinue chemotherapy prematurely. Further, where patients present late, sometimes because of stigma, transmission of the disease in a community increases, and consequently, hinders control efforts. Finally, patients who report late may suffer deformities and disabilities, which could have been prevented if they had reported earlier.

The objectives of this paper are:

1. To describe the cognitive and affective dimensions of leprosy.
2. To use socio–psychological theories to explain the process of stigmatization in leprosy.

The approach that has been used for this paper is first, to describe the dimensions in leprosy in relation to certain characteristics of the disease, and secondly, to explain the process of stigmatization in leprosy using socio–psychological theories. This approach has been adopted because interventions aimed at solving the problem of stigma in leprosy are unlikely to be effective unless one understands how the various dimensions of the disease influence the process of stigmatization.

The biomedical course of leprosy

The bio-medical course of leprosy describes the illness experience as based solely in pathology. Figure 1 describes the bio-medical and social courses of leprosy from the stages of impairment, through disabilities, handicaps and dehabilitation to destitution. It also describes the psychological changes leprosy patients experience following the appearance of these bio-medical changes. This is a modified version of the WHO model on the bio-medical and social course of leprosy.[6] The WHO version does not clearly illustrate the psychological changes which occur in the leprosy patient: this model describes how the cognitive perceptions in the patient eventually cause loss of self-esteem. Another drawback of the WHO model is that it categorizes personality disorders as an impairment due to leprosy. This creates the impression that leprosy affects one's mental function, a fact which is not supported by scientific evidence.

Leprosy damages nerves. The function of nerves is to provide sensation to the skin, control mobility of the body and to stimulate glands in the skin to keep the skin moist and supple. Consequently, damage to nerves results in loss of feeling, dryness of the skin and paralysis. Without adequate care, secondary changes may occur including ulcers, contractures, shortening of the fingers and toes, as well as bone destruction. In addition, the disease may cause damage to the eyes, leading to blindness.

It may also cause infiltrations in the face, which may result in facial disfigurement. These changes in the structure and function of certain parts of the body are referred to as impairments. Impairments are loss or abnormality of psychological or anatomical structure or function.[7] Impairment may be primary or secondary. Primary impairment results from

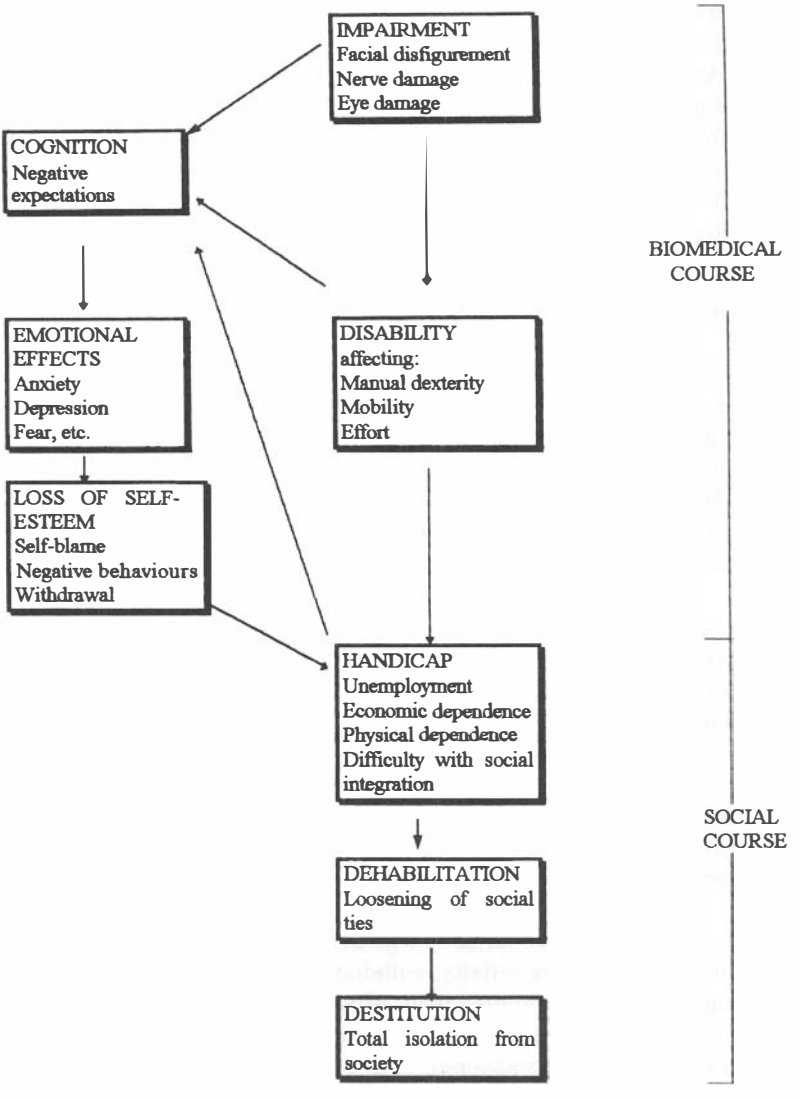

Figure 1. Diagram of the bio-social course of leprosy (modified version of WHO model on bio-social course of leprosy, 1993[6]).

direct damage by the bacterium, whereas secondary impairment results from neglect of primary impairment. A deformity is a visible impairment or a visible consequence of an impairment inside the body.[7] When there is an impairment (primary or secondary), the affected person may find it difficult or impossible to carry out certain activities. This is referred to as a disability, that is, any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being.[7] Leprosy patients often suffer from a variety of disabilities. For example, manual dexterity (skilful use of the hand) may be affected because of insensitivity and muscle paralysis. Walking may become difficult because of ulcers or disintegration of bones of

the foot. Orientation of space, mobility and many other aspects of living may become difficult or impossible, if the eyesight becomes poor.

The impairments and disabilities lead to psychological changes in the leprosy patient, which influence the social course of the disease. Impairments are interpreted as negative perceptions by the patient. As a result, the patient develops negative expectations of himself with respect to life. This is likely to generate a variety of emotions, including anxiety, fear and depression. Eventually the patient loses self-esteem and may become withdrawn or adopt negative behaviours.

Social course of leprosy

The social course of leprosy indicates that the disease develops in a local context where economic, moral, cultural and social factors powerfully affect the lived experiences of leprosy patients. According to Kleinman,[8] the social course varies according to the different local worlds, social networks and social histories. Thus the social dimensions of leprosy are closely interwoven with the cultural traditions of a society. Every society considers health and disease, life and death in different ways and this influences the attitudes taken by a community towards leprosy patients as a consequence of their illness.

A persistently disabled person may experience many disadvantages that limit or prevent that person from fulfilling his or her normal role in society. These disadvantages are known as handicaps (Figure 1). Leprosy patients with disabilities experience and suffer from a variety of handicaps. For example, they may lose their jobs, and consequently their economic independence. This means that they cannot support their families. In addition, those who are severely disabled may lose their physical independence, since they need others to care for them. Other consequences of stigma include loss of self-esteem, difficulty in finding a marriage partner, and generally a lower quality of life. Indeed, in some cases the mere diagnosis of leprosy is sufficient handicap for the affected person, even when there is no disability.

The adverse reactions of the community tend to devalue the status of the leprosy sufferer. This manifests itself by fear, insensitivity, withdrawal, etc. Eventually, the leprosy sufferer loses social status and becomes progressively isolated from the society, family and friends. Frustrations with employment, crippling deformities and social ostracism may finally force him into alcoholism, begging and adoption of a hostile attitude towards society. This stage is known as dehabilitation.

Eventually, a leprosy patient may be forced to leave his or her home and settle in a rehabilitation home or in a leprosy colony with other leprosy patients. This final stage is known as destitution.

Dimensions of stigma

Cognitive dimensions describe how much influence a mark has in interpersonal interactions.[3] They are also useful in understanding the stigmatization process, including how a condition emerges as a socially degrading mark, as well as how a stigmatized individual develops a negative self-concept. Indeed, it is the perceptions people have about leprosy rather than the disease itself which significantly influences their attitude towards leprosy and leprosy

Table 1. Cognitive dimensions in relation to characteristics of leprosy

Cognitive dimensions	Characteristics of leprosy
Concealability	High visibility of stigmatizing 'marks': on head, hands or feet
Course	Curable but generally perceived to be incurable; chronic course
Disruptiveness	No specific characteristic relevant to this dimension
Aesthetic qualities	Deformities
Origin	Depends on culture, religion, etc. For example, punishment by god, inherited, physical causes, witchcraft
Peril	Mildly contagious but generally perceived to be very contagious

patients. Jones *et al.*[3] describe six cognitive dimensions of stigma. These are concealability, course, disruptiveness, aesthetic quality, origin, and peril. Table 1 describes the various cognitive dimensions as well as the characteristics of leprosy under each dimension.

Cognitive dimensions

CONCEALABILITY DIMENSION

According to Jones *et al.*,[3] concealability describes the extent to which certain characteristics of marks make themselves obvious or can be made obvious to all who are involved in a relationship. It may depend on the visibility of the mark, what the afflicted individual says or does, on the characteristics of those interacting with the victim or on the circumstances of the interaction. At one extreme, stigmatized persons can be in a position where no one knows about the problem. At the other extreme, they always have to be conscious of the social effects of their affliction. In general, among stigmatizing conditions leprosy fares poorly on the concealability scale, because most of the deformities occur on the head, the hands or the feet. Consequently, they are very visible. A patient with severe deformities of the hands, feet or head continually bears the mark of the disease and, consequently, stands in perpetual danger of being stigmatized. It must, however, be added that even a patient who bears no external mark of the disease may suffer some stigma if he discloses his history.

COURSE DIMENSION

The course of a mark focuses on the pattern of change over time and its ultimate outcome. Gussow and Tracy[9] described eight criteria that ultimately influence social rejection. Three of these are related to the course of a disease. These are, that the condition should be progressively crippling and deforming, that it should be non-fatal and chronic, and that it should appear to be incurable. Leprosy meets all three criteria. However, so does a condition like rheumatoid arthritis. And yet the former is very stigmatizing whilst the latter is less so. This implies that even though the course dimension may be significant in the stigmatization process, there are other dimensions which make leprosy more amenable to stigmatization. As noted by Jones *et al.*,[3] the course dimension appears to be bound to other dimensions of stigma. Further, it is also important to distinguish between actual changes in the course in contrast to beliefs held by the labeller involved about the pattern the mark will follow in time to come. Indeed, it appears that it is the cognitive perceptions held by the labeller about the course rather than the actual course which is more important in the process of stigmatization.

For example, an air hostess in Ghana had early signs of leprosy without any disabilities or deformities, received adequate treatment and was cured. Yet she continued to suffer social rejection from her colleagues at work and eventually had to quit her job. The patient noted actual changes in her condition, and yet her colleagues continued to hold the belief that the course (or perhaps other dimensions of the disease) had not changed.

DISRUPTIVENESS DIMENSION

The third dimension of stigma is disruptiveness, which means the property of a mark that hinders, strains and adds to the difficulty of interpersonal relationship.[3] The authors refer to any condition that makes appropriate interaction patterns uncertain and unpredictable, and that blocks or distorts the communication process. How relevant is this dimension in stigmatization of leprosy patients?

Leprosy does not affect mental functioning. Arguably, the mark in leprosy that is likely to draw attention to itself and perhaps affect communication is the disabilities and deformities. In leprosy, this dimension is inextricably linked with other dimensions, for example, concealability, perceived threat and aesthetics. It is the opinion of the authors that this dimension is unlikely to play a significant role in the stigmatization of leprosy patients. Indeed as noted by Jones *et al.*,[3] this dimension must be viewed as tentative and its usefulness more in doubt, because it is inherent in various dimensions of blemishing conditions.

AESTHETIC DIMENSION

The fourth dimension according to Jones *et al.* is aesthetics. This refers to what is beautiful. Though scholars have long discussed the nature and determinants of aesthetic appeal, we are a long way from understanding why one object is beautiful and another generally considered ugly.[3] In spite of the cliché that 'beauty is in the eye of the beholder', some people seem ugly to most observers. A leprosy patient with numerous large nodules on the face or one who has lost all her fingers would hardly be described by most people as beautiful. But to what extent does aesthetics contribute to stigmatization in leprosy? Is it culturally determined?

English[10] argues that a number of studies suggest that the aesthetic factor strongly influences social and personal preferences of non-disabled for disabled persons. People generally respond to others as though they agree with the statement that physical beauty is a sign of interior, spiritual and moral beauty. This is perhaps why people on first sight are attracted to others with well-proportioned features and not to those with less well proportioned features. The aesthetic dimension appears to engender a primitive affective response which is in sharp contrast to the cognitive, attributional, stigmatizing processes elicited by other conditions.[3] Indeed, it is doubtful whether leprosy would be associated with such stigma were it not for the distortions it causes to personal beauty.

But familiarity as determined by cultural standards of beauty also appears to influence our concept of beauty. Society's concept of beauty is not static and, indeed, is inherent in prevailing cultural values. In occidental societies, great value is placed on physical beauty, so there is a tendency for anyone with physical deformity to be socially devalued.[12]

ORIGIN DIMENSION

The fifth dimension of stigma, according to Jones *et al.*[3] is origin. This dimension refers to how a mark came to be, including when the mark originated during the course of life, the

rapidity or slowness of its onset and the afflicted individual's role in engendering his own mark. In leprosy, this dimension covers areas such as the perceived cause of the disease and the interpretations made of the perceived cause. How significant is this dimension in the entire stigmatization process in leprosy? Does it matter whether leprosy is perceived to be caused by a witch or a punishment for a transgression against a deity? It would appear to the authors that the significance of the perceived origin is related to the cultural environment of the leprosy patient as well as the perceived role the individual has in bringing about his affliction.

A few issues need to be raised in reaction to Jones's categorization. Will a child with leprosy suffer the same level of stigma as an adult? If not, are there other factors that determine such evaluations? Does rapidity of onset of the mark influence the degree of stigma in leprosy? Research on these issues with respect to leprosy is scant.

PERIL DIMENSION

The last dimension, peril, focuses on the threat posed by the stigmatized individual. Threat may be perceived when the disease is believed to be contagious, or where leprosy patients are considered to be ritually unclean, or where, as in certain cultures leprosy patients are believed to be witches. Indeed, even a weak and deformed hand may be perceived as a threat. For example, one of the authors personally observed a 10-year-old enter a bus. Unknown to the boy, he sat next to a leprosy patient with severe deformities of the hand. As soon as he saw the deformed hand, he quickly moved away from the patient. When the author asked him later about his behaviour he replied, 'I feared he would knock me on the head with his hand'. Unknown to him, that hand was too weak to even give a knock.

Affective dimensions

The emotional reactions that individuals, groups or communities develop towards leprosy patients may include pity, anger and fear. Figure 2 describes the affective responses that

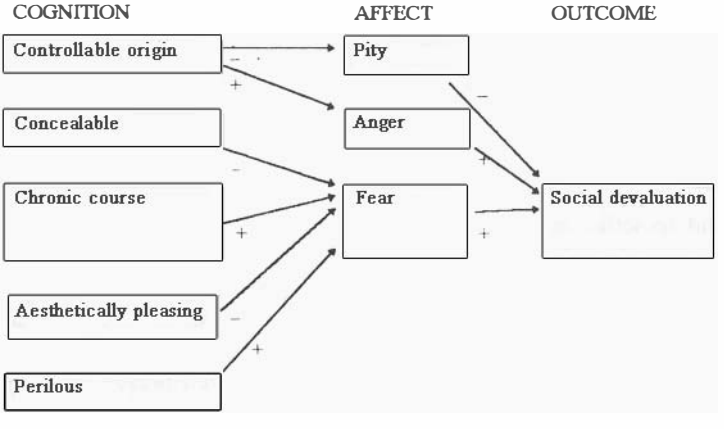

Figure 2. Schema of stigmatization in leprosy.

mediate between the cognitive dimensions and the outcome (stigma). The cognitive dimension which will be most relevant antecedents to these affective responses will depend on the knowledge, beliefs and values of individuals, groups or communities.

FEAR AS MAJOR AFFECTIVE DIMENSION

It appears that in leprosy, the element of fear is more likely to lead to rejection than any other affective dimension. It is the perceived risk of physical harm and pain that serves as the stimulus for fear. Jones *et al.*[3] remarked that leprosy is surely the most striking of the afflictions prompting fears of contagion. What are the reasons for this assertion? First, there are a number of neurological diseases which present similarly to leprosy, but which do not attract the same degree of stigma that leprosy does. For example, a patient was admitted for 3 months in a Teaching Hospital in Ghana with deformities of both hands. He received considerable sympathy and support from the nurses. At the time, leprosy was not suspected, and a non-contagious neurological condition was diagnosed. After several investigations it became clear that the condition was leprosy. As soon as the nurses became aware that the patient had leprosy, their attitudes became negative and they demanded that he should be transferred to the Contagious Diseases Centre. Second, normal people acceptable to others when alone may, by association with a leprosy patient, suffer similar negative social reactions. This may explain why close relations and sometimes health workers attending to leprosy patients also suffer some stigma. Goffman[5] has recognized this phenomenon and labelled it 'courtesy stigma'.

A leprosy patient may be treated with pity where the perceived cause of the disease is presumed to be beyond the volitional control of the patient. However, where the cause of leprosy is perceived to be under the patient's volitional control, it is likely to generate anger towards the patient.

Process of stigmatization

Diseases are feared, but it is people who are stigmatized. Katz[13] observed that the reaction of the majority group observer to the stigmatized individual would seem to have two basic components: first, the perception of a negative attribute, and second, the global devaluation of the possessor. This would suggest that stigmatization of the leprosy patient has two basic components: perception of a negative attribute(s) to leprosy and devaluation of the leprosy patient.

ATTRIBUTIONS TO LEPROSY

Individuals and societies make attributions to phenomena in order to make sense of their world. Attributions describe the processes of explaining events and the behavioural and emotional consequences of those explanations. To be stigmatized is in many ways similar to being a 'failure'.[4] As 'failures,' leprosy patients elicit causal search and attributions from others and themselves. According to Attribution Theory,[4] the perceived cause of a stigma should determine affective reactions towards the stigmatized person (e.g. anger, pity, and fear), future expectations regarding that individual (e.g. the likelihood of recovery), and a variety of behavioural responses. Thus the attributions a given society, group or individuals

make on leprosy influence significantly the emotions they develop towards the disease and, consequently, their behaviour towards leprosy patients. Why then do some societies adopt different affective responses towards the disease?

First, it may be that in some societies, physical abnormality is associated with moral bankruptcy. This is probably likely to hold true in societies that explain diseases as resulting from a transgression against a divinity. Second, among certain cultures and religions, ethical norms do not demand explanations of the type that are called for in the majority of societies For example, Moslems believe that every outcome (success or failure) is ordained by God. Consequently, it should not be surprising if ardent followers of this religion do not display resentment towards leprosy patients. This may, perhaps, explain why Shiloh[15] observed little stigma among the Hausa in Northern Nigeria, who are predominantly Moslem. Third, social psychologists[3] have proposed that this derives from the norm of social responsibility, which requires that we help those who are dependent.

Weiner[4] described three major dimensions of attributions: locus of causality, controllability and stability. Locus of causality is the perception that the location of the source is either due to factors internal or external to the person. Controllability is the extent to which causes are believed to be under volitional control. Stability is a person's location of cause(s) on a continuum according to how stable or unstable that cause is perceived. According to the theory, if society, groups or individuals perceive the cause of leprosy as controllable by the leprosy sufferer, it is likely that anger will be directed towards the leprosy patient (Figure 2) and, as a consequence, the patient will suffer social rejection. On the other hand where the cause is perceived to be uncontrollable, this is likely to generate pity and help-giving (Figure 2). For example, if the cause of leprosy is attributable to uncontrollable factors such as physical causes in the environment, this is likely to generate sympathy or pity for the sufferer. On the other hand, where the disease is attributable to controllable factors such as religious transgression or sexual indiscretion, this elicits anger, revulsion, and social rejection.

In leprosy, the locus of causality may be perceived as internal where it is believed that the source of the disease is infectious or contagious. This attribution is likely to generate fear. However, where the source of the disease is perceived to be external to the patient, for example, due to physical factors such as the weather, this is likely to generate pity.[4]

CONTEXTUAL FACTORS

Does the affective response exhibited by individuals, groups or communities remain static? Do other factors such as situational or individual characteristics influence this? A study by Gussow and Tracy[14] found that leprosy is not salient in the minds of Westerners. In this study, even though people ranked the disease among the top 10 serious diseases, they generally viewed it with less apprehension than diseases like cancer or mental illness. This finding was unanticipated in view of the prevailing presumption of strong stigma against leprosy. The authors concluded that leprosy was not salient, because the disease was relatively rare, and therefore people did not see it as an imminent threat. Does this mean that familiarity and direct experience with the disease is the basis for the observed Western attitude? Other studies do not, however, support this viewpoint. In a study of leprosy among the Hausa of Northern Nigeria, Shiloh[15] observed little or no stigma against leprosy patients even though the prevalence of the disease was high in those communities.

Conclusion

Stigma may be a hindrance to leprosy control. An understanding of the determinants of stigma and the process of stigmatization is, therefore, an essential step towards developing interventions to address the problem. Sadly, Stigma in leprosy is one area where there is a paucity of empirical data. Research is required into the relative importance of the various cognitive dimensions in engendering stigma in specific communities or cultures. Research would also be required into how the characteristics of the patient or the disease influence the degree of stigma. For example, would a child with similar disease characteristics as an adult suffer the same degree of stigma? Would a leprosy patient who is influential or assertive in his community be less stigmatized than one who withdraws from society? Would a patient with multiple nodules on the face be less stigmatized than one with claw hands?

Further, in the search for interventions that address the issue, research would also be required. For example, to what extent does modelling by care providers to leprosy patients influence stigma against leprosy patients? What informational or instrumental supports need to be given to close relations of leprosy patients to assist them to cope effectively with stigma and, in addition, assist the patient to cope with it? Are integrated leprosy control programmes more successful at addressing the issue of stigma than vertical programmes?

It is when studies have been conducted into stigma in leprosy that we can develop interventions through a planned and systematic approach and application of socio–behavioural and cultural theories.

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Histological studies in primary neuritic leprosy: changes in the apparently normal skin

SUJAI SUNEETHA*, S. ARUNTHATHI*, SUSHIL CHANDI#, NISHA KURIAN* & CHINOY J. G. CHACKO*

**Schieffelin Leprosy Research and Training Centre, Karigiri, Tamil Nadu—632 106, India; #Christian Medical College and Hospital, Vellore, Tamil Nadu—632 004, India*

Accepted for publication 10 July 1998

Summary The visually normal skin of 196 patients diagnosed clinically to have primary neuritic leprosy was studied histologically to determine whether there were any specific changes due to the disease in this site. Histological changes due to leprosy were seen in 32·1% of the patients, and included, indeterminate leprosy in 19·4%, borderline tuberculoid leprosy in 6·6% and borderline lepromatous leprosy in 6·1%. The remaining biopsies showed mild non-specific dermal inflammation, mild nerve changes or no significant lesion. The nerve inflammation and/or granulomas were mostly in the deep dermal nerves or neurovascular complexes. This study shows that there is a cutaneous component to primary neuritic leprosy and the disease is not totally confined to nerves. The absence of visible hypopigmented patches in these patients is probably related to the deep location of the dermal inflammation.

Introduction

Primary neuritic leprosy (PNL) presents as a peripheral neuropathy with either pure sensory or combined sensory and motor nerve dysfunction. The characteristic clinical skin lesions of leprosy are absent.[1] No definite information is available as to the extent of involvement of the apparently normal skin in PNL. Histological studies of skin in PNL are few[2,3] and have only suggested mild dermal nerve involvement in the skin. An earlier study of skin biopsies from PNL patients at Karigiri has shown changes consistent with leprosy in 11 out of 17 patients, including two with a borderline tuberculoid (BT) and one with a borderline lepromatous (BL) histology.[4] This prompted us to make a more extensive study of the histological changes in the skin of PNL patients even though they do not have clinically visible skin lesions.

Correspondence to: S. Suneetha, Director, Dhoolpet Leprosy Research Centre, Karwan Post, Hyderabad-500 006, India

0305-7518/98/069351+07 $1.00

Materials and methods

A total of 196 patients seen at the Schieffelin Leprosy Research and Training Centre, Karigiri between 1978 and 1991 were clinically classified as PNL based on the following criteria: sensory or sensory and motor dysfunction, negative skin smear and no detectable skin lesions.[5] A diagnostic cutaneous nerve biopsy was performed on all these patients (radial cutaneous nerve, 94; musculocutaneous nerve, 73; ulnar cutaneous nerve, 15 and sural nerve, 14). Histological confirmation of leprosy was present in 158 patients. Although the remaining 38 patients had no nerve biopsy confirmation, they were classified and treated as PNI, since they had definite nerve thickening with sensory or sensory and motor nerve deficit.[6] Other causes for a peripheral neuropathy, such as congenital, traumatic and diabetic neuropathy, were excluded in these patients.

Biopsies were usually taken from the skin over the cutaneous nerve selected for biopsy to establish a diagnosis of PNL. An elliptical piece of skin was taken from the edge of the skin incision. This was sometimes within the area of sensory change and on occasions outside it. Skin biopsies were also obtained from other parts of the body that had sensory changes such as anaesthesia, hypoaesthesia, paraesthesia or dryness. The biopsied skin samples were fixed in formal–Zenker's fixative for 4–6 h and then transferred to 70% alcohol. They were subsequently routinely processed and embedded in paraffin. Serial 5 μm sections were cut and stained with haematoxylin and eosin and a modified Fite's stain for acid fast bacilli.[7] In all, 182 of these patients were followed up for varying periods ranging from 6 months to 12 years to look for any changes in the pattern of the disease.

Results

A total of 196 patients clinically diagnosed as PNL were studied. Skin biopsies were taken from the nerve biopsy site in 147 patients (75·3%) and from other sites in 49 patients (24·7%). These were from areas of anaesthesia in 133 patients and from areas of normal sensation in 63 patient s. Their histological classification is given in Table 1.

INDETERMINATE LEPROSY

The skin biopsies of 38 patients (19·4%) in the study showed changes of indeterminate leprosy. The deep dermal nerves were usually enlarged and showed definite intraneural

Table 1. Histological classification of skin

Classification	No. of patients (%)
Indeterminate	38 (19·4)
Consistent with indeterminate leprosy	52 (26·5)
Borderline tuberculoid leprosy	13 (6·6)
Borderline lepromatous leprosy	12 (6·1)
Non-specific inflammation	44 (22·5)
No significant lesion	37 (18·9)
Total	196

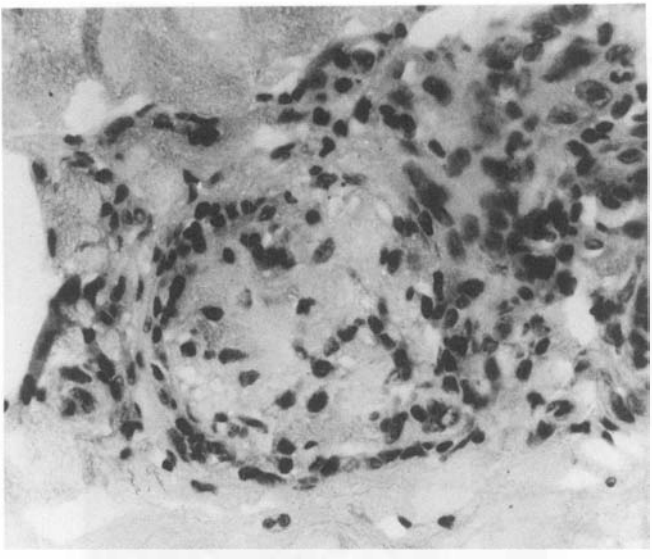

Figure 1. Indeterminate leprosy, showing a deep dermal nerve with a few intraneural lymphocytes and dense perineurial inflammation (H&E × 200).

infiltration by lymphocytes (Figure 1). Additionally, 66% showed perineural inflammation with lymphocytes and histiocytes. Associated mild perivascular and adnexal inflammation was common.

Acid fast bacilli were present in six cases, in nerve alone (two cases), nerve and macrophages (two), nerve and smooth muscle (one) or endothelial cells of blood vessels (one).

CONSISTENT WITH INDETERMINATE LEPROSY

This classification was ascribed to 52 skin biopsies (26·5%) which showed mild to moderate degrees of perivascular and adnexal inflammation including smooth muscle involvement and enlarged deep dermal nerves with perineurial lymphohistiocytic infiltration. Acid fast bacilli were not seen.

BORDERLINE TUBERCULOID LEPROSY

The biopsied skin of 13 patients (6·6%) showed histological features of borderline tuberculoid leprosy. These consisted of epithelioid cell granulomas involving neurovascular complexes in the deep dermis and sometimes blood vessels and adnexal structures (Figure 2). The granulomas contained moderate numbers of lymphocytes either as focal collections or diffusely scattered in the granuloma. Giant cells were present in the epithelioid cell aggregates in eight of the biopsies. Nerve inflammation consisted of intraneural lymphocytes and occasionally intraneural histiocytes and epithelioid cells. An occasional acid fast bacillus was identified in the dermal nerves in five biopsies and in the endothelial cells of a blood vessel in one.

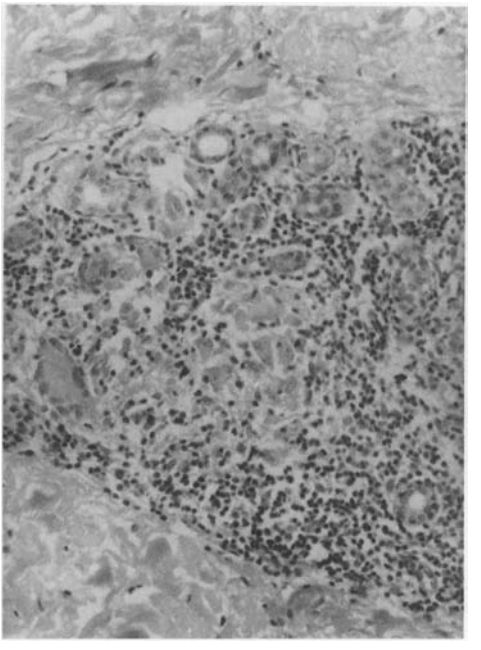

Figure 2. Borderline tuberculoid leprosy, with a dermal granuloma consisting of epithelioid cells, Langhan's giant cells and a cuff of lymphocytes (H&E × 100).

BORDERLINE LEPROMATOUS LEPROSY

In 12 patients (6·1%), the skin revealed deep dermal nerve inflammation accompanied by collections of lymphocytes, histiocytes and macrophages close to nerves, neurovascular complexes and other skin adnexal structures (Figure 3). A few bacilli were present in nine biopsies and moderate numbers of bacilli in three biopsies. The bacilli were present in nerves and macrophages (five cases), nerves alone (four), nerves, macrophages and smooth muscle (one), in macrophages alone (one) and in endothelial cells (one).

NON-SPECIFIC INFLAMMATION

In 44 patients (22·5%), the skin biopsies showed non-specific inflammatory changes, such as a few small perivascular lymphohistiocytic collections around upper dermal blood vessels and skin adnexal structures. Dermal nerves were within normal limits in 37 patients (18·9%) and were slightly enlarged with prominent perineurial cells and Schwann cell prolipheration in seven patients (3·6%). Acid fast bacilli were not present.

NO SIGNIFICANT LESION

In 37 patients (18·9%) there was no evidence of dermal inflammation, neuritis or acid fast bacilli. These skin biopsies were designated as having 'no significant lesion'.

The relationship between the sensory status of the biopsied area and histological diagnosis is given in Table 2. Biopsies taken from an area of sensory change revealed

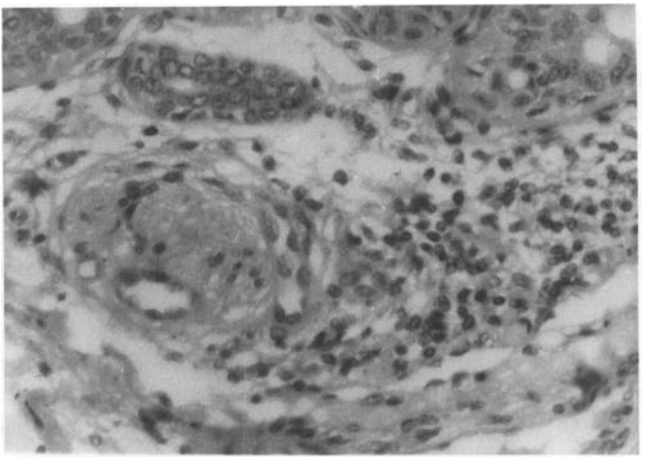

Figure 3. Borderline lepromatous leprosy, showing a macrophage granuloma involving a sweat gland complex as well as perineurial lamination and inflammation. Fite stained sections revealed acid fast bacilli in the macrophages (H&E×200).

inflammation of dermal nerves in 65·4% of the patients whereas those from an area of normal sensation showed nerve inflammation in only 44·4% of the patients ($p < 0{\cdot}001$).

Among the 182 patients followed up in the study, 29 (15·9%) developed visible skin lesions during the follow-up period.

Discussion

The apparently normal skin in lepromatous, borderline, tuberculoid and indeterminate leprosy has been studied by different workers[8–10] but relatively few histological studies of the skin in PNL. A few case reports and studies on small numbers have found specific changes due to leprosy in the skin in PNL[2–4] but there are also reports to the contrary.[6,11]

In the present study, there were histological changes due to leprosy in the skin of 32·1% of the patients with PNL, though they did not have skin patches of leprosy. In all, 12·7% of the patients revealed either epithelioid or macrophage granulomas. The granulomas were located

Table 2. Relationship between anaesthesia and histology

	Sensation		
Histological classification	Anaesthesia	Normal	Total
Borderline lepromatous leprosy	9	3	12
Borderline tuberculoid leprosy	11	2	13
Indeterminate leprosy	67	23	90
Non-specific inflammation	25	19	44
No significant lesion	21	16	37
Total	133	63	196

mostly in relation to the deep and mid-dermal nerves and neurovascular complexes. This would account for the somatosensory and autonomic neuropathic manifestations of the disease[12,13] in the absence of the characteristic skin lesions. The absence of visible hypopigmented skin lesions in these patients is probably related to the deep location of the granulomas in the dermis, beyond the scope of exercising any direct influence by proximity on the melanocytes in the epidermal stratum bacillus.

It would appear that it is only when the dermal inflammation reaches the superficial dermal regions, is it likely to produce a visible skin patch. Follow-up studies suggests that this may be true, since 29 of the patients in this cohort subsequently developed skin patches. The perineurial inflammation seen in 52 patients designated 'consistent with indeterminate leprosy' and the intraneural inflammation seen in 'indeterminate leprosy' may represent steps in the progression to granuloma formation and determined forms of the disease.

The present study suggests that leprosy primarily affects the nerve from where it breaks out into the dermis to produce cutaneous lesions, with individual patients exhibiting histological features of the disease in varied forms and stages of evolution. Haematogenous spread of infection from a primary lesion in the nasal mucosa is a distinct possibility, in view of the inflammatory infiltrate predominantly involving neurovascular complexes and blood vessels. In recent years, there is increasing experimental evidence in favour of the nasal mucosa as the primary site of entry of *Mycobacterium leprae*.[14,15]

The present study has shown that a skin biopsy from an area of anaesthesia is more likely to show evidence of dermal nerve inflammation and/or granuloma than a biopsy from an area with normal sensation.

In conclusion, there are specific histological changes due to leprosy in the skin of PNL patients although they do not manifest skin patches. The deep dermal location of the inflammation may account for the absence of hypopigmented skin lesions. The presence of an inflammatory reaction in dermal nerves, with granulomas and acid fast bacilli in the skin indicates widespread dissemination of the disease, even when it clinically appears to be confined to a few major nerves.

Acknowledgements

We wish to thank Dr C. K. Job, Dr P. S. S. S. Rao and Dr Steve Withington for their advice and suggestions during the preparation of this manuscript, and Mrs Reeny and Mr K. Ramana Babu for secretarial assistance.

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Lepr Rev (1998) **69,** 358–366

Histological studies in primary neuritic leprosy: changes in the nasal mucosa

SUJAI SUNEETHA*, S. ARUNTHATHI*, ANAND JOB#, ANAND DATE#, NISHA KURIAN* & CHINOY J. G. CHACKO*

**Schieffelin Leprosy Research and Training Centre, Karigiri, Tamil Nadu–632 106, India; #Christian Medical College and Hospital, Vellore, Tamil Nadu–632 004, India*

Accepted for publication 1 September 1998

Summary The nasal mucosae of 39 cases of primary neuritic leprosy (PNL) registered at Karigiri were studied histologically to determine nasal mucosal involvement in PNL and its relevance to the pathogenesis of the disease. Specific changes of leprosy were seen in 20 (51%) biopsies, ranging from macrophage granulomas with acid fast bacilli, to epithelioid granulomas and nerve inflammation. The remaining biopsies revealed chronic inflammatory changes of the mucosa or mild non-specific nerve changes. These findings show that there are widespread effects of the disease even in PNL patients in whom the disease is believed to be confined to the peripheral nerves. The findings also show that early leprosy involvement can be found in the nasal mucosa even before lesions become apparent in the skin or other parts of the body. The nasal mucosa could be one of the sites for the primary lesion in leprosy. Clinical and histological examination of the nasal mucosa may be useful and important in the early diagnosis of leprosy and especially in contacts.

Introduction

Although leprosy is primarily a disease of the nerves and skin, other tissues like the nasal mucosa, the anterior segment of the eye, and the testis are known to be affected by the disease.[1] Involvement of the nasal mucosa in lepromatous,[2,3] indeterminate, tuberculoid and borderline leprosy has been reported.[4] Furthermore, studies in the nine-banded armadillo and nude mice suggest that the nasal mucosa may be an important site for entry and dissemination of lepra bacilli.[5,6]

Primary neuritic leprosy is characterized by signs and symptoms of a peripheral neuropathy, no recognizable skin lesions and skin smears that are negative for acid fast bacilli.[7] The pathogenesis and evolution of this form of leprosy is still poorly understood. The

Correspondence to: Dr. Sujai Suneetha, Director, Dhoolpet Leprosy Research Centre, Hyderabad–500 006, India

 0305-7518/98/069358+09 $1.00

present study was undertaken to determine if there are histological changes due to leprosy in the nasal mucosa of patients with PNL and its relevance to the pathogenesis of the disease.

Materials and methods

Nasal mucosal biopsies from 39 consenting patients with PNL seen at the outpatient department at Karigiri were studied. A diagnosis of PNL was made based on the following clinical criteria; signs and symptoms of a peripheral neuropathy, absence of skin patches and negative skin smear.[8] A cutaneous nerve biopsy was done in all these patients. A histological confirmation of leprosy was available in 32 patients. The remaining seven patients were treated as leprosy, based on finding definite nerve thickening and the other clinical criteria for PNL.[9] Other causes of a peripheral neuropathy were excluded.

A cotton swab soaked in 2% xylocaine with adrenaline was placed in the nostril for a few minutes to produce local anaesthesia and reduce the risk of bleeding. The biopsy was taken from the mucosa over the anterior end of the inferior turbinate bone using a Takahashi nasal biopsy forcep and the specimen was immediately immersed in Formol–Zenker's fixative for 4 h and then transferred to 70% alcohol. It was then routinely processed and embedded in paraffin. Serial 5-μm thick sections were cut. Some sections were stained with haematoxylin and eosin and others with Job and Chacko's modification of the Fite Faraco stain for acid fast bacilli.[10] The yield of diagnostic lesions in the nasal mucosa was then determined.

Results

Based on histological examination the biopsies were classified as in Table 1. A brief description of the histological changes is given below.

NERVE INFLAMMATION

Nine of the 39 nasal mucosal biopsies (23%) showed inflamed nerves in the nasal mucosa (Table 1). The nerves were enlarged (Figure 1) and showed dense perineurial and mild intraneural infiltration by lymphocytes (Figure 2). There was usually an accompanying chronic perivascular, adnexal and subepithelial inflammation of the mucosa. Four of them (44%) revealed acid fast bacilli in the Fite stained sections.

Table 1. Histological findings in nasal mucosa

Histological diagnosis	No. of patients (%)	Biopsies with AFB (%)
Nerve inflammation	9 (23)	4 (44)
Macrophage granulomas	9 (23)	9 (100)
Epithelioid granuloma	2 (5)	0
Non-specific inflammation	19 (49)	0
Total	39	13

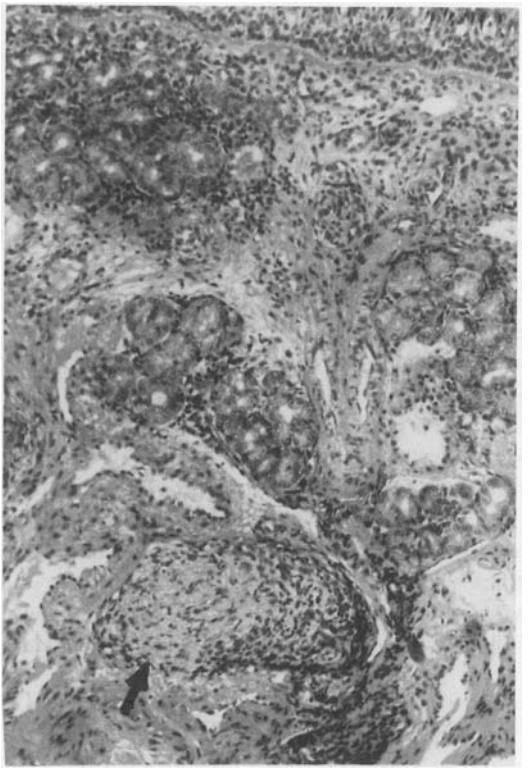

Figure 1. Photomicrograph of the nasal mucosa showing mild inflammation of the submucosa and an enlarged and inflamed nerve (H&E × 100).

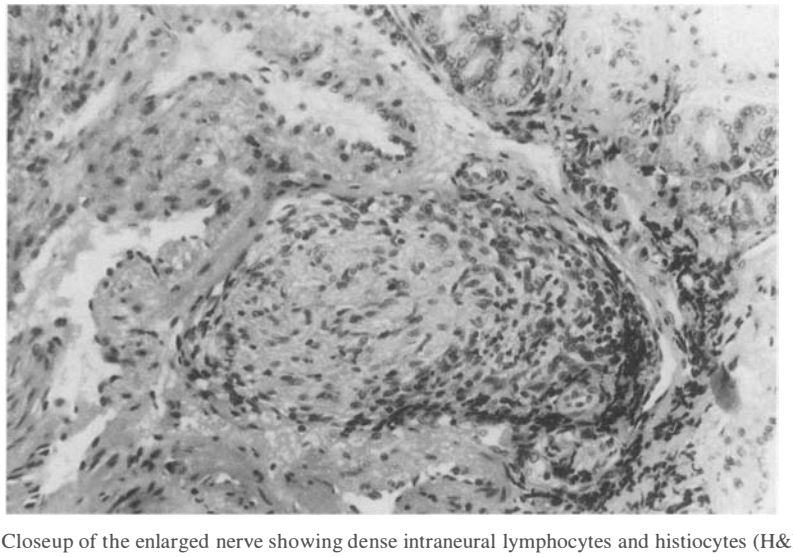

Figure 2. Closeup of the enlarged nerve showing dense intraneural lymphocytes and histiocytes (H&E × 200).

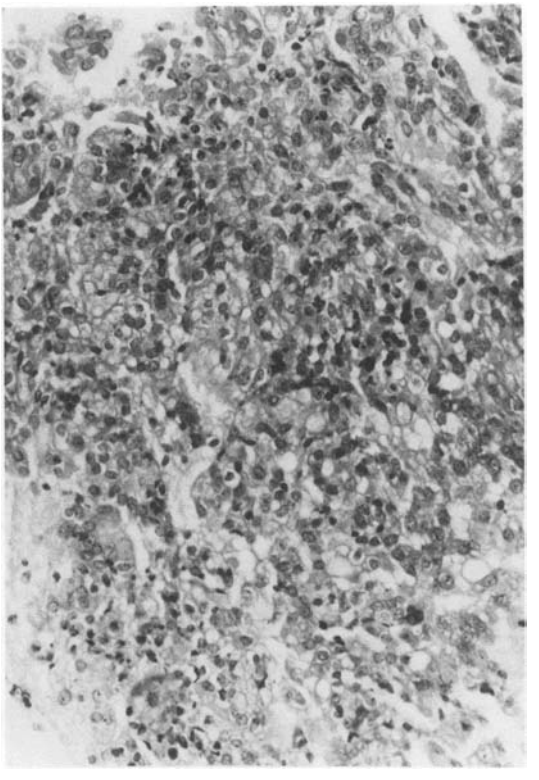

Figure 3. Photomicrograph of the nasal mucosa showing macrophages in the loose stromal connective tissue (H&E × 400).

MACROPHAGE GRANULOMAS

Macrophage granulomas were seen in nine (23%) of the biopsies. The macrophages were present in the nasal mucosa in relation to mucosal glands and in the loose stromal connective tissue (Figure 3). Fite stained sections revealed acid fast bacilli in all these nine cases, in the macrophages (Figure 4), nerves and in endothelial cells of blood vessels.

EPITHELIOID GRANULOMAS

Aggregates of epithelioid cells cuffed by lymphocytes were seen in the nasal mucosal biopsies in two patients (5%). These epithelioid cells were present in relation to mucosal glands (Figure 5), and there was accompanying nerve inflammation and chronic inflammatory changes in the mucosa. Acid fast bacilli were not seen.

NON-SPECIFIC INFLAMMATION

Nineteen biopsies (49%) revealed non-specific inflammatory changes in the mucosa consisting of perivascular and periglandular infiltrate of lymphocytes, histiocytes and plasma cells with no evidence of nerve inflammation or bacilli. In five of these biopsies, the nerves showed prominent Schwann cell nuclei and prominent perineurial cells.

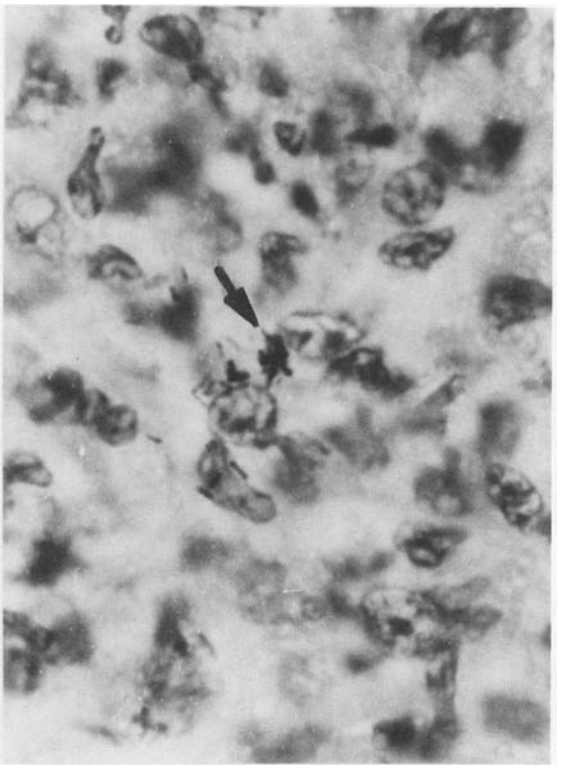

Figure 4. Acid fast stain showing clumps of bacilli in macrophages in the nasal mucosa (modified Fite's stain × 1000).

The relationship between the nasal biopsy findings and nerve histology is given in Table 2. Of the 17 patients who had a multibacillary histology [lepromatous leprosy (LL) and borderline lepromatous leprosy (BL)] in the nerve, 10 (59%) showed nerve inflammation, acid fast bacilli or granulomas in the nasal mucosa. Among the 15 patients who showed a borderline tuberculoid (BT) or indeterminate leprosy histology in the nerve, five displayed nerve inflammation; one had a epithelioid granuloma and the majority (nine) revealed non-specific inflammation in the nasal mucosa.

Discussion

The nasal mucosa is a rich reservoir of infection. While no organisms are shed from the intact skin of even highly bacilliferous lepromatous patients,[11] large numbers of *M. leprae* are disseminated in the nasal secretions of lepromatous leprosy patients.[2] These bacilli are viable and capable of multiplication in a new host.[12] Therefore nasal secretions of a multibacillary patient may be a very potent, if not the only source of *M. leprae* and droplet infection is a distinct possibility. Animal studies have shown that when immunosuppressed nude mice were placed in an environment containing aerosolized *M. leprae*, they developed the disease.[13] Introduction of *M. leprae* into the lung of mice by tracheostomy did not result

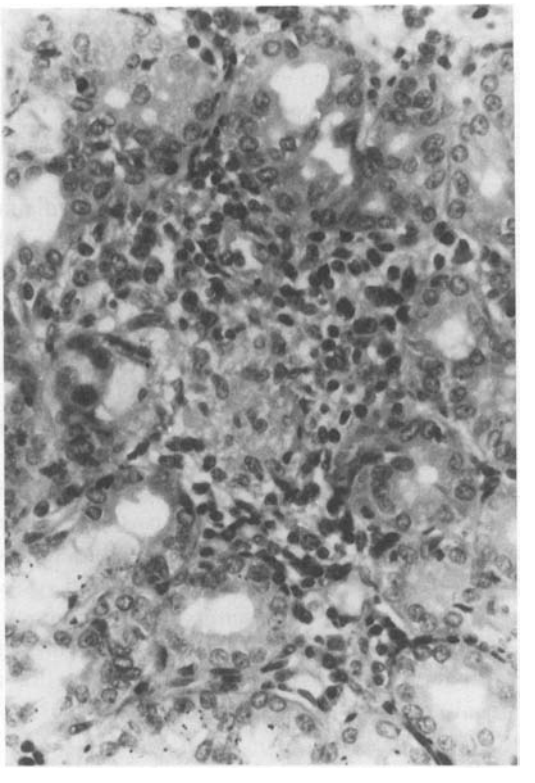

Figure 5. Photomicrograph of nasal mucosa showing a closeup of an epithelioid cell collection surrounded by lymphocytes and plasma cells (H&E×400).

in disease, whereas delivery of *M. leprae* into the nostril in a saline suspension was associated with invasion of the nasal mucosa producing a localized nodule and disseminated disease 15 months later.[5] In addition, recent biochemical studies have characterized an *M. leprae* gene encoding a fibronectin–integrin receptor present on nasal epithelial cells resulting in internalization of the bacteria.[14,15]

Table 2. Relationship between nasal histological findings and nerve histology

	Nerve biopsy diagnosis					
Histological findings in nasal mucosa	LL	BL	BT	Ind. Lep.	*NSL	Total
Nerve inflammation	–	2	2	3	2	9
Macrophage granulomas	1	6	–	–	2	9
Epithelioid granulomas	–	1	1	–	0	2
Non-specific inflammation	–	7	1	8	3	19
Total	1	16	4	11	7	39

*NSL, no significant lesion, LL, lepromatous leprosy, BL, borderline lepromatous leprosy, Ind. Lep., indeterminate leprosy.

In the present study, there were specific changes due to leprosy in the nasal mucosa in over half the patients, confirming that the nasal mucosa is involved in PNL. The histological finding of nerve inflammation, bacilli and even granulomas in the nasal mucosa, which is a site distant from the peripheral nerves, suggests that there are widespread effects of the disease even in PNL patients where the disease is believed to be confined to the peripheral nerves.

Nineteen patients (49%) were found to have non-specific inflammatory changes in the mucosa. These could, in some cases, be due to a nasal smear being taken from the same site prior to the biopsy. Alternatively, the perivascular and periglandular location of the infiltrate may indicate early changes specific to leprosy.[16] The prominent nerves seen in five of these patients may also be a step in the progression towards specific nerve inflammation. All these observations establish that there is a generalized infection in PNL and that the disease is not confined to the peripheral nerves. Furthermore, over 30% of these patients also revealed specific changes due to leprosy in the apparently normal skin from an area of sensory change.[17]

The findings of this study are consistent with the nasal mucosa being one of the sites for the primary lesion in leprosy. From this primary focus, the organism may spread via the bloodstream and/or lymphatics to lodge in nerves, skin and other sites, where the secondary lesions occur. The findings of bacilli in endothelial cells of blood vessels and the perivascular infiltrate is consistent with haematogenous dissemination of infection.

The histological changes in the nasal mucosa, which range from epithelioid granuloma with no bacilli to macrophages with acid fast bacilli, may indicate that the factors that influence local mucosal immunity may determine the future course of the infection.[18,19]

All seven of the patients who revealed macrophages in the nasal mucosa had a lepromatous or borderline lepromatous nerve histology. However, one of the patients who showed epithelioid granulomas in the nasal mucosa showed borderline lepromatous features in the nerve. Such a discrepancy between skin and nerve histology in the same patients has been shown by us and others,[20,21] and suggests that the nasal mucosa (like the skin) is an immunologically open site and may respond differently from nerve tissue, which is considered an immunologically privileged site.[22]

Interestingly, four of the seven patients who did not show any significant pathology in the nerve revealed specific changes–macrophage granulomas with acid fast bacilli (two) and nerve inflammation (two) in the nasal mucosa (Table 2). These findings could suggest that early leprosy involvement can be found in the nasal mucosa before the disease can be identified pathologically in the skin, nerve or other parts of the body. Nasal symptoms may be the first clinical manifestation of leprosy.[3,23] Clinical examination and histology of the nasal mucosa may be useful and important in the early diagnosis of leprosy and especially in contacts.

More recently, a population endemic for leprosy was screened for nasal carriage of *M. leprae* using the sensitive polymerase chain reaction (PCR) technique and found 7.8% positivity.[24] Its significance to infection and disease will need to be investigated. Nasal mucosal biopsies and clinical follow-up of such individuals will throw light on the significance of the bacilli in the nose, the role of nasal mucosal immunity and the possible progression of the disease.

In conclusion, the present study establishes that there is nasal mucosal involvement in PNL. The findings of nerve inflammation, bacilli and granulomas in the nasal mucosa of

patients with PNL (even when the nerve lesion is at a site distant from the nose) suggests that there may be disseminated disease even in these patients and shows that PNL can no longer be considered as confined to peripheral nerves. Nasal mucosa could represent one of the sites for the primary lesion in leprosy. Clinical and histological examination of the nasal mucosa may be useful in the early diagnosis of the disease.

Acknowledgements

We thank Dr C. K. Job, Dr. P. S. S. S. Rao and Dr Steve Withington for their comments and suggestions during the preparation of this manuscript, and Ms Amala and Mr K. Ramana Babu for secretarial help.

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Lepr Rev (1998) **69,** 367–375

A field trial of detection and treatment of nerve function impairment in leprosy—Report from national POD pilot project

J. JIANG*, J. M. WATSON**, G. C. ZHANG* & X. Y. WEI*

**Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, 12 Jiangwangmiao Street, Nanjing, 210042, People's Republic of China*

***The Leprosy Mission International, 80 Windmill Road, Brentford, Middlesex TW8 0QH, UK*

Accepted for publication 1 September 1998

Summary As part of a collaborative project between the Ministry of Health of China (MOH) and The Leprosy Mission International (TLMI) on leprosy rehabilitation and prevention of disability (POD), a total of 1407 patients was monitored for possible nerve function impairment (NFI) through standardized clinical nerve function assessment between May 1995 and February 1998. Of these, 191 patients were found to have NFI and were put on a fixed regimen of prednisolone. In this study, 36·7% of NFI occurred before diagnosis of leprosy, 35·6% developed during MDT and 25·7% after their release from MDT. Overall, 7·5% (105 out of 1407) of all patients, or 55·9% of patients with NFI, suffered from silent neuropathy. Of the affected nerves, 62·6% had silent neuropathy. Sensory impairment responded to prednisolone satisfactorily, giving a recovery rate of 73·8%, 76·5% and 81·0% in ulnar, median and posterior tibial nerve, respectively. Sensibility in patients even with a NFI duration longer than 6 months made significant improvement ($p < 0·05$). Motor function improvement was less satisfactory, especially in ulnar and c. popliteal nerve. The possible reasons are analysed. Our findings with regard to sensibility changes confirm that once it becomes clinically detectable, NFI is no longer at the 'early' stage. More sensitive tests are necessary to detect real 'early' sensory impairment in the field. Our study also indicates that with well-trained field staff and proper equipment for nerve function assessment, early detection and treatment of NFI can be practical and effective.

Introduction

Leprosy is an infectious disease which causes deformity and disability, due to damage to peripheral nerves. It has been increasingly recognized that prevention of disability (POD)

Correspondence to: J. Jiang

0305-7518/98/069367+09 $1.00

activities are an integral part of leprosy control services. The most important aspect of POD is early detection and adequate treatment of neural impairment. Corticosteroids are fairly well known to be effective in the treatment of leprosy reactions and recent nerve function impairment (NFI) in leprosy.[1–3]

The introduction of treatment in the field of recent NFI using a standardized corticosteroid regimen has been encouraged in China, particularly since 1991 when the collaborative pilot project on POD and rehabilitation between MOH and TLMI was undertaken.[4,5] As part of the project activities, a pilot study was established to detect NFI through standardized clinical examination and to treat NFI patients with prednisolone. The pilot project involved 14 provinces with different leprosy prevalence from 1995 to 1998. The objectives of this study were:

1 To determine the progress of sensory and motor function recovery with prednisolone therapy.
2 To analyse results with respect to duration of impairment, the relationship of NFI to MDT, the proportion of silent neuritis and the feasibility and effectiveness of leprosy field staff in dealing with NFI.

Materials and methods

CASE SELECTION

Patients in the pilot areas on MDT treatment or released from MDT during the past year were considered to be at risk of neuritis and were monitored for possible neuritis. All newly detected cases during the study period were included. The total number of cases monitored and followed up was 1407.

DEFINITION OF NERVE FUNCTION IMPAIRMENT (NFI)

NFI refers to a clinically detectable impairment of motor, sensory or autonomic nerve function and may occur in an obvious way or silently. Patients were considered to have neurological impairment when the scores in the deterioration of voluntary muscle test (VMT) and/or the touch sensitivity test (TST) occurring in the same nerve trunk distribution area were one or more points and two or more points higher, respectively, compared with the previous result. If previous VMT and TST results were not available, a patient was considered to have motor impairment when his VMT score was one or more points above the normal score; and sensory impairment, when his TST score was 2 or more points above the normal score. When it had existed for 6 months or less, NFI was considered to be 'recent'. Where patients had NFI for more than 6 months (7–12 months), especially in newly diagnosed cases, they were also put on prednisolone. Silent neuropathy was defined as NFI without skin manifestation (of RR, ENL), without complaints of nerve pain and without awareness of nerve tenderness.

NERVE FUNCTION ASSESSMENT

TST

Touch sensibility was tested by a light touch of the tip of a ballpoint pen. In one province

Table 1. Muscle strength scoring in this study

Muscle strength finding	Score
S – Full ROM*, full resistance	0
R – Full ROM, reduced resistance	1
M – Reduced ROM, some joint movement	3
P – Paralysis	5

Muscle testing in this study for each nerve: Facial, lid gap on light eye closure (nm); Ulnar, abduction of little finger; Median, abduction of thumb; Radial, extension of wrist; Popliteal, dorsiflexion of foot.

*ROM = range of movement.

(Sichuan) we tried the nylon monofilament in the field and also provided extra National Centre training and supervision. Pressures of 4 g and 10 g, respectively, were taken as the protective thresholds for hand and foot separately. On the hands, 10 standard points were tested: four on the ulnar part of the palm and six on the median part. On the feet, 10 points on the sole were tested, including the pulp of each of the five toes, the first, third and fifth metatarsal head, the base of the fifth metatarsal and the heel. One insensitive spot was calculated as one point.

VMT

Muscle strength was graded as strong (S), resistance reduced (R), range of joint movement reduced (M) and paralysed (P). In the case of lagophthalmos, the lid gap was recorded. Muscle strength scoring system is presented in Table 1.

Nerve pain or tenderness

The nerves of ulnar, median, posterior tibial and c. popliteal were recorded in terms of pain (Pn) and/or tenderness (Td). Radial and facial nerves were not examined because they were difficult to access and less affected.

PREDNISOLONE REGIMEN

The standardized prednisolone treatment started with a daily dose of 40 mg in the morning. However, the initial dosage was adjusted for body weight and also for the severity of reaction/NFI. The dosage tapered down at the rate of 10 mg per month until the dosage was 20 mg, after which it was reduced by 5 mg per month, thus giving a course duration of 6 months. This tapering also depended on the progress of the individual patient. Patients with recent NFI who had no other concurrent severe disease, such as untreated tuberculosis, were given systemic steroid treatment.

MONITORING AND FOLLOW-UP ROUTINES

New patients were monitored once a month over a period of 6 months when the diagnosis of leprosy was established. Patients on MDT as well as those on the first year of surveillance

were assessed every 3 months. Once NFI was detected, the assessment of nerve function was repeated monthly during prednisolone treatment and every 3 months after finishing prednisolone therapy. Patients were taught to come back to the staff if there were any signs of nerve function deterioration. The treatment was given mainly on an outpatient basis. The nerve function assessment and NFI treatment were carried out by trained local leprosy staff and supervised by provincial, national and TLMI supervisors.

The data from the study were used to establish a database which was analysed using STATA 3·0 version, a computer software for the statistical analysis. The Student's *t*-test was applied on the differences between group means at the level of statistical significance of $p < 0{\cdot}05$.

Results

A total of 1407 leprosy patients (MB 1118, PB 289) was monitored and their nerve functions were regularly assessed during the study period. Out of 1407 patients, 191 patients (MB 159, PB 32) were found to have NFI, the overall incidence rate was 4·7 per 100 person years at risk. In MB and PB, the incidence rates were 4·9 and 3·9 per 100 person years at risk, respectively. The mean age of patients with NFI was 38·7 years (range: 11–75 years). The mean follow-up period after the completion of prednisolone treatment was 14·8 months (range: 1–23 months). Table 2 shows the basic information of patients with NFI in this study. More than one-third (36·7%) of NFI took place before the diagnosis of leprosy, 35·6% on MDT and 25·7% after release from treatment (RFT). Four hundred and thirty-two nerves were affected, including 124 ulnar nerve (sensory 107, motor 47), 74 median (sensory 68, motor 28), 179 posterior tibial, 27 c. popliteal, 21 facial and seven radial. The posterior tibial nerve was the most frequently involved, the facial and radial nerves the least. The percentage of silent neuropathy of the total affected nerves was 62·6% (Table 3). The total number of patients with silent neuropathy was 105, which was 55·9% of all NFI patients.

Figure 1 illustrates the effect of prednisolone on affected nerves. Sensory function improved in 73–81% of the nerves either partially or completely. The full recovery of sensibility in ulnar, median and p. tibial nerve is 62·6%, 55·9% and 57·4%, respectively. A high percentage of motor function improvement was found in facial and radial nerves but much less in ulnar and peroneal nerve.

Table 2. Basic data of patients with NFI in the study

	Sex		Type of leprosy		Relationship of MDT and NFI			
Age at diagnosis of NFI	M	F	MB	PB	Pre-MDT	On-MDT	RFT	?
≤14	2	0	2	0	1	0	1	
15–29	37	11	40	8	20	19	8	
30–39	38	14	46	6	18	23	11	
40–49	34	9	32	11	14	16	12	
50–59	28	5	27	6	11	8	12	
≥60	10	3	12	1	6	2	5	
Total	149	42	159	32	70	68	49	4

Table 3. Details of nerve involvement and percentage of silent neuropathy among affected nerves

Nerve	Total affected nerves	Silent neuropathy		Nerve pain	Nerve tenderness
		Nerves	%		
Facial[a]	21				
Ulnar	124	72	58·1%	12	40
Median	74	50	67·6%	7	17
Radial[a]	7				
C. popliteal	27	18	66·7%	2	7
P. tibial	179	113	63·1%	21	45
Total	432	253	62·6%	42	109

[a]Facial and radial nerves were not required to record pain/tenderness in this study.

Tables 4 and 5 set forth the details of response to prednisolone in different nerves associated with NFI duration. Using Student's *t*-test to analyse sensibility score before and after prednisolone therapy, significant improvements in all nerves, even in those with a NFI duration longer than 6 months, were obtained. Motor function recovery was much less encouraging. There were no significant differences ($p > 0{\cdot}05$) between the mean motor score at the diagnosis of NFI and at the end of follow-up in both ulnar and c. popliteal nerves. On the other hand, the median nerve with a short duration of NFI presented a significant change ($p < 0{\cdot}05$). We analysed facial nerve as a whole group because of the small number and obtained a highly significant outcome ($p < 0{\cdot}01$).

Common sense would suggest that NFI treated at an 'early' stage should respond better to

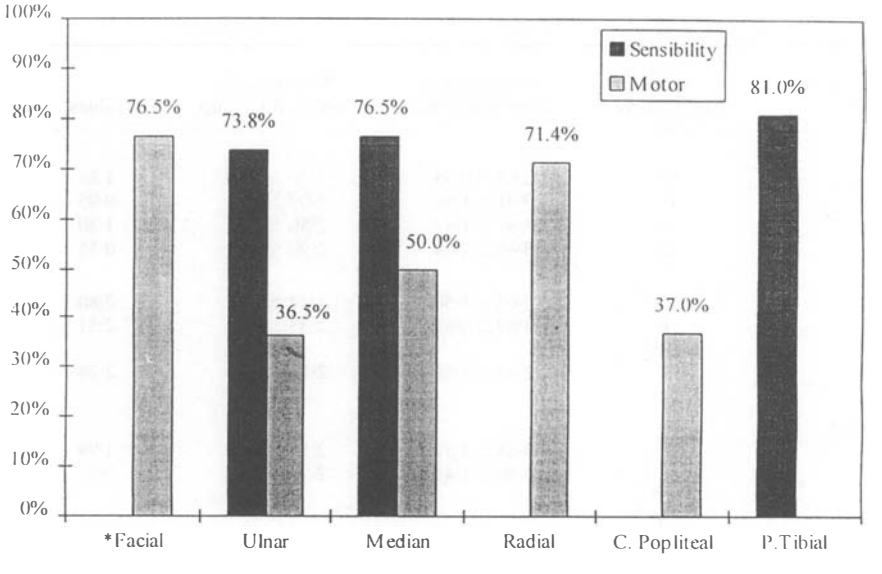

Figure 1. Percentage of nerve function improvement with prednisolone treatment in individual nerves. Two patients with bilateral facial nerves were excluded, because they were only on prednisolone for 1 and 2 months, respectively, when data were collected.

Table 4. Sensitivity changes with prednisolone treatment associated with NFI duration

Duration of NFI (months)	No. of nerves	Mean score at diagnosis of NFI	Mean score by end of follow up	*t*-values	*p*-values
Ulnar					
<1	25	2·80 ± 0·88	0·2 ± 0·5	12·84	<0·01
1–3	43	3·19 ± 0·93	1·58 ± 1·76	5·30	<0·01
4–6	18	2·50 ± 0·99	0·38 ± 0·70	7·42	<0·01
≥7	21	2·95 ± 1·02	1·47 ± 1·69	3·44	<0·05
Median					
<1	15	3·33 ± 1·63	0·27 ± 0·79	6·54	<0·01
1–3	25	3·88 ± 1·92	2·04 ± 2·41	2·99	<0·01
4–6	10	2·90 ± 1·97	1·00 ± 1·49	2·43	<0·05
≥7	18	2·94 ± 1·55	1·67 ± 1·78	2·28	<0·05
P. tibial					
<1	47	5·21 ± 2·91	0·38 ± 0·99	10·77	<0·01
1–3	61	5·36 ± 3·12	2·26 ± 3·06	5·54	<0·01
4–6	35	6·14 ± 2·95	1·58 ± 2·80	6·63	<0·01
≥7	36	7·17 ± 1·62	4·52 ± 3·91	3·76	<0·01

treatment than if treated at a 'late' stage. This is confirmed by Table 6, which reveals a significant difference in sensibility changes between the group with NFI duration less than 1 month and any other groups with longer duration, with the exception of t1–t3.

Table 7 presents the changes of nerve scores which were calculated by individual person instead of by individual nerve. Comparisons of nerve score changes by calculating the difference of scores at diagnosis of NFI from that at the completion of follow-up show highly

Table 5. Motor function changes with prednisolone treatment associated with NFI duration

Duration of NFI (months)	No. of nerves	Mean score at diagnosis of NFI	Mean score by end of follow up	*t*-values	*p*-values
Ulnar					
<1	17	2·88 ± 0·65	1·76 ± 1·86	1·86	>0·05
1–3	11	3·91 ± 1·64	3·09 ± 2·34	0·95	>0·05
4–6	9	3·67 ± 1·41	2·56 ± 2·13	1·30	>0·05
≥7	10	3·40 ± 1·84	2·90 ± 2·23	0·55	>0·05
Median					
<1	11	2·64 ± 1·50	1·27 ± 1·42	2·80	<0·05
1–3	6	4·67 ± 0·82	2·33 ± 2·34	2·31	<0·05
4–6	4[a]				
≥7	7	2·43 ± 1·52	2·14 ± 1·86	2·24	>0·05
C. popliteal					
<1	11	3·55 ± 1·57	2·18 ± 1·66	1·99	>0·05
1–3	8	3·50 ± 1·41	2·75 ± 2·19	0·81	>0·05
4–6	3[a]				
≥7	5[a]				
Facial					
≤6	17	2·59 ± 0·87	0·88 ± 1·17	4·84	<0·01

[a]Numbers are too small to make any meaningful statistical analysis.

Table 6. Comparison of mean differences in sensitivity associated with duration of NFI (the difference of score at diagnosis of NFI from that at the completion of follow-up)

Nerves by groups	No. nerves with NFI		Difference (mean ± SD)			
A B	A	B	A	B	*t* values	*p* values
Ulnar						
u1–u2	25	43	2·68 ± 0·9	1·79 ± 1·77	2·34	<0·05
u1–u3	25	18	2·68 ± 0·9	2·11 ± 0·94	2·01	=0·05
u1–u4	25	21	2·68 ± 0·9	1·48 ± 1·51	3·33	<0·01
u2–u3	43	18	1·79 ± 1·77	2·11 ± 0·94	0·72	>0·05
u2–u4	43	21	1·79 ± 1·77	1·48 ± 1·51	0·69	>0·05
u3–u4	18	21	2·11 ± 0·94	1·48 ± 1·51	1·52	>0·05
Median						
m1–m2	15	25	3·07 ± 1·39	1·84 ± 1·99	2·1	<0·05
m1–m3	15	10	3·07 ± 1·39	1·90 ± 1·30	2·1	<0·05
m1–m4	15	18	3·07 ± 1·39	1·28 ± 1·97	2·96	<0·01
m2–m3	25	10	1·84 ± 1·99	1·90 ± 1·30	0·09	>0·05
m2–m4	25	18	1·84 ± 1·99	1·28 ± 1·97	0·91	>0·05
m3–m4	10	18	1·90 ± 1·30	1·28 ± 1·97	0·89	>0·05
P. tibial						
t1–t2	47	61	4·83 ± 2·90	3·10 ± 3·52	2·73	<0·01
t1–t3	47	35	4·83 ± 2·90	4·51 ± 3·18	0·47	>0·05
t1–t4	47	36	4·83 ± 2·90	2·67 ± 2·75	3·44	<0·01
t2–t3	61	35	3·10 ± 3·52	4·51 ± 3·18	1·96	=0·05
t2–t4	61	36	3·10 ± 3·52	2·67 ± 2·75	0·63	>0·05
t3–t4	35	36	4·51 ± 3·18	2·67 ± 2·75	2·61	>0·05

u, ulnar u1, u2, u3, u4 indicate the duration of NFI <1 month, 1–3 months, 4–6 months, ≥7 months, respectively.
m, median m1, m2, m3, m4 as the same as ulnar nerve.
p. tibial t1, t2, t3, t4 as the same as ulnar nerve.

significant differences between matching groups of I–II and I–III, and significant difference between groups I–IV. There is no significant difference among each matching groups of II–III, II–IV and III–IV. In group I, extra intensive training was given annually by experts at national level, and the nylon monofilament instead of ballpoint was applied in the sensitivity test in the present study.

The months taken to reach a maximum improvement in each nerve are: ulnar 3·52 ± 1·90, median 3·54 ± 1·84, posterior tibial 5·37 ± 2·87 for sensation and ulnar 4·71 ± 2·78, median 4·31 ± 2·09, c. popliteal 4·40 ± 3·00, facial 4·92 ± 2·53 for motor.

Discussion

This study is part of a collaborative project between the MOH of China and TLMI on leprosy rehabilitation and POD, and is primarily concerned with the feasibility and effectiveness of treating NFI with a standardized regimen of prednisolone in the field. Nerve function assessment and NFI treatment were implemented by experienced leprosy control staff who received intensive training in POD courses, which included the very important aspects of early detection and treatment of NFI. The results of this study are encouraging.

Table 7. Comparison of nerve score changes in individual person between groups (the difference of score at diagnosis of NFI from that at the completion of follow-up)

Comparison between groups	No. with NFI		Difference (mean ± SD)			
A B	A	B	A	B	*t* values	*p* values
I–II	97	36	7·08 ± 5·59	4·11 ± 4·17	2·90	<0·01
I–III	97	46	7·08 ± 5·59	4·33 ± 4·39	2·93	<0·01
I–IV	97	20	7·08 ± 5·59	3·90 ± 4·56	2·38	<0·05
II–III	36	46	4·11 ± 4·17	4·33 ± 4·39	0·23	>0·05
II–IV	36	20	4·11 ± 4·17	3·90 ± 4·56	0·17	>0·05
III–IV	46	20	4·33 ± 4·39	3·90 ± 4·56	0·36	>0·05

Group I Pilot areas in Sichuan province (Leprosy endemic areas, with a monofilament trial and intensive training from national centre).
II Pilot areas in Yunnan province (leprosy endemic areas).
III Pilot areas in Fujian, Guangxi, Hubei, Anhui and Shaanxi provinces (non-endemic areas anymore, but have not attained the goal of elimination).
IV Pilot areas in Shanghai, Jiangsu, Yangzhou, Shangdong (have already achieved the goal of elimination).

The occurrence of NFI varies in different studies.[7,8] In our study, the overall incidence rate of NFI in PB group was 3·9 per 100 person years at risk which compares well with that of Richardis', but in MB group, it was 4·9 per 100 person years at risk, which is lower than that of Richardis' 7·5%.[9] In this study, 36·7% of NFI occurred before the diagnosis of leprosy. That means the history of this group was dependent on the observations and recollection of patients. Others developed on-MDT (35·6%) and after release from MDT (25·7%). Quite a number of patients develop new NFI after their release from MDT and a nerve function assessment should be given at regular intervals during the first year after RFT. The frequency of silent neuropathy varies according to different studies.[5,10] Overall, 7·5% of all patients (105/1407), or 55·9% of NFI patients, suffered from silent neuropathy; and the percentage of silent neuropathy in NFI nerves was 62·6%. Some authors had even observed over 65% of patients with recent NFI who did not present complaints spontaneously.[9] In one study, 33% of patients were found with silent neuritis.[5] Without regular and proper ST/VMT assessment, the high percentage of 'silent neuropathy' will undoubtedly result in impairment and disabilities in many patients.

Sensory impairment responded to prednisolone satisfactorily, giving a recovery rate of 73·8%, 76·5% and 81·0% in ulnar, median and posterior tibial nerve, respectively. Where NFI had existed for a short period, the chances for recovery were better. In our study, nerve function may attain significant improvement in those patients with a duration of NFI (sensation) longer than 6 months, especially in posterior tibial nerve (Table 4). Thus, the duration of 6 months of NFI is not a strict demarcation line between giving or not giving conticosteroid therapy.

Motor function recovery varies in different nerves. Facial nerve presented a satisfactory result (76·5%) which is in line with another study.[3] The recovery rates of ulnar, median and c. popliteal nerve were low as shown in Table 5, in which there is no significant difference of motor scores at diagnosis of NFI and at completion of follow-up in ulnar and c. popliteal nerves. The possible reasons are:

1 VMT tests in this study only include four grades for practical reasons.

2 VMT tests seem more difficult than ST tests for field staff and may result in more mistakes.
3 We noted some persons affected by leprosy who only had motor function loss without sensation loss. This phenomenon showed that sensory impairment recovered in the past without recovery in motor impairment.

We can try to explain the variation of sensibility recovery associated with the duration of NFI. The changes in sensory scores are calculated by using the scores at diagnosis of NFI minus those at the completion of follow-up. The groups are divided by NFI duration (Table 6). We find that only the group with NFI duration less than 1 month had score changes significantly different from each of the other groups (NFI duration 1–3, 4–6, ≥7 months). Differences in score changes between the other groups are not significant. It is clear from available pathological evidence that extensive neuropathy is already present before the patients had any sign and/or symptom of NFI. Motor and sensory nerve conduction velocity measurements are able to pick up NFI before it becomes clinically evident.[11] Once it becomes clinically detectable, NFI is not at the 'early' stage. That there is no significant difference in score changes among those groups with NFI duration of 1–3, 3–6 and ≥7 months seems to prove the above point. Therefore, it is important to develop more sensitive equipment to detect the real 'early' sensitivity impairment in the field.

Our study also indicated that with well-trained field staff and proper equipment for nerve function assessment, NFI management is more effective.

Acknowledgements

We would like to thank all the staff who are involved in this project for spending a lot of time on visiting patients and performing detailed nerve function assessments. We are grateful to Dr P. D. Samson and Miss A. Piefer for their financial and technical support. Thanks are also due to Dr X. S. Chen and Mr C. B. Zhu for their substantial help in statistical analysis.

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β_2-Glycoprotein I-dependence of anticardiolipin antibodies in multibacillary leprosy patients

P. FIALLO*, C. TRAVAGLINO**, E. NUNZI* & P. P. CARDO*

**Servizio di Immunopatologia Cutanea e Sezione di Dermatologia Tropicale, Ospedale San Martino, Università di Genova, Genova, Italy*

***Hansenian's Eritrean Welfare Organization (HEWO), Asmara, Eritrea*

Accepted for publication 15 August 1998

Summary This study was undertaken to investigate the influence of β_2-glycoprotein I (GPI) on anticardiolipin antibody (aCL) titration in leprosy. The study group consisted of 140 sera from patients with multibacillary leprosy (46 borderline, 94 lepromatous). The group included newly diagnosed, previously untreated patients, patients under treatment and patients released from treatment. GPI addition enhanced significantly the aCL titres in sera from lepromatous leprosy but not in those from borderline leprosy. Moreover, when the patients were classified according to their bacteriological status, aCL titres were found to be significantly higher in skin smear positive patients compared to bacteriologically negative patients. Thus, the present study demonstrates that aCL in multibacillary leprosy patients are mainly of the GPI-dependent type and emphasizes the importance of GPI addition for aCL titration in leprosy.

Introduction

Anticardiolipin antibodies (aCL) are immunoglobulins that react with negatively charged phospholipids. aCL have been frequently detected in blood samples from patients with systemic lupus erythematosus (SLE) and in patients with infectious diseases such as syphilis, HIV-infection and mycobacterioses.[1]

aCL have been reported in 50–80% of multibacillary leprosy patients.[2–4] Their production and clinical significance in leprosy is still unknown. We have previously reported that aCL titration is a useful tool to improve significantly the specificity of leprosy serodetection when it is combined with an anti-phenolic glycolipid-I antibody immunoassay.[5]

Recently, it has been shown that some aCL require β_2-glycoprotein I (GPI, also called

Correspondence to: Dr Paolo Fiallo, Institute of Dermatology, University of Genoa, Viale Benedetto XV, 7-16132 Genoa, Italy

 0305-7518/98/069376+06 $1.00

apolipoprotein H), a plasma cofactor, for optimal detection in ELISA assays. The addition of GPI to aCL ELISA identifies two distinct types of aCL, GPI-independent aCL, which recognizes only CL, and GPI-dependent aCL, which binds to the CL/GPI complex.[6]

In view of these recent findings, we studied the influence of GPI on aCL binding to CL in blood samples from patients with multibacillary leprosy. We also attempted to establish whether the presence of aCL is related to the bacteriological status of leprosy.

Materials and methods

SERA

The study group consisted of sera from 140 patients with multibacillary leprosy. Sixty-three of these patients were from Italy, 46 from Eritrea and 31 from other areas (Latin America, Asia, North Africa). Leprosy was diagnosed on clinical and bacteriological grounds and confirmed by histopathology in a minority of cases. Patients were classified at the time of initial examination according to the Ridley-Jopling scale and grouped as borderline (including multibacillary BT, BB and BL) and lepromatous (LL). The disease status was established at the time of blood collection. The patients were classified as bacteriologically positive or negative on the basis of their skin smear status. The study group included newly diagnosed, previously untreated patients, patients under antileprosy treatment and patients released from treatment. Detailed information on the leprosy group is summarized in Table 1.

One hundred and four sera from SLE patients and 123 sera from healthy volunteers served as positive and negative controls.

ANTICARDIOLIPIN ASSAY

Serum from all subjects was assayed for aCL in the absence (CL-ELISA) and after addition of GPI (GPI-CL-ELISA) using a technique previously described.[7] Briefly, ELISA plates (ICN Linbro, #76-381-04)) were coated with cardiolipin (Sigma) in ethanol (2·5 μg/50 μl per well) at 4°C overnight. In order to evaluate the different aCL subpopulations, the even columns of each plate were incubated with a source of GPI (GPI-CL-ELISA). In a pilot experiment with autoimmune sera, postcoating with fetal calf serum (FCS) as a source of GPI produced similar

Table 1. Clinical classification, bacteriological status and drug history of leprosy patients

	Borderline ($n = 46$)	Lepromatous ($n = 94$)
Smear-positive		
untreated	22	16
under treatment	3	33
Smear-negative		
released from treatment	18	31
under treatment	3	14

results to purified GPI (OD CL/FCS versus OD CL/GPI had $n = 12$, $t = 1{\cdot}081$ with $p = 0{\cdot}305$) as also previously reported by other authors.[8,9] When test samples were replaced by purified IgG, the results were unchanged. This indicated that endogenous GPI depending on sera dilution was irrelevant for antibody determination at the working serum dilution of 1:100. In view of this pilot study, the even columns of each plate were washed with phosphate buffered saline (PBS) and incubated with 50 μl of 10% FCS in PBS for measurement of GPI-dependent aCL and the odd columns were incubated in PBS alone for measurement of GPI-independent aCL. Incubation was at 20°C for 2 h. After washing with PBS (120 μl/well), the plates were blocked with 0·3% gelatin or 1% electrophoretically purified bovine serum albumin (BSA, Sigma) in PBS (100 μl/well) at 20°C for 1 h. Diluted control samples (normal human serum and aCL high-titre serum) and test sera (1:100 in 1% BSA/PBS) were then added in duplicate in odd and even columns in order to evaluate GPI-independent and GPI-dependent antibodies on the same plate. After incubation at 20°C for 3 h and three washings with PBS, 50 μl of peroxidase-conjugated rabbit anti-human IgG (DAKO1, 1:1000 on 1% BSA/PBS) were added in each well and incubated at 20°C for 1 h. After three washings with PBS the plates were incubated with freshly prepared ABTS (ICN-Flow, 2,2′-azino-di-[3-ethyl-benzthiazoline sulphonate]/H_2O_2, 100 μl/well). The reaction developed in the dark at 20°C and its strength was read when the 414-nm optical density (OD) of the standard high-titre wells reached 0·9–1·1 values. Blanks obtained from uncoated wells on the same plate were subtracted to account for non-specific binding.

Optical density values were converted into a range in which 30 IU/ml was the upper limit. Such a value corresponds to 100 GPL units when compared with a standard curve using commercial aCL standard sera (Antiphospholipid Associated, Louisville, KY, USA).[10]

Antibody titres follow a log-normal distribution and were transformed before analysis. Results below the lower limit of detection of the assay were assigned the value of the lower limit of detection (6 IU/ml) to allow more accurate comparison by parametric methods after log transformation of data. Laboratory ranges were determined from the healthy subject group. Normal values (< mean + 3 SD) were taken as <42·6 GPL for CL-ELISA and <38·6 GPL for GPI-CL-ELISA.

STATISTICAL ANALYSIS

The significance of the differences between the two ELISA assays was tested by Student's test for continuous variables, and McNemar's test for categorical values. Comparison of antibody titres within each ELISA assay was done by ANOVA.

Results

To characterize GPI dependency, sera from patients with multibacillary leprosy, patients with SLE and healthy subjects were compared for their antibody binding to CL in the presence and absence of GPI. Addition of GPI enhanced significantly antibody binding in both the leprosy group (mean 49·83, SD 55·75, 95% CI 10·23, −1·06, $p = 0{\cdot}0076$) and the SLE group (mean 36·4, SD 35·2, 95% CI 0·41, 7·10, $p = 0{\cdot}0283$) but not in the control group (mean 9·3, SD 11·1, 95% CI −3.78, 0·22, $p = 0{\cdot}0812$).

Table 2. Antibody titres in the leprosy subgroups, expressed as GPL ± SD

	n	CL-ELISA	GPI-CL-ELISA	95% CI for difference	*P*[a]
Borderline					
smear-positive	25	35·0 ± 41·0	37·2 ± 37·6	−8·87, 4·43	0·4978
smear-negative	21	46·6 ± 33·3	44·3 ± 30·7	−6·04, 10·78	0·5629
Lepromatous					
smear-positive	49	69·1 ± 43·8	84·4 ± 30·9	−24·5, −6·00	0·0018
smear-negative	45	38·5 ± 34·7	40·2 ± 31·4	−8·55, 5.12	0·6241

[a]Paired *t*-test (two-tailed) among assays within each group.

Comparison of categorical values was done on the leprosy group. Of the 140 leprosy sera, GPI-independent aCL were detected in 76 (54·3%) sera. When GPI was added to the assay system, 93 (66·4) sera resulted to be positive. These included 72/76 sera that were GPI-dependent aCL positive and 21 sera which became positive only after GPI addition.

For further evaluation, leprosy sera were divided in four subgroups according to clinical form and bacteriological status. We found that GPI addition enhanced significantly aCL titres (Table 2) and the proportion of aCL-positive patients (Table 3) only in sera from bacteriologically positive LL. In contrast, there was no significant enhancement in any of the other three leprosy subgroups.

To determine whether the presence of either GPI-independent aCL or GPI-dependent aCL is related to leprosy activity, antibody binding in bacteriologically positive and negative leprosy was compared. There was a significant difference of antibody titres between smear-positive LL and smear-negative LL in both the CL-ELISA (mean 69·1, SD 39·7, $F = 13·949$, $p = 0·0003$) and the GPI-CL ELISA (mean 84·4, SD 31·1, $F = 47·189$, $p < 0·0001$). The significant difference resulted also by comparing categorical values ($p = 0·00151$). By contrast, there was no difference between sera from smear-positive borderline leprosy and sera from smear-negative borderline leprosy.

Table 3. Results of the two aCL assays in the leprosy subgroups

	n	CL-ELISA positive	GPI-CL-ELISA positive		*p*[a]
Borderline					
smear-positive	25	9	11	(8)[b]	0·3085
smear-negative	21	11	11	(10)[b]	0·1572
Lepromatous					
smear-positive	49	35	47	(35)[b]	0·0015
smear-negative	45	21	24	(10)[b]	0·2248

[a]McNemar's test.
[b]Sera in which CL-ELISA and GPI-CL-ELISA were both positive.

Discussion

For solid-phase immunoassays of aCL, optimal concentration of GPI is critical for recording valid and consistent results. Most of the previous studies on aCL in leprosy did not describe in detail the ELISA method they employed. It is quite likely that they used adult bovine serum (ABS) to block the plates and to dilute the serum samples as recommended by Harris *et al.*[11] If this was the case, the assays may have detected GPI-dependent aCL. Binding of GPI-dependent aCL, however, requires the presence of GPI in a dose-dependent fashion; in these assays, GPI concentration was neither established nor optimized.

In our study, GPI influence on aCL titration was investigated by using two ELISA assays, CL-ELISA and GPI-CL-ELISA. Each serum was tested by the two assays on the same plate, in order to exclude errors due to inter-plate variations. The first intention of our study was to investigate whether GPI is relevant for enhancing antibody binding in leprosy patients. Analysis of variance of antibody titres and comparison of categorical values demonstrated that optimal addition of GPI enhances significantly aCL titration in sera from multibacillary leprosy and in those from SLE. This is not surprising, because lepromatous leprosy has been associated with serological features traditionally linked to autoimmune disorders, such as polyclonal B cell activation with multiple antibodies including antinuclear antibodies.[12]

Our findings, however, are different from those reported by Hojnik *et al.*[13] In their study, these authors reported a surprisingly high frequency of aCL antibodies in leprosy sera. In addition, they found that sera that gave increased aCL levels in the CL-ELISA without GPI, displayed increased levels also in the modified aCL-ELISA with GPI. Accordingly, they concluded that leprosy-induced aCL do not show any consistent dependency on GPI. The discrepancy between their results and our study may be due to differences in the sampling of the study group and/or in the technical procedures (e.g. blocking agent, diluting buffer).

An important question is whether GPI, not CL/GPI complex, is the true antigen for aCL. In a previous study,[7] we reported that sera that were positive in our GPI-CL-ELISA showed no binding to plates coated with purified GPI, as confirmed by immunoblotting using purified GPI. This indicates that both GPI and CL are necessary to form the epitope to which GPI-dependent aCL are directed. Nevertheless, whether the epitope is a complex epitope formed by both GPI and CL or a neoepitope exposed on either of the components by their mutual interaction remains unknown.

The second aim of our study was to investigate whether the presence of aCL is related to the form and the bacteriological status of the disease. For this purpose, the leprosy group was divided in four subgroups: smear-positive LL, smear-negative LL, smear-positive borderline, smear-negative borderline. Our study demonstrates that GPI addition is significantly relevant only in those patients with bacteriologically positive LL. Of interest was the observation that aCL titres were significantly higher in skin smear positive LL compared with smear-negative LL in paired tests in both assays. This difference was even more evident in the GPI-CL-ELISA.

In conclusion, the present study demonstrates that aCL in multibacillary leprosy patients are mainly of the GPI-dependent type. This emphasizes the importance of optimal addition of GPI in the immunoassay for aCL detection in leprosy. Although the clinical significance of GPI-dependent aCL in leprosy, if there is any, is not known, the relationship between aCL and bacteriologically positive lepromatous leprosy strengthens our previous report[7] on the

potential use of aCL titration, in association with species-specific serological tests, to improve serodetection of subclinical lepromatous leprosy.

Acknowledgement

The authors thank 'Associazione Italiana Amici di R. Follereau', Via Borselli 4, 40135 Bologna, Italy, for supporting leprosy research in Italy.

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Explanatory models and help-seeking behaviour of leprosy patients in Adamawa State, Nigeria

N. VAN DE WEG*, E. B. POST**, R. LUCASSEN*,
J. T. V. M. DE JONG† & J. VAN DEN BROEK
**University of Maastricht, the Netherlands*
***TBL Control Programme Adamawa State, Nigeria*
†Transcultural Psychosocial Organisation, Amsterdam, The Netherlands
Royal Tropical Institute, The Netherlands

Accepted for publication 10 September 1998

Introduction

The main strategy for leprosy control programmes consists of early case finding and treatment with multidrug therapy,[1] which are still major challenges.[2]

The first decision of patients to go for care, and to whom to go, is influenced by many personal and social factors, such as gender, ethnic group, socio-economic status, costs, distance, availability of helpers and fear of stigmatization.[3–6] Treatment choices are also influenced by the explanatory model the patients are using for their illness.[7] Kleinman[3] defines the explanatory model as 'the notions about an episode of sickness and its treatment that are employed by all those engaged in the clinical process'. They are held by both patients and practitioners, and they 'offer explanations of sickness and treatment to guide choices among available therapies and therapists and to cast personal and social meaning on the experience of sickness'.

In 'traditional' societies, help seeking is often diverse, and the position of indigenous healers within the medical system is an important one.[8] Although indigenous healers are competent in healing chronic and self limiting ailments as well as minor psychological disorders, this does not seem to be the case for severe, acute diseases.[9]

The medical system can be divided into three overlapping sectors. The *popular sector* comprises the lay, non-professional domain which includes self-medication, lay management and advice of relatives, friends, neighbours, village heads, religious leaders, other patients and chemists. The *folk sector* includes sacred and secular folk healers as well as barbers. The *professional sector* comprises the organized, legally sanctioned healing professions.[3]

In Adamawa State in Nigeria, the majority of the population choose modern medicine as

Correspondence to: E. B. Post, c/o: Netherlands Leprosy Relief Association, Wibautstraat 137-k, 1097 DN Amsterdam, The Netherlands

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their treatment of first choice, especially for a variety of chronic diseases. Traditional medicine followed closely, and was in some cases even preferred.[10] In the case of leprosy, use of traditional treatments might be one of the factors causing delay.

In Adamawa State, approximately 20% of leprosy patients appear to have visible deformities at the time of diagnosis, pointing to late reporting of patients and thus to the need to strengthen case finding activities.

To improve case finding, it is important to understand what happens in the phase before patients contact modern health care facilities and how they label and understand their sickness. This study focuses on explanatory models and help seeking behaviour of leprosy patients.

The study was performed in 1994 in Adamawa State, in the north-eastern part of Nigeria. It is a rural area, known for its many ethnic groups, which all have their own language and customs. Hausa is a widely spoken second language. The registered prevalence rate of leprosy in 1993 was 4·1/10,000 and the case detection rate 1·2/10,000 population.

Materials and methods

A questionnaire was used that focussed on help-seeking behaviour and explanatory models.[11] First signs and symptoms were asked for in an open question, leaving space for patients' explanatory model, after which an interpretation was done by the investigator following the lines of modern categories of dermatological symptoms, nerve function impairment, general symptoms and others. From the time these first signs and symptoms developed, each help-seeking step was explored: patients were asked to whom they went for treatment, who took the initiative to seek care and what kind of treatment they received. For each help-seeking step, the explanatory model the patient was using was elicited; this included questions about the labelling of their problem and perceived cause.

The study can be divided into two steps:

1. INTERVIEWS WITH KEY INFORMANTS

To gain a first impression about leprosy-associated beliefs at the population level, several key informants were interviewed: persons who occupy a position of respect and trust and have contact with many people within the community. Two folk healers (one male and one female), a village head, a schoolteacher, a Muslim leader and a Christian police officer were interviewed. The information thus obtained was used to adjust the questionnaire and to get a better understanding of the general socio–cultural context.

2. INTERVIEWS WITH PATIENTS

Patients ($n = 60$) were selected whose treatment duration at the time of the interview was 24 months or less and had never been treated before in a leprosy hospital or control programme. The majority of these patients ($n = 49$) was interviewed in 28 different outpatient clinics. The remaining 11 patients were interviewed at the leprosy hospital in Garkida.

Two Dutch medical students performed the interviews with the help of two interpreters. To increase inter-rater reliability, the first five interviews were done together. After 30

interviews, the completed questionnaires were discussed in order to trace possible differences in interpretation of the questions, which were absent.

The interpreters were leprosy supervisors who were unknown to the patients. They were carefully instructed about the purpose of the study and the use of the questionnaire. Most patients were interviewed in Hausa. In 11 cases (18%), a second interpreter had to be used. The duration of the interviews ranged from 45 to 120 min.

Patients younger than 12 years were excluded.

Results

In Table 1, the characteristics of the patients in this study are summarized. Of the 60 leprosy patients, 15 (25%) were classified as paucibacillary and 45 (75%) as multibacillary.

PERCEIVED CAUSES OF LEPROSY

Table 2 summarizes the perceived causes of leprosy reported by leprosy patients answering an open-ended question. They answered the question after they already had received some form of health education.

An overwhelming majority of the patients (58%) used traditional beliefs to explain the cause of leprosy. Food was perceived by 14 patients (23%) as the main cause of leprosy. The foodstuffs most frequently mentioned were goat meat, groundnut and (mud-) fish, which are important ingredients of the day-to-day diet. They did not seem to be speaking about sorcery, neither was it taboo to eat these foodstuffs. Many patients had only stopped eating goat meat *after* they were told they had leprosy. Many respondents (27%) perceived leprosy mainly as 'God's wish', without further explanation.

Sixty percent of the patients started treatment in the last 3 months before the interview, 15 patients (25%) were diagnosed as leprosy patients less than 2 weeks before the interview.

The modern concept of contagion was less frequently mentioned (20%). Ten leprosy

Table 1. Main characteristics of the interviewed patients

Sex: male 37 (62%), female 23 (38%)
Age: mean 33·1 (±13·1) years
Major ethnic groups: Fulani 11 (18%),
Higgi 5 (8%),
Koma 5 (8%),
Mumuye 5 (8%),
In total 26 different ethnics groups
Religion: Muslim 30 (50%), Christian 28 (48%), Animist 1 (2%)
Education: No formal education or only Koranic school: 40 (67%)
1–4 years formal education: 13 (22%),
5 or more years formal education: 7 (12%).
Only 13 (22%) patients were literate.
Source of income: 43 (71%) farmers.
Disability grade 1 (WHO): 6 (10%)
Disability grade 2 (WHO): 29 (48%)

Table 2. Perceived causes of leprosy by leprosy patients ($n = 60$, first answer counted). Fisher's exact (male/female) = 0·422

Cause	Male ($n = 37$) (%)	Female ($n = 23$) (%)	Totals ($n = 60$) (%)
Traditional beliefs (food, god, witchcraft, taboo, spirits)	19 (51)	16 (70)	35 (58)
Modern concepts (contagion)	9 (24)	3 (13)	12 (20)
Other (heredity, hygiene, physical)	5 (14)	1 (4)	6 (10)
Don't know	4 (11)	3 (13)	7 (12)
Total	37 (100)	23 (100)	60 (100)

patients considered germs or bacteria to be the cause of leprosy, other patients mentioned 'contact with leprosy patients' (eating together, bathing in the same water, etc.).

Most respondents (65%) thought everybody could get leprosy, 15% thought only some persons could get the disease, for reasons closely connected to their perceived cause, while 8% were not sure. Twelve percent of the respondents thought that each person had the disease in the body, but that in most cases the disease didn't 'come out'.

No significant difference was found between male and female patients concerning their concept of leprosy (Fisher's exact = 0·422).

DELAY AND HELP-SEEKING

The duration of delay between noticing the first signs and symptoms and the first contact with the leprosy services ranged from 0 to 10 years, with a median total delay of 36 months. In the majority of the cases (68%), more than a year passed before the patient started effective treatment. Once a lay diagnosis of leprosy was made, 27% of the patients found their way to the leprosy services within 3 months. The median delay after the lay diagnosis was 12 months.

Multivariate analysis using Cox regression analysis showed no significant correlations between delay on the one hand and sex, age, religion, level of education or leprosy classification on the other. There were correlations, however, with visible deformity at the time of interview ($p = 0{\cdot}008$ with a 95% confidence interval of 0.413–0.876) and illiteracy ($p = 0{\cdot}019$ with a 95% confidence interval of 0.064–0.785). No difference in delay was found between patients with either grade 0 and grade 1 disability (WHO). The delay in diagnosis was, however, consistently larger among patients with visible deformities at the time of interview, as evidenced by a Kaplan Meier analysis (Figure 1).

The flow diagram (Figure 2) shows to whom people went for treatment or advice before they started modern treatment for leprosy. Surprisingly, 19 (32%) respondents went straight to the leprosy services without another help-seeking step in between: women (43%) more so than men (24%). The folk sector was the most frequently [22 times (37%)] consulted as a first step, followed by the popular sector [14 times (23%)]. The professional sector was consulted as a first step only 5 times (8%).

Although folk healers denied treating leprosy and said that they referred such patients, in fact none of their consultations resulted in referral. Their treatment ranged from modern medicines to herbal treatments, dietary advice, hygienic measures, to 'writings', where

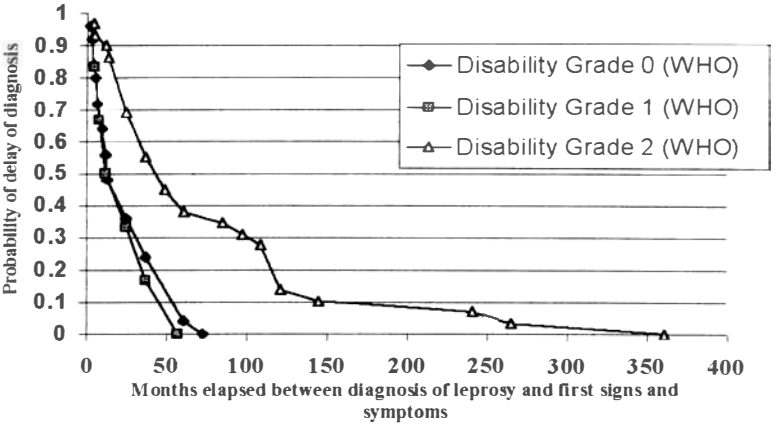

Figure 1. Kaplan Meier analysis of the delay of diagnosis of leprosy since first signs and symptoms.

Koranic verses were written on a wooden slate and washed off with water which was given to the patient to drink.

The total number of help-seeking steps ranged from one to six steps; most patients had a total number of two (27%) or three (32%) help-seeking steps; only 11% had four or more help-seeking steps before reaching the leprosy services.

In general, patients tended to consult different practitioners one *after* the other; rarely did they use two treatments at the same time. When they evaluated their treatment as not effective, they usually 'tried their luck' somewhere else. There was no clear pattern in the sequence of practitioners consulted.

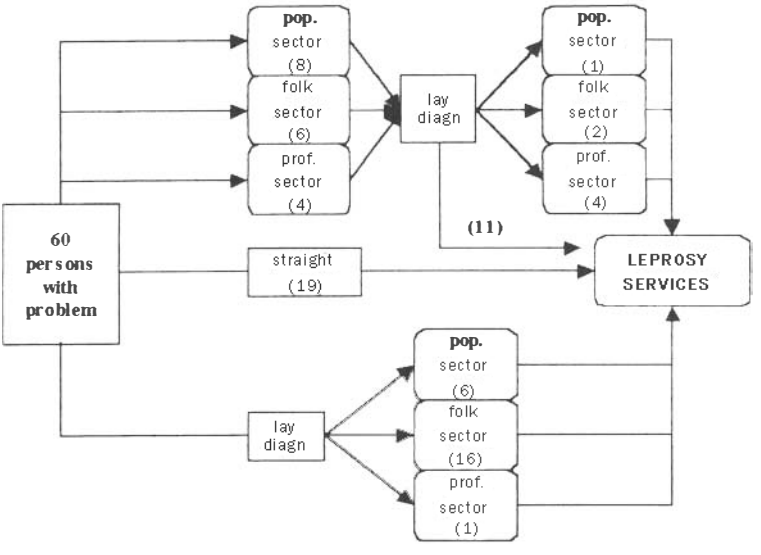

Figure 2. Where leprosy patients go with their (leprosy) problem before starting modern treatment.

Discussion

This study has shown that a majority of the patients had a total delay of more than a year from the first signs and symptoms to consultation of the leprosy services. A longer delay was correlated with visible deformities and illiteracy.

The large proportion of patients labelling their problem as leprosy *before* their first contact with leprosy services and the high percentage of diagnoses being made by others than the health workers suggests that many people in the community are aware of the early signs and symptoms of leprosy. In contrast with other studies performed in India[12] and Pakistan,[13] patients rarely denied their diagnosis of leprosy. A majority of the patients thought their condition would get worse if they did not go for treatment. This shows that unawareness of possible deterioration is not a likely explanation for delay. Most thought leprosy could be cured with modern treatment, but could not contact the leprosy services in an early stage, resulting in a high proportion of disabilities (48% visible disabilities in this study).

Consultation of other practitioners seemed to be the main reason for delay. The finding that many patients consulted other practitioners before reporting to leprosy services is in line with other studies.[12–14] The professional sector seemed to be under-consulted, but we lack information on help-seeking behaviour for other ailments. It is our impression, however, that peripheral health units were generally under-utilized, to which factors like costs and poor availability of essential drugs might have contributed.

In this study, no significant difference in delay could be found between men and women. The lower number of registered female leprosy patients can thus not be easily explained by possible women's restricted mobility, as was found in Nepal.[4] Other factors have to be looked into. Ethnic differences in help-seeking behaviour have been found in Nepal,[4] but could not be analysed in this study, due to the large number of ethnic groups in Adamawa State.[15,16] General considerations as expressed in the 'etic-emic' debate[17] also point at the significance of the cultural context in relation to people's view on sickness and consequently sickness behaviour. In this study, however, no significant difference was found between male and female patients concerning their concept of leprosy.

The fact that only few patients report personal problems or fear of discrimination suggests that leprosy patients in Adamawa State are not severely stigmatized, which has been observed by others as well.[18,19] This contrasts with the study of Mull *et al.*[13] in Pakistan, where 54% spoke of severe personal problems.

Comparison with other studies shows that perceived causes of leprosy differ from culture to culture.

Food was a frequently mentioned cause in Pakistan,[13] Bombay[12] and northern Nigeria, but not in Thailand.[14] Whereas in Pakistan, patients explained this as an imbalance between 'hot' and 'cold', this did not seem to be the case in northern Nigeria, nor did sorcery or a taboo seem to be the underlying reason.[18]

The high number of respondents attributing the disease to God was specific for northern Nigeria. Lewis Wall[18] described leprosy as one of the 'Ciwon Allah' (diseases of God), 'regarded as a not quite comprehensible manifestation of the power of God and accepted as such'. This is in line with the (official) Muslim view, where all events, including disease, are caused by the will of God irrespective of causes, but are not considered as punishment by God for sins or wrong-doings.[20] Whereas in Nepal one study suggested that fear of stigmatization led patients to travel farther for treatment in order to disguise their diagnosis,[4] this did not seem to be the case in this study. Most patients sought treatment at their local clinic.

Contagion was a frequently mentioned cause in northern Thailand,[14] Bombay[12] and northern Nigeria.

Conclusion

Based on the findings in this study, several measures can be taken to improve early case finding. First of all, it seems to be important to involve folk healers in case finding activities. They are the ones most frequently consulted as an alternative to the leprosy services.

The lay referral system (the general public and chemists) could be further exploited by improving health education, not merely about early signs and symptoms of leprosy but also about where to go when leprosy is suspected. For example, the use of radio programmes would not only reach a wide audience but would also address illiteracy as an obstacle in finding the leprosy services.

Summary

In northern Nigeria 60 leprosy patients, 49 outpatients and 11 in-patients, were interviewed about their help-seeking behaviour and explanatory models before their first contact with the leprosy services. Most patients showed a delay of more than 1 year. After leprosy was provisionally diagnosed by lay persons, 27% of patients found their way to the leprosy services within 3 months. Chemists (popular sector) and the professional sector frequently missed the diagnosis. If early case finding is to be improved, it is important to involve them in case finding activities and to train them in adequate diagnostic skills.

No significant correlations were found between total delay and sex, age, religion or leprosy classification, except with visible deformity at the time of the interview and illiteracy.

Consultation of folk healers was the major reason for delay. Most patients consulted folk healers, who, although they claimed to have a positive attitude towards modern medicine in the case of leprosy, never referred patients to the leprosy services.

While many patients held a variety of causes responsible for leprosy, most patients explained the disease in traditional terms (58%), while only a minority used modern concepts (20%). This emphasizes the need for continuous attention for health education of diagnosed patients and their families. No significant difference was found between male and female patients concerning their concept of leprosy.

Denial of the leprosy diagnosis was rare.

Acknowledgements

This study was supported by a grant from the Stichting Wetenschappelijk Onderwijs Limburg. The authors are particularly grateful to Mr Thomas Abalan and Mr Satburi Jared for their excellent interpretations of the interviews. Also, we wish to express our warmest thanks to the many leprosy patients who shared their time and stories to help us learn from their experiences.

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FURTHER EDUCATION

Surgery of common paralytic conditions

FRANK DUERKSON
Health Sciences Centre, 700 William Avenue, Winnipeg, Manitoba, Canada R3E 0Z3

Involvement and loss of function of nerves, cutaneous as well as trunk nerves, is the main cause of impairment. The subsequent disability leads to a handicap in leprosy.

Early intervention at the stage of impairment is the best way to prevent deformity, disability, the stigma and fear of leprosy. The next best is intervention at the stage of early deformity and disability before it becomes established and irreversible.

Early surgery can correct deformity and disability; the earlier it is done the better is the restoration of form and function.

A positive attitude and motivation on the part of the patient, doctor and all involved in this work, is essential.

The surgical team consists of a willing patient, a specially trained surgeon, trained physical and occupational therapists, a social worker and the operation theatre staff.
Trunk nerve decompression can often help in restoring the function of a damaged nerve, especially when done early.

Nerve decompression surgery

The different procedures are:

1. External decompression, e.g. carpal tunnel release.
2. Epicondylectomy.
3. Anterior transposition.
4. Epineurotomy.
5. Internal decompression or neurolysis.

Successful surgery in leprosy is a result of teamwork, not only during but also before and after surgery, including at periodic follow-up visits for at least a year after surgery.

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Nerve surgery

Surgical decompression of a trunk nerve is indicated when medical treatment for nerve damage has failed or there is a nerve abscess. If after 4–6 weeks of corticosteroid treatment the neurological evaluation and symptoms do not show improvement, then surgical release of the nerve is indicated.

METHODS

In most cases, external release of compressing factors is adequate. In instances where the nerve is swollen with a thick epineurium, incision of the nerve sheath should be done. This needs an experienced surgeon and magnification with a loop during surgery. In case of a nerve abscess, careful removal of all infected necrotic tissues is required.

Ulnar nerve

This is the most common nerve often requiring surgical decompression to prevent trauma by compression, stretch and friction.

SURGICAL DECOMPRESSION OF THE ULNAR NERVE AT ELBOW

The ulnar nerve just above the elbow is commonly involved. It is thickened, sometimes nodular, with pain on movement of elbow, tenderness and a varying degree of sensory and motor paralysis. Sometimes there is severe tenderness; warmth and swelling indicating nerve abscess (Figure 1).

Occasionally the nerve has no pain or tenderness, but there is reduced nerve function; this is labelled as a quiet nerve paralysis. The role of surgery here is not yet established.
The various techniques of surgery are:

1. Release of the roof of the fibro–osseous tunnel, the epitrochleo–olecranon canal. This is sufficient in most cases. The roof is formed of fibrous bands and the arching origin of flexor carpi ulnaris muscle. This has to be incised.
2. Some surgeons advocate other procedures like anterior transposition (subcutaneous or under the muscles) or epicondylectomy in order to eliminate traction injury. No conclusive evidence is available at present that any of these techniques are better than a simple release of external compressing factors.
3. Epineurotomy is release of the compressing thickened nerve sheath. This is indicated when the nerve sheath is much thickened and opaque. This surgery is delicate and needs experience and magnification during surgery.

Median nerve

The median nerve is compressed at the wrist in the carpal tunnel. A standard carpal tunnel release is indicated. Sometimes an epineurotomy is also required, as in the case of the ulnar nerve. The results of early surgery are good.

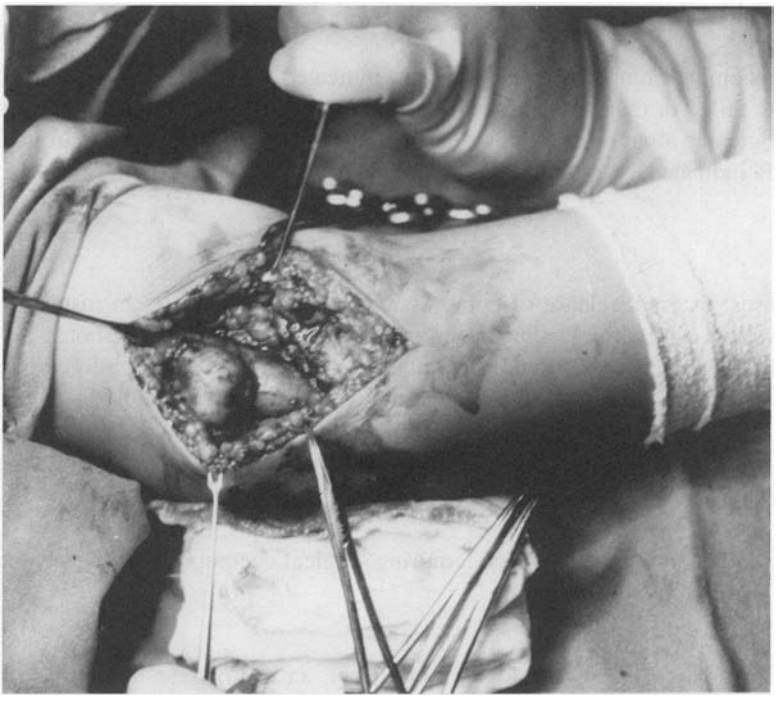

Figure 1. Ulnar nerve abscess.

Posterior tibial nerve

The posterior tibial nerve is compressed behind the ankle, in the tarsal tunnel. This is probably the most important nerve to release since permanent damage here leads to paralysis of the sensory supply of the whole of the sole of foot and paralysis of intrinsic muscles. At this site, the nerve and blood vessels travel together within a common neurovascular sheath. The artery often provides the main blood supply of the foot. Because of involvement and swelling of the nerve, the artery is secondarily compressed reducing the vascular supply of the foot. Early decompression releases from pressure both the artery and the nerve. The method of release is incision of the flexor retinaculam, of the neurovascular sheath, of the constricting calcaneal bands and sometimes epineurotomy. More work is required to establish this benefit.

The common peroneal (lateral popliteal) nerve

The common peroneal nerve is less frequently involved and responds better to conservative treatment with rest, splinting and steroids.

Occasionally decompression of this nerve is required, especially in case of a nerve abscess. The procedure is release of the fibrous bands overlying the nerve at the level of the neck of the fibula and release of the fibrous arch in the peroneal muscles through which the nerve passes.

In leprosy, absence of controls in the study of nerve surgery has deprived it of an established place in prevention of deformity and disability. Individual experiences are, however, quite encouraging.

Surgical treatment of deformities and disabilities secondary to permanent nerve damage

This section describes the commonly performed reconstructive surgery procedures for restoration of form and function of the hand and foot in leprosy. Early diagnosis and treatment is the best prevention, next best is early treatment of nerve damage aimed at restoration of nerve function. When there is established paralysis and resultant deformity, early reconstructive surgery is desirable.

For most such deformities of hands and feet, very successful surgical solutions are available. The success depends on teamwork involving an experienced surgeon, physiotherapists and well-motivated patients. Care of the part with loss of sensation is of course essential to maintain the form and function restored by surgery.

RECONSTRUCTIVE SURGERY OF HAND

Tendon transfers can correct or improve most problems caused by paralysis of the hands and feet in leprosy.

Co-operation from an experienced physiotherapist and the availability of an experienced surgeon, who knows how to handle tissues gently and understands the biomechanics of tendon transfer surgery, is essential.

The hand has to be made fully mobile before surgery by methods of physical therapy including exercises, wax therapy correction of any contractures, correction of any adaptive shortening of the long flexors, erasing of trick movements and other measures.

Next comes training of the muscle–tendon complex to be transferred and explanation to the patient of the maximum restoration of form and function that this surgery is aiming at in his case and the nature of the co-operation required.

Protection of the transfer during the first 3 months by avoiding excessive stress and strain and repeated reinforcement of integration of the transfer at follow-up visits is essential to achieve a good result. The patient has to be encouraged to use the operated hand, but with care.

Surgery for ulnar nerve paralysis (Figure 2)

Clawing of the hand can easily be corrected by a variety of surgical techniques. Surgery is delicate and very exact, and must be accompanied by the patient learning techniques of care of the parts with loss of sensation since surgery only corrects the motor component.

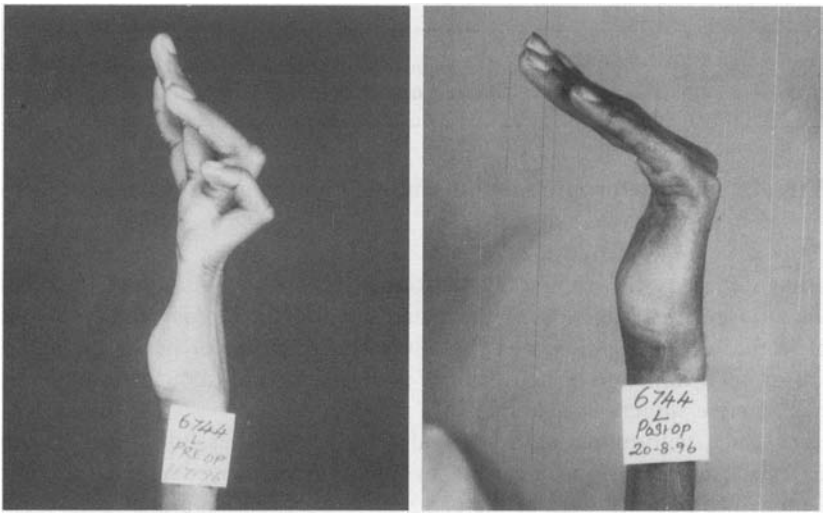

Figure 2. Ulnar paralysis repair. Four-tailed transfer of extensor carpi radialis longus into fibrous flexor pulleys. The tendon of flexor superficialis of one finger (usually the ring) or the palmaris longus is looped around all flexors, tunnelled to the radial side of the hand and inserted in the tendon of abductor brevis or flexor brevis of the thumb to restore pinch power.

PROCEDURES

The principle is correction of the muscular imbalance at the level of the metacarpophalangeal (MP) joints of the fingers and thumb. The common techniques are:

1. The transfer described by Dr Brand using the extensor carpi radialis longus as a motor extended by a graft, tendon or fascia lata. The insertion is into the lateral bands of the extensor expansion of the fingers in the proximal phalanx. The tendon is routed in front of the wrist and MP joints.
2. Transfer of flexor superficialis of the long or middle finger (first described by Bunnel) to the extensor expansion as above.
3. Zancolli's 'lasso' operation principle where the transfer, ECRL of flexor superficialis is inserted into the A1 (and part of A2) fibrous flexor pulley. This technique is specially useful in hypermobile fingers, where other techniques could cause a swan neck deformity.

Surgery for median nerve paralysis (Figure 3)

The disability involves loss of opposition and instability of the MP joint of the thumb.

The aim of surgery is restoration of stability of the MP joint and restoration of a three-finger pinch grasp.

METHOD

Replacement of opposition and of flexor brevis action by: (1) a single tendon transfer where the tendon is divided into two slips. Usually this tendon is the superficial flexor of the

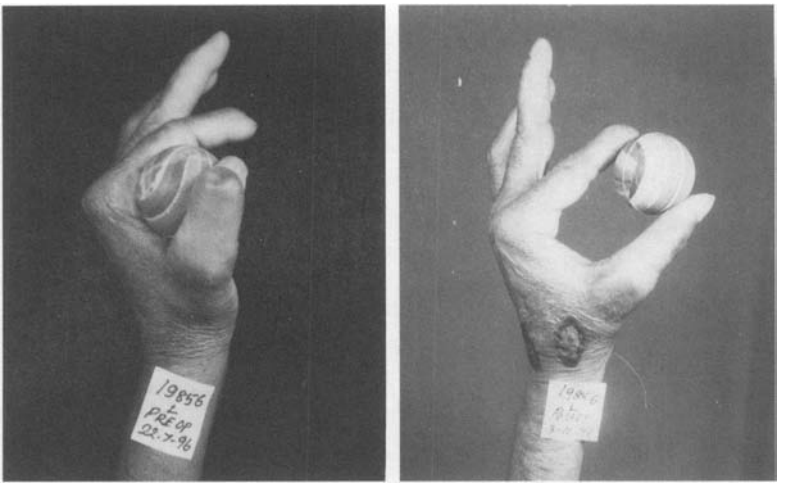

Figure 3. Surgery for median nerve paralysis.

ring finger as recommended by Dr Brand. Another popular transfer is using the extensor indicis proprious tendon routed around the ulnar border of the wrist to the thumb; (2) the second method is 'two-tendon transfer', also described by Dr Brand. One tendon restores abduction-oppositions and another the flexor brevis function.

For restoring the loss of opposition of the thumb, many procedures have been described. We routinely use the single tendon transfer described by Dr Brand. The flexor superficialis (sublimis) tendon of the ring finger is detached and then tunnelled from the ulnar side of the wrist to the thumb and divided into two slips. One goes around the neck of the thumb metacarpal and is sutured to the adductor pollicis tendon. This provides opposition. The other slip goes to the radial side of the thumb, volar to the axis of rotation of the MP joint and is inserted into the extensor pollicis longus tendon. This slip provides stability to the MP joint in flexion.

CORRECTION OF ATROPHY OF THE FIRST INTEROSSEOUS SPACE

The first web space becomes hollow because of wasting of the first interosseous muscle. This noticeable deformity is often a cause of stigma. Correction by a silicon implant or a dermal flat implant successfully corrects the deformity.

Correction of foot-drop and clawed toes

SURGERY OF COMMON PARALYTIC CONDITIONS OF THE FOOT IN LEPROSY

The two common conditions are foot-drop and clawed toes. Foot-drop can be partial or complete where all the dorsiflexors and peroneii are paralysed. Claw toes can be mobile or fixed with bony or soft tissue contractures.

Surgical correction prevents development of lateral border ulceration, rigid equinovarus foot and excessive pressure under the metatarsal heads leading to plantar ulcers.

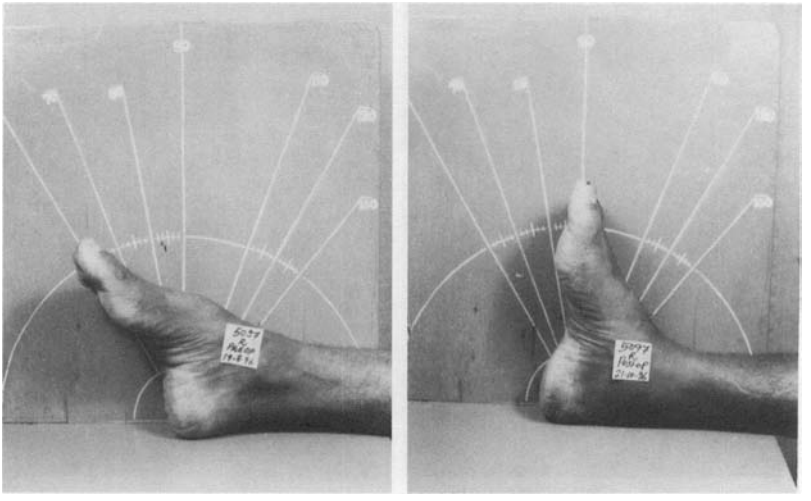

Figure 4. Correction of foot drop. Lengthening of the Achilles tendon, two-tailed tibialis posterior transfer and flexor to extensor transfer for claw toe.

FOOT-DROP CORRECTION (FIGURE 4)

The most common tendon transfer used is that of the tibialis posterior either through the interosseous membrane or subcutaneously around the medial aspect of tibia. Insertion is done either by two slips or by one slip. The two-slip insertion is done usually into the extensor hellucis longus and the extensor communis (of all lateral four toes) tendons. Insertion by single slip is often done either into bone or joint capsule in the middle of the foot.

Provision of appropriate footwear in maintaining a trouble-free foot cannot be overstressed.

CLAWED TOES

Clawing of toes often needs correction at the same time as correction of foot-drop. This is done, when the toes are mobile, by transfer of the toe flexors to the toe extensors thereby creating a new MTP flexor. When the clawing is fixed. it is corrected by joint fusion procedures.

Rigid equinovarus foot deformity is corrected by remodelling arthrodesis together with tibialis posterior transfer.

Lepr Rev (1998) **69,** 397–399

CASE REPORT

Fixed drug eruption due to rifampin

STEPHEN S. JOHN
St Joseph's Hospital, Dindigul-624 001, Tamil Nadu

Accepted for publication 17 August 1998

Summary A case of fixed drug eruption due to rifampin in a leprosy patient is described. Fixed drug eruption due to rifampin with the classical residual hyperpigmentation has not been described before.

Introduction

Rifampin is a semisynthetic broad spectrum antibiotic widely used in the treatment of leprosy and tuberculosis. A number of side effects have been reported with rifampin. However, cutaneous side effects due to rifampin are rare.[1] Though an urticarial form of fixed drug eruption has been described earlier,[2] the classical form of fixed drug eruption due to rifampin with residual hyperpigmentation has not been reported as yet. This is a report of a case of classical FDE due to rifampin occurring in a leprosy patient.

Case report

A 30-year-old woman presented with asymptomatic hypopigmented ill-defined and well-defined, flat, dry, anaesthetic patches over the posterior aspect of the right thigh, right leg, right arm and right interscapular area. The right lateral popliteal nerve was thickened but non-tender. Skin smear was negative for AFB. A diagnosis of borderline tuberculoid leprosy was made and the patient was put on once monthly rifampin 600 mg and once daily dapsone 100 mg.

The patient complained of a pruritic rash over the abdomen and thighs following the fourth dose of rifampin. On examination, 2–3 cm size well circumscribed, round, dusky red macules were seen, four on the abdomen and four on the right thigh (Figure 1). These lesions did not in any way involve the existing hypopigmented patches due to leprosy. A diagnosis of fixed drug eruption (FDE) was made. Since FDE is a well established side effect of dapsone, dapsone was thought to be the offending drug and this drug was stopped. Clofazimine was added to the regimen instead. The itching and the erythema subsided in 2 days, but the grey-black pigmentation remained at the site. Following the next monthly dose of rifampin, the patient developed itching over the original lesions and mild oedema was seen at these sites. This time, rifampin was suspected as the possible cause for the FDE, and dapsone was restarted. The symptoms did not recur. In the following month, the sixth and final dose of

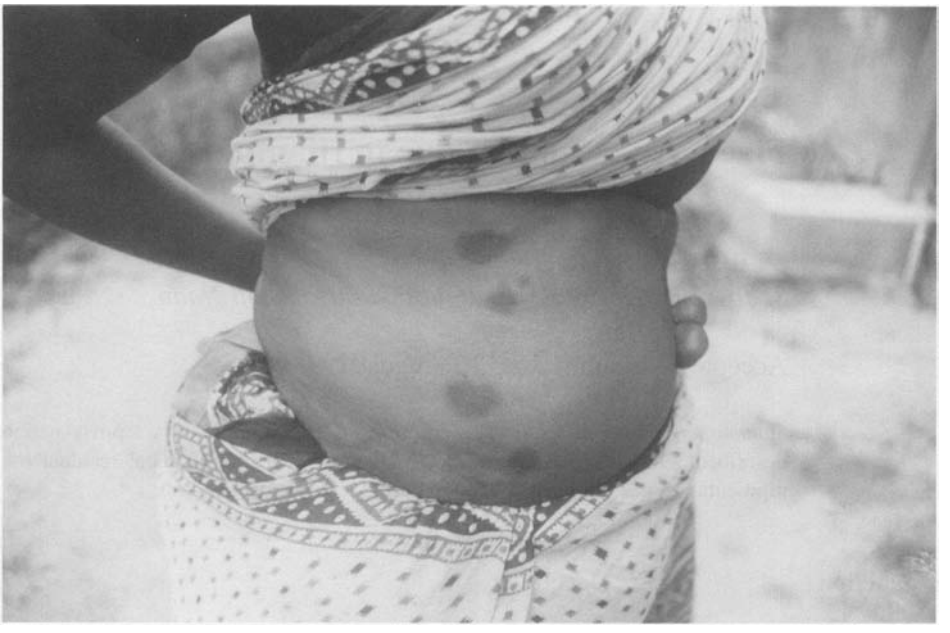

Figure 1. Macules due to fixed drug eruption.

rifampin was given and the patient was kept under observation. She developed itching within 1 h of rifampin administration and one new lesion was seen on the chest the same evening. By next evening, the itching had subsided. The patient has since been released from treatment and is presently under surveillance.

Discussion

Fixed drug eruption was first described by Bourns in 1889. However, it was Brocq who introduced the term FDE.[3] Since then, many drugs and various chemical substances have been reported to cause FDE.[4–6]

The cardinal morphological feature of FDE is pigmentation, varying from dusky slate to brownish black. The diagnostic hallmark is its recurrence at previously affected sites.[7]

The exact pathogenic mechanisms of FDE is not known. However, the studies reported so far[8–11] seem to incriminate the immune system.

The drug in circulation is thought to act as a hapten, and binds to some protein component in the lower epidermal cells. The Langerhan cells then process and present this drug–protein complex to lymphocytes in the dermis or regional lymph nodes. Subsequently, lymphocytes are stimulated, producing lymphokines and antibodies that eventually cause inflammation. Antibody-mediated cellular cytotoxicity has been implicated in inducing damage to keratinocytes.[12]

The exact reason for preferential localization of fixed lesions to certain skin sites is still not known.

Rifampin when given in the usual doses is well tolerated. However, adverse effects of

rifampin are well documented. Cutaneous side effects with rifampin have been reported in less than 5% of patients. Though some of the adverse effects, for example flu syndrome, shock, shortness of breath, haemolytic anaemia and renal failure, occur only with intermittent rifampin administration, cutaneous side effects may occur to either daily or intermittent rifampin administration.

The cutaneous side effects of rifampin described in the literature include: pemphigus[13,14] exfoliative dermatitis,[15] acneiform lesions,[16] urticaria,[17] maculopapular lesions,[18] itching with or without rash,[18] contact dermatitis,[20] anaphylaxis,[21] anaphylactoid reactions[22] and an urticarial form of fixed drug eruption.[2]

There has been only one report of FDE to rifampin, which was an urticarial form. The classical form of FDE with residual hyperpigmentation as seen in this patient has not been described as yet.

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Lepr Rev (1998) **69,** 400–401

Letters to the Editor

SKIN PATCHES HERALDING RELAPSE IN A TREATED CASE OF NEURITIC LEPROSY

Editor,

A 36-year-old soldier, an old case of pure neuritic leprosy with initial involvement of left ulnar and right common peroneal nerves, who had received MDT-MB for 2 years, presented 3 years after successful completion of MDT with complaints of pain in the left periorbital region, increased weakness of the left hand and right foot, and hypopigmented skin patches over the left forearm and right thigh of 3 months duration.

Examination revealed two large ill-defined hypopigmented hypoaesthetic skin patches over the right thigh and left forearm, respectively. Left infraorbital, left ulnar, right common peroneal and posterior tibial nerves were uniformly thickened and tender. Weakness of the left orbicularis oculi (Gr. IV/V), grip left hand (Gr. III/V) and dorsiflexors of right foot (Gr. III/V) was evident clinically. Muscle power in the ulnar nerve supplied muscles of the left hand had been 4/5 on completion of MDT and 4/5 for the dorsiflexors of the right foot. There was no weakness of the left orbicularis oculi and the muscle power of left hand/dorsiflexors of right foot was Gr. IV/V on completion of MDT-MB. Slit skin smears for *M. leprae* from the right ear lobe and left eyebrow were negative for *M. leprae*. Skin biopsy from the patch over the left forearm revealed a dermal foamy macrophage granuloma (Figure 1) with the presence of AFB in Fite-stained sections.

Relapse was considered in view of the insidious appearance of skin patches, new nerve involvement, histopathological findings and inadequate response to 4 weeks therapeutic trial with oral steroids.

Transition from neuritic to leprosy with cutaneous lesions has been reported by several workers, more so when treatment is irregular and the patient is on monotherapy .[1,2,3] In a follow-up study on evolution of disease, it has been found that a large proportion of patients (almost two-thirds) with suspicious disease pass through a short-lived phase of neuritic disease before developing skin

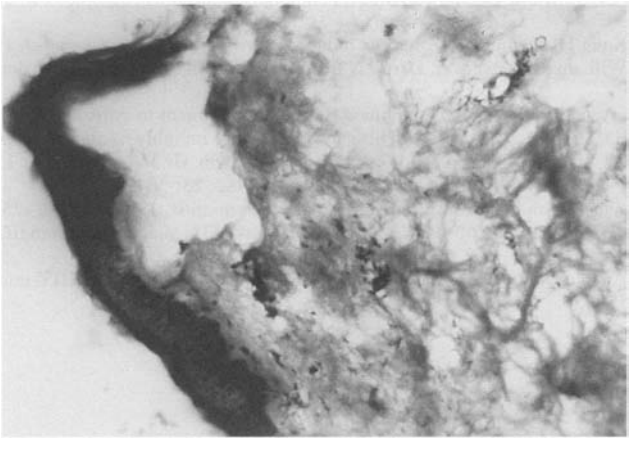

Figure 1. Dermal foamy macrophage granuloma (haematoxylin and eosin stain, ×450 magnification).

manifestations.[4] The appearance of skin lesions in neuritic leprosy has been suggested to be a part of the reversal reaction.[5,6] However, the appearance of a skin patch heralding relapse in an adequately treated case of neuritic leprosy is an interesting observation in this case.

Department of Dermatology & STD
Command Hospital (Air Force)
Bangalore-560 007
India

GURCHARAN SINGH
K. DASH
S. GROVER
P. SANGOLLI

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COMMENT: LEPROSY, HIV INFECTION AND LEPRA REACTIONS

Editor,
It was interesting to read the case reports of lepra reactions occurring in HIV-seropositive multibacillary leprosy patients (*Lepr Rev*, 1998; **69:** 173–177). The report raises two controversial points.

1. In each of the three cases, reversal reaction has been diagnosed on the basis of clinical findings and a single biopsy picture each of skin and nerve lesions. On this basis, it would have been more appropriate to refer to them as type-1 lepra reactions rather than reversal reactions. These reactions could have been downgrading reactions, as there is no record of pre-reaction biopsy and further biopsy was not carried out after the reaction subsided. In the early and acute reactions, it is not possible to know by the histological picture whether the patient is upgrading, downgrading or neither.[1] It is obviously easier to determine the course of reaction if a pre-reaction biopsy is available for comparison. The reported cases may have been of downgrading reactions which were controlled with the treatment given. Lepromin positivity during reaction is not an absolute proof of reversal, as the lepromin test could have been more strongly positive earlier.

2. The authors state that the occurrence of reversal reaction in HIV-seropositive patients is paradoxical. It is not so because in the early stages of HIV infection, the CD4 cell count may be more or less normal and some degree of immune competence is retained. The immune function gradually deteriorates till the patient develops full-blown acquired immune deficiency syndrome (AIDS). Occurrence of a reversal reaction in a patient with full-blown AIDS would definitely be a paradox, but not so in the early stages of HIV infection. None of the reported patients apparently had reached the stage of full-blown AIDS. Moreover, the authors have not reported on the CD4 + cell counts of these patients, which would have given some indication of the degree of immune dysfunction.

Skin Clinic
Runwal Raisoni Plaza
41/12, Karve Road
Pune 411004, India

ANIL H. PATKI

Reference

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Lepr Rev (1998) **69,** 402–405

Obituary

DR M. S. NILAKANTA RAO, 1927–1998

Dr M. S. Nilakanta Rao, former Director, Gandhi Memorial Leprosy Foundation, passed away in February 1998.

Born on April 5, 1927, Dr Nilakanta Rao had his education in the erstwhile Mysore State. Having obtained a BSc degree from Central College Bangalore, he joined the Medical College in Mysore in 1946. As an undergraduate in the Medical College, he had a bright academic record. After obtaining a medical degree, he worked for about 3 years as a lecturer in Kasturba Medical College, Manipal. In 1957, he left for the UK for postgraduate studies and specialized in chest diseases. On his return from the UK in 1961, he joined Gandhi Memorial Leprosy Foundation (GMLF) and worked as a Medical Officer for 3 years. He was later drawn into administrative work as Joint Director and subsequently as Director of GMLF. During his tenure as Director of GMLF, he was involved in the National Leprosy Eradication Programme, as an expert consultant. He played an active role in the National Leprosy Organization (NLO), a confederation of voluntary organizations in the field of leprosy. As the President of NLO, he was able to co-ordinate the work of various voluntary organizations. In appreciation of his valuable contribution to leprosy work, Dr Nilakanta Rao was awarded the title 'Padmashri' by the Government of India.

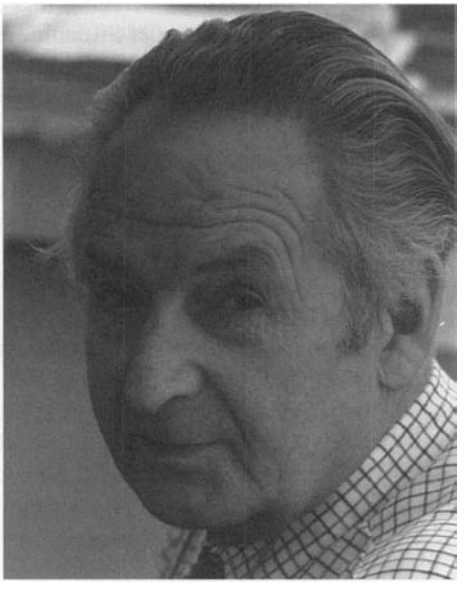
Retiring from GMLF, Dr Nilakanta Rao settled in Bangalore, carrying out private practice in tuberculosis and leprosy. The Government of the State of Karnataka utilized his services as a member of the Expert Committee on Leprosy. He was thus able to guide the leprosy programme in Karnataka and also to co-ordinate the work of voluntary organization in the State. By his death, India has lost a prominent leprologist.

K. V. DESIKAN

0305-7518/98/069402+01

Obituary

Dr R. J. W. REES



Richard John William 'Dick' Rees, CMG, FRCP, FRCPath died on October 3 aged 81. He was one of the most influential leaders in the fight against leprosy, a fight which has seen remarkable advances in recent years. During a research career spanning more than 4 decades, he dedicated himself to bringing the benefits of modern medical science to some of the poorest and most ostracized people in the world.

Dick was educated at Sheen County Secondary School, before studying medicine at Guy's Hospital. After qualifying from Guy's in 1942, he served as a captain in the Army Blood Transfusion Service in the North Africa and Italian campaign. At the end of World War II, he returned to Guy's and started what was to become a remarkable career in experimental pathology. In 1949 he made the defining move in his career; Philip D'Arcy Hart was establishing the Medical Research Council's new Tuberculosis Research Unit in London. Dick Rees was recruited to the National Institute for Medical Research at Mill Hill to carry out laboratory-based research on TB, research which was to underpin the Unit's activities. The study of tuberculosis was changing rapidly; the discovery of streptomycin in 1944 was to be the start of a new era of successful chemotherapy. Other drugs against TB quickly followed, and the TB Research Unit became the major focus of research on the

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use of these new compounds for treating TB. Dick's early work, in collaboration with Philip D'Arcy Hart and Sir John Cornforth, involved an investigation of the anti-tuberculous activity of a group of compounds which appeared to act through a host cell-mediated mechanism. These compounds, now called 'calixarenes', are the source of renewed interest, since they represent a novel approach to understanding how macrophages can inhibit mycobacterial multiplication.

Although research in tuberculosis was creating much excitement in the early 1950s, Dick Rees made another important change of direction. He heard of a lecture, ostensibly about TB, in which the speaker drew the audience's attention to the fact that the related disease of leprosy had attracted virtually no interest from medical researchers, and like many of its sufferers, was isolated from the mainstream of medicine. Dick gradually started to shift his focus; drawing on the TB Unit's experience in successfully bringing together high quality laboratory-based research and clinical research carried out under difficult field conditions, he turned his attention to leprosy. Meticulous observation enabled him to establish the relationship between viability of the leprosy bacillus and its staining properties. This enabled him to establish the concept of the morphological index, or MI, as a measure of therapeutic progress, thus providing the first laboratory correlate of successful chemotherapy.

Although useful, the MI lacked the precision and sensitivity required to carry out precise comparisons of therapeutic regimens. However Dick instantly recognized the importance of the research being carried out by Charles Shepard at CDC in Atlanta; if *M. leprae* could be reproducibly grown in the footpads of mice, then here at last was a method for reliably monitoring the viability of the bacteria isolated from patient tissue. Dick confirmed Shepard's findings and extended them by using immunosuppressed mice which permitted greater bacterial multiplication. From his base at Mill Hill he began to establish an international network of collaborators in leprosy research. Field units were set up, first in Sungei Buloh in Malaysia and later in Addis Ababa and then Hyderabad, South India. It was these interactions in particular, with discoveries made in the Rees laboratory at Mill Hill underpinning the clinical research of Dr Michael Waters in Malaysia and Dr John Pearson in Addis Ababa which transformed the way in which leprosy was studied, and ultimately how leprosy patients are treated.

Using the mouse footpad technique Rees and his colleagues demonstrated the emergence of secondary drug resistance, then primary drug resistance. By utilizing the greater sensitivity of thymectomized-irradiated mice they were able to demonstrate the presence of a population of drug-sensitive bacteria which remained viable for several years following treatment, the so-called persisters. It was these findings which provided the impetus for the recommendation of multiple drug therapy by the World Health Organisation in the early 1980s.

In the same way that he had instantly appreciated the importance of the mouse footpad work, Dick also recognized the potential of using the armadillo as a source of large numbers of *M. leprae*. The mouse had provided a tool to support his clinical research; now the work of Dr Eleanor Storrs in the USA at last offered the possibility of carrying out basic studies on the immunology, physiology and ultimately the molecular biology of *M. leprae*. A colony of infected armadillos was established in the UK, and with the support of the World Health Organisation the ''IMMLEP Bank'' was set up, with Dick providing a range of *M. leprae* ''products'' to the research community. We can anticipate that within the next 12 months we will have the complete genome sequence of the leprosy bacillus; how fitting that the material supplied by Dick's IMMLEP Bank should ultimately reveal the most fundamental secrets of the organism which he spent his life trying to understand.

Even before he was officially appointed Head of the Medical Research Council's Laboratory for Leprosy Research at Mill Hill in 1969, Dick Rees' remarkable scientific abilities and commitment to the cause of leprosy had become widely recognized. In 1963 he became Chairman of the Medical Advisory Board of the charity LEPRA (The Leprosy Relief Association); he was a central figure in leading the research and disease control activities of LEPRA for more than a quarter of a century and remained closely associated with the charity until shortly before his death. He also played a leading role in the World Health Organisation's leprosy programme. Although Dick officially retired in 1982, he continued to work both for LEPRA and WHO, and was a profound influence on the leprosy work of both organizations long into his retirement years.

Dick Rees was a modest man, communicating his ideas in a quiet but forceful way to his colleagues and students all over the world. The many visiting workers who trained with him and then returned to their home countries to work on leprosy received life-long support and encouragement. There are few people working in leprosy today, be it in the scientific laboratory or in the remotest part of the world where leprosy remains an important health problem, that have not been influenced by his enthusiasm and devotion. A world without leprosy was a dream which inspired his research career; it is a dream which he more than most has helped to bring within our grasp.

Lepr Rev (1998) **69,** 406–407

Book Review

'Don't treat me like I have leprosy!' Tom Frist
ILEP, London, UK, 1996.

The author sets out to guide three categories of people; 1) those presently involved in Hansen's disease work, 2) those who have no experience now but may become involved, and 3) people interested in helping any stigmatized and discriminated group.

Part I provides an overview of the leprosy problem as he sees it. Frist looks at the goals of leprosy work, progress in achieving these goals in relation to the physical, psychological, spiritual, social and economic aspects of the problem. He discusses issues such as who speaks for leprosy sufferers, integration, roles of various agencies, resources and the 'correct' image of leprosy.

Frist posits the final goal of Hansen's disease work as 'to eradicate the disease and to help persons affected by it ''normalize'' their lives and achieve true social integration.' He claims that this can take place only when there are changes in persons providing services and the public as a whole as well as in persons affected by the disease.

The author touches on the crux of the matter under psychological goals, that is, the failure of present and past health education efforts by care providers and educators to reduce stigma attaching to leprosy. He then asserts that 'For leprosy stigma to reduce, the public, the provider ... and the person affected by the disease must learn the new reality of the disease ... not only learn, but come to truly believe that the old images of leprosy are no longer true,. Only then will their attitudes and behavior change'.

Frist's description of the problem is thorough and methodical, the facts provided are useful and enlightening and the framework claimed to be holistic. Unfortunately, his framework lacks cultural and religious elements and so is likely to miss crucial deeper understanding which could lead to effectively removing of the problem. Leprosy occurs in many countries where western, scientific, secular notions of health and illness, treatment and cure are not commonly held. Such cultures often have their own unique medical systems, their own way of explaining illness and their own means for dealing with it.

Foreign care providers in such settings need to be aware of the traditional cultures in which they operate. In this area of inquiry trained social scientists can lend vital insights into the culturally specific aspects of stigmatization.

Frist's first model for attitude change is that knowledge leads to change of belief which then leads to change in attitude and behaviour. This is attractively straightforward but misleadingly simple. The wealth of literature and research on attitude change serves to illustrate that the process of change is complex and protracted. Studies in other fields could help those who attempt to bring about attitude change in relation to leprosy. Some examples are 'diffusion of information' based on programs to reduce smoking, raise the rate of childhood immunizations. Distinct elements of attitudes need to be studied to identify which are most likely to be 'changeable'.

Part II provides a plan of action to promote normalization. There follows the Frist formula for achieving this. In order to bring about ''normalization'' changes must be brought about on three fronts, that of the people affected by leprosy, the society in which they live and finally in the service providers themselves. In order to be successful, programs designed to bring about 'normalization' need to be relevant, effective, efficient, sustainable and fair.

The primary step in this formula is to change ourselves. Here Frist suggests a second model of attitude change; if we base our behavior, not on our prejudices, but on sound scientific knowledge, then after such changed behavior 'we will often find that our attitudes will soon change as well'.

Next comes the identification of 'prime movers' or allies in society in the process of social change. Prime movers are to be organized and a project set up after investigating the problem in the area, gathering information in relation to the medical, psychological, socio-economic, support services related to the problem. What are the obstacles to social integration? Analysis of information will lead to the plan of action and identification of areas to be addressed. Detail is given on setting up support services and in such a way transforming the society in relation to leprosy.

Detail is also given on transforming the leprosy world. Integration and the dismantling of segregatory institutions and programs are advocated. '...it is imperative for all Hansen's disease-specific organisations to review their missions, ... names, ...symbols, ... fund raising strategies...'

Finally, Frist deals with who pays, the reduction of expenses and the evaluation needed to assess the progress of transformation. He provides a suggested Normalization Index for calculating progress in physical, spiritual, social and economic normalization for both the individual and a community.

Here the author presents his formula in a systematic and logical way with accurate and clear information. His formula advocates a systems approach to transforming society, to change services, infrastructures and community based programs.

Unfortunately Frist has also fallen into a trap when he said 'Health practitioners, because of their activist orientation, have an understandable tendency to begin with inputs (interventions) ... and assume that the outcome (desired changes) will occur automatically'. Frist's formula seems to be an input assuming a desired outcome. If it is applied in cross cultural situations regardless of the specific cultural insights, it may well lead to undesired negative effects. It is a pity that Frist has not consulted experts like Green and availed himself of the wealth of research literature available on attitudes and attitude change, stigma and stigma reduction.

Most would agree with Noordeen, who in 1991 mentioned several factors including social stigma which '...led to leprosy control losing considerable ground...'. Unfortunately, the WHO response of introducing MDT and the push for 'elimination', while reducing registered prevalence dramatically, has not addressed the stigma issue. Future prospects of leprosy control may be bright with 'major reductions in prevalence foreseen'; however, issues of social stigma are left unresolved.

One wonders if Frist's systems approach and formula for transformation has actually been used anywhere? What were the effects? Perhaps such a project should be tried as a pilot? It would be useful to have information on the actual successes and shortcomings of such an approach.

Frist is correct to suggest that the reduction of stigma with all its ramifications remains a long term aim of leprosy work. While his book may 'fill part of the literature gap' in this area, it remains to be seen if his formula provides an adequate framework to bring about changes or whether its weakness—that of disregarding traditional cultural and religious basis for much prejudice—will prove to be a fatal flaw.

Jeanette Hyland

Lepr Rev (1998) **69,** 408–418

Teaching Materials and Services

Schieffelin Leprosy Research & Training Centre

SCHEDULE OF COURSES FOR 1999

Courses	Qualifications	Duration	Commencing date
Medical Officers	Medical personnel engaged in Leprosy work	6 weeks	Jul. 26–Sep. 04
Non-Medical Supervisors	Qualified Para Medical Workers with a minimum of 5 years experience	3 months	Apr. 01–Jun. 30
Physiotherapy Technicians	+2 or P.U.C. passed. (with science subjects)	12 months	Jul. 01–Jun. 30
Laboratory Technicians	+2 passed. Science graduates preferred	12 months	Jul. 01–Jun. 30
Smear Technicians	+2 passed (with science subjects)	3 months	Jan. 11–Apr. 10 Sep. 06–Dec. 04
Paramedical workers	+2 passed. Graduates preferred	6 months	Jul. 01–Dec. 31
Shoe-Makers	V-standard with knowledge of English preferred	6 months	Jan.04–Jun. 30 Jul. 01–Dec. 31
Diploma in Prosthetic & Orthotic Engineering	+2 passed. Graduates preferred (with science subjects)	30 months	Jul. 01–Dec. 31 (2001)
Ophthalmic Aspects in leprosy	Medical personnel	1 week	Jul. 19–24
Eye Care in Leprosy	Non-medical Personnel	1 week	Sep. 6–11

For further details, please contact: Director/Registrar Training Unit, Schieffelin Leprosy Research & Training Centre, Karigiri 632 106, Vellore District, Tamil Nadu, India. Tel: +91 416 74221; Fax: +91 416 74274.

Science funding opportunities at the Wellcome Trust, UK, 1998

The following information appeared in Issue 15 Q2, 1998 of *Wellcome News* (Research & Funding News from the Wellcome Trust, 210 Euston Road London NW1 2BE. Telephone 0171-611-8888. Fax 0171-611-8545).

INFECTION AND IMMUNITY PANEL

Remit: Fundamental and applied research relating to infectious diseases, and mechanisms of immunity and allergy—ranging from the genetics of host susceptibility or resistance, through epidemiology, immunology and pathology of infection, to the genetics and molecular structure of the aetiological agents of disease. Disease vectors, chemotherapy and vaccine developments are also covered.
Programme Manager: Pat Goodwin
Scientific Officers: Cathy Fletcher, Anne Wood
Grants Officers: Iqbal Khanem, Sheila Pickard, Chris Sainty
Preliminary enquiries: Contact scientific staff, preferably in writing, with an outline of proposed research (plus brief CV and details of current funding). Preliminary application form for project grant support is available on the Trust Web site (www.wellcome.ac.uk).
Tel: +44 (0)171 611 8435
Fax: +44 (0)171 611 8352
E-mail: s.parkes@wellcome.ac.uk

MOLECULAR AND CELL PANEL

Remit: All areas within molecular and cell biology, including biochemistry, molecular immunology, developmental biology and genetics; proposals may involve basic, clinical or veterinary research.
Programme Manager: Barbara Skene
Scientific Officers: Helen Fisher, Jane Itzhaki, Pam Reid
Grants Officers: David Clayton, Joan Saitch, Louise Williams
Preliminary enquiries: As for Infection and Immunity Panel.

INFRASTRUCTURE PANEL

Remit: Funding of large items of equipment and refurbishment of laboratory facilities.
Programme Manager: Siân Thomas
Scientific Officers: Gavin Malloch, Sally Woodward
Grants Officers: Roger Crimp
Preliminary enquiries: Details of schemes and eligibility are provided on the Wellcome Web site (www.wellcome.ac.uk). Contact above scientific staff with preliminary enquiries for support.
Tel: +44 (0)171 611 8320
Fax: +44 (0)171 611 7277
E-mail: infrastructure@wellcome.ac.uk

GENETICS ADVISORY GROUP

Advises on any matters relating to research in and involving genetics; provides advice on the needs of UK genetics research and other policy issues. Has responsibility for the Sanger Centre at the Wellcome Trust Genome Campus at Hinxton and the Wellcome Trust Centre for Human Genetics at Oxford.
Tel: +44 (0)171 611 8690
Fax: +44 (0)171 611 8363
E-mail: mcp@wellcome.ac.uk
Neurosciences Panel
Remit: Research relating to the brain and nervous system in health and disease—encompassing cellular neurobiology to problems in the pathology and treatment of common neurological, ophthalmologic and psychiatric diseases.

Programme Manager: John Stephenson
Scientific Officer: John Williams
Grants Officers: Michael Kilbane, Julian Pais, Jane Stone
Preliminary enquiries: As for Infection and Immunity Panel.
Tel: +44 (0)171 611 8419
Fax: +44 (0)171 611 7208
E-mail: neuroscience@wellcome.ac.uk

PHYSIOLOGY AND PHARMACOLOGY PANEL

Remit: Physiology and pharmacology in its broadest context, ranging from basic cellular and molecular studies in model systems to whole organ and animal studies and clinical investigations. Epidemiological and mathematical studies are also covered.
Programme Manager: Michael Wilkinson
Scientific Officers: Jacob Sweiry, Anthony Woods
Grants Officers: Rachel Davies, Nick Potter, Tim Hudson
Preliminary enquiries: As for Infection and Immunity Panel.
Tel: +44 (0)171 611 8420
Fax: +44 (0)171 611 8211
E-mail: ppp@wellcome.ac.uk

Programme Manager: Celia Caulcott
Scientific Officer: Jill Kent
Grants Officer: Jane Sinclair
Tel: +44 (0)171 611 8431
E-mail: j.sinclair@wellcome.ac.uk

BEOWULF GENOMICS

Remit: Sequencing genomes of pathogenic organisms.
Programme Manager: Celia Caulcott
Grants Officer: Jane Sinclair
E-mail: beowulf@wellcome.ac.uk
Web: www.beowulf.org.uk

SIR HENRY WELLCOME AWARDS FOR INNOVATIVE RESEARCH

Remit: Sir Henry Wellcome Commemorative Awards for Innovative Research ('Showcase' awards) provide funding for speculative and highly innovative research projects.
Programme Director: Andy Robertson
Grants Officer: Jennifer Hill
Tel: +44 (0)171 611 8391
Fax: +44 (0)171 611 8688
E-mail: a.robertson@wellcome.ac.uk

BASIC SCIENCE INTEREST GROUP

Remit: Runs personal support schemes for scientifically qualified graduates, including PhD schemes, Research Career Development Fellowships and Senior Research Fellowships in Basic Biomedical Science.

Programme Manager: Patricia Chisholm
Scientific Officers: Candace Hassall, Peter McOwan
Grants Officers: Michael Brophy, Tracey Glenister, Niamh O'Sullivan
Preliminary enquiries: Most schemes are held in annual or twice yearly competition; they are advertised in the scientific press and on the Wellcome Web site (www.wellcome.ac.uk).
Tel: +44 (0)171 611 8888
Fax: +44 (0)171 611 8687
E-mail: cdg@wellcome.ac.uk

CLINICAL INTEREST GROUP

Remit: Provides an overview of the Trust's support for clinical research. Runs numerous personal support schemes for medical, dental and veterinary graduates, from Entry-level Fellowships to Senior Research Fellowships in Clinical Science. Also responsible for health services research, Cardiovascular Research Initiative and Clinical Research Facilities.
Programme Manager: Helen Cope
Grants Officers: Michael Brophy, Margaret Hurley, Niamh O'Sullivan
Preliminary enquiries: As for Basic Science Interest Group.
Tel: +44 (0)171 611 8888
Fax: +44 (0)171 611 8687
E-mail: cdg@wellcome.ac.uk

VETERINARY MEDICINE INTEREST GROUP

Remit: Advises on matters relating to veterinary research and on the profession's research training needs.
Programme Manager: Patricia Chisholm
Grants Officer: Tracey Glenister
Preliminary enquiries: Schemes are advertised in the veterinary and scientific press, or contact Dr Chisholm.
Tel: +44 (0)171 611 8888
Fax: +44 (0)171 611 8687
E-mail: cdg@wellcome.ac.uk

INTERNATIONAL INTEREST GROUP

Remit: Developing international research strengths, through fellowship exchange and collaboration. Senior fellowship schemes are run in several overseas countries.
Programme Managers: Mary Phillips, Ian Scott
Scientific Officers: Michael Chew, Gek Kwan-Lim
Grants Officers: Laura Chambers, Sheila Dykes, Marilyn Westland
Preliminary enquiries: See Wellcome Web site (www.wellcome.ac.uk) for portfolio of schemes. Contact above scientific staff with preliminary enquiries for support.
Tel: +44 (0)171 611 8816
Fax: +44 (0)171 611 7288
E-mail: international@wellcome.ac.uk

TROPICAL MEDICINE INTEREST GROUP

Remit: Provides advice on matters relating to international health. Runs training and career development schemes for overseas and UK researchers. Also responsible for Biodiversity Initiative.

Programme Manager: Ian Morris
Scientific Officers: Cathy Davies, Jane Prosser
Grants Officers: Sean Hussain, Joanna Lucas
Preliminary enquiries: As for International Interest Group.
Tel: +44 (0)171 611 8409/8641
Fax: +44 (0) 171 611 7288
E-mail: tropical@wellcome.ac.uk

POPULATION STUDIES PANEL

Remit: Research aimed at improving reproductive health, and on the socioeconomic and environmental impact of demographic change. Considers applications for personal support (including Master's research training) and project grants, and funds special initiatives.
Programme Manager: Wendy Ewart
Scientific Officer: Gunvanti Goding
Grants Officer: Ralph Pine, Martin Sexton
Preliminary enquiries: As for International Interest Group.
Tel: +44 (0)171 611 8710
Fax: +44 (0)171 611 7288
E-mail: population@wellcome.ac.uk

WELLCOME TRUST UK EXPANDS OVERSEAS SENIOR RESEARCH FELLOWSHIP TO ENCOMPASS INDIA

To help strengthen India's research capacity, the Wellcome Trust recently expanded its overseas Senior Research Fellowship scheme to encompass India. Launched early in April, the scheme was advertised in international journals as well as local Indian biomedical journals and newspapers. The response was immediate: more than 50 applications came through in the first week, mostly from Indian researchers working in the USA wishing to return to their homeland.

The decision to include India reflected its long-standing research tradition, as well as the numerous successful Wellcome Trust-funded research projects that have been based in India. The new scheme's aims are broad; support will be provided for scientists undertaking fundamental research as well as those addressing local issues. A committee of eminent Indian scientists based in India, the UK and the USA will act as advisers for the scheme, which will provide some three to five fellowships a year.

For enquiries and forms contact
Dr Mary Phillips
International Programmes Manager
The Wellcome Trust
183 Euston Road
London NW1 2BE
Tel: +44 (0)171 611 8410
Fax: +44 (0)171 611 7288
E-mail: m.phillips@wellcome.ac.uk
Further details of the schemes are available on the Wellcome Trust Web site (www.wellcome.ac.uk).

WHO REPORT OF A MEETING ON THE FUTURE ROLE OF LEPROSY TRAINING AND/OR RESEARCH INSTITUTIONS

The above meeting was held in Addis Ababa, 25–26th February 1998.

The main objectives of the meeting were:

1. To review current activities of the institutions in the areas of service delivery, field work, training and research, and their relevance and importance in the light of changing needs.
2. To identify and discuss feasible activities by the institutions for the next 10 years.
3. To identify training needs in the light of changing needs and define the future roles of leprosy institutions in meeting those training needs.
4. To identify research areas needing support for the future.

During the final session of the meeting, conclusions and recommendations were drawn up and the drafts were discussed. Several more points were discussed as follows:

One proposal was to create a committee for the development of standardized, basic curricula for field workers that could be applied anywhere in an integrated setting. The feeling of the meeting, however, was that no global prescription could be made—only principles could be laid down—on which each country would have to develop its own training programme. These principles would include decentralization of training, a task-oriented content and courses of as short a duration as possible.

On the need for the institutions to diversify, there was much debate as to how strong the recommendation should be. Some felt that institutions 'must' diversify to survive, while others felt that they 'may' diversify if necessary.

After leprosy elimination is achieved, there is the possibility of a decline in the capacity of the general health services to manage leprosy. The institutions may then be required to play a more prominent role than is expected at present This may be notably true for disability prevention and rehabilitation activities. However, a different point of view was that both the national programmes and the institutions would be under the same financial constraints, so a major change back to institutional activity would be unlikely. Therefore, the emphasis was on the need for diversification, recognizing that persons disabled by leprosy will be around for a long time and will require certain services. The public health aspects of leprosy will become a small but important part of communicable disease control programmes.

Dr Noordeen formally closed the meeting and thanked the participants for achieving the objectives of the meeting. It was clear that, in partnership with others, the leprosy training and research institutions have an important role to play, not only in reaching the goal of eliminating of leprosy, but far into the future.

The Conclusions & Recommendations were the following:

6.1 In view of the rapidly changing situation of leprosy and the increasing integration of leprosy work within the general health services, the role of leprosy training and research institutions needs to be redefined.
6.2 The essential roles of training, service and research need to be retained, with a renewed focus on elimination and post-elimination issues.
6.3 All future activities must have close collaboration and two-way communication with national leprosy control programmes.
6.4 Leprosy institutions should network with other centres involved in training, research and rehabilitation, including those outside the field of leprosy.
6.5 The institutions will continue to provide the required expertise to train leprosy specialists at the national and regional levels and to provide advice to the national programmes on training at district and peripheral levels. The training should be decentralized, task-oriented and as short as possible.
6.6 In order to preserve expertise and sustain tertiary referral services for leprosy patients in a cost-effective manner, institutions should consider diversifying according to local capacity and needs.
6.7 The institutions should take the lead in proposing appropriate standards and guidelines for the prevention and management of disabilities, and the rehabilitation of persons affected by leprosy.
6.8 There remains a need for continued research into improving patient care and operational research

into elimination issues. Capacity, particularly for operational research, needs to be built up. Basic research in leprosy should be maintained.

The document reference is WHO/LEP/98.1. WHO, 1211 Geneva 27, Switzerland.

Revista de Leprologia

We are grateful to the Director, Dr Jośe Terencio de las Aguas, Sanatorio de Fontilles (Prov. de Alicante), España, for the latest issue of the *Revista*. Apart from the valuable information it routinely includes on training courses, meetings, and workshops, the reviews of published work, with extensive summaries in Spanish, must surely be of great interest to people working in many parts of south and central America, and Mexico. The headings cover bacteriology and immunology; pathology, physiopathology and biochemistry; clinical aspects and diagnosis; therapeutics; surgery, physiotherapy and physical rehabilitation; epidemiology, prevention and control. Address as above. Tel: 96 558 33 50. Fax: 96 558 33 76.

Biomedical Research & Training Institute, Harare, Zimbabwe

The Biomedical Research and Training Institute (BRTI) are pleased to announce their programme of courses for the period 1998–99. The Institute was established to provide a centre for coordination of research training and support for biomedical research in the Southern African Development Community (SADC). It aims to assist researchers from the region in identifying sources of cooperation and funding, to organize training courses to strengthen the capacity of laboratory personnel, researchers and research managers and to promote the formation of networks for research collaboration. BRTI is a non-profit organization which works together with institutes and laboratories having compatible interests throughout the SADC region.

1. Health Sector Reform for Eastern and Southern Africa: (BRTI/CHSA)	1–10 December 1998
2. Data Handling, Biostatistics and Use of SPSS for Windows: (BRTI/DBL)	7 Sept–3 Oct 1998
3. African International Course in Serological Diagnostics Techniques (BRTI/UZ)	5 Feb–17 March 1999
4. Research Methodology Course for Disease Control Managers (BRTI/DBL)	15–27 March 1999
5. Interpretation and Quality Control of Laboratory Diagnosis of Infectious Diseases (BRTI/UZ)	26 April–8 May 1999
6. Data Handling, Epidemiology and Statistical Analysis using: Epi Info (BRTI/DBL)	10 May–6 June 1999
7. Health Sector Reform for Eastern and Southern Africa:	July/December 1999
8. Data Handling, Biostatistics and Use of SPSS for Windows: (BRTI/DBL)	Sept/Oct 1999

Further information about the courses can be obtained from:
The Training Programmes Manager
Biomedical Research and Training Institute
P O Box CY1753, Causeway
Harare, Zimbabwe
Telfax: 263-4-723997 870403

E-mail: brti@samara.co.zw
brti@healthnet.zw

WHO. Selected Annotated Bibliography on Essential Drugs

This remarkable bibliography, published by WHO in May 1994, runs to 277 pages, plus Subject Index and includes information on no fewer than 709 publications, directing the reader to '... key reports, articles and books related to essential drugs and national policy.' The contents list includes assurance of quality; audiovisuals; drug information; economics and finance; health aspects; human resources and training; monitoring and evaluation; periodicals; pharmaceutical industry; policy and regulation; selection; supply; use; author index; country and subject index. The Introduction reads as follows:

The pharmaceutical sector is increasingly complex. While the number of drugs available on the global market increases, funds to purchase drugs are diminishing in many countries. There is also considerable evidence that drugs are not being used rationally. Governments, prescribers and consumers may have to make difficult decisions about what they can afford, what represents value for money, what meets real health needs and how the rational use of drugs can be promoted. The essential drugs concept, embodied in the WHO Model List of Essential Drugs, and the analytical instruments, operational reports and practical guidelines developed by WHO and others, are intended precisely to assist such decision making, and to contribute towards the appropriate use of drugs.

Information is a vital element. Information on strategies and policies in different parts of the world; on pitfalls and constraints; and on available practical tools, is invaluable to countries, organizations and individuals developing rational drug policies and programmes.

This third edition of the annotated bibliography provides an updated entry point to the literature. It directs the reader to key reports, articles and books related to essential drugs and national drug policy. The bibliography is not exhaustive. Some publications were excluded because of space and time constraints, and because of their limited circulation and accessibility. In addition, most of the material is from English language sources only.

The publications are organized in alphabetical order by author/corporate author. Each is placed, according to its main focus, into one of 13 sections: assurance of quality; audiovisuals; drug information; economics and finance; health aspects; human resources and training; monitoring and evaluation; periodicals; pharmaceutical industry; policy and regulation; selection; supply and use. Keywords highlight specific subject areas and countries that are covered in each publication. A list of keywords relating to each section follows this introduction. The material is indexed by author, corporate author, subject area and country.

Most of the WHO publications should be available in national libraries. In case of difficulty it is suggested that the libraries of the WHO Regional Offices be approached for assistance.

WHO depository and reference libraries in each country (addresses available from WHO Headquarters) hold copies of all WHO publications. WHO publications may also be purchased from the WHO sales agents (listed overleaf) or the Distribution and Sales Office in WHO Headquarters. Please note that WHO documents (unlike WHO publications) are not for sale and can only be obtained from the headquarter's programme or regional office indicated in each bibliographic reference.

Users' comments on the bibliography, as well as suggestions, for inclusion or deletion of material, are most welcome. These should be sent to: Action Programme on Essential Drugs, WHO, 1211 Geneva 27, Switzerland.

Practical Pharmacy: newsletter to ensure the safe and rational use of drugs

Practical Pharmacy is a newsletter (two sheets of A4 paper, using four sides), which aims to ensure the

safe and rational use of drugs world-wide by increasing knowledge and understanding of drug management and supply, and improving work practices. It has been written for individual health workers who may have no specific pharmacy qualifications, and as a resource for training activities. It is edited and produced by Georgina Stock, Heatherlands, Lydford, Okehampton, Devon EX20 4AU, United Kingdom, with the help of an advisory group of people experienced in pharmacy in developing countries. The first issue was distributed in April 1996, following Georgina Stock's return to the UK after 2 years in Tanzania, working with *Voluntary Service Overseas* (VSO). To date, there have been nine issues with the following headings: (1) The use of disinfectants; (2) Storage of drugs; (3) Donations of drugs; (4) Stock control; (5) Generic drugs; (6) Dispensing; (7) Giving information to patients; (8) What is rational drug use?; and (9) Drugs in pregnancy and breast feeding.

Starting from scratch in 1996, the circulation has now grown to 2500 and copies will soon be available in French. *Practical Pharmacy* is available free of charge to applicants from developing countries; otherwise in the USA $12 to students, $24 to individuals elsewhere and $48 to institutions elsewhere. A number of experts in the field of information transfer have already expressed their admiration and approval for this initiative, which appears to be extremely successful at remarkably low cost.

Health Information Forum; improving access to reliable information in developing countries

A workshop on *Meeting the information needs of the isolated health worker* was held on 14 July 1998 at the Royal College of Physicians in London in the context of improving access to reliable information for health care workers in developing and transitional countries. It was chaired by Dr Richard Smith, Editor of the *British Medical Journal*, and participants included Professor K. G. M. M. Alberti, President of the Royal College of Physicians. Guest speakers were Andrew Chetley (Healthlink Worldwide, formerly AHRTAG), Georgina Stock (Practical Pharmacy) and Pauline Monro (Neurology International Partnership Programme). Other participants included representatives from Nigerian Medical Forum; Continuing Medical Education, Uganda; South Thames Library and Information Services; *Africa Health* and *Medicine Digest*; British Medical Association; Sheffield University; Cochrane Collaboration; Book Aid International; Essential Drugs Project; Partnerships in Health Information (formerly SatelLife, UK) and Royal College of General Practioners. A full report of the proceedings and main conclusions may be obtained from Dr Neil Pakenham-Walsh, Programme Manager, INASP-Health, International Network for the Availability of Scientific Publications, 27 Park End Street, Oxford OX1 1HU, United Kingdom. Tel +44(0)1865 24999. Fax +44(0)1865 251060. E-mail (INASP-Health): 101374.3615@compuserve.com. WWW: htpp://www.oneworld.org/inasp.

New Atlas of Dermatology on CD-ROM

Springer-Verlag London Ltd have recently sent out information on their new CD-ROM, described as '...the world's leading and most comprehensive image collection of skin diseases.' Their brochure reads:

- This atlas contains more than 3,000 colour pictures relating to over 500 dermatologic diseases.
- Search possibilities via names of diseases or via differential diagnoses are provided for and corresponding symptoms are mentioned.
- This is the only dermatologic atlas which offers such a wide range of pictures and thus makes it an ideal reference book for every dermatologist and medical practitioner dealing with diseases of the skin.

Two years ago the University of Erlangen placed a dermatologic online atlas in the internet. This project is known world-wide now and more than 1,000 users visit the site daily.

This CD-ROM has the advantage of a faster availability and also offers the relevant differential diagnoses which are not presented in the internet.

1998. CD-ROM for Macintosh
Approx. DM 78; £34; FF 294; Lit. 86.140; US $52.35; öS 569.40; sFR 69
ISBN 3-540-14669-5
*Suggested retail price plus local VAT
Due March 1998

System Requirements:

- 486 PC or higher (Pentium recommended)
- 8 MB of RAM
- CD ROM drive
- Microsoft Windows (96 or NT)
- Display adapter with at least 32.768 colors
- Browser with frame extension
  (i.e. Internet Explorer 3.0 or Netscape Navigator 2.02)

Address: Springer-Verlag London Ltd, Sweetapple House, Catteshall Road, Godalming, Surrey GU7 3DJ

The British Council

The British Council, registered in England as a charity no. 209131, is Britain's international network for education, culture and development. It has offices in 109 countries and 160 library and information service points.

Through its libraries, information and books programmes the Council supports the development of local book industries, access to information, books and reading. The Council focusses on improving professional standards in book industries, policy development and research, supporting intellectual property and developing sustainable local book market structures. Training in authorship, publishing, copyright, distribution and information skills is a priority.

The Council operates a coupon scheme to reduce the problem of foreign exchange availability for institutional book and journal purchase. The scheme operates in Malawi, Morocco, Nigeria, Sierra Leone and Zambia, Bulgaria, Romania and Myanmar. Institutions buy coupons in sterling denominations from British Council offices in exchange for local currency. The purchaser can exchange the coupons for books, periodicals or other published products in Britain through the usual export channels or use them to pay royalties to publishers on rights or licence contracts.

The Council organizes training courses and consultancy in book distribution and retailing for developing and transitional economies, including India, Zimbabwe, Tanzania and the Ukraine. It has organized study tours for publisher trainers in South Africa and seminars on curriculum development and textbook design for teachers, authors, publishers and educational managers. It has organized seminars with a Kenyan NGO on the development of science authorship, illustration, publishing and book marketing skills for educational book publishing. The Council has organized rights workshops for publishers in Poland and Lithuania and produced handbooks and guides in Lithuanian and Polish on copyright contract and negotiation practice based on individual copyright law.

British Council
Information Group
Books and Information Development Services
Medlock Street
Manchester
M15 4AA
UNITED KINGDOM
Contact: Stephan Roman
Telephone: (44 161) 957 7170
Fax: (44 161) 957 7168
E-mail: stephan.roman@britcoun.org

Lepr Rev (1998) **69,** 419–432

News and Notes

Goodbye AHRTAG – Hello Healthlink Worldwide

There is a new name in the world of health information—Healthlink Worldwide.

But it's a name with 21 years of experience behind it. Healthlink Worldwide is the new name for AHRTAG (Appropriate Health Resources and Technologies Action Group) which has been putting health information to work since 1977.

The new name reflects the organisation's focus on health and describes its way of working worldwide – linking information and health workers, linking partners, linking policy and practice.

Healthlink Worldwide continues AHRTAG's aim of improving the health of poor and vulnerable communities by strengthening the provision, use and impact of information.

Healthlink Worldwide works with more than 30 partner organisations in developing countries including governments, non-governmental organisations and academic institutes to run programmes to support particular health needs. These include continuing education and training for health workers in Africa and the Middle East, AIDS and Sexual Health, Child Health and Disability.

Healthlink Worldwide's practical training and education materials is printed and electronic forms reach nearly two million health and development workers worldwide. Healthlink Worldwide provides technical support to partner organisations and others in setting up and developing resource centres and information services. This work draws upon the UK's largest collection of health learning materials from developing countries, based at Healthlink Worldwide's resource centre.

For further information, contact
Andrew Chetley
Communication and Information Manager
Healthlink Worldwide (formerly AHRTAG)
Farringdon Point
29–35 Farringdon Road
London EC1M 3JB, UK

or visit our web site:
http://www.healthlink.org.uk

Tel: +44 171 242 0606
Fax: +44 171 242 0041

E-mail: general enquiries: info@healthlink.org.uk
chetley.a@healthlink.org.uk

LEPRA: Annual General Meeting July 1998: Report & Financial Statements for 1997

On the occasion of the *Annual General Meeting of LEPRA* in London, 21 July 1998, those invited received a copy of the *Report and Financial Statements for 1997*, which included information about the Association's main objective, policies, activities and future developments.

Objectives of the Association

The main objective of the Association is to carry out the investigation of and promote research into the causes, treatment, cure and prevention of the disease of leprosy and any allied disease, and give and grant relief and assistance to any person suffering or believed to be suffering therefrom, or the family or dependants of such persons of any description, including financial assistance. (Extract from the Memorandum of Association).

There are more than 1 million people suffering from leprosy and an estimated 4 million others who have disabilities as a result of the disease. For the foreseeable future there will be at least 600,000 new patients diagnosed each year and a proportion of these will be disabled. This means that more than one person is found to have leprosy every minute of every day. A significant number of people affected by leprosy are in areas which are difficult to reach and where often there is a lack of infrastructure. Tuberculosis is once again a world epidemic and many leprosy patients are at risk of contracting this disease, especially in areas of dense population, e.g. India. HIV infection is also on the increase in a number of countries where LEPRA operates. The cost of medical research into these diseases has increased significantly over the last 5 years. All these diseases have stigma associated with them and, unfortunately, in endemic regions not only the general public but also some less well-informed medical personnel may ostracise the patients.

LEPRA aims to maximize the use of staff, infrastructure and local resources by adding further programme elements to existing control programmes and to general health service programmes. These include, for example, Prevention of Disability, Eye Care, Income Generation Programmes, Social Aspects of Leprosy, TB control and HIV Awareness and Education. LEPRA's prime objective will, however, remain the eradication of leprosy.

Policies

- High quality services are given to patients through the running and support of leprosy control programmes.
- Medical research into the causes and cure of the disease is undertaken.
- Services to leprosy patients are integrated into local health services.
- Where possible, leprosy control is integrated with TB control and HIV awareness raising programmes.
- High priority is given to prevention of disability in all programmes.
- Surgical and, where possible, socio-economic rehabilitation programmes are undertaken.
- Medical Consultancy and Advisory Services are continued.
- LEPRA continues to publish Leprosy Review, LEPRA's scientific journal.
- High quality Training Programmes are run in all programmes LEPRA supports.
- Education and Awareness Raising Programmes are run in all programmes LEPRA supports, including the United Kingdom.
- LEPRA will establish closer working relationships with Government and Non Governmental Organisations at both local and international levels.

Review of Activities

1997 was another remarkable year for LEPRA and as planned all the activities that were proposed in the last Report and Financial Statements were undertaken.

The highly successful Blue Peter Appeal reached £1·762m at the end of 1997, making a total from that Appeal of £2·734m.

The Appeal not only enabled us to strengthen existing programmes and open new ones, but also significantly raised LEPRA's profile in Britain.

A successful application for funding was made to Novartis for funding a programme in Brazil.

We continued to support and expand leprosy work, which includes research in Africa, Asia and Latin America.

At the end of 1997 LEPRA's work and standing were acknowledged, by the election of the Director as President Elect of the International Federation of Anti-Leprosy Association (ILEP). The Presidency of ILEP is for a 4 year period commencing December 1998.

Africa

We were particularly pleased that despite the continuing civil conflict in Sierra Leone, the National Programme was able to continue to diagnose and treat patients with the assistance of LEPRA Funds.

We have agreed to take responsibility for the leprosy/TB control programme in Zambezia Province, Mozambique.

We have entered into discussions regarding supporting the National Programme in Madagascar.

We continue to support the training of nurses in leprosy control in Cameroon.

We have continued to support the All Africa Leprosy & Tuberculosis Rehabilitation Training Centre in Ethiopia.

Malawi

We were able to strengthen the infrastructure at our Research Centre in Malawi, prior to the centre receiving major research funds from the Wellcome Foundation.

After more than 30 years of successful work in Malawi, we were able to hand over the responsibility for the National Leprosy Control Programme to the Malawian Government.

We were delighted that our representative, Rev. Peter Garland, was presented with the Order of the Lion of Malawi, and that LEPRA has been invited to sit on the National Research Committee.

Brazil

Two new state programmes in Brazil, namely Paraíba and Rio Grande de Norte, were strengthened through LEPRA Funds.

A new programme to assist patients and ex patients with disabilities was started in the south of Ceará.

The leprosy reference centre in Fortaleza, Ceará was totally renovated, which has strengthened the programme there considerably.

The patient organisation, MORHAN, in Ceará was assisted by the provision of transport helping patients who have to travel to clinics for treatment.

We were particularly pleased that in the National Leprosy Eradication Campaign, launched by Pelé, the programmes supported by LEPRA identified more new patients than any other in Brazil, indicating the high quality of work being done.

India

New programmes were commenced in Orissa and Andhra Pradesh where significantly high numbers of new patients have already been identified and have started treatment.

Plans for a further programme in Orissa were made in order for a programme to start at the beginning of 1998.

Through the appointment of four new staff in India, socio-economic rehabilitation programmes were started, thereby assisting some of the poorest patients in those areas covered by our programmes.

The upgrading of the research laboratory in Hyderabad took place, after LEPRA took over the responsibility for it from the Church of South India. A new Director was also appointed.

A new laboratory and offices were also acquired in Orissa and a new ward was built to increase the capacity of the surgical unit there.

The programme we support in Basti, Uttar Pradesh, was greatly expanded and now covers a population of 550,000.

We began discussions with the ILEP agencies and with the National and State Government regarding co-ordination of all the leprosy work in the state of Andhra Pradesh.

After discussions with the Department for International Development (DfID), we undertook a new project in Andhra Pradesh to examine the spread of HIV infection.

We have upgraded our computer systems in India and have appointed an IT specialist.

Future Developments

We are discussing the possibility of supporting work in a further State in Brazil.

We have begun the process of registering LEPRA in Brazil.

We aim to provide mobile education units to all our programmes in India.

We will restructure our Head Office to meet growing need.

We are investigating the possibilities of opening a Leprosy Training Centre in India.

We are considering starting further new programmes in Orissa.

We are looking at the possibility of supporting a programme in Nepal and a further programme in Bangladesh.

We will discuss assistance to the Indian Government for TB control programmes in Andhra Pradesh with DfID India.

Death and disability from road accidents. Red Cross Report on World Disasters, 1998

The Red Cross have recently published a detailed and important Report on world disasters, drawing attention to the fact that road crashes worldwide already claim 500,000 lives each year and cause 15 million injuries. They will overtake tuberculosis, war and HIV as one of the world's biggest killers by the year 2020. *The Guardian* newspaper account of 24 June, 1998 (UK) included the following:

Traffic accidents are the leading cause of death for men and the fifth most frequent for women in the 15–44 age band. Children under 15 account for 15 per cent of traffic fatalities in developing countries compared with 6 per cent in the developed.

Even in rich countries the poor are the more likely to die in accidents.

Only clinical depression and heart disease will kill more people than traffic accidents in 20 years, the report says. Ethiopia has by far the worst record: 175 road deaths for every 10,000 licensed vehicles, compared with the second country, Nepal, with 80. By comparison Australia and Japan have two deaths per 10,000 vehicles.

The report argues that the cost of road deaths places a severe and needless strain on national resources. Crashes cost underdeveloped countries as much as the aid they receive. The average costs of accidents in most countries is now at least one per cent of the gross domestic product.

Traffic accidents damage progress by killing the economically active, seek out the most vulnerable, and are forecast to do more harm through death and disability than many of the health threats currently given greater priority for assistance.

In many countries there is no road safety training in schools. The Red Cross suggests as a first step that national road safety councils are established in each country to examine the problem.

Further enquiries: Oxford University Press Bookshop, 116/117 High Street, Oxford OX1 4BZ, United Kingdom. Telephone 01865-242913. Fax 01865-241701. Price UK £15·99.

Freeplay, 'wind-up' radio now available with integral solar panel

The original model of the BayGen Freeplay Radio (affectionately known as the 'Clockwork' or 'Wind-up' radio), invented by Trevor Baylis, Twickenham, UK, has already achieved wide distribution, with sales in 1997 reported to be around 500,000 sets per year. It utilizes personally generated power, and there is no need for batteries or an external power source. The energy storage and release mechanism is based on energizing a textured carbon steel spring by winding it from one spool to another. As the spring returns to its original position, it releases its energy and applies a rotational torque into a transmission. This consists of a gearbox, which drives a direct current generator, providing energy for the radio receiver. A solar powered, translucent, AM/FM, wind-up radio with integral solar panel has now been produced by BayGen, which operates on both solar and spring energy. The radio draws energy from available light and switches automatically to spring energy only when needed. It gives unlimited playing time in direct sunlight.

Enquiries: UK phone 01285-659559. International phone +44-1285-659559. UK Fax 01285 659550 E-mail baygen@lineone.net.

Regression with AIDS-related Kaposi's sarcoma during therapy with thalidomide

Writing from The University Children's Hospital, Zurich, Switzerland, the Division of Virology, Department of Medical Microbiology and the MRC HIV Clinical Trials Centre, University College London Medical School and University College and University College London Hospitals NHS Trust, London, RA Solèr and colleagues describe an interesting response to thalidomide, summarized as follows–

> 'A 14-year-old girl with HIV infection and subcutaneous Kaposi's sarcoma (KS) received thalidomide therapy for oral ulcers, resulting in regression of KS lesions, disappearance of KS-associated herpesvirus (KSHV) DNA from blood, and reduced viral load in tumor tissue. Administration of granulocyte colony-stimulating factor resulted in clinical exacerbation of KS and reappearance of KSHV DNA in blood.'

The authors are, however, cautious about the implications of the response observed in one case and the final paragraph of the Discussion runs as follows–

> 'Although this case suggests that thalidomide may be efficacious in the treatment of a patient with HIV-related KS, conventional chemotherapy, radiotherapy, and IFN-α should remain first-line therapeutic options. However, we suggest that thalidomide should be further studied as a therapeutic agent for the treatment of HIV-induced KS and that its use may be justified in patients with disseminated KS who are considered unsuitable for or who are unable to tolerate conventional therapeutic interventions.'

(One of the co-authors, Professor David Nadd, Zurich, has kindly supplied further information: after publication of the case report above, the patient developed further Kaposi's sarcoma lesions despite continued medication with thalidomide. She died 2 months later and autopsy was refused.)

Leprosy and leprophilia

The following is taken from *World Health* No 2, March–April 1998–

> 'I want it eliminated'
> In his novel *A Burnt-Out Case*, set in a 'leproserie' in central Africa, the novelist Graham Greene invented the word 'leprophil' for people who appeared to prefer the disease to the

people who suffered from the disease. The physician in charge, Doctor Colin, says: 'You remember that little leproserie in the bush that the nuns ran. When DDS [dapsone] was discovered to be a cure, they were soon reduced to half a dozen patients. Do you know what one of the nuns said to me? 'It's terrible, doctor. Soon we'll have no lepers at all.' There surely was a leprophil.'

Another character comments: 'All the same, doctor, you've said it yourself, leprosy is a psychological problem. It may be very valuable for the leper to feel loved.' Doctor Colin replies: 'A patient can always detect whether he is loved or whether it is only his leprosy which is loved. I don't want leprosy loved. I want it eliminated.'

Green dedicated his novel, published in 1961, to Dr Michael Lechat whose leprosy hospital at Yonda in the Congo he had visited. The forward expressly says: 'I hope you will accept the dedication of this novel, which owes any merit it has to your kindness and patience. ... Doctor Colin has borrowed from you his experience in leprosy and nothing else.' Professor Michel Lechat is a distinguished leprologist. Formerly President of the School of Public Health, Catholic University of Louvain in Brussels, he is President Emeritus of the International Leprosy Association (ILA) and President of the International Leprosy Union (ILU). (Read his article 'History of a Disease' on page 8 of the May–June 1996 issue of World Health.)

Professional fundraising

This publication is aimed at charities and the non-profit sector and claims to be '... the only magazine dedicated to workers in these sectors. It carries information on management strategy, the internet, legacy giving, direct mail campaigns, planning of fund-raising events, telemarketing, corporate giving, industry profiles, regular international news and feature articles'. The July 1998 issue includes sections on The Netherlands non-profit sector; The Imperial Cancer Research Fund, Intermediate Technology. The British Lung Foundation: The British Red Cross; Fight for Sight and Sight Savers International. The three end-pages of this issue carry information on address management systems; consultants; copywriters; database services; design consultancy; sponsorship and mailing lists.

Enquiries: Professional Fundraising, TM and D Press Ltd, (Dept G2), 39–41 North Road, London N7 9DP, United Kingdom. Telephone 0171 700 3479. Fax 0171 700 2049. e-mail tmd.press@-btinternet.com

USA allows thalidomide for leprosy sufferers

The following appeared in *The Guardian* newspaper, 17/7/98–

The United States yesterday became one of the first countries to relicense thalidomide—35 years after it banned the controversial drug—when government health officials authorised it for sale.

But the decision by the federal Food and Drug Administration was hedged with unprecedented restrictions aimed at ensuring that there can be no repeat of the thousands of birth defects which turned thalidomide into one of the most notorious drugs of all time, and triggered a legendary 1960s British lawsuit between the victims and Distillers, the UK parent company of the firm marketing the drug.

After months of speculation, the FDA said yesterday that thalidomide was an effective treatment for a small number of leprosy patients who suffer from a serious inflammation called erythema nodosum leprosum. However, in authorising the use for this small

group—there are said to be around 50 cases in the US each year—the FDA imposed a raft of tight restrictions.

Every patient who uses the drug will be required to enrol in a government monitoring programme. The makers of thalidomide, the New Jersey-based firm Celgene, will be allowed to supply the drug only to authorised chemists and dispensers. Women patients will be required to undergo pregnancy tests, and all patients for whom thalidomide is prescribed will be told to use contraception at all times.

However, the FDA said it could not require doctors not to prescribe thalidomide for other appropriate conditions, and it is known that the drug is being tested for possible use in treating Aids-related ulcers and wasting. Thalidomide is quite widely available illegally in the US as an Aids-related treatment, and the FDA acknowledged that it may in due course be prescribed more widely in these and other cases.

Thalidomide was banned worldwide 35 years ago after it was blamed for birth defects in more than 12,000 babies, many of whom were born without arms or legs, and with defective organs.

The drug had been prescribed widely during the 1950s and 1960s as a sedative and treatment for morning sickness for pregnant women in 48 countries, including Britain.

Ironically, the FDA won widespread praise at the time because of its work in preventing the drug from going on sale in the US. A few Americans nevertheless took thalidomide in clinical trials or had it prescribed in other countries.

A number of other countries, including Brazil and Mexico, have recently authorised the limited availability of thalidomide.

InDevelop

InDevelop Uppsala AB (International Development Consultant Services) is an independent Swedish consultancy company specializing in social development, especially within the health sector. The company was established in 1986 and is owned jointly by the University of Uppsala and HifabGruppen AB in Stockholm.

InDevelop works in a tradition of strong commitment to health development in the developing countries. The company seeks in particular to focus on vulnerable groups such as women, children and disabled. In its work the company adheres to principles of long term sustainable development with true participation in the decision making of those who are at the receiving end of the international assistance.

The company manages long-term projects focused on technical assistance in ministries and other organisations in developing countries. On behalf of Sida, NORAD. Unicef, the European Union and the World Bank, InDevelop is engaged in planning of large scale health programmes in countries like Vietnam, Cambodia, India, Uganda, Tanzania, Ethiopia, Eritrea and Angola. The company is also running clinics for overseas personnel in several countries.

InDevelop is most experienced in arranging study and exchange programmes between Swedish and foreign organisations and institutions. Through its association with the University of Uppsala, InDevelop can offer facilities for study visits and training under guidance of prominent researchers.

The main office of InDevelop is situated in Uppsala, close to Stockholm. Through the permanent staff and short-term experts, InDevelop can provide expertise in many technical areas. Overseas the company has a number of persons employed on long-term contracts.

Through the company's subsidiary Sodeco (Social Development Consultants) in the university town of Lund in southern Sweden, services are also offered within other fields related to social development. Among the areas in which InDevelop and Sodeco together can offer services are:

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Social impact assessments
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Human resources development

Address:
InDevelop Uppsala AB,
S:t Olofsgatan 6,
S-753 12 Uppsala, Sweden
Telephone: +46 18 15 71 55
Fax: +16 18 10 15 13
E-mail: info@indevelop.se

Why conjugate vaccines protect longer

The British Medical Journal, volume 316, 23 May 1998, www.bmj.com, page 1571, included the following information on conjugate vaccines–

> 'The effectiveness of polysaccharide vaccines against diseases such as meningococcal meningitis is limited because they do not stimulate a T cell response, which is required to activate long term immunological memory. Also, polysaccharide vaccines induce poor responses in infants. Up to 40% of cases of meningitis in the United Kingdom are caused by *Neisseria meningitidis* type c; *N meningitidis* is particularly virulent in young babies and teenagers. Because the polysaccharide vaccine against meningitis A and C does not induce the production of immunological memory cells and is relatively ineffective in children aged under 2, it does not protect these vulnerable groups.
>
> Conjugate vaccines are being developed to overcome this lack of long term memory. Conjugation involves attaching the required polysaccharide component of the bacteria against which the immune response is to be directed to a protein. This conjugated complex then behaves more like a protein and is presented and processed in a T cell dependent manner. Activated T cells then secrete cytokines that elicit a long term memory response, which includes the production of antibodies and cell mediated immunity. This response occurs at all ages.
>
> Conjugated vaccines against meningitis A and C are likely to undergo clinical trials within 2 years. Developing a vaccine against meningitis B is harder because the risk of a cross reaction between certain HLA antigens and the B capsule polysaccharide, which could result in an inappropriate autoimmune response.
>
> Conjugate vaccines are also being developed against pneumococcal disease: 11 of the commonest childhood pneumococcal serotypes have been conjugated together with a protein in one vaccine, which should offer long term immunity against otitis media, community

acquired pneumonia, septicaemia, and meningitis. This vaccine is being assessed in clinical trials; results are expected in 1999—Abi Berger, *Science editor, BMJ.*''

Professor Douglas Young, Imperial College School of Medicine, London has kindly commented as follows:

'Conjugate vaccines certainly look excellent in the case of the encapsulated bacteria for which antibodies to surface components confer protection, but their application for mycobacterial disease is less clear. Antibodies may well modulate mycobacterial infection in some way—maybe altering details of their interaction with macrophages—but I don't think they play the same decisive role in protection. The generally favoured view is that T cell recognition of protein antigens is the main contributor to protection, though there has been recent interest in T cells that recognise non-protein antigens in mycobacteria. (Fairhurst R. M. *et al.* CDI-restricted T cells and resistance to polysaccharide-encapsulated bacteria. *Viewpoint Immunology Today.* Volume 19. Number 6. Pages 257–259.)

A vaccine for malaria?

The following article by Drs Howard Engers & Nina Mattock of the Special Programme for Research & Training in Tropical Diseases (TDR), WHO, appeared in *World Health* No 3, May–June 1998–

In the last decade, considerable progress has been made in the search for a malaria vaccine, and the turn of the century is expected to see one or more such vaccines being actively developed by the pharmaceutical industry.

Globally, malaria is a major public health problem. The story of mosquito resistance to insecticides and parasite resistance to drugs impeding malaria control is a familiar one. And while there are renewed efforts to combat malaria both through conventional and novel drugs and through vector control activities, an effective vaccine would constitute a powerful addition to these tools.

Natural exposure to malaria leads to the development of partial immunity in humans, but repeated re-infection is required to maintain this immunity. Inactivated sporozoites (parasite forms living in the mosquito which are infective to humans) have been shown to be highly effective at inducing immunity in humans. Unfortunately, it is not possible to produce inactivated sporozoites in the enormous numbers required to make this a feasible method of vaccination. However, we now have new technologies at our disposal. Nucleic acid-based DNA vaccine technology, for example, allows us to identify promising immunogenic molecules much more rapidly, and this considerably expands the number of potential vaccines. Novel adjuvants—neutral substances that enhance the body's immune response to antigens—are becoming available for clinical use. Other delivery systems (live vectors such as salmonella or vaccinia which incorporate antigen gene sequences, and DNA vaccines) are under development and starting to be evaluated in humans.

This improved knowledge and the availability of new technologies give us reason to believe that vaccination against malaria is possible.

What sort of vaccines are being developed?

The malaria parasite has a number of different stages in its life cycle. Candidate vaccines are based on various antigens derived from these different stages:

- *Pre-erythrocytic vaccines* prevent the malaria parasite sporozoite stage from entering or developing within liver cells. Such vaccines would prevent the severe and life-threatening consequences of malaria in non-immune individuals. About 20 human clinical trials with various *Plasmodium*

falciparum pre-erythrocytic vaccine candidates have been conducted to date. One highly promising candidate, 'RTS,S', is currently in field trials in the Gambia.

- *Asexual blood-stage vaccines* prevent the parasite merozoite stage from entering or developing with red blood cells. Immunity against the asexual blood stages of the parasite, which are responsible for the symptoms of malaria, would have a direct impact on disease morbidity and death in the individual but would not necessarily prevent people from getting infected. At least six asexual blood stage vaccines have been tested clinically or are currently undergoing human trials.
- *Transmission-blocking vaccines* inhibit development of the sexual stages of the parasite within the mosquito. The sexual forms of the malaria parasite develop in the red blood cells a few weeks after infection, and are infective for mosquitos biting infected individuals. With wide coverage these vaccines could reduce transmission of the disease in endemic regions by reducing the number of mosquitos infected. Several transmission-blocking candidate vaccines are already undergoing clinical trials for safety and immunogenicity in the USA.

Vaccines currently under development include:

- Vaccines based on cocktails of antigens (multicomponent vaccines). The first multicomponent synthetic peptide vaccine SPf66, developed by Dr Manuel Patarroyo in Colombia (representing three asexual blood stage antigens and a sporozoite antigen), is the most widely tested vaccine to date. It has given mixed results in field trials in South America, Africa and South-East Asia.

  Another multicomponent vaccine, engineered in attenuated vaccinia virus and expressing three pre-erythrocytic proteins, three asexual blood-stage antigens and a transmission-blocking candidate, gave limited protection in a human clinical trial in the USA. A third multicomponent asexual blood-stage vaccine under development by Australian scientists is currently undergoing clinical trial in Papua New Guinea.

Second-generation vaccines include those that contain modified malarial peptides or novel adjuvants; DNA vaccines (nucleotide sequences encoding the antigen in question), which have shown promising results in rodent models; and antitoxic or anti-disease vaccines.

WHY IS A VACCINE FOR MALARIA PROVING SO ELUSIVE?

We don't yet have a vaccine for any human parasitic disease. For malaria, there is the problem of not being able to grow malaria parasites in large enough quantities to make vaccines in the traditional way, either from live but weakened organisms or from crude antigen preparations. Hence the focus on synthetic peptides, recombinant proteins or DNA vaccines. One difficulty is that, in clinical trials so far, most vaccines have failed to live up to the potential they have shown experimentally in animal models. This situation may be overcome when novel, more powerful adjuvants for human use become available.

Then there is the difficulty of evaluation. The fact that there are no good *in vitro* surrogate screening systems to assess the efficacy of different vaccines in the laboratory is a significant limitation, and means that vaccines have to be tested experimentally, often in expensive, time-consuming animal model systems, including monkeys.

Another problem is that, unlike less complex organisms, parasites have developed ingenious ways of avoiding the host's immune response. For instance, the malaria parasite expresses different antigens at each stage of its life cycle, and is often able to change these antigens when the host mounts an immune response towards them. Different strains or isolates of the parasite can also express different forms of the same antigens. A multicomponent vaccine, aimed at covering several of the antigens, could overcome this problem but would be highly complex and difficult to develop. And finally, there is the complexity of conducting the clinical and field trials themselves, when researchers are confronted with measuring the reduction of morbidity and mortality following vaccination with a candidate vaccine.

Research on vaccines against malaria is mainly supported by a variety of international agencies, organizations, foundations and national funding agencies, including the governments of some countries

and various research institutes. There is also greater involvement of the private sector when vaccine candidates have reached advanced stages of development.

WHERE DO WE GO FROM HERE?

There is no guarantee that the current promising approaches to malaria vaccine-development will result in a cost-effective malaria vaccine. Nevertheless, new technologies are becoming available and there is intensified political and financial support for research on malaria. The UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) is committed to evaluating the currently available leading *P. falciparum* malaria vaccine candidate in clinical trials by 2005. If all goes well, a malaria vaccine could be ready for use sometime in the next decade.

'VICTORY OVER LEPROSY DRAWS NEARER'

The following article appeared in a recent issue of *World Health*, No 2, March–April 1998:

As early as 1914, the Office International d'Hygiène Publique (OIHP)—a forerunner of WHO—ordained that there should be compulsory notification, as well as surveillance or isolation, of cases of leprosy. The disease was very clearly an international public health problem, and in the year of WHO's founding, 1948, the International Leprosy Association was among the first nongovernmental organizations to be brought into official relations with the infant organization. Shortly afterwards, an expert advisory panel was established whose members helped to prepare for the first meeting of the Expert Committee on Leprosy, held in Rio de Janeiro and São Paulo in 1952.

That Expert Committee confirmed two important points: 'that leprosy is not in most cases a highly infectious disease, and that, with the introduction of sulfone therapy, a good proportion of cases can be cured'. The experts also 'accepted that temporary isolation might still be necessary, though for infectious cases only, but it was suggested that ambulatory and domiciliary treatment could be safely and satisfactorily given to most patients'.

The First Ten Years of WHO, published in 1958, reported that the clinical results of treatment with diaminodiphenylsulfone—also known as dapsone—'tend to confirm the favourable results already reported in medical literature on the treatment of leprosy patients in specialized institutions'. Over-optimistically, it claimed that 'leprosy patients no longer tend to avoid treatment because of its possible association with segregation. They now come forward spontaneously'. There was also a mention of trials with BCG vaccination (the anti-tuberculosis vaccine) and of vaccines prepared with other mycobacteria, 'which appear to offer a certain degree of protection against leprosy'.

In 1968 *The Second Ten Years of WHO* reported: 'Participants in the seminar on leprosy control organized at Belo Horizonte, Brazil, in 1958 were agreed that compulsory isolation of patients should be abolished and replaced by effective control of foci through the treatment of all patients and surveillance of their contacts—hospitalization being restricted to cases in need of special medical or social care.' Later that year, the Seventh International Congress of Leprology, held in Tokyo, stressed that, from the epidemiological point of view, 'it is more advantageous to reduce infectiousness in many patients than to eliminate infectiousness in a few'.

POOR PATIENT COMPLIANCE

The Second Ten Years struck a gloomy note. 'Poor follow-up and attendance of out-patients for regular treatment continue to be a main obstacle in leprosy control programmes. Leprosy control has been based primarily on chemotherapy with sulfones, and surveys have shown that 73% of lepromatous patients require more than three years to become bacilli-negative. Unfortunately, the longer treatment continues, the less regular it tends to become,' It went on: 'The specialized leprosy control services need the active cooperation of the general health services, and leprosy control should be progressively integrated into the work of the health centres at the local level.'

All this was remarkably farsighted. There was the insistence that leprosy patients should not be segregated or isolated from their communities. There was the tantalizing vision of a drug that would actually cure leprosy without requiring many years of treatment. And there was the problem of maintaining patient compliance with drug regimens. Above all, there was the strong recommendation that leprosy control should be integrated with general health services, in fact with what was later to be called primary health care.

Certainly the drug dapsone seemed to offer some light at the end of the tunnel. Its use spread around the world in the next decades, thanks largely to the work of WHO and of its partner nongovernmental organizations, many of them members of what was to become the International Federation of Anti-Leprosy Associations (ILEP). But then dapsone ran into trouble. The long duration of treatment made patient compliance a big problem; it was rather a lot to expect a possibly disabled person to travel several miles every month to a health post to obtain the drugs. A patient who noticed an improvement—perhaps the disappearance of skin lesions—saw no further point in going on taking the pills. Worse still, *Mycobacterium leprae*—like so many other agents of disease that plague our planet—began to develop resistance to the drug. It looked as if mankind's only safe weapon against leprosy was about to become useless.

BETTER DRUGS NEEDED

The WHO Expert Committee on Leprosy, in its fifth report published in 1977, struck a note of alarm when it declared 'there is an urgent need for controlled clinical trials of combined chemotherapy in multibacillary leprosy' and called for research into alternative drugs to dapsone, with the cooperation of research institutes and the pharmaceutical industry. In due course, newer and better drugs came on the scene, in particular rifampicin and clofazimine, which proved to be both highly effective and well-tolerated by patients. As a result, a WHO Study Group which met in Geneva in October 1981 proposed a multidrug regimen consisting of these two drugs in combination with dapsone, since they did not merely kill *M. leprae* in quick time but also prevented the bacillus from developing resistance to any of the three.

It was this multidrug therapy or MDT which provided the breakthrough that at least made it possible to envisage putting an end to leprosy. Today, even people with the more severe form of the disease, multibacillary leprosy, can be guaranteed a total cure within the space of 12 months. Relapses—the recurrence of the disease after stopping treatment—are very rare, constituting well under 1% of cases. One unexpected result of the amazing success of MDT has been to put the never very hopeful quest for a viable vaccine on the back burner.

At the World Health Assembly in May 1991, the Member States of WHO made a formal commitment to bring about the elimination of leprosy as a public health problem by the year 2000. This means reducing the number of cases to less than 1 case per 10,000 people. A full account of how WHO and its partners are prosecuting the war against leprosy appeared in the May–June 1996 issue of *World Health*. In the mid-1980s, there were an estimated 12 million cases (and 5.4 million registered cases) in the world. Today that estimate has been revised to only around one million, while the number of registered cases—therefore receiving MDT—stands at around 800,000. Where there were 122 countries with prevalence rates above 1 per 10,000 in 1985, there are today fewer than 50. So the goal of elimination is not far away—but neither is the target date of the year 2000.

Aside from the purely medical aspects of the drive against leprosy, there is the human and social side. While the cure is certain for every person with leprosy who comes forward for MDT, many still face ostracism from their own communities, even from their own families. The social suffering lingers on and, together with the totally unjustifiable loss of human rights, adds a heavy psychological burden to the physical damage that they have undergone. So it is essential for everyone concerned in public health to spread the word that leprosy is curable, and it is extremely hard to 'catch,' and that sufferers need not and must not be shunned. Unless this message reaches every patient in every village, and unless they come forward for the drugs—which should be available at every clinic and primary

health care centre in the leprosy-endemic countries—the disease will still lurk in isolated and dangerous pockets.

It is important to avoid triumphalism and the tendency to count our chickens before they are hatched. But provided the impetus is maintained and provided there is no shortfall in the human and financial resources required we should be able to put paid to this age-old disease and ensure a leprosy-free world in the 21st century.

Former leprosy sufferers sue Japanese Government

Under the heading 'Forgotten leper outcasts return to haunt Japan', *The Guardian* newspaper of August 10th, 1998, carried the following:

Thirteen former leprosy sufferers are suing the Japanese government for keeping them in quarantine for more than 40 years after the discovery of an effective treatment.

The 1·5 billion yen (£6·2 million) suit is the first attempt to make the government legally liable for its quarantine policy.

Under Japan's 1953 Leprosy Prevention Law, sufferers were kept in remote sanitariums with little or no access to the outside world. Pregnancies were also forcibly terminated in the mistaken belief that leprosy is hereditary.

Despite a recommendation by the World Health Organisation in 1960 that such policies were no longer necessary, the Japanese government abolished the quarantine law only 2 years ago. By then, most of the residents in Japan's 15 sanitariums were too old to leave—about 5,200 stayed on.

The plaintiffs have spent an average of 46 years in the sanitariums. In their suit, launched last week at the Kumamoto district court in southern Japan, they claim the government violated their constitutional rights by retaining the isolation policy. They also claim the authorities failed to rehabilitate them adequately after the law was scrapped.

Many of the plaintiffs want to remain anonymous because of the social stigma attached to the disease.

Among those who spoke out, however, was Isao Tateyama, aged 49, who was sent to a colony in Kagoshima prefecture when he was 13.

'Because of the isolation policy, I lost my family, my hometown, my life, everything', he said. 'I believe all of us are entitled to be happy to make up for all the tears we have shed.'

The health and welfare ministry said the case was unexpected. 'I thought the patients wanted government support for medical costs and welfare projects, not individual compensation,' said a spokesman, Hiroki Nakatani.

Although the disease is contagious, it rarely spreads through person-to-person contact. Since 1941 it has been possible to arrest most of the symptoms with medication.

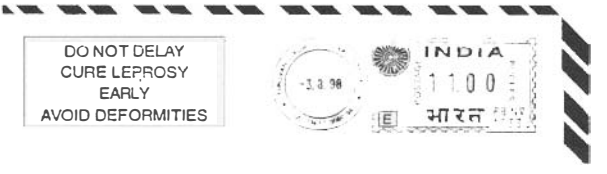
NSL (Netherlands) changes to NLR

Komme L Braber, Director of the newly named *Netherlands Leprosy Relief*, abbreviated NLR, has written to draw attention to the change of housestyle and the development of a new logo, showing hands together, symbolizing collaboration, solidarity and care. The former NSL logo should not be used any longer. *Enquiries*: Netherlands Leprosy Relief, PO Box 95005, 1090 HA Amsterdam, The Netherlands.

Indian Postal Department carries message about leprosy in postage franking machine

Mr K. Subramahyan, Assistant Editor of the *Indian Journal of Leprosy* has kindly confirmed that the

message (below) on letters from India appears with the blessing of the Indian Postal Department which permits the use of a logo or message of specified dimensions. We reproduce it here in the hope that it may be valuable in other leprosy-endemic countries.



Note

Dr Johannes Schäfer's current address (*Lepr Rev* (1998) **69**, 267–278) is: Friedhof Str. 23, 75365 Calio-Stannheim, Germany.

Lepr Rev (1998) **69,** 433–436

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VOLUME 69 (1998)

Instructions to Authors

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

It is understood that the article is offered to Leprosy Review alone, that it will be subject to editorial revision, and that its copyright becomes the property of LEPRA.

Format. Articles should be submitted double spaced, on one side of A4 (297 x 210 mm) paper, with wide margins (4 cm all round) in triplicate. 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.

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

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

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

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Typeset and printed by the Alden Group, Oxford.

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