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Leprosy Review

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

British Leprosy Relief Association
LEPRA

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

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

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Editorial

REDEFINING HEALTH EDUCATION IN LEPROSY: A PERSONAL VIEW

Most textbooks and published guidelines on leprosy state that health education is a requirement for leprosy control or makes an important contribution to it. Similar views are expressed at international conferences on leprosy and in discussions with field staff.

Despite these statements, while training leprosy workers in health education.* I have been faced with a number of unresolved issues. These are not confined to any particular country and emerged in workshops conducted in West Africa, East Africa and South East Asia. In my opinion, four of them need urgent attention. Let me briefly state them.

First, health workers expect health education to solve questions of misunderstanding about leprosy, but also to radically change beliefs and practices of communities with respect to the disease and its sufferers. Health education should make the defaulter not default, the ulcer patient to rest his limbs, the discharged patient not to claim further medicine and so on. Are such expectations realistic or, more to the point, are they justified?

To answer the question we need to examine the assumptions made by health workers about the nature and practice of health education and to see whether they are in agreement with what is currently known about the field and accepted by its practitioners. I will argue that many health workers tend to assume that health education in leprosy is mainly concerned with dispensing facts about the disease and its treatment. I will then discuss three assumptions about health education practice which all health workers should be familiar with and which constitute a framework to define health education in leprosy.

A second issue concerns the deficiency in health workers' skills in communication and human interaction.

Health education activities at treatment sessions or health talks for village groups tend to be 'one-way messages'. It is common to hear health workers ask: 'How can we make our talks more attractive? Should we use other media? Why are we receiving so little feedback from patients? Why are our patients forgetful? Why don't we see much evidence of changes in patients' behaviour?' Some health workers become discouraged and medical officers and supervisors report a lack of interest among health workers to health educate patients and families. Nevertheless, health workers are very much aware of the 'precept'

* Since 1984, Workshops on Health Education in Leprosy have been conducted for 20 to 25 participants (medical officers, supervisors and paramedical workers) at national or district level in the following countries: Côte d'Ivoire, Sierra Leone, Burkina Faso, Mali, Congo, Tchad, Senegal, Niger, Madagascar, Ethiopia, Pakistan and India.

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that health education 'should' be given to patients and communities. It is not just a popular activity.

In my view the current gap between 'precept' and actual communication 'performance' is based on a misconception about the acquisition of communication skills and, on the ways in which health workers have been trained in medical schools or in schools for paramedical workers. I will then propose how skills in communication and human interaction can be improved.

Thirdly, despite the emphasis on health education to achieve leprosy control objectives, few leprosy control programmes make administrative provisions to support and reward health education activities. Managers of leprosy control programmes have questions about: who should provide health education and where should it be done? What type of set-up is required to develop, support and monitor health education activities of staff? What guidelines are available or should be proposed to leprosy staff working in outpatient departments, field clinics, rehabilitation departments and hospital wards?

In order to answer some of these questions we need a common view and a set of principles about what constitutes health education in a leprosy control programme. Towards that end I will set out three principles of health education and discuss their implications for leprosy programme organization.

Finally, I find that available research on health education or on social science issues in leprosy does not provide the insights health workers need to justify their approach towards patients and communities. For example, health workers will ask: how can we change the traditional beliefs of patients which are harmful because they delay early detection? Or how should we handle a patient who denies he has leprosy? How can we be more successful in teaching self-care in our clinics to patients with loss of sensation in hands, feet or eyes? Can we change some of the unfair ways in which communities treat leprosy patients?

In my view social science and health education research should focus less on cultural particularities of leprosy care in different countries and more on 'basic themes' related to the psychosocial mechanisms and processes used by patients to give meaning to their disease and make decisions about care. These themes are strikingly similar in different countries. I will propose three orientations for research studies so that health workers are able to formulate a more reasoned explanation for their work instead of proceeding on the basis of an 'intuitive' grasp of the problem.

Let me now turn to a separate discussion of the issues.

Need for a framework

INFORMING PATIENTS AND ORGANIZING CAMPAIGNS

In countries that I have conducted workshops, I found two prevalent views about the nature and practice of health education. First, health education is seen as informing patients about accepted medical facts concerning leprosy (its cause, spread, symptoms, progression, prognosis, treatment and rehabilitation). Secondly health education is seen as organized campaigns in urban or rural settings aimed at raising awareness about the disease or at combating social stigma.

These views are correct but incomplete. They are limiting by not adequately explaining why certain problems arise and what suitable strategy should be employed.

Their limiting character stems from two underlying assumptions: that enlightenment of patients or the public is a sufficient condition to change their behaviour; and that such enlightenment is achieved by one-way communication.

Most health workers agree that these assumptions are inadequate to understand and deal with problems of late detection, defaulting, self-care or social stigma. Yet why is it that in the practice of leprosy work health education is still largely based on those assumptions? One reason may be historical.

Informing, convincing and exhorting population groups to avail themselves of new insights about common illnesses and their treatment and to apply these insights to daily life, was the major task of public health workers in Western Europe in the early 20th Century. No one doubted the soundness of this strategy. The strategy and its underlying assumptions were passed on to successive generations of health workers through curricula in schools of medicine and public health. Even today most curricula maintain that unhealthy ways of life should be altered by a combination of social pressure (laws, regulations) and the enlightenment of the public.

Another reason may be that some of the major publications on leprosy unwittingly reinforce a limiting outlook on health education. For example, Jopling's *Handbook of Leprosy*, p. 82[1] refers to health education as: 'propaganda to dispel ignorance, fear and prejudice'. Films on leprosy are suggested as a main tool to provide adequate information to health workers and the public (op. cit. p. 116). Thangaraj's and Yawalkar's text on *Leprosy for Medical Practitioners and Paramedical Workers*, p. 95[2] states the following: 'Health education of the patients and the public should be organized on an intensive scale . . ., . . . the enlightened participation of the whole population is essential . . .'. And a leading French textbook on leprosy by Pattyn *et al.* p. 58[3] does not mention health education at all although the section on how to organize leprosy control is quite detailed. Reference is made to the importance of a good doctor–patient relationship in obtaining drug compliance.

Bryceson & Pfaltzgraff's[4] accessible exposé on leprosy has no explicit reference to health or patient education but the authors are aware of the psychosocial reality of leprosy. This is evident in the section on 'Rehabilitation' which discusses physical, psychological and social strategies (op. cit. p. 114). The book on leprosy edited by R S Hastings[5] has one page on health education under the heading 'Control Programmes' it is mainly a summary of WHO's thinking about the aims and principles of health education (op. cit. p. 261). However, considering the size of the textbook (319 pages) this one-page reference is a meager treatment of the subject.

Fortunately, publications in the 1980's start to reflect a different view on health education in leprosy. For example the ILEP booklet on *Guidelines for the Campaign against Leprosy*[6] carries a succinct and readable statement about aims and requirements for health education in leprosy (op. cit. pp. 12–3). Similar good advice comes from Pearson[7] who summarizes the main principles of health education in leprosy and further states that, 'health education is not merely instruction or one-way communication' (op. cit. p. 42).

The 1988 *Guide to Leprosy Control*[8] by the World Health Organization provides a fairly balanced view on health education in leprosy. The section on health education (op. cit. pp. 62–4) goes beyond the view that health education consists of explaining facts about disease and treatment. It draws our attention to four specific points: health education can be required for patients, their families, for health workers and for

communities. As a method it is needed at all stages of leprosy control. It is a duty for all health workers, and good health education practice requires an understanding of the psychological and social situation of the patient.

A modern view of health education

We define 'Health education as a set of activities based on processes of communication and learning and designed to help people decide to behave in a healthy, not harmful way'. There are three main assumptions underlying such a definition?

1 HEALTH BEHAVIOURS AND HEALTH OUTCOMES

First, we assume that what people do is relevant to their health, either positively (taking prescribed drugs, wearing sandals, continuing to work or to stay in one's household) or negatively (defaulting; moving to another area without notifying health staff). The consequences of particular decisions people make are reflected in the state of their health, such as, the early or late detection of cases in an area, the rates of compliance and of deformity, measures of social integration. Thus not only 'physical events' (size and number of patches, degree of nerve damage) but also 'behavioural events' determine health outcomes.

The relationship between what people do and their health constitutes the justification for health education. Without such a relationship health education is not needed nor justified. In other words there is no health education problem.

Therefore, health workers should be able to state for any health problem that they are working on, its behavioural reference point. For example, when you give a health talk to a group of teachers to increase their awareness of early signs of leprosy, behavioural reference points may be that school teachers fail to teach children about early signs of leprosy or do not present themselves readily to a health worker, or do not encourage any other person to do the same.

The ability of health workers to define health education problems can be sharpened by analysing case histories. A case history reveals the profile of decision-making by the patient, his relatives and often the surrounding community.* It is useful for health workers to reflect on those decisions in terms of the consequences of these decisions for early detection and complete treatment.

Key decisions in leprosy (alternatively called 'normative', 'critical' or 'prescriptive' behaviours†) of patients and communities are listed in several publications.[6,8–12]

* In the Workshops on Health Education in Leprosy participants are requested to interview a patient and to elicit a narrative account of what the person has done from early signs to the current stage of his treatment. Emphasis is placed on how the patient views his illness and care, on his decisions and on his social network. Examples of such case histories can be found in '*The Manual on Health Education in Leprosy*'.[9]

† 'Normative' behaviour is used in the sense that there is a consensus among health experts about what constitutes proper individual and collective behaviour to prevent and control a particular disease. Some normative behaviours are debatable because of insufficient evidence concerning their relationship to the outcome of health or because of conflicting values society concerning the proposed behaviour. This is especially the case for sensitive areas such as sexuality and family planning.

Sometimes they are grouped together under the heading 'participation in leprosy care' calling our attention to the fact that health workers advise, people decide.

2 CHANGING HEALTH BEHAVIOUR THROUGH EDUCATION

We assume that we are able to modify people's decisions through health education. That behaviours change is a fact of daily life. Why they change is a different story and still more elusive is the question, how we can contribute to changes which are positive to a person's health. Research and practice indicates that we need not be unduly pessimistic or optimistic about behaviours and their change.

What people do for their health is far less stable than is usually thought. Case histories illustrate this point clearly. For example people with a patch will try a 'remedy', then abandon it, then try another one, or change their minds again and now follow a friend's advice, or they show up at the clinic and so on.

Another point is that the decisions we are talking about (i.e. voluntary and conscious decisions) are not made at random but are influenced by a set of specific forces of differing strengths. For example, the decision to default can be based on lack of perceived improvement in health condition, traditional beliefs suggesting another approach (going to Holy Water, offering prayers in the Temple), financial needs, difficult access to health services, conditions of climate or geography, or a lack of trust in the health worker. We should find out which forces are dominant for a particular patient and adjust our approach accordingly.

A last consideration about changing people's decisions relates to the intrinsic nature of health education activities. The health education approach, as compared to legislative measures or structural changes, is specific in that it activates a learning process to obtain changes in decision and behaviour. This of course limits the potential of health education to influence decision making about health. We are all aware that we may stop smoking cigarettes in places where smoking is forbidden; that the type of service offered to leprosy patients may determine how they feel about themselves as leprosy patients, how independently they will pursue their own life projects or how much they will remain in the charge of the community.

The practical significance of the above is that different types of strategies should complement each other or, conversely, not to expect health education to be the only strategy able to affect changes in decision and behaviour.

3 PRINCIPLES OF COMMUNICATION AND LEARNING

A third and last assumption states that methods of health education follow a set of general rules and principles which can be laid down, learned, applied and validated.

The central reference point for all methods of health education is their contribution to effective learning. Therefore rules and guidelines will be derived from our knowledge of the communication and learning processes. In practice, I have witnessed examples of ineffective health education because of insufficient insight into conditions which affect communication and learning. For example, long explanations to a patient who is sick or tired; dispensing audiovisual messages in noisy and crowded waiting rooms; diffusing messages to a general and not a specific target group. In the next section on skills in communication and human interaction, I will discuss some of the general rules of communication and learning.

Overcoming three deficiencies in communication and human interaction

Communication is health education's major tool. It therefore needs careful consideration.

In the field and at workshops I have observed different levels of communication skills among health workers. Three deficiencies are readily apparent.

COMMUNICATION AS TALKING

First, most communication by health workers, be it in clinics, villages or wards, is confined to talking. Patients are instructed about medication and follow-up visits; they are taught self-care measures for insensitive hands, feet and eyes; advice is given about work and about continuing family relationships. However, what is not used in educating patients are the concurrent skills in listening, observing, using non-verbal signs and symbols. These skills are as much a part of communication as talking.

It is a fundamental rule of communication that it is impossible not to communicate.[13] In other words, all interactions between health worker and patient (or public) have 'communication-value'.

Imagine, for example, that you are a patient and you come to the health worker's desk who is busy filling out his records. You will have received communication even without a word being uttered. Another example. A patient comes to the clinic and starts by saying: 'Doctor, I have been taking these tablets for two months and I don't see any improvement'. Many health workers will reply: 'Don't worry; be patient; continue taking your medicines'. Some will even turn suspicious and ask, 'Have you been taking your medicine?' None of these replies are advisable because they show that the health worker is not 'listening' to what is on patient's mind. He could start by saying: 'You want to talk about this?' or 'You don't see any improvement?' or other 'open' listening responses.

Also observation skills are not properly used. They are easily confused with interpretation. When health workers are asked, for example, to describe a patient they have observed they may say: she wore a green dress; she had a patch on the upper left arm; she was depressed. How did they know she was depressed? What did they look for and see? Perhaps the patient said something; had a particular facial expression; walked slowly; hunched her shoulders?

Talking, observing and listening interact and influence each other. It is the mastery of these three elements for a specific purpose (an interview, a health talk . . .) that characterizes an effective communicator.

COMMUNICATION AS CONTENT

A second problem that health workers have in communicating with patients or the public is a too exclusive emphasis on the 'content' of the communication, i.e. the ideas or advice the health worker wants to pass on.

A knowledge of the correct facts is important. However, it is only part of what makes communication effective or ineffective. The other part, which is intrinsically present in all forms of communication, has to do with the way in which a health worker, or for that matter a patient, wants his message to be understood. So people always communicate on two levels: the idea and how I want you to understand the idea. The last part is technically called meta-communication.[13] Full exchange of meaning between sender and receiver,

which is what communication is all about, occurs when both health worker and patient are tuned in at both levels. For example, a health worker tells a patient, 'I want you to take these tablets'. The patient will understand that the health worker talks about 'tablets', and not about surgery, or hospital admission or preventive measures. However, the impact of the idea on the patient will depend on how he interprets the meta-communicative part of the message. Specifically, how strong is the 'appeal' in this message? What does the message reveal about the health worker as a person? Is he expressing concern or anger? This is the 'expressive' function of a message. Also the message about tablet taking is formulated in the context of a specific relationship between health worker and patient. If the relationship is distant or formal, the message, 'I want you to take these tablets', will be perceived more as an order. If the relationship is less distant and both respect each other, and the health worker wants the patient to decide, then the message is more likely to motivate a patient to take the tablets.

The health worker or patient may not be clearly aware of the meta communicative aspects in communicating. However they are present in all human interactions and influence communication effectiveness. They are most clearly revealed when health worker and patient face communication problems. For example, a patient does not fully trust the health worker. A health worker is annoyed with a patient who reveals little about himself. An instruction lacks appeal. We sense instinctively that trust, annoyance, lack of expression or appeal will affect the message. Therefore, we should learn to identify these aspects of communication and apply them in our health education work.*

COMMUNICATION AS ONE WAY TRANSMISSION

Health workers have difficulty in formulating advice, instructions and explanations from the patient's or the public's point of view which is called 'receiver-orientation'. For example, when we advise a patient do we consider what it means to him to take drugs every day for six months or two years? What about advice on wearing sandals for insensitive feet? Do we think about how a farmer or a young lady look at the prescribed advice?

More receiver-orientated health workers will spontaneously make their message more attractive. They will use words the patient uses himself, discuss contra-arguments to wearing sandals (and not brush these arguments off as irrelevant), demonstrate and give feedback, use examples, listen to patient's objections and practical concerns. However, some health workers do not sense what a receiver-orientation is or they do not know how to put it into practice. The result is one-way communication from a 'health worker' perspective. Such communication is ineffective and does not satisfy either health worker or patient.

WHY DO THESE DEFICIENCIES IN COMMUNICATION SKILLS EXIST AND WHAT CAN BE DONE?

Knowledge about the rules, principles and practice of effective communication exists and has been validated in situations of business relationships, mental health counselling, and

* The Workshop on Health Education in Leprosy comprises specific training modules on communication skills where health workers learn to identify and correct specific deficiencies in this area.

marketing. However, curriculum analysis of training programmes in different countries shows that little or next to nothing is being taught about communication and human interaction to health workers.*

In my view this situation is related to two misconceptions about communication skills for health workers.

Some feel that since communication is part of human life it is acquired naturally and should not be learned. Differences in communication skills are explained by differences in basic personal aptitudes, about which not much can be done.

The other misconception relates to an overestimation of the traditional clinical method. Mastery of the clinical method by health workers is considered sufficient to deal with the essential requirements of patient care and community health. So, health workers should be able to detect and interpret signs and symptoms of disease, know the tools for gathering clinical evidence, be able to arrive at proper diagnostic conclusions and to apply proper treatment.

I do not question the power and efficacy of the clinical method as learned by health workers. However, I do question the claim that mastering the method is sufficient to effective patient and health care.

First, the method focuses on physical events only which are relevant to detect and follow the disease processes. But illness or 'dis-ease' cannot be reduced to physical events. Having leprosy cannot be reduced to bacilli, or to their damage to the peripheral nerves, the state of body immunity and so on. Having a disease is a psychosocial event. People give meaning to their signs, symptoms and misfortunes. Communities react to diseases; and differently to malaria than to leprosy.

Secondly, traditional medical circles do not ignore psychosocial events but place them in a loosely defined category of 'bedside manners' or natural empathy for patients without acknowledging that such events can be properly identified, classified or that skills can be learned to deal with the non-disease aspects of a person's health problem. The main reason for not taking these events more seriously is that they are not considered 'scientific', i.e. open to observation and verification. This is nonsense. A person's behaviour is as open to objective scrutiny as a bacillus under a microscope. In this respect we may want to heed Cassell's observation on medicine's twin goal which is to cure disease and to relieve suffering: 'Considering that medicine's warrant to exist is (also) to relieve suffering, a profession grounded in the belief that it cannot have real knowledge of whether someone is suffering has lost its way' (in Stewart & Roter,[14] p. 15).

How then can we improve the communication skills of health workers? A first and general requirement is accepting the limiting nature of the traditional clinical method based on a 'biomedical' perspective and the need to pass on knowledge and tools to health workers to deal more effectively with the psychosocial reality of disease and health. A second requirement is the organization of training in the health education and social aspects of leprosy for health workers in basic and in inservice training programmes.

The Workshops on Health Education in Leprosy may serve as a useful model for their adaptation is being discussed by the ALERT and Karigiri Training Centres. However, not all health workers attend regional training centres. Some are trained at national level (e.g. MAC in Pakistan), others may receive inservice training at district

* There is an encouraging new trend in selected schools of medicine and institutes for paramedical workers and a resurgence of interest in the process of communicating with patients.[14]

level. Therefore from 1990 onwards the training of selected health workers as 'future teachers' in health education is being organized.

Attention to inservice training only has a drawback in that much time is spent to 'unlearn' specific habits picked up from teachers and mentors during basic training. It is therefore advisable to include teaching modules on the health education and social aspects of leprosy as part of the current efforts reported by McDougall and Georgiev to introduce basic leprosy teaching into the curricula of medical students and other cadres of health personnel.[15]

Funding a place for health education in leprosy control programmes

What health education activities are implemented in leprosy control programmes? We have no reliable information on the subject. Current reporting through the annual ILEP forms is incomplete and misleading. If activities are reported they tend to be those which are highly visible and which can be stated quantitatively. For example, a programme has conducted a large-scale leprosy awareness campaign in Madras or in Bombay; 50 talks have been held in schools in Control Area 3 of Sierra Leone; 10 meetings about leprosy have been arranged with medical and nursing societies in Karachi. Other reported activities may include World Leprosy Day events, participation in health fairs, leprosy messages sent through press, radio or TV.

But much health education goes unreported, especially patient education during home visits, in clinics, in physiotherapy departments.

A first step should be to obtain a better picture of current health education activities and needs. I suggest regional meetings of programme directors as a tool for data collection since there is no commonly accepted terminology for the coding of health education activities, making written reports therefore unreliable.

Most leprosy control managers I have met in different countries want to include health education activities in the programme, but have questions about the effectiveness of current activities; about who should be responsible for health education and about where and how to introduce health education in the scheduled activities of the leprosy control programme.

These questions should be discussed and answered within the framework of three principles.

1 HEALTH EDUCATION IS NEEDED AT ALL STAGES OF LEPROSY CONTROL

Health education in leprosy tends to focus on problems of late detection or on the teaching of self-care for the prevention of deformities. I suggest we define health education activities in other areas as well, such as the first contact of people with leprosy services for diagnosis and eventually treatment. Health workers should provide proper conditions for communication to help new patients accept the disease and the proposed treatments.

Another area is the promotion of regular treatment and ensuring appropriate post-surveillance behaviour among patients. Are proper communication skills applied? Does the clinic setting and its organization favour effective communication between health

workers, patients and relatives? Finally, what is being done educationally to prevent social isolation of leprosy patients? Are problems of family or of community support sorted out?

Thus health education contributes to effective leprosy control in the following areas: through promoting early detection, helping with the acceptance of disease and treatment, ensuring regular treatment and appropriate follow-up; preventing deformities by teaching self-care and preventing social isolation. These are the major headings under which we should define specific health education practices.

Examples of successful practice in those areas are scattered throughout different leprosy programmes. It would be useful to exchange and share these experiences amongst leprosy control managers and people interested in health education in leprosy.*

2 ALL HEALTH WORKERS INVOLVED IN LEPROSY WORK ARE HEALTH EDUCATORS

This statement is deceptively simple but contains important implications for the organization of leprosy programmes.

I will first discuss the common practice to appoint one or two persons in a leprosy programme who carry the title 'health educator' and who are officially charged to conduct health education activities; then the requirements of an 'integrated approach' where all health staff perform health education tasks.

Appointing a special health educator is not an advisable arrangement. It is impossible for one person to carry out the health education functions specified in the above-mentioned programme areas. Secondly, it de-motivates other health staff to health educate whenever they see a need amongst patients they care for. Furthermore, the practice of referring patients who have a 'health education problem' to a special health education section does not make good educational sense. Patients and families with learning needs want them to be solved by the health worker they know and have come to see as their resource.

Is there then a place for a specially appointed health educator? The answer is a qualified yes, provided he/she is a respected capable and experienced leprosy worker and provided the health education duties are of the 'support' and not of the 'delivery' type. Examples of support activities are: organizing inservice training for health staff on communication skills or on how to organize group sessions; developing teaching materials for staff in field clinics, OPD, physiotherapy; assessing progress or problems in the health education performance of staff and assisting the programme manager and the field staff to organize specific activities in the community, including campaigns.

How to make a strategy succeed whereby all health staff participates in health education at their own level of work?

I am not aware of any reported experience of leprosy programmes with fully integrated health education services. However, feedback from workshop participants indicate two conditions: a sufficient level of training of staff in communication skills and the provision of administrative support to apply those skills with patients and

* A beginning of sharing of programme experience was initiated at the International Leprosy Congress, The Hague, 1988. During a pre-congress workshop 15 participants, leprosy control managers and health educators from 12 countries, discussed issues concerning health education work in leprosy programmes. The proceedings of the Workshop, published in an 80-page booklet, are available from TLMI, Brentford, UK,[16] free of charge.

communities. Support requirements may vary from the need for teaching materials, to transport, to rearrangement of patient load. In my opinion there is no standard solution. Possible arrangements should be discussed on their merits within the context of the programme.

I would like to add a third condition which also has been raised by some programme managers: the need to provide health workers with standardized guidelines for health education work in a number of situations, very much in the same way as guidelines exist for skin smear taking or VMT assessment.

Some programmes have made headway in this regard. For example, the Marie Adelaïde Leprosy Centre in Karachi published a *Leprosy Skill Book*,[17] containing guidelines for health education tasks and also forms to be filled out by leprosy workers (National Training Institute MAC). The Leprosy Control Programme of the Phillipines has developed detailed sets of tasks for multipurpose health workers on leprosy, including health education tasks.[18] Such work should be shared with other control programmes and reviewed for applicability in other settings. Furthermore, a few texts with advice to health workers on how to conduct health education, are available. Jane Neville's *Guide to Health Education*[10] in leprosy is well known and Jean Watson's book on *Preventing Disability in Leprosy Patients*[11] has a fine section on patient teaching (op. cit. 97–106). Guidelines for health workers' educational tasks in specific situations such as promoting early detection, acceptance of disease, drug compliance and prevention of deformities, have been prepared as hand-outs for participants of the Workshops on *Health Education in Leprosy*.[19] However, most guidelines need further refinement and especially validation.

Two final notes on the place of health education in leprosy control programmes.

What would be a proper administrative focal point for health education? Currently, focal points exist in Departments of Physiotherapy or Ergotherapy (ALERT, Karigiri) or at the central office level (Sierra Leone). In view of the supportive function of a specialized person I would argue not to place such a person in a particular section of the programme but to associate him with the training department or with training activities.

Secondly, our discussion on where to place health education activities in leprosy programmes should be seen in the context of changing patterns of programme organization due to the introduction of MDT requirements and to the integration of leprosy services in primary health care systems. It is said that a reduced caseload will provide more time for community education and for working on issues of social rehabilitation. I am sceptical about this, unless we witness a radical change in the views of programme managers and health workers from a biomedical to a psychosocial perspective.

Integration or linkage of leprosy services with other health services will considerably expand the volume of health education work as communication will be needed to address several priority diseases. In my opinion, if a good job is done on health education within the leprosy control programme, the extension and/or integration will not pose great problems because principles and strategies of health education in leprosy apply to other diseases as well.

3 HEALTH EDUCATION PRACTICE SHOULD BE BASED ON RESEARCH

I will discuss this point under the next heading.

Refocusing research on health education and social aspects of leprosy

Two recent papers in the *International Journal of Leprosy* have reviewed health education and social science research in leprosy.[20,21] In my opinion, a distinction between health education and social science research is not meaningful since there is none. Both focus on the cultural, socioeconomic and psychological problems related to leprosy. Health education research will perhaps focus more on communication methods while social science more on stigma and culture, but these are matters of degree, not of substance.

Most research studies are based on questions such as: why are patients defaulting? What knowledge, misconceptions and fear exist in communities about leprosy? What is stigma? How is it expressed? What are the effects of awareness campaigns on leprosy knowledge and early detection?

Reflecting on these studies in terms of their usefulness to health education practice and to communication activities of health workers, I would say: a, that too much attention has been given to research on the outcome (e.g. defaulting) and not enough to the underlying processes (e.g. what is the coping mechanism of a patient which explains his defaulting); b, the patient has been over-researched and more attention should be given to the health worker as a focus of research attention; and c, cultural differences receive considerable attention in research studies, such as, what different people believe to be the cause of leprosy, but what strikes me more is the 'similarity' in different countries of basic mechanisms explaining patient and community beliefs and behaviour.

I would suggest three lines of research.*

1 We need studies of basic processes which guide individual and community decisions about leprosy. Two themes merit attention: an investigation into belief systems and strategies of their modification; and studies about the nature of coping with leprosy and its treatment.

There is evidence of a new way of looking at beliefs about leprosy and about the use of simple tools to assess those beliefs in the social and cultural matrix of a community.[22] Still health workers need to know more clearly what, if anything, they can do about existing beliefs. Beliefs are not curious aberrations from a biomedical explanatory perspective nor caused by ignorance of the patient. If they are vital elements to people in helping them to make sense of unexpected events (such as signs, symptoms), how do you approach them? More particularly, can one influence a belief-system and if so, how?

Studies about coping as a psychodynamic mechanism for guiding a patient's responses towards illness and care would be useful to make sense out of observed decision profiles of patients. These studies could also suggest fruitful approaches health workers can take at particular stages of a patient's disease.

Patients have their own ways of dealing with illness and misfortune and their behaviours are not at random. They follow what Senkenesh calls 'care seeking stages'.[23] These stages are adaptive or coping responses to an illness as well as to the proposed care (treatment, surgery, the health worker, an institution). They represent a process every person goes through.

Such stages have been identified for diseases such as cancer.[24] Identifying similar stages for leprosy would be useful. The health worker would have a better insight into

* A more detailed account of research priorities on health education in leprosy control is available as an internal 4-page document submitted to ILEP, May 1989.

problems which occur such as, non-acceptance of the disease; patient's use of other healers; his claiming of drugs after discharge, and so on. Such behaviour of patients would then not be considered in isolation (requiring, as often is thought, an extra dose of health education) but as an expression of a coping response which requires a specific and appropriate approach. For example, a health worker when faced with a patient who is complaining that his patches are not disappearing and that he does not feel well will tend to respond with a 'don't worry, after a few more months the patches will disappear'. In fact, the health worker should understand that the patient is going through an accommodation stage of his illness and is re-assessing the meaning of his disease within the context of his personal life projects. Armed with this knowledge health workers could initiate a discussion on personal concerns about the consequences of the disease on a person's life rather than to suggest not to worry.

In a more general sense, unless we better understand the nature of suffering of a person, we are not able to help effectively. On the contrary, health workers who fail to understand the nature of suffering can engage in medical interventions that (although technically adequate) not only fail to relieve suffering but may become a source of suffering itself'.[25]

2 A second line for research should focus on the health worker. It has been suggested that health workers may contribute to misconceptions and fear about leprosy.[21] If so, it is an important observation requiring closer analysis and possibly a review of current training practices.

Several studies acknowledge the possible beneficial effect of a sound health worker–patient relationship with respect to patient attendance, drug compliance and other indices. Yet can we describe the parameters of a sound relationship? How do those with a sound relationship behave compared to those with an ineffective relationship? How much do we know about the attitudes of health workers towards patients compared to the amount of research on the attitudes of patients towards disease and care? And, what about studies of job satisfaction and commitment of the health worker towards leprosy care and particularly towards the educational and social aspects of his task? We know little about this area. Yet a satisfied worker is an effective worker.

3 A third and final area for research which I would like to suggest deals with the evaluation of communication strategies and methods.

Although we possess an interesting set of rules and principles for communicating with patients and communities, several communication practices need validation. For example, how do we translate medical concepts into words and a language people readily understand? Is 'health belief synthesis', which attempts to bridge the gap between scientific and cultural concepts about leprosy, an effective procedure?[26] Another research theme concerns the specifics of community participation strategies. What are the steps? Are there simple tools to assess opinion leaders and the influence of social networks in decision-making? Who are the main informants about leprosy and its care? What is the role of traditional healers in this respect? What types of relationships are viable between leprosy services and healers?

Conclusion

I have discussed the need to redefine health education in leprosy. Some of the thoughts expressed in this paper may be useful to programme managers and health workers. They

are intended for discussion and comments. In my opinion, a redefined view on health education will help reduce unrealistic expectations about health education in leprosy, provide health workers with effective tools to do their educational work, ensure a supportive programme structure and increase our understanding of basic themes which not only cut across cultural variations but also will influence the way in which people are cared for.

Does ILEP have a role in all this?

Being a coordinating body to ILEP-member associations, ILEP could for example, promote and coordinate health education activities in leprosy; secure expert advice on this matter to leprosy programmes funded by Member Associations; and establish a network of contacts among people responsible for or interested in health education in leprosy programmes.

In 1989 an Expert Group on Health Education was established to provide a focal point for ILEP on the above. The Group is part of the ILEP Medical Commission Training Discipline and works closely with TALMILEP. The Group welcomes information on health education from national leprosy programmes, including particular needs and encourages the establishment of regional task forces to work in depth on some of the issues raised in this article.*

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The pathology of the eye in armadillos experimentally infected with *Mycobacterium leprae*

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Summary One hundred and twenty-seven eyes from 66 *Mycobacterium leprae* inoculated armadillos were studied histologically and some ultrastructurally.

Inflammatory reactions were found in the following extraocular tissues: the eyelid, including the orbicularis muscle and the third eyelid, extraocular muscles, tear gland and Harder's gland.

The early and slight changes of the intraocular tissues, small amounts of lymphocytes, plasma cells and macrophage infiltrations were confined to the area around the anterior angle specifically within the trabeculae and the adjacent ciliary body, the root of the iris and the limbus region of the cornea.

But in the cases with severe lesions the whole uvea was densely infiltrated with large, foamy macrophages intermingled with small amounts of lymphocytes, plasma cells and frequently, neutrophils. No specific necrosis of the granulomas was seen. No explanation for the neutrophil infiltrations was given.

The lesions in the cornea were significantly less severe than those in the uvea. Retinal lesions comprised of macrophage infiltrations were all obvious extensions of the adjacent uvea lesions. Acid-fast bacilla (AFB) were found within all tissues. The infection of the intraocular tissues in the armadillo eyes seemed to be mainly, if not solely, haematogenous.

Introduction

Although the incidence of leprosy is declining in many parts of the world the prevalence of this disease is still considerable in many countries. The eyes of leprosy patients are

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damaged either by the disease itself or because of lagophthalmos and insensitivity of the eyes.

The clinical aspects of eye diseases in leprosy have been well documented, but the pathological studies of the eye in human patients are few,[1] this is due to the fact that eye specimens of patients are hard to get. Whenever eyeballs were available, they were almost always at the end stage of disease and had been treated over a long period of time. What we know about the pathology of the whole human eyeball in leprosy is based on limited observations of human specimens. In order to gain an overview of the pathology of the eye in leprosy, and to know the pathogenesis of it animal model studies are necessary.

Since the discovery that armadillos could be artificially infected with *Mycobacterium leprae*,[2,3] these animals have been used both as a source of the causative organism for other research and as an animal model of human leprosy in different fields of research.[4] In order to know more about the pathology of the eye lesions in this animal model, 130 eyes from 68 experimentally infected armadillos were studied histologically and in several cases ultrastructurally.

Material and methods

One hundred and thirty eyes were studied from 68 *M. leprae* infected armadillos (*Dasypus novemcinctus*). The eyes came from the following research institutes: Forschungsinstitut Borstel of West Germany, Royal Tropical Institute of Amsterdam, Holland and Florida Institute of Technology, Melbourne, Florida, USA. Six of these animals had only one eye specimen available.

The animals were inoculated intravenously with *M. leprae* through the femoral vein and with a dosage of 10^8 bacilli in 1 ml of saline. Between 5 and 60 months after inoculation the animals were put to sleep and the eyes removed, 59 of them with the eyelids and intraorbital tissues intact. The specimens were fixed in buffered formaldehyde or glutaraldehyde. Paraffin sections of these specimens were made and stained either with haematoxylin-eosin, with modified Fite–Faraco (FF) method for acid-fast bacilli (AFB) after depigmentation with potassium permanganate,[5] with Gomori or with PAS methods. The eys of 3 armadillos fixed in glutaraldehyde were studied ultrastructurally under a Philip electron microscope, after having been embedded in Epon and cut with an LKB microtome.

We categorized the lesions of the eyes of these animals into four groups according to the severity of the reactions: the group with minimal lesions (+ −) included the eyes with very small amounts of lymphocytes and/or plasma cell infiltrations, usually around the anterior angle, in the ciliary body and occasionally in the iris and choroid. If there were small numbers of macrophages present, the cytoplasm in the macrophages was not very abundant. The one plus group (+) included the eyes with lymphocytes plasma cell and large macrophage (with extensive cytoplasm) infiltrations around the anterior angle and in the iris, ciliary body and choroid. The two plus (+ +) group included the cases with significant infiltrations of plump macrophages in the ciliary body, iris and choroid, with slight to moderate thickening of these structures. The three plus (+ + +) group included the cases with the whole uvea tract densely infiltrated with plump macrophages and the uvea significantly thickened.

Results

Of the 130 eye specimens from the inoculated armadillos, one eye was excluded from the study because of its autolytic changes. Both eyes from another animal were also excluded because there was acute keratitis in both eyes with neutrophile infiltrations in the whole cornea stroma and no AFB or other significant lesions in other ocular tissues.

In the remaining 127 eyes, the following changes in various tissues were found, see Tables 1 and 2.

EYELID

In 59 of the 127 eye specimens, eyelids were present. In the skin of 56 of these eyelids (95%), granulomatous lesions were found. There were gatherings of large macrophages and foam cells in the dermis, usually intermingled with small numbers of lymphocytes, plasma cells and neutrophiles (Figure 1). Where the infiltrations were not very dense, the lesions were more prominent around the adnexa of the skin and around the nerves and blood vessels. The perineurium of some nerves was thickened with perineurial cell proliferation. In 21 of the 52 eyes (40%) in which the orbicularis muscles were visible, the muscles were infiltrated with macrophages or foam cells and other inflammatory cells

Table 1. Number of eyes with lesions in various ocular tissues

	Lesion group				
	+ −	+	+ +	+ + +	Total
Number of eyes in this group	42	52	21	12	127
No. of eyes with lesions found in the tissue of:					
Cornea	4 (10%)*	7 (13%)	10 (48%)	9 (75%)	30 (24%)
Sclera	1 (2%)	3 (6%)	5 (4%)	9 (75%)	18 (14%)
Limbus	20 (48%)	40 (77%)	18 (86%)	11 (92%)	89 (70%)
Trabeculae	37 (88%)	52 (100%)	21 (100%)	12 (100%)	122 (96%)
Iris	6 (14%)	32 (62%)	21 (100%)	12 (100%)	71 (56%)
Ciliary body	35 (83%)	52 (100%)	21 (100%)	12 (100%)	120 (94%)
Choroid					
Ant.	9 (21%)	45 (87%)	21 (100%)	12 (100%)	87 (69%)
Mid.	6 (14%)	30 (58%)	17 (81%)	12 (100%)	65 (51%)
Post.	6 (14%)	23 (44%)	13 (62%)	11 (92%)	53 (42%)
Retina	0/42 (0%)†	0/52 (0%)	2/19 (11%)	6/12 (50%)	8/125 (6%)
Optic nerve	0/19 (0%)	0/22 (0%)	0/7 (0%)	0/5 (0%)	0/53 (0%)
Lens	8/28 (29%)	14/45 (31%)	12/18 (67%)	6/11 (55%)	40/102 (39%)

* The figure represents the number of the eyes in which lesions were found in that tissue. The figure in parenthesis represents the percentage of the eyes in which lesions in that tissue were found.

† The numerator represents the number of eyes in which AFB were found. The denominator represents the number of the eyes in which that tissue was distinct and AFB had been looked for. The figure in the parenthesis represents the percentage of the AFB positive cases.

(Figure 2). Different quantities of AFB were found both within these infiltrated cells and outside them.

CONJUNCTIVA

Infiltrations of macrophages with foamy cytoplasms and AFB were found both in the bulbar and lid conjunctiva in 84 eyes (66%) (Figure 3).

In the conjunctiva of the eyelid and fornix, small nodules of lymphocyte gatherings were observed. Scattered lymphocytes, plasma cells and Russell's bodies had infiltrated the conjunctiva elsewhere. In one case hair follicles with sebaceous glands were found in the palpebral conjunctiva facing the nictating membrane.

THE THIRD EYELID, NICTATING MEMBRANE

The nictating membrane was seen in 45 of the 127 eyes. In the connective tissues of 43 (96%) of these third eyelids, large amounts of macrophages or foam cells, with many AFB in their cytoplasms were observed. Sometimes giant cells and neutrophiles and other cells were found (Figure 4). The cartilages of these eyelids appeared to be normal, but AFB were discovered both in the perichondrial cells and in the chondrocytes in 5 cases.

Table 2. Number of eyes and intraocular tissues in which AFB were found

	Lesion group				
	+−	+	++	+++	Total
No. of eyes in this group	42	52	21	12	127
No. of eyes with AFB looked for	42	51	20	12	125
No. of eyes with AFB found	13	46	20	12	91/125 (73%)*
AFB found in the tissues of:					
Cornea	9/42 (21%)*	25/50 (50%)	16/20 (80%)	10/12 (83%)	60/124 (48%)
Limbus	11/42 (17%)	37/50 (74%)	16/20 (80%)	11/12 (92%)	75/124 (60%)
Trabeculae	12/42 (29%)	36/49 (73%)	17/18 (94%)	11/11 (100%)	76/120 (63%)
Iris	5/42 (12%)	28/49 (57%)	17/19 (89%)	11/11 (100%)	61/121 (50%)
Ciliary body	13/42 (31%)	43/51 (84%)	19/20 (95%)	11/11 (100%)	86/124 (69%)
Choroid	13/42 (31%)	46/51 (90%)	20/20 (100%)	12/12 (100%)	91/125 (73%)
Retina	2/41 (5%)	9/50 (18%)	6/17 (35%)	10/11 (91%)	27/119 (23%)
Sclera	7/42 (17%)	33/50 (66%)	19/20 (95%)	12/12 (100%)	71/124 (57%)
Optic nerve	1/14 (7%)	2/16 (13%)	1/2 (50%)	2/6 (33%)	6/38 (16%)
Lens	0/19 (0%)	1/37 (2%)	0/15 (0%)	3/9 (33%)	4/80 (5%)
Blood vessel	3/42 (7%)	6/51 (12%)	4/20 (20%)	5/12 (42%)	18/125 (14%)

* The numerator represents the number of eyes in which AFB were found. The denominator represents the number of the eyes in which that tissue was distinct and AFB were looked for. The figure in the parenthesis represents the percentage of the AFB positive tissues found.

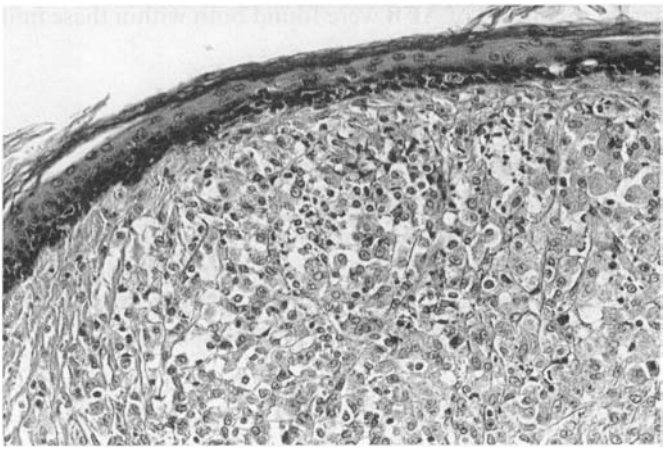

Figure 1. The cells infiltrating the dermis are mainly foam cells and smaller macrophages mixed with a small amount of other cells, including neutropheles. HE 284 ×.

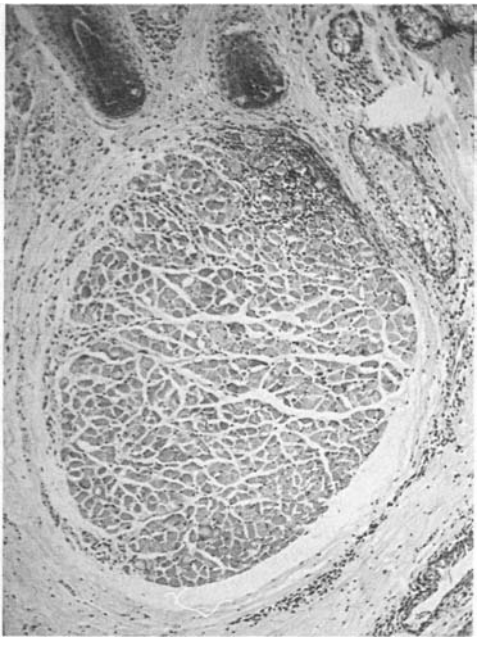

Figure 2. The obicularis muscle in the eyelid is infiltrated by inflammatory cells. HE 71 ×.

LACRYMAL GLAND

Lacrymal and/or accessory lacrymal glands were found in 91 eyes. In 51 (56%) of the 91 eyes lymphocyte infiltrations were found, some with macrophages and some with the gland partially destroyed (Figure 5). AFB were found in 43 (55%) of the 78 glands studied.

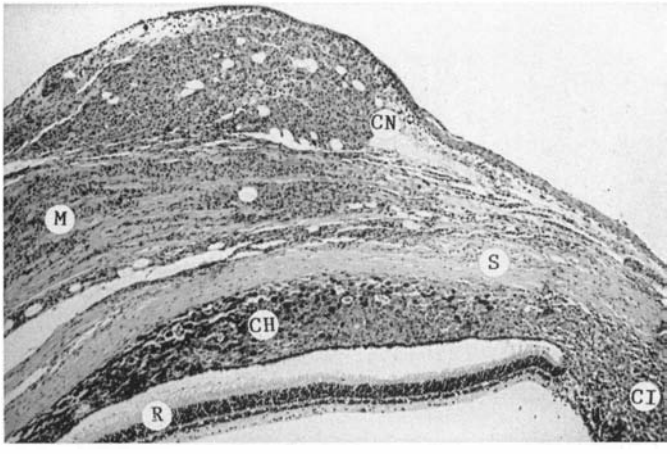

Figure 3. In the bulbar conjunctiva (CN), a focus of macrophage infiltration is bulging outward. The infiltrations in the extraocular muscle (M), choroid (CH) and ciliary body (CI) are also prominant. R, retina; S, sclera. HE 71 ×.

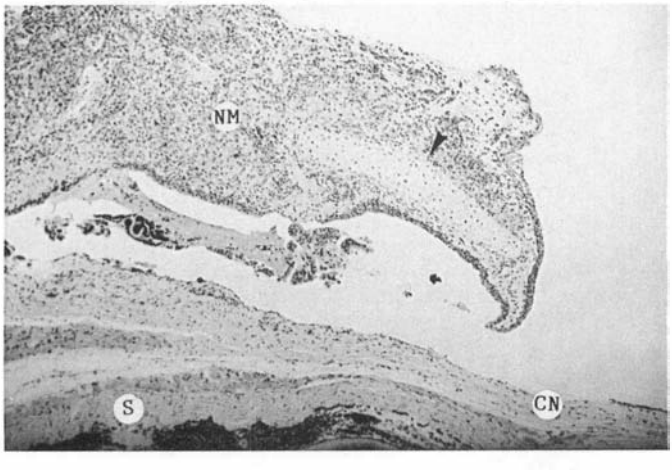

Figure 4. The stroma of the nictating membrane (NM) is heavily infiltrated with inflammatory cells, but the cartilage (arrow head) in the third eyelid seems intact. CN: conjunctiva, S: sclera. HE 71 ×.

EXTRAOCULAR MUSCLES

Although 83 of the 127 muscles were intact, the muscles in 44 cases (35%) were infiltrated with large macrophages or foam cells in great numbers (Figures 3 and 6). In some cases parts of the muscle had been replaced by there infiltrated cells and only a few muscle cells remained among a great number of foamy macrophages. Hypertrophy of the remaining muscle cells could be observed. A lot of AFB were to be seen in the infiltrating cells (Figure 7) in the muscle bundles. In the muscle cells of several animals, parasite sarcocystes were found filling the cytoplasm, usually with no inflammatory reaction involved.

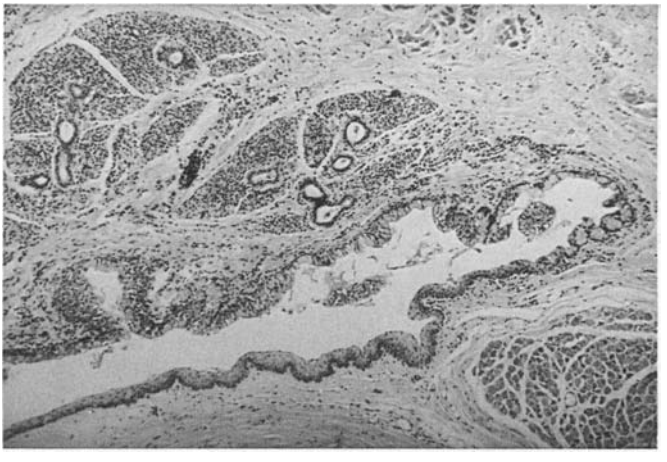

Figure 5. The accessory lacrimal gland within the palpebral conjunctiva is significantly infiltrated with macrophages. HE 71 ×.

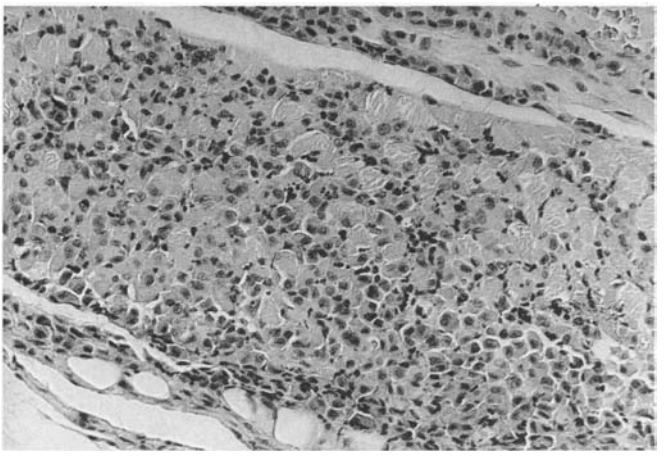

Figure 6. The extraocular muscle is infiltrated with large macrophages. Significant neutrophiles can be observed intermingling with these cells. HE 284 ×.

CORNEA

The cell infiltration in the cornea was not extreme; usually only minimal cell infiltrations at limbus were found (Figures 8 and 9). The infiltrating cells were mostly comprised of some small or large macrophages, lymphocytes, plasma cells and sometimes neutrophiles. In some cases there were small round cells scattered around the small blood vessels, a normal constituent of the cornea of this species. In most of the cases, the epithelium and the endothelium of the cornea showed no changes, though in others some of these cells were swollen. In some specimens, sheets of endothelia were detached, leaving bulla-like spaces between them and the Descemet's membrane. AFB were found in the epithelium cells, in cells infiltrated between the lamellae of the stroma cells and within the

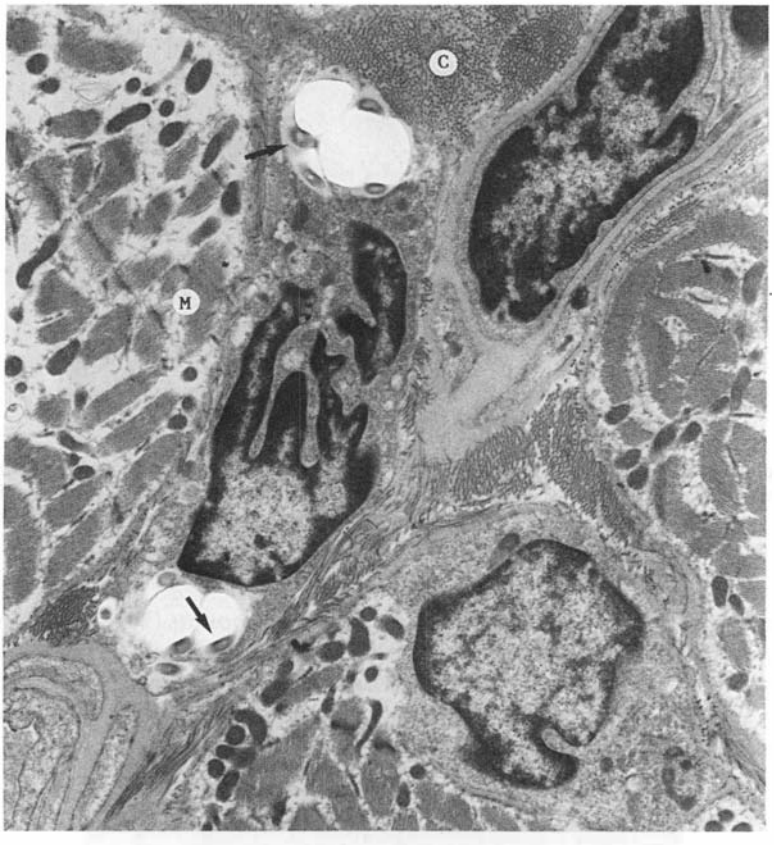

Figure 7. Within the cytoplasm of the infiltrating macrophage among the muscle cells (M), many *M. leprae* (arrows) could be seen. C, collagen. Electronmicrograph. 24000 ×.

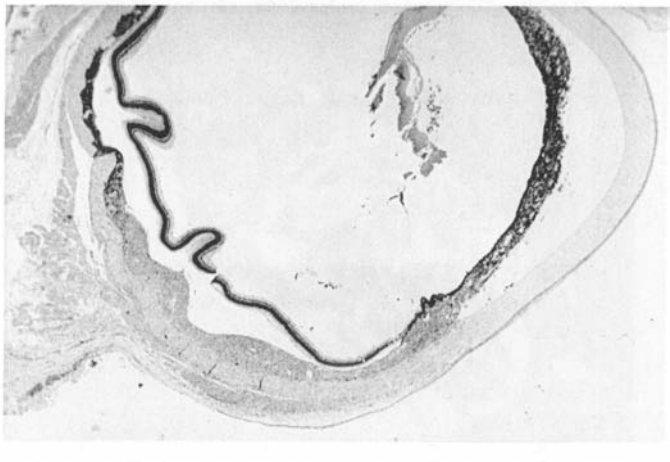

Figure 8. The cornea is not significantly infiltrated. But the iris, ciliary body, the choroid, even in the posterior segment of the eyeball, the sclera and the extraocular muscle are significantly infiltrated with inflammatory cells. HE 21 ×.

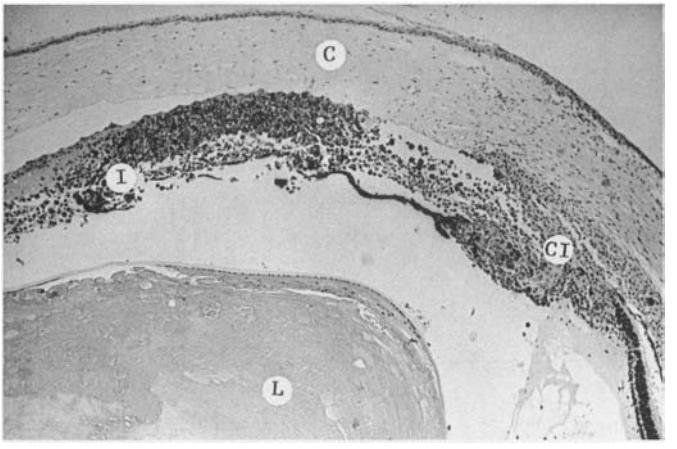

Figure 9. The cornea (C) is significantly infiltrated with inflammatory cells only at the limbus region. The iris (I) and ciliary body (CI) are more or less destroyed and infiltrated by the inflammatory cells. Some fluid and cell exudates are filling the anterior chamber. The lens (L) shows Morgagni globules beneath the anterior capsule. HE 71 ×.

endothelium, in the latter case sometimes in very large amounts (Figure 10). In one case, though the cornea of an eye in the + − lesion group was basically normal, several AFB were found in the superficial and basal epithelial cells of the cornea. Sometimes small round cells and macrophages had attached to the endothelium of the otherwise normal-looking cornea (keratic precipitates, KP).

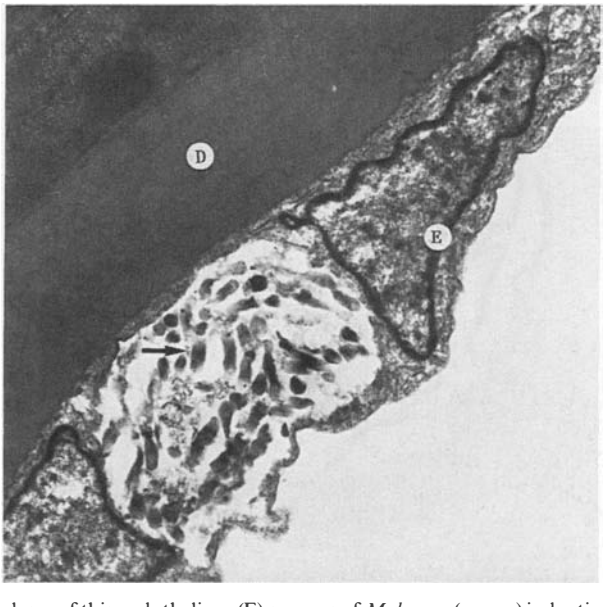

Figure 10. In the cytoplasm of this endothelium (E) swarms of *M. leprae* (arrow) indenting the nucleus are seen. D, Decement's membrane. EM 20000 ×.

SCLERA

In the sclera around the vicinity of ciliary bodies and choroid, there were large amounts of macrophages (Figure 11). There were also some scattered-cell infiltrations around small vessels and nerves within the sclera. In some cases the cell infiltrations in the choroid seemed to be continuous with the extraocular infiltrations, e.g. those in the conjunctiva and in the extraocular muscles through the sclera. AFB were found in the infiltrating cells and within the nerves traversing the sclera.

TRABECULAR MESHWORK OF THE ANTERIOR CHAMBER ANGLE

In the eyes with minimal alterations, the most significant change within the whole eyeball was almost always found around this region. Infiltration of small numbers of lymphocytes and plasma cells with or without plump macrophages were seen in the trabecular meshwork, around the Schlemm's canal and in the adjacent tissues of the ciliary body and iris (Figure 12).

When the infiltrations were denser, the cells dominating the picture were macrophages with abundant cytoplasm, within which there were different quantities of melanin granules. Sometimes the infiltrations tended to be continuous with the infiltrations in the limbus of the cornea and in the ciliary body and iris (Figure 13). These infiltrating cells were also found unattached in the anterior chamber. Among the free macrophages in the chamber, a giant cell was found in one case. AFB were present in the infiltrating cells.

IRIS

In some cases, the iris seemed normal, thin and without infiltrations. But in those with severe change, the iris was greatly thickened, infiltrated by large amounts of macrophage. The normal structure of the iris was obscured (Figure 9). In some cases the infiltrating cells were lymphocytes, plasma cells and various amounts of neutrophiles and eosinophiles.

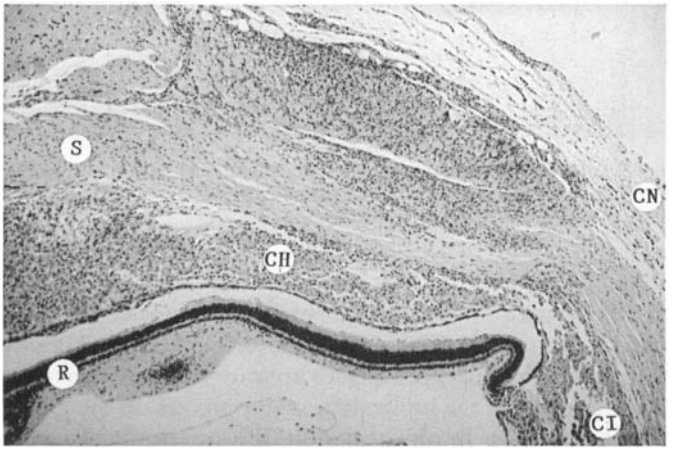

Figure 11. The sclera (S) adjacent to the heavy infiltrations of the choroid (CH) and extraocular muscle (M) is infiltrated with macrophages and other cells. CN, conjunctiva, CI, ciliary body; R, retina. HE 71 ×.

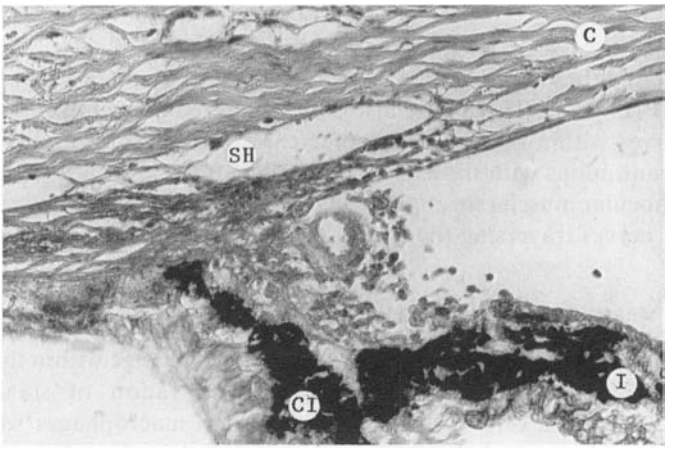

Figure 12. In the anterior angle area of this eye with slight lesions, tens of small macrophages and lymphocytes are seen in the meshwork, around the Schlemm's canal (SH), root of the iris (I) and in the adjacent ciliary body (CI). In the cytoplasm of these macrophages shown here, a large amount of AFB was seen. C, cornea. FF staining after depigmentation. 284 ×.

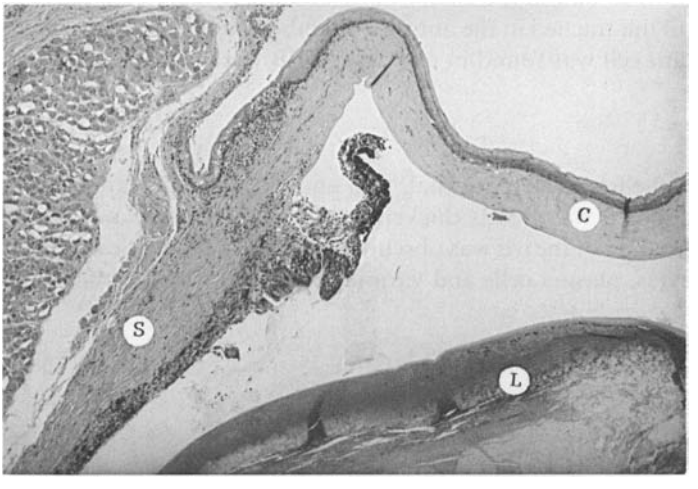

Figure 13. The anterior angle area is infiltrated with inflammatory cells. The infiltration extends to the limbus region of the cornea (C) and seems to be continuous with that of the bulbar conjunctiva. The bulk of the cornea is not infiltrated. L, lens; S, sclera. Depigmented. HE 71 ×.

Occasionally giant cells with one or several small or big nuclei were present among the other infiltrating cells (Figure 14). The sphincter muscle of the pupil of some of the iris was infiltrated with some inflammatory cells. Both anterior and posterior synechiae of the iris were seen. AFB were found in the infiltrating macrophages, in the giant cells mentioned above and in the muscle cells. In one armadillo the anterior surface of the iris and the anterior angle area were covered by endothelial cells continuous with those in the cornea (endothelialization).

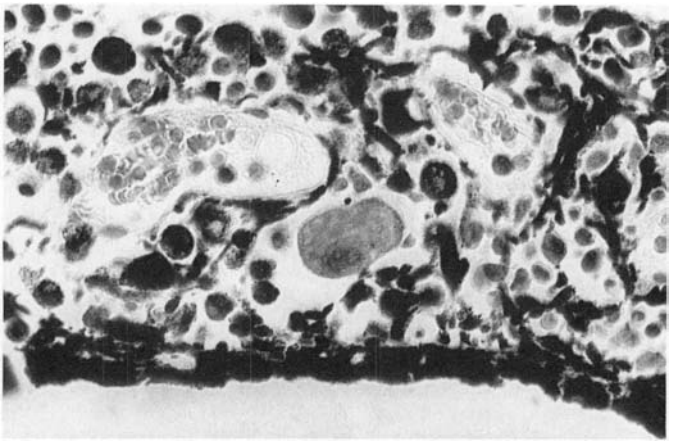

Figure 14. The iris is infiltrated with macrophages, lymphocytes and other cells. A giant cell with several nuclei is prominant among them. Within this giant cell, several AFB were seen. FF. 710 ×.

CILIARY BODY

In some cases there were only small round cell infiltrations. But in others the whole ciliary body was swollen tremendously with large numbers of full-blown macrophages engulfing some melanin granules and with the tissue of the ciliary body destroyed. The muscular structure could not easily be recognized (Figure 9). Large amounts of AFB were found within these macrophages as well as in the pigment and non-pigment epithelial cells lining the ciliary processes (Figure 15). No fibrotic change was found.

CHOROID

In those cases with slight changes, the choroid was thin and without significant cell infiltrations. Only occasional, small round cells were found. In the cases with severe lesions, the choroid was thickened to several times the normal size, crowded with abundant macrophages and other cells, including some neutrophiles (Figure 16). The thickening appeared segmental and not uniform. Usually the anterior part was swollen the most, but sometimes only the posterior part was thickened and even more swollen. AFB were found in the infiltrating macrophages and stroma melanophores (Figure 17).

RETINA

In most cases the retina was observed to be devoid of any significant change. In armadillos the entire retina was abruptly joined to the epithelium of the ciliary body, and there was no obvious transitional zone corresponding to the ora serrata in humans. In seven eyes, in this anterior end of the retina adjacent to the heavily infiltrated choroid, many large macrophages had infiltrated. In another eye, at a place near the equator of the eyeball, where the choroid was heavily infiltrated with plump macrophages and the Bruch's membrane was destroyed, a lot of macrophages infiltrated the retina destroying the retina tissue (Figure 18). Large amounts of AFB were found there, both in the choroid and the

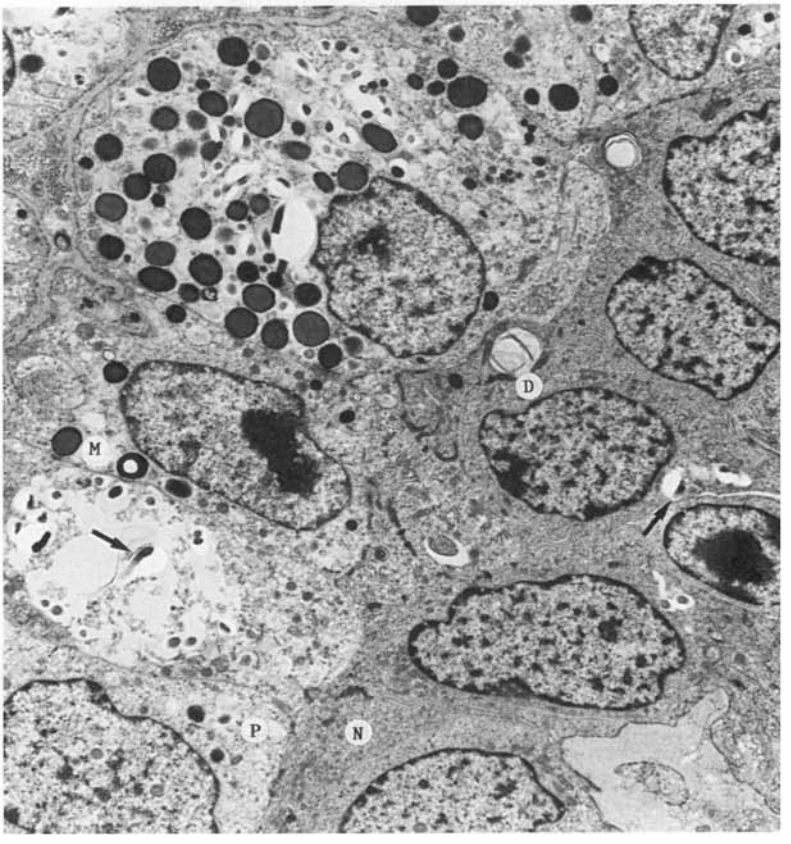

Figure 15. *M. leprae* (arrow head) in the cytoplasm of the pigmented (P) and non-pigmented (N) epithelium of the ciliary body. The melanosomes (M) and desmosomes (D) of the cells are very distinct. EM 12000 ×.

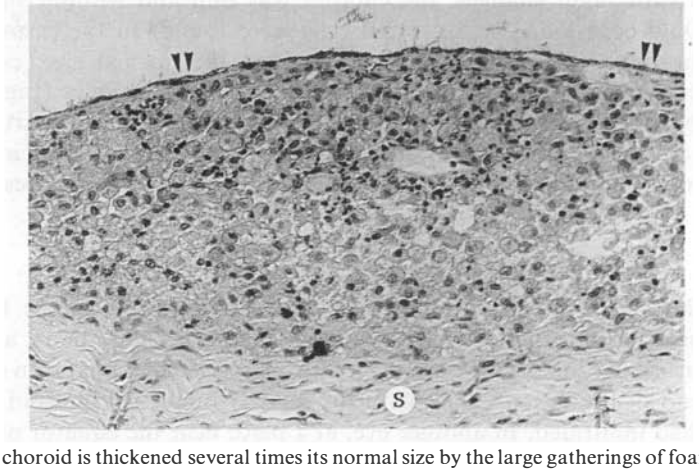

Figure 16. The choroid is thickened several times its normal size by the large gatherings of foamy macrophages. Within the cytoplasm large amounts of AFB were seen. Note the neutrophiles scattered among the macrophages. The pigment epithelium layer (arrows) is at the top and the sclera (S) is at the bottom of the picture. HE 284 ×.

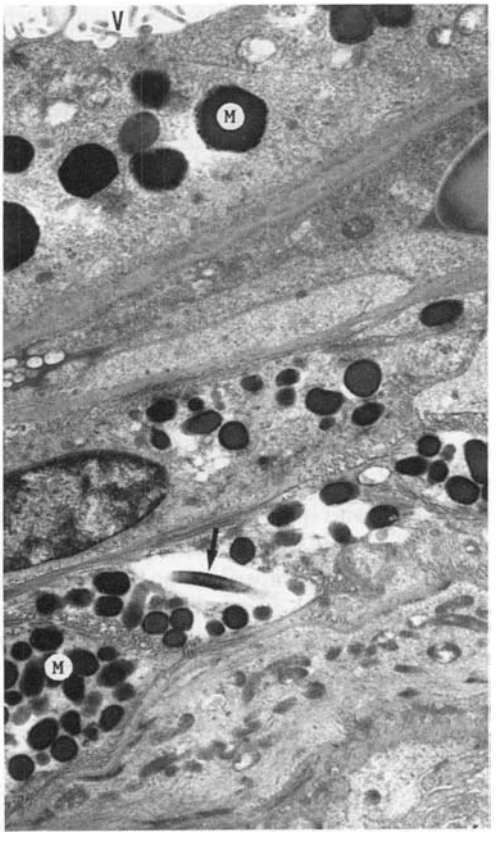

Figure 17. *M. leprae* (arrow) in the cytoplasm of a melanophore in the choroid. M, melanosome; V, microvilli of the pigment epithelium of the retina. EM 20000 ×.

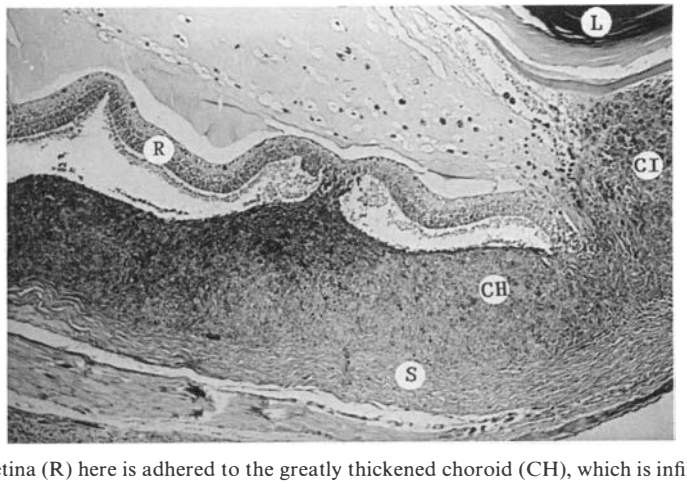

Figure 18. The retina (R) here is adhered to the greatly thickened choroid (CH), which is infiltrated with huge amount of foamy macrophages engulfing swarms of AFB. The lens (L) is at the top right-hand corner and the ciliary body (CI) is also greatly engorged. S, sclera. FF. 71 ×.

retina. In nineteen cases AFB were also visible in the ganglion cell layer, in the inner and outer nuclear layer, between the photoreceptors and pigment epithelium of the otherwise normal retina (Figure 19). In several cases the retina was detached and fluid had gathered under the detached retina. In two cases segments of retina were atrophic; in those cases the retina had been reduced to a one-cell layer structure, but the adjacent choroid was normal.

OPTIC NERVE

No significant lesions were found in the optic nerves observed in 39 cases, but AFB were found in the meninges surrounding the optic nerve in five eyes and in the nerve itself in one (Figure 20).

LENS

Focal globular thickenings of the lens capsule with flattened epithelial cells were seen in thirteen lenses (13%) of the 102 eyes with the lens in the sections. Morgagni globule or small vacuole formations were found in 34 cases. The thickening of the lens capsule and the degenerative change of the lens fibres in the same eye appeared in seven lenses. In four eyes a few AFB were observed under the capsule. One bacillus seemed to be located within a vacuole of the cell (Figure 21). In one eye the lens capsule was disrupted and the lens substance provoked an acute inflammatory reaction around it (phacogenic endophthalmitis).

ENDOTHELIUM OF THE BLOOD VESSELS

Some AFB were found in 18 eyes in the cytoplasms of the endothelial cells, or in the cells within the lumen of the blood vessels in various tissues, e.g. the limbus of cornea, choroid, sclera and iris.

In 85% of the cases, both eyes of an animal had the same degree of lesion. In 9% of the

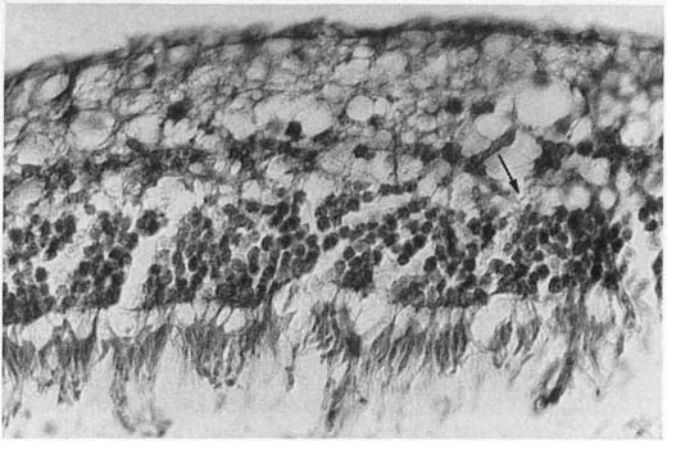

Figure 19. In various layers of the retina without significant lesions, *M. leprae* were observed, as shown here (arrow). FF. 710 ×.

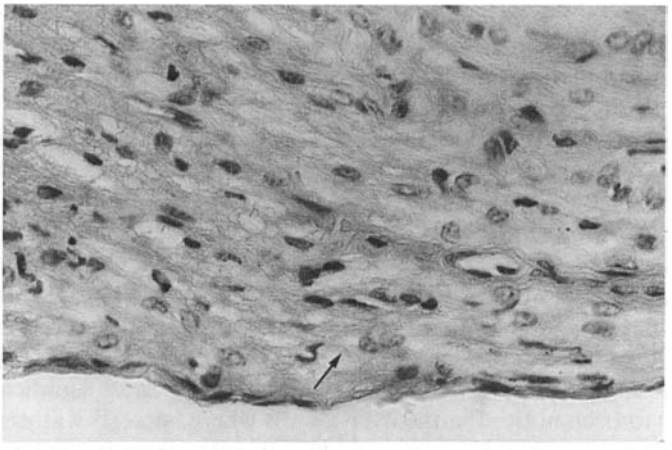

Figure 20. A *M. leprae* in the optic nerve. FF. 710×.

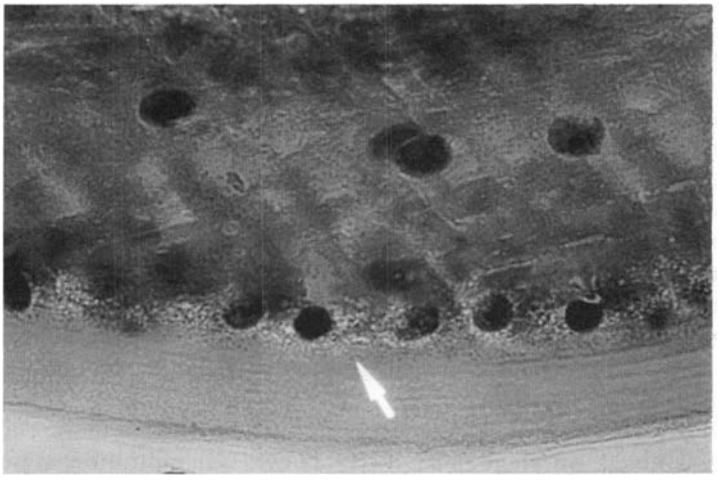

Figure 21. A *M. leprae* (arrow) in a vacuole of the epithelium of the lens under the capsule (C). FF. 710×.

animals the degrees of the lesions of their two eyes were not identical, but of an adjacent degree. In only 6% out of all the armadillos were the eye lesions differing by two or more degrees.

Discussion

Of the 66 armadillos which were experimentally infected with *M. leprae*, no AFB were found in the liver or in the spleen in five animals at the time of their deaths. However, in the eyes of these five animals, minimal cell infiltrations around the anterior angle area

were found (group + −), although no AFB were found in these eyes. Since AFB were observed in other eyes in the + − group, the + − lesion may represent either an early and slight leprosy inflammation or a mild, nonspecific reaction to some other irritants.

All the other 61 experimentally infected armadillos in this study had disseminated leprosy infections upon death. The amount of the bacilli in their spleens and liver and the presence of granulomata in the soft tissue within their bodies seen in post-mortem examinations verified the nature of their systemic lepromatous infection. The eye lesions are simply a part of the manifestations of the general infection.

The granulomatous reaction in the intraocular and extraocular tissues was manifested by macrophage infiltrations, and the cytoplasm of these cells was sometimes not extreme, and at other times very abundant and foamy. Among these cells there were usually some neutrophiles. Often there were some lymphocytes and plasma cells intermingled, whether the lesion was in the eyelid, in the iris, in the choroid, or most significantly in the iris. Neutrophiles had been noticed in the liver lesions where necrosis was present[6,7] and had been mentioned as a particular component of cell infiltrations in the eye.[1] In the eyes of this study the neutrophiles were present both in the intraocular and the extraocular lesions where there were no obvious signs of necrosis. What this exudation means remains to be determined. There were two possible routes for the bacilli to get into the anterior angle area, namely invasion through the cornea or adjacent extrabulbar tissues (via nerves or by direct extensions from conjunctiva, extraocular muscles and fibra-fatty tissues) and haematogenous seedling.

When the lesions within the eye were slight (group + −), they were almost always confined to the anterior angle region, with cell infiltrations around the trabeculae, at the limbus region of the cornea and in the adjacent ciliary body and the root of the iris. AFB were also found in these places, sometimes in quite large numbers, even when the cell infiltration was not very severe.

When the lesions became more severe the ciliary body and iris were affected more. The lesions in the choroid, when present, seemed to be commonly more severe in the anterior part, though in some cases the posterior part was equally, if not more severely, affected. The lesions in the anterior angle area might be the initial intraocular lesions in these intravenously infected animals.

Inflammatory cells were seen only occasionally in the stroma in the corneas of 30 of the 127 eyes examined. Although in 89 of the 127 eyes cell infiltrations were found in the limbal regions, the cell infiltrations were not dense and there was no frank granuloma or significant lepra cell infiltrations in the stroma of the cornea in the central part, as seen by others.[8–11] In comparison to the severity of the lesions with that in other eye tissues, the corneal lesions were slight. Although AFB were found in the epithelium of the cornea, it seemed that *M. leprae* cannot have entered the eye initially through the cornea.

In view of the fact that the lesions of the extraocular tissues in the vicinity were insignificant in those eyes with slight leprosy lesions in the angle area, the continuous invasion route did not seem to be of significant importance.

The large amount of AFB within the endothelia of the cornea and epithelia of the ciliary body in some cases was of interest. That meant that the bacilli could multiply and accumulate within them and shed into the fluid phase within the eyeball.

The intraocular circulation of the aqueous humor with the trapping and concentrating of particulate matters and cells (might be bacilli-laden) between the meshworks of trabeculae might be a factor in the early cell infiltrations there; the lower temperature of

the anterior parts of the eyeball might also be a factor in the early lesions there. The ciliary body receives an enormous blood supply. Bacilli in the bloodstream might gather more easily at the site where the blood supply is greater. Choroid also receives a large amount of blood; nearly as much as that of the ciliary body. If only the number of AFB in the blood supplied to these parts were concerned, as the ultrastructures and permeability of the capillaries of choroid and ciliary body are about the same, the severity of the lesions in these two parts should be similar. That was true in some cases we examined, but we observed cases in which the lesions in these two structures were not the same, usually with heavier lesions in the ciliary body, but also with heavier lesions in the other. The cause of these differences might be solely a matter of chance, but tissue preference or other factors must also be considered.

Retinal lesions in leprosy have rarely been seen.[9–11] In the present studies, retinal lesions were observed in 8 of 125 cases. In seven cases, the lesions were at the beginning part of the retina adjacent to the ciliary body and choroid where there were heavy macrophage infiltrations. In another animal, a focal lesion was found in the retina at about the equator of the globe, where there were also heavy macrophage infiltrations in the choroid. Here the retina and the Bruch's membrane were destroyed. The retinal lesions in these 8 cases were obviously extensions of the adjacent choroid and/or ciliary body lesions. But AFB were found, too, in the retina without obvious lesions in another 19 cases. These AFB might be blood borne, since bacteremia might be a constant event in this systemic infection. The reason why so few retinal lesions were seen, after the possible constant bacteremia, might be attributed to the properties of the blood-retinal barrier or to some other properties of the microenvironment in the retina.

The finding of a few AFB within the lens in four eyes was unexpected. It is not easy to imagine how the bacilli could penetrate the thick lens capsule. Since they were seen under the microscope at the levels of the cell organelles and some were in vacuole-like structures and not at the top of tissue, they probably were not dislodged bacilli resettled there during slide preparations.

The endothelialization of the anterior surface of iris in one case, the phacogenic endophthalmitis in one and the focal atrophy of the retina in two cases might not be directly related to leprosy infection. The sarcocystis seen in the muscle fibres in several armadillos is a common parasite of various laboratory animals and sometimes of human beings, and it usually does not provoke strong reactions, if any, in the host.

Applying the findings of the eye lesions of the armadillos to human patient treatment may not be done directly. But since we saw small amounts of cell infiltrations around the anterior chamber angle, and some free cells in the chamber with acid-fast bacilli in them, and as the early lesions in the intraocular tissues showed no obvious inflammatory reactions in the iris in the armadillos, we may suggest that the early lesions in human eyes could also be similar to those seen in the armadillos. Other findings in the eyes of armadillos infected with *M. leprae* are also similar to the eye complications in leprous patients. As in humans, the ocular involvement is mostly symmetrical, just as it happens that 94% of the armadillos showed similar grades of ocular involvement in both eyes.[12] The inflammation of the *M. orbicularis* has been shown by electromyography[13] and is one of the reasons for lagophthalmus. And if the lacrimal gland in humans were involved in the disease as in the animal, it must be expected that tears are infectious, especially in multibacillary patients. We cannot say whether the inflammatous infiltrations of the extraocular muscles may cause paralysis in armadillos, but in humans such complications have not been observed.

The early, distinct involvement of the anterior segment, of the trabecule and of the ciliary body in the armadillo eye is very similar to the situation in the human eye. This is also true for the presence of AFB in the aqueous humor.[14] Keratitic precipitates and iritis are common in leprous patients too.[15] The way in which the AFB enter the eyeball has often been discussed, but we would like to emphasize that the AFB may also leave the eye via nerves or vessels, as shown in the armadillos. Scleritis is also a common eye complication in leprosy in humans. However, in the lens of inactive leprous patients no AFB were found.[16] To the best of our knowledge the lens of active multibacillary cases have not been examined with that in mind. Similar to leprosy in humans,[17,18] the involvement of the posterior segment has been observed in only a few cases.

Our findings, according to which the grade of the lesion in the eye of the armadillo was correlated with the number of AFB found in it, may not easily be transferred to ocular leprosy among humans. Therefore we think that routine studies of eye tissues taken from patients during surgery, like iridectomies, cataracts, enucleations and other operations including autopsies, would be much more useful than the study of eyes of an animal in the prevention of blindness and for the elucidation of ocular problems in leprosy patients.

Acknowledgments

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Experiences with *Mycobacterium leprae* soluble antigens in a leprosy endemic population

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Summary Rees and Convit antigens prepared from armadillo-derived *Mycobacterium leprae* were used for skin testing in two leprosy endemic villages to understand their use in the epidemiology of leprosy. In all, 2602 individuals comprising 202 patients with leprosy detected in a prevalence survey, 476 household contacts and 1924 persons residing in non-case households were tested with two antigens. There was a strong and positive correlation ($r = 0{\cdot}85$) between reactions to the Rees and Convit antigens. The distribution of reactions was bimodal and considering reactions of 12 mm or more as 'positive', the positivity rate steeply increased with the increase in age. However, the distributions of reactions to these antigens in patients with leprosy, their household contacts and persons living in non-case households were very similar.

These results indicate that Rees and Convit antigens are not useful in the identification of *M. leprae* infection or in the confirmation of leprosy diagnosis in a leprosy endemic population with a high prevalence of nonspecific sensitivity.

Introduction

There are several unanswered questions in the epidemiology of leprosy. There has been a long-felt need for a test that could recognize infection with *Mycobacterium leprae* and thereby serve as a marker for the postinfection phase.[1] Lepromin testing does not fulfil this need because studies[2] have shown lepromin positivity in leprosy non-endemic populations, as well as its occurrence on account of other mycobacterial infections. Also, it is widely believed that the late lepromin reaction (Mitsuda reaction), which serves as a tool to classify patients with leprosy,[3] helps to identify persons susceptible to the lepromatous form of leprosy.[4,5] Reaction to lepromin is expected to be negative in such persons, although infected with *M. leprae*. In addition, lepromin has been documented as a miniature vaccine.[6] Drs Rees and Convit have prepared soluble antigens from *M. leprae* of armadillo origin, known as Rees and Convit antigens, which have been used in different parts of the world to understand their use in the epidemiology of leprosy.[7] Rees

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and Convit antigens were supplied to our Unit by the IMMLEP programme of the World Health Organization. After obtaining the necessary clearance from the Drugs Controller of India, we used these antigens for skin testing in a leprosy endemic population, and our findings are reported here.

This study was particularly relevant to us as our Unit is proposing to undertake a leprosy vaccine trial. Identification of *M. leprae* infected population and also the population at risk of suffering from leprosy, particularly the multibacillary form, will be highly relevant in a leprosy vaccine trial situation.

Materials and methods

This work was done during the period February to April 1987, in a population of 2602 persons from two leprosy endemic villages in Sriperumbudhur Taluk of Chengalpattu District in Tamil Nadu. Initial screening for leprosy prevalence in this population was done by trained paramedical workers. All the suspects and cases of leprosy detected by the paramedical workers were reexamined by a medical officer or one of two senior technical assistants, who had more than 15 years experience and had been trained in standardized clinical diagnosis of leprosy. Diagnosis of leprosy was based on clinical parameters and was supported by skin-smear examination for acid-fast bacilli. Patients were classified into different types following the system adopted by the Indian Association of Leprologists.[8] In Chengalpattu District, BCG immunization was not undertaken by the health services, as this district was kept free from BCG coverage. However, each person was examined by a trained technician for the presence or absence of a BCG scar and the result recorded.

In the various observations reported here, the following antigens were used for skin tests:

(1) Tuberculin PPD (RT 23, 1 TU per dose) from BCG Vaccine Laboratory, Madras.
(2) Rees antigen (Batch CD-19), supplied by Dr Rees (1 mcg protein per dose).
(3) Convit antigen (Batch SA-IND, 1.16.86) supplied by Dr Convit (dose as standardized by Dr Convit).

For skin testing and reading standard procedures were followed.[9] Skin testing was done by an assessed tester by superficial intracutaneous injections of 0·1 ml of antigens. Tuberculin test was given on the mid-volar side of the left forearm. Rees and Convit antigens were randomly allocated to the upper dorsum of the two forearms. Reactions to Rees and Convit tests were read after 48 hr and that to the tuberculin test after 72 hr. The interval of 48 hr for Rees and Convit antigen readings was based on our previous experience, where we took serial readings after 24, 48 and 72 hr.[10] Tuberculin skin tests are routinely read after 72 hr.[9] Transverse diameters of the indurations were measured in millimetres, by an experienced reader. The same tester and reader were used throughout the study. Skin testing was done in all age and sex groups, excluding infants up to the age of 1 year.

After initial standardization studies for skin testing,[10] about 2400 individuals from one village (TT01) were tuberculin tested and read. Three months later, Rees and Convit antigen skin tests were performed in the same population. Data from 888 individuals who were tested and read for all the three skin test antigens, tuberculin, Rees and Convit, has

been used to compare the skin test reactions to these three antigens. In this village 126 individuals were tested and read for the Rees and the Convit antigens, but not for tuberculin.

Skin testing was performed using Rees and Convit antigens in an adjoining village (TT02). Tuberculin was not used in this village.

The skin test responses to the Rees and the Convit antigens were studied in the population from both the villages with respect to age, sex, clinical evidence and type of leprosy, as well as according to the household contact status with leprosy patients. From village TT01, 96 patients, 143 household contacts of these patients and 812 individuals living in households without a case of leprosy were test read. From village TT02, these figures were 106, 333 and 1112 respectively. In all, 2602 individuals, comprising 202 clinically diagnosed patients with leprosy during the prevalence survey, 476 household contacts of these patients and 1924 individuals living in households without a case of leprosy were tested and read for the Rees and Convit antigens. Of the 476 household contacts, 444 individuals were contacts of paucibacillary cases and 32 were contacts of multibacillary cases.

Results

COMPARISON OF REACTIONS TO REES AND CONVIT ANTIGENS AND TUBERCULIN

Correlation between reactions to Rees and Convit antigens in 888 individuals from village TT01 is presented in Table 1. There was a strong and positive correlation between the two indurations with a correlation coefficient of 0·85 which was statistically highly significant ($p < 0{\cdot}001$). However, the mean size of reaction to Rees antigen (14·1 mm) was slightly higher than that to the Convit antigen (12·8 mm). The mean difference between the two reaction sizes was 1·2 mm ($p < 0{\cdot}001$). This relationship was similar in different age and sex groups as well as in patients and their household contacts. The relationship was also similar in the 1551 individuals from village TT02 (correlation coefficient 0·80; $p < 0{\cdot}001$).

Similar comparisons were made between reactions to Rees antigen and tuberculin, as well as between reactions to Convit antigen and tuberculin in the 888 individuals from

Table 1. Correlation between reactions to Rees and Convit antigens in 888 individuals from village TT01

Reaction to Rees antigen	Reaction to Convit antigen (mm)							
	0–3	4–7	8–11	12–15	16–19	20–23	24–27	Total
00–03	14	4	5	—	1	—	—	24
04–07	11	140	18	3	1	1	—	174
08–11	1	35	46	18	4	1	—	105
12–15	3	14	35	77	23	5	—	157
16–19	2	5	11	75	126	13	1	233
20–23	—	—	2	17	91	35	7	152
24–27	—	—	—	—	7	25	10	42
28–31	—	—	—	—	—	—	1	1
Total	31	198	117	190	253	80	19	888

village TT01 (Table 2). It was seen that there was a positive but weak correlation between reactions to Rees antigen and tuberculin (correlation coefficient 0·44; $p < 0·01$) as well as between reactions to Convit antigen and tuberculin (correlation coefficient 0·44; $p < 0·01$). The mean difference in sizes of reaction to Rees antigen and tuberculin was 2·7 mm ($p < 0·001$) and that between Convit antigen and tuberculin was 1·5 mm ($p < 0·001$).

Bimodality in the frequency distributions was seen for all the three antigens with the antimode at 8–11 mm (Figure 1). In analogy with tuberculin reactions, considering the first curve with reactions of 0–11 mm to represent 'reaction negative' individuals and the second curve with reactions of 12 mm and above to represent 'reaction positive' individuals, the proportions with 'positive' reactions to the Rees and the Convit antigens were 66% and 61% respectively. This difference was statistically significant ($p < 0·05$).

Comparison between reactions to the Rees antigen and tuberculin showed that, in general, Rees antigen positivity was higher in the tuberculin positive individuals. Patients of leprosy as well as individuals in whom BCG scars were present were excluded for the sake of this comparison. The results are based on skin test reactions in 702 individuals. It was seen that in the younger age group of 1–9 years, the Rees antigen positivity was much higher among tuberculin positives (66%) as compared to that among tuberculin negatives (24%). This difference was statistically highly significant ($p < 0·001$). However, in the higher age groups the differences were small and not statistically significant.

In the village TT01, 126 individuals who were not tested for tuberculin were tested and read for the Rees and Convit antigens. Distributions of reactions to the Rees and the Convit antigens in these individuals were very similar to the ones in the 888 tuberculin

Table 2. Correlation between reactions to Rees, Convit antigens and tuberculin in 888 individuals from village TT01

Reaction (mm) to	Reaction to tuberculin (mm)							
	0–3	4–7	8–11	12–15	16–19	20–23	24–27	Total
Rees antigen								
00–03	5	3	3	5	6	2	—	24
04–07	59	79	3	10	14	5	4	174
08–11	21	42	7	8	16	10	1	105
12–15	10	50	21	29	33	12	2	157
16–19	12	49	28	48	69	21	6	233
20–23	4	12	9	40	66	18	3	152
24–27	1	2	3	7	23	6	—	42
28–31	—	—	1	—	—	—	—	1
Total	112	237	75	147	227	74	16	888
Convit antigen								
00–03	4	6	4	5	8	4	—	31
04–07	68	87	4	12	21	2	4	198
08–11	14	54	10	10	17	11	1	117
12–15	13	52	24	41	38	21	1	190
16–19	9	31	25	60	95	23	10	253
20–23	4	6	7	16	36	11	—	80
24–27	—	1	1	3	12	2	—	19
Total	112	237	75	147	227	74	16	888

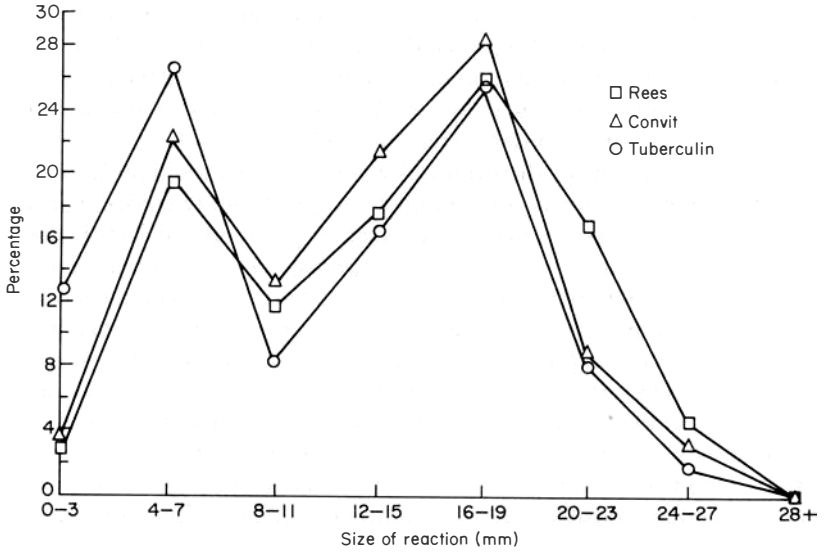

Figure 1. Distribution of the 888 persons by size of reaction to Rees and Convit antigens and tuberculin.

tested individuals. The mean reaction sizes for the Rees antigen were 14·3 mm and 14·1 mm and that for the Convit antigen 12·9 mm and 12·8 mm in the two groups of 126 and 888 individuals respectively. The proportion of individuals with positive reactions were also very similar in the two groups. 67·5% of the tuberculin tested and 65·9% of those not tested with tuberculin gave positive reactions to the Rees antigen. Similar figures for the Convit antigen were 62·7% and 61·0% ($p > 0{\cdot}5$, in both cases).

INFLUENCE OF BCG SCAR ON REES ANTIGEN POSITIVITY

The 2602 individuals from the two villages who were Rees antigen tested and read were also examined for the presence of a BCG scar. As mentioned earlier, this area was kept free from routine BCG vaccination and as such the prevalence of BCG scars was low. By the age of 10 years a high proportion of persons (68%) were showing Rees antigen positivity, and only children aged 1–9 years were considered in the study of the influence of BCG scars on the Rees antigen positivity. Of the 688 children aged 1–9 years who had been examined for BCG scars, 79 (11·5%) had BCG scars. Eighteen (22·8%) of the 79 with a BCG scar and 173 (28·4%) of the 609 without a BCG scar showed Rees positivity. This difference was not statistically significant ($p > 0{\cdot}2$).

It was also seen that the tuberculin positivity was similar in persons with a BCG scar and in those without. Considering the age group 1–9 years, 15 (11·2%) of 134 with a BCG scar and 54 (10·5%) of 515 without a BCG scar showed positive reactions to tuberculin ($p > 0{\cdot}9$).

REES SKIN TEST POSITIVITY IN PATIENTS AND NON-PATIENTS OF LEPROSY

Skin test results from the two villages with respect to the positivity to the Rees antigen was marginally different. It was slightly higher in village TT01 as compared to that in village

TT02. This difference was consistent in different groups of individuals (Table 3). However, distributions of reactions to the Rees antigen in both the villages were similar and bimodal with the antimode at 8–11 mm. Therefore, the information from the 2602 individuals in the two villages is merged for studying the pattern of reactions to Rees' antigen. Considering 12 mm and above as the criterion for positivity, 11·9%, 41·8%, 68·0% and 76·9% were 'positive' to Rees antigen in the age groups 1–4, 5–9, 10–14 and 15+ years, respectively. Figure 2 provides the information on Rees skin test positivity in different age groups separately for the 202 patients with leprosy, 476 household contacts of these patients and 1924 individuals living in households without leprosy.

Of the 202 patients, only 14 (7%) had multibacillary forms of leprosy and thus only 32 of the 476 household contacts were contacts of patients with multibacillary leprosy. Fourteen (43·8%) of the 32 contacts with multibacillary leprosy and 270 (60·8%) of the 444 contacts of patients with paucibacillary leprosy were 'positive' to the Rees antigen. This difference was not statistically significant ($0{\cdot}10 > p > 0{\cdot}05$). The Rees antigen positivity was 22·2% (4 of 18) and 41·2% (84 of 204) in the age group 1–14 years and 71·4% (10 of 14) and 77·5% (186 of 240) in the age group 15+ years in the contacts of multibacillary and paucibacillary cases respectively. These differences were also not statistically significant ($p > 0{\cdot}1$).

Considering the 202 patients with leprosy, frequency distributions of Rees antigen skin indurations are given separately for the different types of leprosy in Table 4. The bimodality of the distribution is observed in patients with leprosy as well. This bimodality is also seen in patients with tuberculoid and the borderline tuberculoid types. Amongst 14 patients with borderline or lepromatous leprosy, 4 showed reactions of 12 mm or more though there was no tendency for bimodal distribution. Since the significance of smaller reactions to the Rees antigen may be different from that to tuberculin, while comparing the results of Rees' antigen test in patients and non-patients of leprosy, the entire range of reactions were considered. Thus, when the frequency distributions (age and sex

Table 3. Rees antigen positivity (% with 12+ mm) according to age in the two villages

		Age group (in years)						
Village	Population	1–4	5–9	10–14	15–24	25–34	35+	Total*
TT01	Patients	—	47·8	63·7	80·0	93·1	78·2	66·5
		(2)	(11)	(15)	(20)	(16)	(32)	(96)
	Contacts	12·7	50·0	61·8	78·4	100·0	78·6	69·1
		(23)	(24)	(16)	(27)	(20)	(33)	(143)
	Others	13·1	43·5	70·5	79·8	84·9	85·1	69·0
		(110)	(123)	(124)	(152)	(116)	(187)	(812)
TT02	Patients	—	50·1	87·3	70·7	74·3	67·0	61·2
		(4)	(10)	(11)	(24)	(18)	(39)	(106)
	Contacts	11·0	49·6	57·4	74·9	91·0	67·7	62·9
		(53)	(54)	(52)	(60)	(32)	(82)	(333)
	Others	11·8	35·6	67·9	73·1	76·1	74·8	61·9
		(136)	(149)	(140)	(226)	(147)	(314)	(1112)

Figures in parentheses give denominators.
* Age-sex standardized.

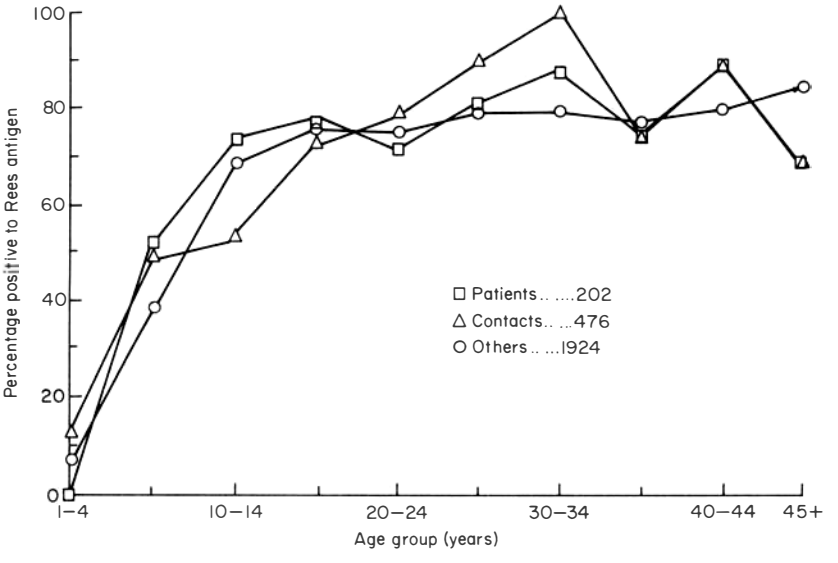

Figure 2. Rees skin test positivity (%) in patients, contacts and others by age.

Table 4. Distribution of leprosy patients by size of reaction to Rees' antigen

Type of leprosy	Size of reaction (mm)							
	0–3	4–7	8–11	12–15	16–19	20–23	24–27	Total
Neuritic	2	5	2	5	3	6	2	25
Indeterminate	1	8	3	13	8	5	3	41
TT and BT	3	16	10	30	32	19	12	122
BL and LL	3	3	4	2	1	1	0	14
Total	9	32	19	50	44	31	17	202

standardized) of Rees antigen indurations for the patients, contacts and the general population (excluding patients of leprosy and contacts) from the two villages were considered, the similarity in the distributions was very striking (Table 5). All the three groups gave a bimodal distribution with the antimode at 8–11 mm (Figure 3).

Discussion

Preparation of *M. leprae* soluble antigens was being viewed as a promising development to detect subclinical *M. leprae* infections. Studies in Venezuela by Convit indicated that the soluble antigen developed by him from the armadillo-derived *M. leprae* would meet the requirements and would be sufficiently sensitive and specific for epidemiological field studies.[11] IMMLEP–TDR under the World Health Organization encouraged studies using these antigens in several worldwide areas.[11]

Table 5. Proportion (%)* of patients and nonpatients of leprosy by size of reaction to Rees antigen

	Reaction to Rees (mm)								
Population	0–3	4–7	8–11	12–15	16–19	20–23	24–27	28–31	Total
Patients	4·0	23·9	8·7	22·3	20·5	13·2	7·4	—	100
Contacts	3·6	19·6	12·0	18·1	23·8	18·8	3·6	0·5	100
Others	4·2	19·7	11·6	18·1	25·9	15·7	4·6	0·2	100

* Age–sex standardized rates.

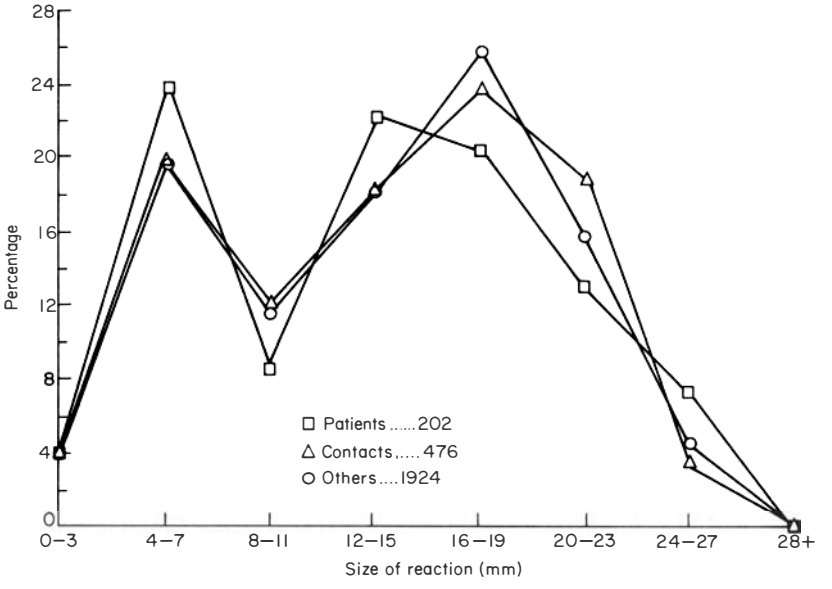

Figure 3. Distributions (age–sex) of patients, contacts and others by size of reaction to Rees antigen.

In the findings reported here, care was taken to avoid the methodological problems on account of batch-to-batch variations and variations due to multiple testers and readers. We found a positive and very high degree of correlation between reactions to the Rees and Convit antigens. The findings were similar in different age and sex groups as well as in patients and contacts of the patients. Since the two antigens were calibrated to different standards, the mean difference of 1·2 mm in the skin-test reactions to the Rees and Convit antigens may just be a dose effect and as such not biologically significant. For the various results presented, for patients, contacts and population, the information is given on the Rees antigen, but the results were very similar for the Convit antigen as well.

In the study reported here, we used CD-19 batch for the Rees antigen and SA-IND, 1-16-86 for the Convit antigen. We have observed earlier, in two independent experiments, that the correlation between reactions to two different batches (CD-19, CD-73) of the Rees antigen was much stronger ($r = 0{\cdot}81$ and $0{\cdot}77$) than that observed for two different batches (SA-IND, 1-16-86 and IB-Lote, 4-6-87) of the Convit antigen ($r = 0{\cdot}53$ and

0·66).[10] One study[12] observed a positive correlation ($r = 0·7$) between postvaccination reactions to Rees (CD-19) and WEL-1 (an antigen prepared using the protocol for Convit antigen) antigens although the responses to WEL-1 antigen were uniformly lower than that to the Rees antigen. They also found that the WEL-1 antigen did not produce pre-vaccination induration in the vast majority of the individuals tested. The protein content of WEL-1 and Rees antigens was 0·5 mcg and 1·0 mcg per dose, respectively.[12] It is difficult to say whether the high degree of correlation observed by us between reactions to Rees and Convit antigens was limited to the particular batches used or the observed dissimilarity on the other occasions was due to variations in the calibration procedures for the Convit antigen. Considering the magnitude of positive correlation observed between reactions to the two antigens, both by us and by Ponnighaus and Fine, the observed differences might be on account of dose or calibration effect.

In the 888 individuals skin tested with Rees, Convit and tuberculin antigens, a low level of positive correlation was seen between reactions to the Rees antigen and tuberculin, as well as between reactions to the Convit antigen and tuberculin. It was seen that this association was significant in the younger age group of 1–9 years only. However, even in this age group as many as 24% of children who were tuberculin negative showed positive reactions to the Rees antigen. It appears that the tuberculin status of an individual would affect the Rees antigen positivity only marginally and also only in the younger children in the study area. Thus tuberculin positivity was at most only partially responsible in producing cross-sensitization to the Rees antigen. It was also seen that prior tuberculin testing did not seem to influence the pattern of reactions to a subsequent test with the Rees antigen.

The differences observed in the two villages with respect to the Rees and the Convit antigen reactions were marginal, though statistically significant (Table 3). The frequency curves, however, followed the same pattern and in all probability the observed difference did not have any biological significance.

The BCG scar status did not influence reaction to Rees antigen in our study. Convit and Zuniga in Venezuela and Fine and Ponnighaus in Malaŵi found cross-sensitization on account of BCG scar status.[7] One study[13] in Sri Lanka did not find any such influence, another study[14] in Agra, India observed that the previous BCG scar status did not influence the leprosin-A (Rees antigen) results in the children studied. However, in a prospective study, they found an increase in the Rees antigen positivity following BCG vaccination.[14] Also, it was seen in our study that even the tuberculin reactions did not depend on the BCG scar status. However, it should be noted that the population in Chengalpattu District was kept free from BCG vaccination programme, and the proportion of persons with a BCG scar was less than 10%. The practice generally followed in India is BCG vaccination at birth. The waning of tuberculin sensitivity after BCG has been documented in Chengalpattu District.[15–16] In a study in Madras city, it was observed that the post-BCG tuberculin sensitivity in newborn babies waned considerably over a period of 12 months.[17] In a study in Sri Lanka involving 740 healthy children given a BCG vaccination in their first month, it was seen that 80% of the children showed tuberculin anergy in spite of having a visible scar.[18] A similar waning effect may also be expected on cross-sensitization, if any, for the Rees antigen.

We obtained a consistent bimodal pattern with both the Rees and the Convit antigens (Figure 1). Based on this pattern, we considered reactions of 12 mm or more as 'positive'. With this cut-off point, 73% (138 of 188) of patients with paucibacillary leprosy were Rees

antigen positive while 71% (10 of 14) of patients with multibacillary leprosy were Rees antigen negative. The cut-off point used by various workers for defining positivity have been different. In the Malawian studies, despite observing a clear bimodal distribution, the investigators arbitrarily called reactions of > 5 mm as 'positives'.[12] The criterion for positivity adopted for the Convit antigen reactions by Convit and his colleagues was 10 mm or more.[19] Stanford and Lema considered indurations of 2 mm or more as a positive response.[20] Different definitions adopted by various investigators will certainly contribute to the observed differences with respect to positivity. The frequency distributions of reactions to the soluble antigens appear to follow different patterns in different areas.[13,21,22] Prevalence of environmental mycobacteria and other organisms, prior vaccination with BCG as well as infection with *M. leprae* are some of the likely causes to affect these distribution patterns.

Results from earlier studies indicate that these antigens might be useful for classification of leprosy and in identifying the population at a high risk for multibacillary leprosy. Data from Malaysia and India showed that patients with lepromatous leprosy were uniformly negative to Rees antigen while tuberculoid patients were positive.[7] Samuel *et al.* have concluded from their work in five different countries, namely India, Uganda, Kenya, Nepal and Bhutan, that the Rees antigen (Leprosin-A) reactions were positive in the high resistant forms of leprosy and were negative in low resistant lepromatous forms.[23] Ponnighaus and Fine also found that 80% of untreated paucibacillary patients with leprosy in Malawi gave positive skin test reactions (> 5 mm) to a Rees-type antigen, whereas, only 35% of a sample of treated patients were positive. All the multibacillary patients, although only a few, were skin test negative.[7] Convit had reported similar results with his antigen in Venezuela.[7] These findings with the soluble antigens are similar to the Mitsuda reaction to lepromin test in leprosy patients.

In the present study we noticed that Rees antigen positivity was 64·0%, 70·7% and 76·2% in neuritic, indeterminate and the TT–BT groups of patients respectively. In the BL–LL groups of patients, however, it was only 28·6%. Thus the skin test results in the study patients from South India followed a similar pattern as reported by other workers. However, the capacity of the Rees antigen to classify the leprosy patients into two groups, paucibacillary and multibacillary, was limited and the dividing line was blurred. Fifty (27%) of the 188 paucibacillary patients were 'negative' and 4 (29%) of the 14 multibacillary patients were 'positive' to the Rees antigen test.

We observed that the distributions of reactions to both the Rees and Convit antigens were bimodal. This observation was true for patients with leprosy, their household contacts, as well as the general population. It was seen that the reaction positivity to the Rees antigen increased sharply with the increase in age in both males and females. Generally, the reaction positivity was higher in males than in females. It is to be expected that the risk of infection will increase with age. However, it is difficult to conceive such a steep rise with age on account of the new infections due to *M. leprae* alone. The similarity in the distributions of reactions to Rees antigen in patients with leprosy, their household contacts and general population became strikingly demonstrable when the age and sex standardized proportions in different reaction sizes were considered (Table 5 and Figure 3). The Rees reaction positivity was also very similar in patients, contacts of both paucibacillary and multibacillary patients with leprosy, and general population in different age groups (Figure 2). In this respect, our results are different from the observations of Convit and Zuniga in Venezuela. Convit and Zuniga extensively used the

M. leprae soluble antigen (Convit antigen) in Venezuela. Their initial objective was to have a test comparable to the lepromin test. They also hoped that the Convit antigen would be useful to determine prevalence and incidence of infection due to *M. leprae*. They found that the prevalence of Convit skin test positivity correlated with the level of prevalence of leprosy in the population. Only 3·5% individuals were positive in nonendemic areas of Chile compared to 46% positives in endemic areas of Venezuela. Contacts of leprosy patients showed higher levels of positivity than that in the general population.[7] Extensive studies have also been done in Malaŵi using the *M. leprae* soluble antigens. Fine *et al.* found a clear bimodal distribution of the skin reactions in the Northern Malaŵi population endemic for leprosy. Based on the rising prevalence rate of positivity with age, they postulated that the skin tests were specific for some mycobacterial experience.[21]

In a study in Bangladesh, Cree *et al.* observed that the Rees antigen (CD-19) positivity ($\geq$5 mm) was similar in 78 household contacts of untreated patients, 34 untreated paucibacillary patients and 50 randomly selected indigenous subjects. It was 56·6%, 56·3% and 55·6% in the three groups respectively.[24]

In a population based study in Sri Lanka, Pinto *et al.* did not find any statistically significant changes in Rees' antigen (CD-19) positivity with respect to age, sex, race or BCG vaccination status.[13]

It is difficult to explain the differences observed in the results of these studies. However, the possible reasons could be the use of different batches of antigens, prevalence of different levels of leprosy endemicity and nonspecific sensitization, as well as the differences in the populations studied.

Variations observed in some of the studies mentioned above could be explained as due to the substantial amount of variations in the skin reactions produced by different batches of these antigens. Such batch-to-batch variations have been observed and documented by us.[10] Similar observation is also reported by Fine *et al.* in the Malaŵi studies.[21] Considerable batch-to-batch variability of skin test antigens was also observed in Venezuela.[7] Rees antigen batch CD-19 was used by us in the study reported here. This batch has been extensively used in different parts of the world. Pinto *et al.*,[13] Cree *et al.*[24] and Ponnighaus & Fine[12] used the same batch in their studies in Sri Lanka, Bangladesh and Malaŵi respectively. The results in these studies varied with respect to the frequency distributions of skin test responses in different groups of populations. The batch-to-batch variations alone, therefore, cannot explain the different patterns of skin test responses to these antigens.

It was also noted that the skin test indurations produced by the Rees and Convit skin tests were extremely soft and needed a considerable amount of training even for standard readers experienced in reading tuberculin reactions.[10] Ponnighaus & Fine, using Rees antigen (batch CD-19) found almost spontaneous conversions and reversions in a substantial proportion of the subjects retested.[12] This problem would also therefore contribute to the differences observed in the various studies.

The leprosy epidemiological situation in Venezuela is different in comparison to that in other areas. Leprosy prevalence in Venezuela is relatively low. There was only one active case under control per thousand population in 1981.[25] In Venezuela it is reported that the leprosy problem has rapidly declined over the past three decades and that there is a relative increase in the proportion of multibacillary cases.[25] In the Malaŵi vaccine trial area, prevalence of clinical leprosy is found to be about 5 per thousand and multibacillary

cases constitute about 7% of these cases.[26] In our study area the prevalence of leprosy is around 40–50 per thousand population and about 7% of these cases are of the multibacillary type.

Categorization of the population into leprosy patients, their contacts and general population in the present study was based on a prevalence survey. It is possible that some individuals who might have been leprosy cases and in whom leprosy lesions had completely resolved at the time of the prevalence survey were considered as non-cases. The majority of the leprosy patients in the study were of the paucibacillary type, only 7% belonged to the multibacillary type. As such the majority of the 'contacts' belonged to households with paucibacillary patients. However, the pattern of reactions in contacts of multibacillary patients was similar to that in contacts of paucibacillary patients. Since the number of contacts of patients with multibacillary leprosy was small and Rees antigen positivity in them was not significantly different from that in other contacts, all the contacts were considered as one group.

Our study area is adjacent to Thiruvallur Taluk in Chengalpattu District, where a BCG prophylaxis trial against tuberculosis and leprosy was conducted, and which had a high prevalence of nonspecific sensitivity.[15] Thus the study area is expected to have a high level of nonspecific sensitization. Studies carried out in different parts of India have demonstrated that nonspecific sensitization is not restricted to Chengalpattu District alone, but is a widespread phenomenon. In the temperate zone the population at higher altitudes had a lower prevalence of nonspecific sensitivity than that among the population in the plains. In the tropical zone, prevalence of nonspecific sensitization was high,[27–29] however, even in Kashmir valley, situated about 1650 m above the mean sea level, prevalence of nonspecific sensitivity was 59%.[30] It is difficult to say to what extent the existing high level of nonspecific sensitization in the study area would have influenced the pattern of results to the skin-test antigens observed by us.

To sum up, the results of the study reported here clearly show that the Rees and the Convit antigen skin tests are not sensitive enough to detect leprosy, they do not appear to be specific enough to confirm the clinical diagnosis of leprosy. Since the present study was conducted in a leprosy endemic area, the differences between contacts of leprosy patients and the general population might not be evident. Almost every individual in the study population was exposed to the *M. leprae* infection. However, the pattern of reactions to these antigens seen in patients and the almost identical pattern observed in other population groups, raise serious doubts about their use in detecting *M. leprae* infection in a leprosy endemic population with a high prevalence of nonspecific sensitivity.

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Lepr Rev (1990) **61,** 145–150

Serodiagnosis of leprosy in patients' contacts by enzyme-linked immunosorbent assay

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Summary Serum samples from 3336 contacts of leprosy patients were tested for antiphenolic glycolipid I antibodies by enzyme-linked immunosorbent assay with the albumin coupled synthetic disaccharide antigen. The overall positivity rate was 9·3%. No significant differences were seen between a group of household contacts of lepromatous patients and those of the other types of the disease. The proportion of ELISA positives was slightly higher in the relatives as compared to workplace contacts and neighbours but significantly different only between the two former ($p < 0{\cdot}05$). Among those contacts with absorbance values higher than 0·100, 5 new leprosy patients were diagnosed, 2 of them with positive skin smears. A sixth contact was detected with a very high absorbance value in whom no single skin lesion was found but whose lepromin reaction was 0 mm and the skin smear showed a bacteriological index of 3+.

Introduction

It has been suggested that since modern chemotherapy rapidly reduces the number of viable *Mycobacterium leprae* spread by an individual, the major source of leprosy transmission is likely to be individuals who do not yet have symptoms.[1] One of the principal goals of leprosy research is to develop tests that will allow identification and early treatment of such individuals, aimed at reducing transmission of the disease.[1] The incorporation of early diagnosis, especially of multibacillary cases, to the activities of integrated control programmes through appropriate methods of case finding is among the specific approaches considered by WHO to prevent and control leprosy.[2]

However, early diagnosis may not always be easy to attain. Symptoms of leprosy are very often absent or minimal, particularly during the early stages of the disease, hence patients do not voluntarily seek relief through the health care system,[3] whereas, in other instances, individuals in whom the disease has already manifested do not look for medical care either because of the social stigma or lack of health education. On the other hand, contact surveillance identifies only a small proportion of the total number of new cases

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occurring in a community[3] and frequently in low endemic areas leprosy is not borne in mind, thus resulting in late diagnosis.

The isolation and chemical characterization of a *M. leprae* species specific antigen, the phenolic glycolipid I (PGI)[4,5] as well as the preparation of an artificial antigen containing the species specific moiety of PGI[6,7] have made the detection and study of anti-*M. leprae* specific antibodies possible by rather simple serological methods. It has been suggested that these antigens have considerable potential as tools in the serodiagnosis of subclinical stages of leprosy infection, early diagnosis of clinical disease and in detecting transmitters of infection.[8–10]

In this report data are presented from a trial based on the enzyme-linked immunosorbent assay (ELISA) using the albumin coupled synthetic disaccharide (ND-A-BSA) antigen to study anti-PGI antibody levels among contacts of leprosy patients and to seek for subclinical transmitters, cases with early clinical stages and individuals at risk of contracting the disease among those presumably infected.

Materials and methods

SERA

Serum samples from 3336 contacts were tested, of these, 660 were from household contacts, grouped according to the leprosy type (Madrid classification) of the index case, 2134 were relatives in whom no separation into household and non-household or leprosy type of the index case was made, 435 were workplace contacts and 107 were neighbours. They were all living in the province of Guantanamo, Cuba, where leprosy is highly endemic. Venous blood samples were taken, sera obtained and kept frozen at $-20°C$ until used.

ELISA

The procedure was the same as that described by Cho *et al.*[11] except that the antigen was not sonicated but dissolved directly in the buffer and added to wells of flexible PVC plates (Flow Laboratories). The ND-A-BSA antigen was obtained from IMMLEP (Gigg DISSACH). The conjugate reagent was goat anti-human IgM-peroxidase conjugated IgG fraction (Cappel Laboratories). The absorbance was read at 492 nm in a Titertek Multiskan MC or in an Organon Technika reader. A serum was considered 'positive' when the absorbance exceeded 0·160 since this value corresponded to the 98th percentile when 100 serum samples obtained from a Havana blood bank were tested to establish the cut-off level.

Dermatological and skin-smear examinations were performed in contacts who showed absorbance values above 0·100 and not in those with lower values. Mitsuda tests with lepromin A, obtained from G. W. Long Hansen's Disease Center, LA 70721, USA, were also included in the clinical study of 200 of such contacts.

Differences between proportions above the cut-off level among the groups of contacts were ascertained by the hypotheses test for two proportions and correlation was also done between the results of ELISA and Mitsuda tests.

Results

The overall ELISA positivity rate of all contacts tested was 9·3%. Table 1 shows the test results for household contacts grouped according to the leprosy type (Madrid classification) of the index case. No significant differences were seen between the contacts of lepromatous patients and those of the other types of the disease.

The data for other relatives (household and non-household), workplace contacts and neighbours of all leprosy patients are shown in Table 2. The proportion of ELISA positives was slightly higher in the relatives as compared to workplace contacts and neighbours but significantly different only between the two former ($p < 0{\cdot}05$).

The observed distribution of absorbance values is shown in Table 3. Of the total, 81·7% were below 0·100, 12·4% were in the range 0·101–0·200, 3·3% in the range 0·201–0·300 and 2·3% above 0·300. Hypochromic macules found in 2 (0·5%) of 417 contacts, in the range 0·101–0·200, hypoaesthetic in 1 of them, led to the diagnosis of indeterminate leprosy (patients 1 and 2). Hypochromic macules and a positive Fite–Faraco stained histological section found in 1 (4·7%) of 21 contacts in the range of 0·401–0·500 led to the diagnosis of the third indeterminate patient. In 1 (50·0%) of 2 in the range 0·701–0·800 clinical signs of lepromatous leprosy and a bacteriological index (BI) of 4+ were found (patient 4). Two contacts were found with absorbance values above 1·000, one of them with skin lesions and a BI of 2+ was diagnosed as a dimorphous leprosy whereas in the other one not a single skin lesion or other dermatological sign was found but the skin smear revealed a BI of 3+ (patients 5 and 6) Tables 3 and 4.

Mitsuda tests were performed in 200 contacts who showed an absorbance value higher than 0·100. The correlation coefficient (r) was $-0{\cdot}18630$ which is out of the $+/-$ 0·13808 critical interval for a $p = 0{\cdot}05$, thus a significant inverse correlation was proved between the lepromin reaction sizes and the absorbance values observed.

Table 1. ELISA results in household contacts grouped according to the leprosy type of the index case

Leprosy type of the index case*	Positive/Total	%
Lepromatous	38/350	10·8
Dimorphous	12/144	8·3
Indeterminate	10/123	8·1
Tuberculoid	5/43	11·6

* Madrid classification.

Table 2. ELISA results in other contacts of leprosy patients

Type of contact	Positive/Total	%
Relatives (household and non-household)	216/2134	10·1
Work place contacts	23/435	5·2
Neighbours	8/107	7·4

Table 3. Results of the serological tests, number of skin-smears performed and new cases detected

Absorbance level	Sera	Skin smears	Cases
<0·100	2728 (81·7)*	NE	NE
0·101–0·200	417 (12·4)	213 (51·0)†	2 (0·5)†
0·201–0·300	111 (3·3)	66 (59·4)	0
0·301–0·400	45 (1·3)	29 (64·4)	0
0·401–0·500	21 (0·6)	13 (61·9)	1 (4·7)
0·501–0·600	7 (0·2)	5 (71·4)	0
0·601–0·700	3 (0·08)	3 (100·0)	0
0·701–0·800	2 (0·08)	2 (100·0)	1 (50·0)
0·801–0·900	0	0	0
0·901–1·000	0	0	0
>1·000	2 (0·05)	2 (100·0)	2 (100·0)

NE, not examined.
*, percentage of the total number in brackets.
†, percentage of the number in the range in brackets.

Table 4. New leprosy cases diagnosed among contacts of leprosy patients

Patient	Leprosy type*	Mitsuda (mm)	ELISA	BI
1	Indeterminate	0	0·109	0
2	Indeterminate	3	0·125	0
3	Indeterminate	5	0·401	0
4	Lepromatous	0	0·755	4+
5	Dimorphous	0	2·125	2+
6	Subclinical infection	0	1·074	3+

* Madrid classification.

Discussion

The ELISA technique with the PGI or its semisynthetic analogues appears to be the most widely used system for the detection of anti-*M. leprae* specific antibodies at present. However not many reports on studies with high risk groups have been published so far. The overall serological positivity rate observed in this study (9·3%) was lower than that found by other workers in Mexico (23%) and Sri Lanka (33%),[12] but had the same definition of positivity ($A_{492} > 0·09$) been used by us it would have been comparable. It was close to those found by Douglas *et al.* (11·2%) in Cebu, Philippines[13] and by Chanteau *et al.* (12·8%) in French Polynesia.[14]

Contrary to what was expected, no significant differences were found between the proportions of positive household contacts grouped according to the leprosy type of the index case. It is likely that the contacts of paucibacillary patients may have been exposed

to the same infection sources of their index cases or to others in the community since they were living in a neighbourhood with a high prevalence rate (5·6 per 1000). Seropositivity in the relatives was higher than in the workplace contacts and neighbours but not statistically significant with respect to the latter. The fact that the group of neighbours was represented by persons living on the same block, where as many as 16 patients also lived, might account for this observation since it can be supposed that the risk of infection was high with so many patients in the vicinity.

Previous work with several immunological tests revealed that infection by *M. leprae* is much more frequent than the number of manifest clinical cases would indicate.[10] While the only accurate way of determining whether the test is useful as a serodiagnostic tool would be to examine clinically and bacteriologically all contacts. In the present study only those with absorbance values above 0·100 were chosen to be studied. The reason was that the work was aimed mainly at assessing the usefulness of the system, by testing serum samples from a rather large number of contacts, for detecting transmitters of infection who might be individuals who did not yet have physical signs and/or cases in very early stages of clinical manifestation, as well as for identifying those presumably infected who might be suspected of incubating multibacillary leprosy and, hence, might be potential transmitters. On the basis of accumulated data, it was assumed that subsequent multiplication of *M. leprae* after infection in such individuals would reach such a bacillary load that it would be reflected in absorbance values higher than 0·100.

In this study the majority of the positive individuals showed low absorbance values which might reflect normal immune responses to *M. leprae* exposures, a few false positive reactions as has been reported[6] and, in some cases, early stages of infection which could progress towards clinical disease. Much caution should be taken with the small number of contacts exhibiting high absorbance values since they are generally associated with multibacillary leprosy. In this connection the finding of a subclinically infected contact with acid-fast bacilli in his skin smears is of great interest, since this lends support to the assumption that these individuals may play an important role in the transmission of the disease.

It has been reported that this assay is not able to detect a high proportion of paucibacillary patients without considerable loss of specificity.[15] However, the usefulness of the system as a test for leprosy infection and its use for control purposes should be discussed in relation to particular epidemiological situations and to the quality of the control programme. There is evidence that the distribution of the different types of the disease may vary between different populations.[16] In Cuba, the proportion of multibacillary leprosy (lepromatous and dimorphous in the Madrid classification) reaches about 50% of the annually detected cases.[17] Therefore, in areas with a relatively high prevalence of multibacillary leprosy, the value of this tool for screening purposes may be important in terms of leading to the detection of a number of early cases and the identification of presumably infected individuals who could be examined and followed up. In addition, the administration of chemoprophylaxis to these latter subjects could also be evaluated.

Acknowledgments

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Evaluation of five treatment regimens, using either dapsone monotherapy or several doses of rifampicin in the treatment of paucibacillary leprosy

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Summary The objective of the present study was to define short-course treatment regimens for PB leprosy and to compare them with the 'classical' dapsone treatment and the WHO–PB regimen. Five treatment regimens were studied and evaluated by the histologic evolution. The regimens were: (1) dapsone 100 mg daily, non-supervised for 3 years; (2) RMP 900 mg supervised, once weekly, 8 doses; (3) idem 12 doses; (4) RMP 600 mg, once monthly, supervised, 6 doses and during this treatment dapsone 100 mg daily unsupervised; (5) RMP 600 mg together with dapsone 100 mg daily, supervised for 6 days. For each of these regimens there were between 114 and 195 person-years of follow-up.

Results are comparable for the 5 treatment regimens, and reach 65–75% cure rates at 36 months and 80–90% at 48 months after the start of therapy. The relapse rate for all groups is about 0·5% per year. The difficulty for the diagnosis of relapse in PB leprosy is discussed.

It is concluded that treatment of PB leprosy can be relatively simple but that a relatively long time is needed to evaluate its effect.

Introduction

Paucibacillary (PB) leprosy patients are estimated to harbour no more than 10^6 *Mycobacterium leprae*.[1] This is 100 to 1000 times lower than the frequency of naturally appearing rifampicin resistant mutants,[2] allowing treatment of PB leprosy with rifampicin (RMP) monotherapy. Furthermore, the potent and rapidly bactericidal activity of RMP allows evaluation of the efficacy of short-course antibacterial treatment regimens in PB leprosy.

In a previous study performed in Burundi and Addis Ababa[3,4] 900 mg RMP was administered once a week during 8 weeks to a small number of patients.

In a later study RMP was administered weekly during 10 weeks, in 900 mg doses in

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Zaire, Rwanda and Burundi and 600 mg doses in the Comores, with very satisfactory results.[5] In the meantime there was a possibility to conduct at the Institut Marchoux in Bamako, Mali, a prospective randomized study on the efficacy, in PB leprosy, of 8 and 12 weekly doses of 900 mg RMP compared with the 'classical' dapsone (DDS 100 mg daily) during 3 years. In a second study in Bamako started in 1984, 2 treatment regimens were compared: the WHO–PB regimen[6] and the same regimen administered during 6 days instead of 6 months.

The results of both these studies are presented in this paper.

Patients and methods

The patients presenting at the Institute Marchoux, Bamako, had a clinical, neurological and bacteriological examination, the results of which were entered, together with the disability scores on a standard form. A copy of this, together with a skin biopsy fixed in 10% formalin were sent to Antwerpen.

Patients were classified as PB when they had clinical TT or BT leprosy, a bacterial index (BI) of no more than 1+ in none of 5–6 skin smears (2 earlobes and 3–4 other skin sites: one or two lesions, the lumbar region and front or chin), and if the skin biopsy showed a TT or BT lesion with a BI not higher than 1.

After informed consent patients were allocated to the different groups by the use of numbered envelopes containing computor randomized treatment regimens.

The regimens were:

DDS: dapsone 100 mg daily, unsupervised, during 3 years, the patients collecting their drugs once a month.

RMP 8× or 12×: RMP 900 mg weekly, supervised during either 8 or 12 weeks, the patients coming to the Institute weekly. Some patients coming from far away in the country were lodged at the Institute for the duration of the treatment.

WHO–PB: RMP 600 mg once every 4 weeks, supervised, 6 doses, together with DDS 100 mg daily, unsupervised.

RMP–DDS 6d: RMP 600 mg and DDS 100 mg daily, supervised during 6 days. Patients were lodged at the Institute during treatment which started on Mondays and finished the next Saturday.

During the second study some patients refused the WHO–PB treatment, preferring the shorter regimen RMP–DDS 6d. This explains the slightly lower number of patients in the WHO–PB regimen. Follow-up examinations were planned on a yearly frequency, but some patients showed up more frequently while many were lost for follow-up. Only those patients seen at least 12 months after the end of the different treatment regimens have been included in this analysis, except for those in the DDS regimen, for whom 3 years of follow-up were required.

During follow-up, clinical and neurological examinations were performed, and a copy of a new clinical file together with a biopsy from the lesion originally biopsied, were sent to Antwerpen. Sometimes when a lesion was entirely replaced with scars from previous biopsies, a biopsy from another lesion was taken.

The criterium for cure was the disappearance of histological lesions, the criterium for relapse was the presence of histological lesions when a previous biopsy had shown cure.

For the analysis of the results the life table technique was applied taking into account the withdrawal of some patients.

Results

Table 1 shows for the 5 treatment regimens: the number of patients analysed, the number of patient-years of follow-up (after the start of the treatment regimens) and the cure rates observed. For the interpretation of this table, the widely differing durations of the treatment regimens should be taken into consideration: 3 years for DDS (the results after 12 and 24 months being obtained during treatment) 2 and 3 months respectively for the regimens RMP 8× and RMP 12×, 6 days for RMP–DDS 6d and 6 months for the WHO–PB regimen.

The histological evolution is comparable in the 5 groups, none of the differences being significant. The cure rates are 65–78% at 3 years, 78–90% at 4 years and for those who presented still later 90–100%. There were no significant differences between patients with less than 3 skin lesions and those having 3 or more. The histological cures in the present studies were obtained somewhat later than in a previous study.[2] There were no neurological reversal reactions leading to significant (more than 1 unit) deterioration in the disability scores.

There was a histological relapse in each treatment group and 2 in the WHO–PB group. For illustration, brief summaries of these cases are presented.

Table 1. Number of patients, patient years of follow-up and annual percentages of histological cures in PB leprosy after different treatment regimens

	Treatment regimens*				
	DDS	RMP 8×	RMP 12×	OMS 6d	OMS PB
	n				
	33	46	40	73	60
	Patient years of follow-up†				
	138	114	173	189	163
Months after start of treatment	Annual percentages (after start of treatment) of histopathological cures				
12	18·2	21·8	22·5	38·7	34·4
24	46·6	43·5	52·5	55·8	58·8
36	68	65·6	67·5	77·9	71·7
48	80	89·5	78·4	89	88·7
60	92	100	89·2	100	100
72	100		94·6		

* See Patients and methods.
† Calculated from the start of treatment.

DDS treatment (IMT 27)

Treatment was started in 1981. Cured in 1984. In 1986, 60 months after the start of treatment, new lesions appeared which were diagnosed indeterminate (peri-neural infiltrations only).

RMP 8× treatment (IMT 54)

Treatment started June 1981, clinical cure during 1982–7 but the last biopsies show BT granulomas in a scarred tissue.

RMP 12× treatment (IMT 45)

Treatment started in May 1981, patient seen twice a year in 1982, 1983 and 1984, clinically cured, no histologic lesions. On two occasions in 1985 a new hypochromic lesion on the elbow was seen with each time a small BT granuloma. Incubation time 48 months.

RMP–DDS 6d treatment (IMT 265)

BT leprosy in 1985. Several biopsies between 7 and 30 months after the start of therapy were negative, when biopsy was once more positive in the presence of new clinical lesions.

WHO–PB treatment

Case (IMT 142) treated in 1984 had a clinical and histological cure at 6 successive examinations. In 1987, at 37 months, in the absence of any clinical signs, 2 small granulomas were detected, no granuloma was found 5 months later.

Case (IMT 179) had a similar evolution. In October 1984 he had BT lesions over his whole body. They disinfiltrated and repigmented progressively and no lesions were found at 5 successive examinations. A biopsy in October 1988, 42 months after the end of treatment revealed a small tuberculoid granuloma.

These histologic relapses appeared after a mean and median interval of 48 months after the start of treatment.

Discussion

The regimens of 8 and 12 weekly doses of 900 mg RMP were included in the first study reported here because at the time of its initiation, 1980, it was not clear whether 8 doses as used in the Addis Ababa–Bujumbura study conceived in 1976 and initiated in 1977[2,3] would be a satisfactory treatment for PB leprosy. The 900 mg dosage of RMP also goes back to 1976 when the optimal dosage of RMP was undecided. In 1980 it was still ethical to study dapsone monotherapy regimen as the first cases of primary dapsone resistant leprosy in Bamako were detected only in 1985, and published in 1987.[9] The administration of dapsone in the RMP–DDS 6d regimen is certainly without any notable antibacterial effect and could have been omitted, its presence results simply from an

attempt to condense the WHO–PB regimen (where there is no need for the antibacterial effect of dapsone) into 1 week.

The results show that there are no differences in cure nor relapse rates between the 5 treatment regimens tested, be it the old classical DDS treatment or regimens based on RMP monotherapy.

All our studies concerning the efficacy of treatment regimens in PB leprosy are based on histopathology, because it produces objective and permanent documentation, certainly when different clinicians examine the patients.

One study[7] has called attention to the discordancies that may appear between different histopathologists in the diagnosis of leprosy. However in the present and previous studies[4,5] the same person examined all the slides. Furthermore, the purpose of the study by Fine *et al.*[7] differs from ours. In the study by Fine *et al.*, efforts were made to diagnose all possible cases of leprosy, whereas in our studies histopathology was applied to exclude all cases that were not histologically documented. Thus we may have excluded false negatives (patients with minimal leprosy in histopathology) but we avoided the inclusion of false positives (patients without leprosy).

It is astonishing that, as far as we know, this is the first study of the histologic evolution of PB leprosy under DDS treatment.

The slowness of the histologic cures was already noted during the first study of our laboratory[4] inasmuch that in the second study[3] skin biopsies at the first follow-up examination, 1 year after the start of treatment, were omitted. There is frequently a delay of the histological cure compared with the clinical one. The contrary is less frequent, although the clinical appreciation is frequently subjective, particularly when only hypochromic patches are present. The discrepancy between the clinicopathological and bacteriological evolution is particularly striking when the DDS treatment is compared with the RMP containing regimens, there being no difference in the clearing of the histopathological lesions after the administration of a very slow, or very rapid, bactericidal drug.[8]

Thus the slow disappearance of the granulomas from the skin points either to a longtime residence of antigens derived from the killed *M. leprae* or to a long natural life of these granulomas.

The results also show that a very small amount of bactericidal treatment is needed to cure a PB patient. This may result from two additive factors: the low number of responsible organisms in the lesions and the considerable immunologic defences of the patient. No cases of primary dapsone resistance were encountered in the DDS monotherapy group. The prevalence of primary dapsone resistance in multibacillary leprosy in Bamako between 1979 and 1983 was 42%[9] but not one case of high degree dapsone resistance, expected not to respond to the classical dosage of 100 mg dapsone per day in man, was found.

Based on the definition of relapse as applied in this analysis, the presence of one or more epithelioid cell granulomas when a previous biopsy had shown none, there were 5 relapses. One case in the WHO–PB and RMP 8 × regimens each concerned intercurrent histologic lesions without clinical symptoms. One case in the RMP 12 × regimen relapsed at the sites of previous lesions; however, if the biopsies were not taken precisely at the correct sites, this case could be a treatment failure rather than a relapse (to take skin biopsies at very precise sites is not always so easy in real practice). Finally, there were two real relapses in the DDS and RMP–DDS 6d regimens at 30 and 60 months respectively,

after the end of treatment. However, since the differential diagnosis between relapse and reversal reaction in PB leprosy is extremely difficult and mostly impossible[10] some of the cases classified as relapse might well be reversal reactions.

The present study illustrates the difficulty to evaluate treatment regimens in PB leprosy within a short period of time, and how needlessly some authors have proposed to prolong the WHO–PB regimen, based on observation periods of only 6 or 12 months.[11,12]

The advantages of short course treatment regimens do not need further justification, and we refer to the patients asking spontaneously for a shorter treatment regimen than the 6 months WHO–PB regimen.

We conclude that treatment of PB leprosy with 6, 8 or 12 doses of RMP administered within 6 days or 2, 3 or 6 months are equivalent, but that a relatively long time is needed to evaluate their effect.

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A study of relapse in paucibacillary leprosy in a multidrug therapy project, Baroda District, India

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Summary In order to judge the value of therapeutic regimens in paucibacillary leprosy, knowledge of incubation time of relapses is essential, as this will define the length of time patients have to be followed up after treatment has been stopped. The prospective study of relapse includes paucibacillary cases of leprosy belonging to a non-lepromatous group consisting of tuberculoid, neuritic and indeterminate. Data are presented on the incubation time of 21 relapses after multidrug therapy in Baroda district; 76·19% of relapses occur during the first 2 years. This figure is most important in the analysis of results of drug trials in paucibacillary leprosy. This figure should also be relevant to regimens including drugs that are more bacteriocidal than dapsone, since the bacteriocidal activity has a bearing on the minimal necessary duration of treatment, but not on the incubation time of relapses.

With the introduction of bactericidal drugs e.g. rifampicin in multidrug therapy, the incidence of relapse are very low, hence relapse rates fall down to a very low level after multidrug therapy. Our study shows a mean relapse rate of 0·19% after multidrug therapy. Factors associated with the occurrence of relapse are discussed.

Introduction

There have been only a few studies on relapse in non-lepromatous and intermediate groups of leprosy cases. The non-lepromatous cases form the bulk of the case load of any leprosy control unit. It is recognized that with an effective treatment regimen these types of leprosy regress much more rapidly compared to the lepromatous type of leprosy. However, a certain amount of care has to be exercised while releasing them from control after inactivity to avoid relapses.[1,2] This study reports risk factors contributing to relapses observed in the multidrug therapy project, Baroda district with the collaboration of the State Government, Government of India and World Health Organization.

Material and methods

The multidrug therapy project was started on 11 June 1984 and the intensive phase of 3

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years was completed on 10 June 1987; the project has been in its maintenance phase since 11 June 1987. The study of relapse in paucibacillary cases in the MDT project was undertaken from January 1985 to January 1989. The study cases included are paucibacillary cases of leprosy belonging to a non-lepromatous group consisting of tuberculoid (TT), borderline tuberculoid (BT), neuritic (N) and indeterminate (I). The classification followed was that suggested by Ridley & Jopling.[9] The criteria followed for diagnosing clinical and bacteriological paucibacillary leprosy cases was as suggested by Job & Chako. These cases include skin smear negative TT, BT, neuritic and indeterminate. The cases were selected on the criteria prescribed under MDT guidelines which included proper clinical assessment of each case and bacteriological examinations of skin smears of patient.[7] Amongst 10,348 old active cases, 9770 (94·41%) were released from treatment up to January 1989 (3478 MB + 6292 PB). New cases detected between commencement of MDT and January 1989 are 9374 (3717 MB + 5657 PB), of which 9291 (99·11%) were brought under treatment (3697 MB + 5594 PB). Total number of new cases discharged as cured between commencement of MDT and January 1989 are 6823 (2020 MB + 4803 PB). Thus a total of 11,095 paucibacillary cases were released from control up to January 1989, of which, only 21 cases relapsed. All of the relapsed cases were diagnosed clinically, bacteriologically and confirmed by histopathology.

These cases of relapse were differentiated clinically from reversal reaction by slow and insidious onset, time interval of 6 months after stopping treatment, new lesions were minimal, lesion showed erythema and infiltration, ulceration does not occur and very slow response to treatment.

TREATMENT

Paucibacillary cases were given dapsone 100 mg daily for 6 months and supervised rifampicin 600 mg once a month for 6 months.[12] 723 PB cases were clinically active, erythema and infiltration were still persisting. Therefore a further extension of treatment for 6 months were given to 723 cases. All PB cases released from treatment were followed once in 6 months for 2 years.

Results/Observations
(Non-lepromatous and paucibacillary used synonymously; RR = Relapse rate)

The observations are given in the tables.

RELAPSE RATE: (Table 1)

It will be observed from Table 1, which gives the number of relapse cases over the years, that the relapse rate has been rising which is natural as the number of cases discharged have been increasing cumulatively. The average relapse rate is 0·19%. All 21 relapsed cases were on multidrug therapy and all cases were also bacteriologically positive.

Table 1 shows the number of cases that relapsed yearly out of the total number of PB cases released from treatment. The first case relapsed in the year 1984–85 out of 1210 PB cases released from treatment. Thus 21 cases relapsed out of the 10,995 PB cases released from treatment with a mean relapse rate of 0·19%. Relapses in leprosy are less common

Table 1. Relapse cases yearwise from total number of PB cases released from treatment

Year	Total PB cases RFT	No. of cases relapsed yearwise	Relapse rate (%)
1984–85	1210	1	0·08
1985–86	2644	4	0·18
1986–87	4404	6	0·13
1987–88	1717	6	0·34
1988–89 (Jan.)	1020	4	0·23
Total	10,995	21	0·19

after giving multidrug therapy compared to relapses after dapsone monotherapy. Our study shows a very low 0·19% relapse rate after multidrug therapy.

AGE AND SEX IN RELAPSE CASES: (Table 2)

The proportion of males to females is more in relapse cases. In fact, the usual male preponderance in the disease prevalence is exaggerated in the relapse cases. Amongst both males and females the higher age groups faced more relapse, especially in the 20–30 and over 40 age groups. Out of 21 relapsed cases only 6 cases were irregular in treatment (28·5%) as shown in Table 2.

CHANGE IN TYPE: (Table 3)

In connection with classification of leprosy in the field it was noticed that patients had been classified as tuberculoid even when there were multiple lesions. Many of these cases would be classified as borderline tuberculoid at the present time. If the modern concept of classification had been applied perhaps cases would not have been released without a longer maintenance treatment. It will be observed that only 4 (23·80%) out of 17 PB originally termed T have been relapsed to T but the remaining 13 have relapsed by changing their types. It can be seen from Table 3 on the number of patches that there were

Table 2. Distribution, age, sex for relapsed cases with treatment regularity

Age groups (Years)	Sex groups		Treatment		Total
	Male	Female	Regular	Irregular	
0–14	1	—	1	—	1
15–25	1	1	1	1	2
26–40	5	2	5	2	7
Over 40	9	2	8	3	11
Total	16	5	15	6	21

Table 3. Changes in types due to relapse

On admission	On relapse							
	TT	I	P	BT	BB	BL	LL	Total
TT	4	1	1	9	1	1	—	17
P. Sec.	—	—	—	1	—	—	—	1
P	1	—	—	—	—	—	1	2
I	—	—	—	—	1	—	—	1
Total	5	1	1	10	2	1	1	21

cases without skin lesions who were either primary polyneuritic or secondary polyneuritic or had infiltration. It will be observed that these cases have been transformed into more serious forms.

In our study of relapse 2 cases were pure neuritic type without any evidence of a history of skin lesions whereas one case was of secondary polyneuritic in which multiple nerves were thickened and tender with a past history of skin lesions.

DEFORMITY STATUS AND RELAPSE: (Table 4)

Out of 21 relapsed cases, 17 cases had no deformities and 4 cases developed deformity on relapse, out of which two had grade 2, one had grade 1 and one had grade 3 deformity. 15 cases were regular in treatment and the remaining 6 cases were irregular out of which two developed grade 2 deformity and one developed grade 3 deformity.

The above table shows time of relapses (release interval) in PB cases after MDT. The

Table 4. Number of cases that developed deformity amongst relapsed cases under MDT project

Total number of relapsed cases	Number of cases that developed deformity grading			
	G1	G2	G3	Total
21	1	2	1	4

Table 5. Time of relapse (relapse interval)

	No. of patients		
	1Yr	1–2 Yr	2–3 Yr
TT	1	4	1
BT	—	10	3
P	—	1	1

majority of relapsed cases in our study after treatment manifest themselves within a period of 3 years. Out of 21 relapses 16 relapses (76·19%) manifested within 2 years of the completion of multidrug therapy and the remaining 5 cases (23·80%) relapsed in the 3rd year.

Discussion

In the early days of sulphone therapy Lowe had observed 11·6% of relapse which had occurred in 6–12 months after stopping treatment.[6] Davey[3] had reported a relapse rate of 6% in tuberculoid cases, among indeterminate and borderline cases the relapse rate was 29%. Ekambaram[4] had reported a relapse rate of 1·8% in patients treated for 5–6 years with 56% occurring within the first 2 years and 73·5% within the first 3 years. Ramu & Ramanujam[8] found a relapse rate of 4·4% in borderline cases treated for 3–9 years after subsidence and no relapses were seen after the 5th year. Girdhar *et al.*[5] found a relapse rate of 2·5% in patients treated according to conventional methods of induction, relapses in leprosy are common after dapsone monotherapy. Repeated relapses in single cases have not been documented though there may be a few such instances. Vellut[11] found that longer maintenance follow-up led to a lower risk of relapse. Relapses after giving multidrugs are expected to be less common compared to relapses after dapsone monotherapy. The present study proves relapses are less common in multidrug therapy, in comparison to the above studies on dapsone monotherapy; out of 21 relapses 16 manifested in the first 2 years (76·19%) and the remaining 5 cases (23·80%) relapsed in the 3rd year. Touw-Langendijk & Naafs[10] observed a 14% relapse among T.T. patients treated for 1·5 years and 28% for patients treated less than 5 years.

Differences in these studies may be the result of differences in the follow-up period or different diagnostic criteria between clinicians. In our study each relapse case was documented by histopathology. It may be that some relapses appearing early after stopping treatment, for instance during the first year, may in reality be upgrading reaction. Where onset is sudden, new lesions are maximum and these lesions may ulcerate, multiple nerve involvement with pain and tenderness and respond to antireactional treatment rapidly. It is frequently argued that the nature of drugs, for example RFM instead of dapsone, will profoundly influence the incubation time for relapses. This results from confusion of two different issues: the incidence of relapses and the moment at which they appear. Indeed, nature and duration of therapy must influence the incidence of relapses, since these are the result of insufficient killing of aetiologic bacilli. However, the moment at which the survivors start to multiply again in most patients must be independent of the kind of anti-bacterial treatment administered. Survivors are survivors, whether the dead ones were killed by dapsone or rifampicin or any other drug.

Relapse is the result of bacterial multiplication starting anew from the survivors remaining after insufficient chemotherapy, due to an insufficiently bacteriocidal drug or to a therapeutic regimen that was too short. It should be mentioned that shortcomings of bacteriocidal activity of drugs is frequently corrected by prolonging the duration of chemotherapy.

In conclusion relapses in leprosy are common after dapsone monotherapy. Relapses after giving multidrugs are expected to be less common compared to relapses after dapsone monotherapy. Our study shows a very low 0·19% relapse rate after multidrug

therapy. The majority of relapsed cases in our study after treatment manifest themselves within a period of 3 years. Out of 21 relapses, 16 relapses (76·19%) manifested within the first 2 years of completion of multidrug therapy and the remaining 5 cases (23·80%) relapsed in the 3rd year. With the introduction of bacteriocidal drugs, e.g. rifampicin, in multidrug therapy, the incidence of relapse are very low, hence relapse rates fall down to a very low level after multidrug therapy. Our study shows a mean relapse rate of 0·19% after multidrug therapy.

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The influence of structural modifications of dihydrophenazines on arachidonic acid mobilization and superoxide generation by human neutrophils

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Summary In this study the effects of nine dihydrophenazine derivatives, relative to clofazimine (B663), on the N-formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP) stimulated release of superoxide anion and on the spontaneous generation of arachidonic acid by human neutrophils were investigated. Previous findings that the pro-oxidative activity of the agents depended largely on the substituion in position 2 of the phenazine molecule and on chlorination in the paraposition of the phenyl and anilino rings were confirmed. Only riminophenazines, but not aposafranone derivatives or the imidazophenazine B621, could enhance superoxide release from activated neutrophils. The lack of chlorination of the phenyl and anilino rings could be compensated for by chlorine substitution in position 7 of the phenazine core.

The priming effect of the agents on FMLP stimulated superoxide generation was completely prevented by the phospholipase A_2 inhibitor 4-*p*-bromophenacyl bromide. Furthermore pro-oxidative activities correlated closely with a stimulatory effect of the agents on arachidonic acid release. It was therefore concluded that dihydrophenazine derivatives with pro-oxidative properties can prime neutrophils for FMLP-stimulated superoxide release by modulation of phospholipase A_2 activity.

Introduction

The dihydrophenazine compound clofazimine (B663; 3-(*p*-chloroanilino)-10-(*p*-chlorophenyl)-2,10-dihydro-2-(isopropyliminophenazine)) is used for the treatment of leprosy due to its antimycobacterial, as well as its immunosuppressive properties.[1] Apart from its direct antimicrobial activity it can also enhance host defence by increasing various phagocyte functions including the respiratory burst.[2,3] It has also been found to augment

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the release of reactive oxidants[4] as well as of prostaglandin E_2 from polymorphonuclear and mononuclear leucocytes,[5,6] both potential mediators of immunosuppression.[7,8] The priming effect of clofazimine on superoxide release by human neutrophils is stimulus nonspecific and has been observed with phorbol myristate acetate (PMA), N-formyl peptides, calcium ionophore, opsonized zymosan and arachidonic acid (AA).[9] Clofazimine can mobilize AA from membrane phospholipids of human neutrophils.[10] AA in micromolar concentrations and by a mechanism which remains to be clearly elucidated, activates NADPH-oxidase, whereas at suboptimal concentrations it can prime neutrophils to subsequent stimulation with N-formyl peptides or the tumour promotor phorbol myristate acetate.[11–14] Since phospholipase A_2 (PLA_2) can cleave AA from membrane phospholipids[15] the priming effect of clofazimine on the release of superoxide from neutrophils could be explained by modulation of the activity of this enzyme.[10]

We have recently shown how structural modifications of the clofazimine molecule can influence the release of reactive oxidants[4] as well as the release of PGE_2 from neutrophils.[16,17] The nature of the chemical group in position 2 of the phenazine ring was found to be particularly important for these activities. In the present study we have extended our previous investigations and attempted to correlate molecular structures with both pro-oxidative activity and the mobilization of AA by human neutrophils.

Methods

CHEMICALS AND REAGENTS

Unless otherwise indicated, these were obtained from Sigma Chemical Co., St Louis, Mo, USA.

SELECTION AND SOLUBILIZATION OF AGENTS

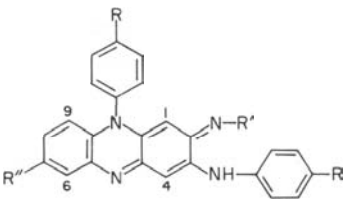
All dihydrophenazine derivatives investigated in this study were synthesized by J F O'Sullivan. On the basis of previously published and unpublished data, nine phenazine derivatives were selected to correlate structural manipulations with effects on the release of superoxide anion and AA by human neutrophils *in vitro*.[16–18] The chemical structures of these derivatives are shown in Figure 1. B663, B980, B670, B1865, B746, B718 and B4021 are riminophenazines while B3722 and B685 are aposafranones, in which the nitrogen in position 2 of the phenazine molecule has been replaced by oxygen. B3722 has a hydroxyl group in position 3, and B685 a ρ-chlorinated anilino ring. B621 is an imidazophenazine in which the phenyl and anilino rings in position 10 and 3 respectively are not chlorinated.

Ten milligrammes of each compound was solubilized in 5 ml dimethyl sulphoxide and further diluted in distilled water to the concentrations required. All agents were compared to the appropriate solvent control.

CELL PREPARATION

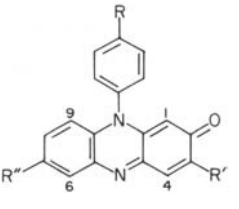
Neutrophils were obtained from heparinized venous blood (5U preservative-free heparin per ml), as previously described.[3] The cells were suspended in indicator-free HEPES (N-2-hydroxy-ethylpiperazine-N′-2-ethanesulphonic acid, 4·2 mM)-buffered Hanks' balanced

Riminophenazines



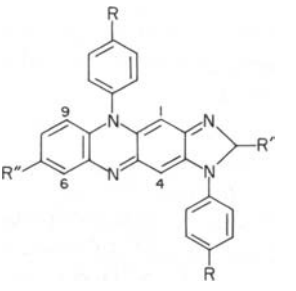
	R	R′	R″
B663	Cl	$CH(CH_3)_2$	H
B670	H	$CH(CH_3)_2$	H
B1865	H	$CH(CH_3)_2$	Cl
B980	F	$CH(CH_3)_2$	H
B746	Cl	C_2H_5	H
B718	H	C_2H_5	H
B4021	H	C_2H_5	Cl

Aposafranones



	R	R′	R″
B685	Cl	$NH.C_6H_4Cl$	H
B3722	Cl	OH	H

Imidazophenazines



	R	R′	R″
B621	H	$(CH_3)_2$	H

Figure 1. Chemical structures of nine dihydrophenazines in comparison with clofazimine, (B663).

salt solution (HBSS; GIBCO Laboratories, Grand Island, NY, pH 7·4) and contained >90% viable neutrophils.

SUPEROXIDE-PRODUCTION BY PMNL

The reaction mixture contained 1×10^6 neutrophils, 0·1 μM of the synthetic chemotactic tripeptide N-formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP), 0·1 mM horse heart ferricytochrome c (cyt-c; type VI) and the agent under investigation at a final concentration of 1 μg/ml, or the corresponding solvent control in a final volume of 1 ml HBSS with or without 100 U of superoxide dismutase (SOD). After preincubation of the neutrophils at 37°C for 5 min, cyt-c and, where applicable, SOD was added followed immediately by the test agents. FMLP was added after 5 min incubation at 37°C and the reaction was stopped after another 5 min by addition of 4 ml ice-cold phosphate-buffered saline (0·15 M, pH 7·1) followed by centrifugation of the tubes. The supernatants were assayed for reduced cyt-c in an SP 1700 UV spectrophotometer (Unicam, Cambridge, England) at 550 nm. The amount of reduced cyt-c was calculated by using an absorbance coefficient of $2{\cdot}11 \times 10^4$ $cm^2/mmol$.[19] Superoxide-dependent reduction of cyt-c is expressed as the difference in cyt-c reduction between reaction mixtures with and without SOD, as nmoles of reduced cyt-c per 10^6 neutrophils.

To investigate the role of PLA_2 in the pro-oxidative effects of the dihydrophenazines, 4-*p*-bromophenacyl bromide (BPB), an inhibitor of PLA_2[20] was added to the reaction mixture directly after SOD and ranged from 0·25 to 5·0 μM. Following an incubation of 30 min at 37°C, the test agents (1–5 μg/ml) and stimulants were added as previously described.

CELL VIABILITY

Neutrophil viability was measured after a 30 min incubation with BPB, according to the release of lactic acid dehydrogenase (LDH), by a standard spectrophotometric procedure.[21]

ARACHIDONIC ACID RELEASE BY NEUTROPHILS

This assay was performed as previously described with some minor modifications.[10] Briefly, 2×10^7/ml neutrophils were incubated with 5 μCi/ml radiolabelled AA (5, 6, 8, 9, 11, 12, 14, 15-^{3}H(N), 100 Ci/mmol, New England Nuclear Corp., Boston, Mass.) for 30 min at 37°C, washed twice and resuspended in HBSS. After prewarming the cells for 30 min at 37°C the agents, administered at 10 μg/ml final concentration, or the corresponding solvent control were added followed by an incubation time of 10 min at 37°C. The final volume in each tube was 1 ml (HBSS). The reactions were terminated by the addition of 5 ml *n*-hexane/isopropanol/concentrated HCl (final concentration 0·1 M) 300:200:4 (vol/vol/vol), followed by vortexing. After incubation at 4°C overnight the tubes were again vortexed and centrifuged at $2200 \times g$ for 5 min to separate the lipophilic and aqueous phases. The upper organic phase was collected and dried under a stream of nitrogen. The lipids were then redissolved in 100 μl of hexane/isopropanol 3:2 (vol/vol). Aliquots of 10 μl were spotted onto silica gel 60 F 254 precoated thin layer chromatography (TLC) plates (Merck, Darmstadt, Federal Republic of Germany) together with 2·7 μg unlabelled AA standard to facilitate visual detection. The plates were developed in chloroform/acetone 96:4 (vol/vol) followed by exposure to iodine vapours. The AA spots were localized and the silica removed and assayed for radioactivity. The results are expressed as fmoles ^{3}H-AA/2×10^7 neutrophils.

EXPRESSION AND ANALYSES OF RESULTS

Results are expressed as mean values with standard error (SEM) for each series of experiments. Statistical analyses were performed by the Student's t-test (paired t-statistics).

Results

SUPEROXIDE PRODUCTION BY PMNL

There was no spontaneous generation of superoxide from resting cells incubated with 1 μg/ml of the dihydrophenazine derivatives (results not shown). The effect of the test agents on superoxide generation of FMLP-activated neutrophils in comparison to clofazimine is shown in Figure 2. Statistically significant stimulation was found with the riminophenazines only, i.e. clofazimine, B980, B1865, B746, B718, B4021, with the exception of B670. Neither of the aposafranones, B685 and B3722, nor the imidazophenazine B621, had any effect on the amount of superoxide released by neutrophils.

The PLA_2 inhibitor BPB, inhibited the generation of superoxide from neutrophils in a dose dependent fashion (Figure 3). In assays where BPB-treated cells were stimulated with 0·1 μM FMLP, (Figure 3(b)) the release of superoxide was only significantly

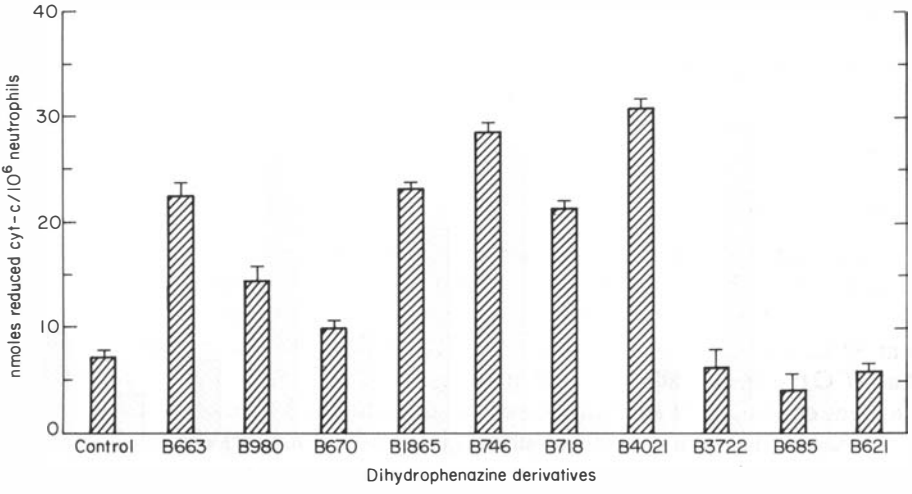


Figure 2. The effects of nine phenazine derivatives relative to clofazimine (B663) and a drug-free solvent control at a final concentration of 1 μg/ml on FMLP (0·1 μM) activated superoxide generation by neutrophils (1×10^6/ml). The results are expressed as nanomoles of reduced cytochrome c and show the mean value $\pm$SEM of four different experiments. Statistically significant stimulation was found with B663, B1865, B746, B718, B4021 ($p < 0{\cdot}005$) and B670 ($p < 0{\cdot}05$).

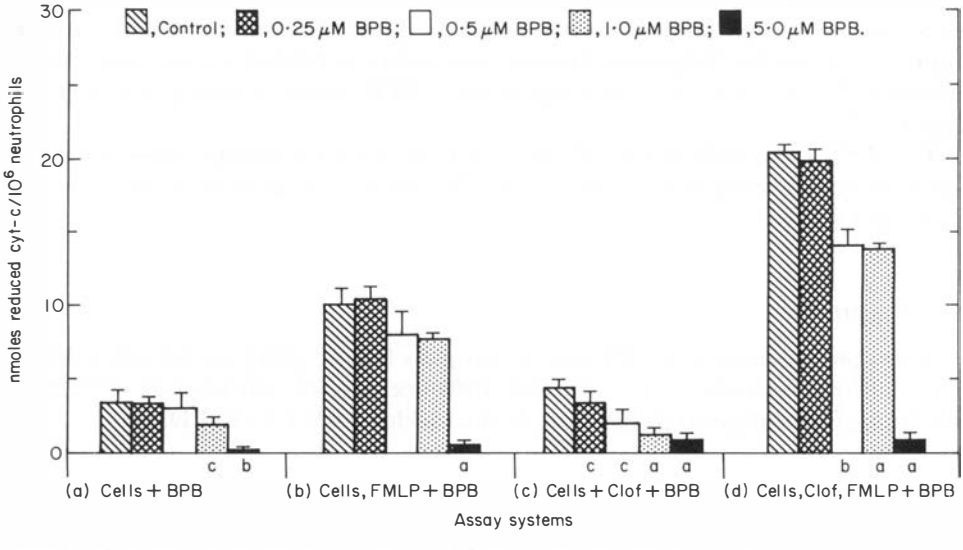


Figure 3. Inhibition by increasing concentrations of BPB (0–5 μM) on FMLP (0·1 μM)-mediated generation of superoxide from human neutrophils (10^6/ml) pre-incubated with 1 μg/ml clofazimine (B663). The results are expressed as nanomoles of reduced cytochrome-c and show the mean value $\pm$SEM for three different experiments. Inhibition of superoxide generation by BPB was significant from concentrations of BPB as low as 0·25 μM. $^a p < 0{\cdot}005$; $^b p < 0{\cdot}01$; $^c p < 0{\cdot}025$.

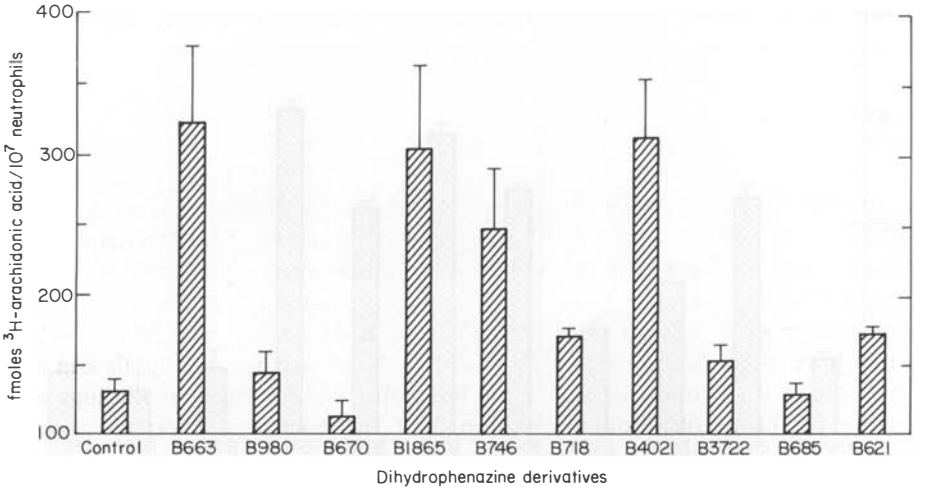


Figure 4. The effects of nine phenazine derivatives relative to clofazimine (B663) and a drug-free solvent control at a final concentration of 10 μg/ml on the release of arachidonic acid by neutrophils. The results are expressed as femtomoles ^{3}H-arachidonic acid per 2×10^{7} neutrophils of four different experiments. Statistically significant stimulation was found with B663, B746 ($p < 0{\cdot}05$), B1865 and B4021 ($p < 0{\cdot}025$).

inhibited at a concentration of 5 μM. However, if the cells were treated with clofazimine (1 μg/ml) prior to stimulation, superoxide generation was inhibited by BPB concentrations greater than 0·5 μM, (Figure 3(d)). Furthermore, BPB only affected superoxide generation from clofazimine-free unstimulated control cells between 1 and 5 μM BPB (Figure 3(a)), whilst clofazimine treated neutrophils exhibited a clear dose response inhibition of superoxide, which was significant at BPB concentrations as low as 0·25 μM (Figure 3(c)).

This BPB-mediated inhibitory effect on superoxide release by neutrophils could not be overcome by increasing the concentration of the dihydrophenazine derivatives to 5 μg/ml (results not shown).

CELL VIABILITY

A 30 min pre-incubation of BPB with neutrophils had no effect on the cell viability as measured by percentage release of LDH. BPB-free control cells released 4·3% ($\pm$0·3) LDH while cells subjected to BPB for 30 min yielded 5·0% ($\pm$1·0) LDH.

ARACHIDONIC ACID RELEASE BY PMNL

The effects of the nine phenazine derivatives relative to clofazimine on the release of arachidonic acid by unstimulated neutrophils are shown in Figure 4. Statistically significant stimulation was observed only with the riminophenazines clofazimine, B1865, B746 and B4021. Dose response studies of these agents over a concentration range of 0–10

μg/ml showed significant dose related increases of AA release at drug concentrations equal to or greater than 5 μg/ml ($p < 0{\cdot}05$–$p < 0{\cdot}01$).

Discussion

In the present study the effects of various dihydrophenazine derivatives on FMLP-stimulated superoxide generation and spontaneous AA release of human neutrophils in comparison to clofazimine were investigated. Possible scavenging or catalytic effects of the test agents on the reduction of cyt-c were excluded using the O_2^--generating xanthine-xanthine oxidase system. B663 (clofazimine), B980, B670, B3722, B685 and B621 have previously been investigated for effects on superoxide release by neutrophils and results similar to those of the present study, have been observed.[4,16] Previous findings on the significance of the substitution in position 2 of the phenazine molecule were also confirmed, i.e. only riminophenazines were potentially pro-oxidative while the aposafranone derivatives B3722 and B685 and the imidazophenazine B621 were inactive.[4,16,17] However, this study indicated that the unchlorinated riminophenazines B670 and B718 had no effect on AA release by neutrophils compared to their chlorinated analogues B663 (clofazimine) and B746, which is also in accordance with previous findings.[16] Lack of chlorination of the anilino and phenyl rings in the paraposition could however be compensated for by a chlorine substituent in position 7 of the phenazine molecule as in B1865 and B4021.

Although the specificity of BPB has been questioned,[22] it is primarily a PLA_2 inhibitor and completely prevented the pro-oxidative effects of the test agents indicating the possible involvement of PLA_2 in the priming mechanism. Furthermore those compounds that stimulated superoxide generation of FMLP-activated neutrophils also increased AA release from the cells, with the exception of the unchlorinated riminophenazines B670 and B718, which had no effect on AA mobilization. This discrepancy especially with B718 which significantly enhances superoxide generation, could be attributed to the absence and presence respectively of a stimulus (FMLP) in the AA and superoxide assays. It is probable that the riminophenazines investigated in this study mediate their pro-oxidative effects by modulation of PLA_2 activity which cleaves AA from membrane phospholipids as was previously found for clofazimine.[10] However alternative pro-oxidative mechanisms related to the redox properties of clofazimine and its analogues may also play a role.[2,23]

Some of the agents have previously been investigated for chemotherapeutic activity in mice experimentally infected with *Mycobacterium tuberculosis*.[24,25] The increase in median survival time of the treated mice relative to untreated controls was measured. Interestingly, the most effective agents were those which we have found to interact pro-oxidatively with human phagocytes. Some discrepancies are evident, e.g. clofazimine (B663) at a daily dosage of 5 mg/kg body mass increased the median survival time by 210 days, while B746 at the same dosage did so by only 45 days.[21] These observations could be attributed to differences in pharmacokinetic properties.

It is concluded that only chlorinated riminophenazines are potent stimulators of spontaneous AA release from neutrophil membrane phospholipids, possibly via modulation of PLA_2 activity. AA can mediate the priming effect of the agents on superoxide release from activated neutrophils.

Acknowledgment

We wish to thank Mr R H Savage for production of the figures, and Mrs Madgwick for expert secretarial assistance.

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Leprosy deformities: experience in Molai Leprosy Hospital, Maiduguri, Nigeria

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Summary A total of 410 patients (288 males, 122 females) aged between 9 and 60 years with an average age of 32·5 years were assessed for deformities of the eyes, hands and feet. The objectives were to find out the number and types of leprosy deformities in the leprosy population of the hospital, the proportion of those deformed among them and to establish the deformity baseline for the hospital. The study lasted 1 year, 38·78% (26·59% males, 12·20% females) of those investigated had one or more deformities. Apart from plantar and palmar insensitivity which accounted for 17·91% and 17·24% of all deformities, the most frequent deformities were mobile claw hand 12·94%, plantar ulcers 10·78% and palmar ulcers 5·97% respectively. With the exception of eye deformities, males accounted for a higher proportion of all deformities. Hand deformities were the most frequent of the three parts of the body studied. The patients' problems were highlighted and the need for adequate management and self-care were emphasized.

Introduction

Leprosy is a chronic infectious disease almost restricted to man. It is caused by *Mycobacterium leprae* and it commonly affects the peripheral nerves and the skin. The estimated total number of leprosy patients in the world is about 15,000,000.[1]

Deformity is an alteration in the form, shape or appearance of the affected part of the body.[2] Leprosy is perhaps better known to the public because of the mutilation and crippling deformities it causes. Many people view these mutilations and gross deformities, which are the result of neglected or poorly managed leprosy, as an integral part of the disease process. This perhaps explains the enormous fear and stigma that the disease instills into members of an ill-informed public.

Disabilities and deformity in leprosy constitute a major problem in the management of the disease,[3] yet they are not an inevitable result of the disease except in a few cases of untreated, advanced lepromatous leprosy.[4]

About 25% of leprosy patients who are not treated at an early stage of the disease

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develop deformities of the hands and feet. And these deformities disfigure, stigmatize and disrupt the lives of the patients and could constitute a handicap for a person's whole life.[1]

Leprosy patients with deformities are a common sight in our public places such as supermarkets, roundabouts, squares, churches and mosques. They patronize these places to display their plight to the public and to solicit alms and solace and perhaps to seek an understanding.

Molai Leprosy Hospital is on the outskirts of Maiduguri, Borno State capital, in Nigeria. It is the only such hospital in the entire state. Patients are drawn from the entire state and from neighbouring states.

This study was motivated by the presence of the many leprosy patients with deformities. The objectives of the study were to find out the number and types of deformities in our leprosy patients, the proportion of those with deformities among the entire patients and, above all, to establish a deformity baseline data for the hospital, upon which the disability prevention programme could be improved and assessed from time to time.

Materials and methods

Leprosy patients who reported to our hospital between 1 July 1987 and 30 June 1988 were used for the study. All the patients who attended the diagnostic skin clinic of the hospital and were confirmed as having leprosy were referred to the physiotherapy department for physical examination for leprosy deformities and assessment of deformities. All the patients were reviewed at 4-month intervals except for outpatients who had some complaints, or those admitted into the wards for one reason or another. They were reviewed as the patients, condition dictated.

Every patient had a physical examination and assessment which entailed examination of the face, hands and feet. The eye examination involved tests for corneal sensation and closure.

The hands were examined for palmar sensation, absorption of digits, finger/thumb weakness, contractures, palmar ulcers, including injury, and deep cracks. The hands were also examined and assessed for wrist drop, mobile claw fingers and thumb.

The feet were examined and information recorded about plantar sensation, foot weakness, claw toes, plantar ulcer, absorption of digits, foot drop and contractures.

Assumptions for the purpose of this study

Incomplete eye closure was one in which the patient was unable to close his/her eyes in such a way that the eyelids did not meet. Eyelid weakness was one in which the patient was able to close the eyes without any lid gap but was unable to do so when the eyelids were gently pulled apart.

Contracture was regarded as stiff joint[4] and no reasonable range of movement was possible either actively or passively through such joints. Mobile claw fingers and thumb were one that were held in hyperextension of the metacarpophalangeal (mcp) joint and flexion of the proximal interphalangeal (PIP) joints and distal interphalangeal (DIP)

joints[5] and the joints of such fingers could completely or almost completely be straightened.[4,6]

Ulcer included injury and deep open cracks large enough to be scored grade two in the World Health Organization (WHO) disability grading system as quoted in one study.[4]

A mobile wrist drop was one that could be moved passively through its full range without or with very minimal resistance.

Foot drop was one in which the foot seemed 'too long' in such a way that when the patient lifted the foot up in walking, the toes trailed on the ground[7] and the patient was unable to pull the foot up.[8] A mobile foot drop was one that was able to be moved through its full range passively without or with very little resistance.

Finger, thumb, wrist and foot weakness were regarded as those in which a full range of movements were possible actively but that could not resist reasonable resistance.

Sensory tests

FACE–EYE

The whole procedure was explained to the patient, and after the patient showed understanding of the procedure and after two trials, the actual tests were conducted.

The patient's face was supported with one hand and the patient was asked to look up to the opposite side being tested. A piece of tissue paper was then used to gently touch the limbus of the cornea, approaching from the side, care was taken not to touch the eye lashes. If the patient blinked, it was recorded present, if no blink, corneal sensation was recorded absent.[4,8] Incomplete eye closure (lagophthalmos) was tested by asking the patient to close his/her eyes as tightly as possible. If the patient closed the eyes in such a way that there was a lid gap, it was recorded as lagophthalmos.[6]

For eye weakness, the patient was asked to close his/her eyes as tightly as possible while the investigator tried to pull the eye lids gently apart. If the patient was unable to resist the pull, it was recorded weak. All tests were carried out while the patients were sitting.

THE HAND

The back of the patient's fingers and thumb being tested was supported with the palm of the investigator's left hand. Care was taken to ensure that there were no joint movements. The procedure was explained and demonstrated with the patient's eyes open. After the patient had shown understanding of the procedure, his/her face was covered with an opaque file jacket so that the patient did not see what was being done. A ballpoint pen held upright was used to gently dent different places of the palm, fingers and thumb and the patient was asked to touch the dented place with the tip of one finger indicating that he/she felt the touch.[6,8]

Finger weakness was tested by placing a card (hospital) between the little and ring fingers of the patient's hand. The patient was asked to hold it as tightly as possible while the card was gently pulled out. If the patient was unable to resist the pull, the finger was recorded as weak. For the thumb, the patient was asked to move the thumb up in such a way that the base of the thumb was fully across and out while the thumb was straight. Pressure was then applied at the side of the thumb in this position. If unable to resist the pressure, it was recorded as weak. Weakness of the wrist was determined by asking the

patient to pull the wrist back fully while gentle pressure was applied downwards. If he/she was unable to resist, it was regarded as weak.[8]

THE FOOT

Plantar sensation was tested for by indenting the sole of the foot in different places with a ballpoint pen held upright. The foot being examined was bent at the knee with the lateral border of the foot resting on the knee of the other leg. With the patient's face covered with an opaque file jacket, and after the procedure had been explained and the patient showed an understanding, the tip of the ballpoint pen was used to gently dent the sole at different places. The patient was asked to touch the place with the tip of one finger any time he/she felt the denting.[6,8]

Foot weakness was determined by asking the patient to pull up the foot fully while gentle pressure was applied at the top of foot.[8] If the patient was unable to resist the pressure and yet when the patient walked, the toes did not trail on the ground, it was recorded as weak. All the data were recorded on the individual patient's sheet and were updated anytime the patient was reviewed. The final data was compiled at the end of the study.

For the purpose of this study, where a patient had a deformity and if eventually it degenerated to something worse, i.e. weakness of the little finger without discernible clawing to mobile clawing, it was the mobile clawing that was recorded against the patient in the final data. Equally for the purpose of this investigation, where a patient had the same deformity bilaterally, i.e. plantar ulcer, it was simply recorded as a plantar ulcer. These assumptions were largely informed by the fact that the study was about to find out what deformities patients presented with, during the period of investigation.

The lower and upper age limits of the patients were determined by the age limits of patients studied. Also 1 July 1987 to 30 June 1988 were chosen so that the duration of the study lasted 1 year.

Results

The 410 leprosy cases (288 or 70·24% males, 122 or 29·76% females) were seen in the hospital between 1 July 1987 and 30 June 1988. Their ages ranged between 9 and 60 years with an average of 32·5. They were made up of both new and old patients who either reported to the hospital on their own volition or were referred from other clinics in Borno

Table 1. Percentage of patients with deformities amongst 410 leprosy patients

	Male		Female		Total	
Deformity/No deformity	No.	%	No.	%	No.	%
Deformities absent	179	43·66	72	17·56	251	61·22
Deformities present	109	26·59	50	12·20	159	38·78
Total leprosy cases assessed	288	70·25	122	29·76	410	100

State or from neighbouring states due to complications or for the confirmation of a diagnosis.

Table 1 and Figure 1 show the number and percentage of patients with deformities among the entire 410 leprosy population of the hospital; 159 (38·78%) of the total number studied were found to have one or more deformities, 251 (61·22%) of the total patients were free of deformities.

Table 2 displays the various deformities found in the 159 patients with deformities, and indicates that the four most frequent deformities were plantar insensitivity (108 or

Table 2. Types of deformities found in 159 leprosy patients with one or more deformities

	Male		Female		Total	
Types of deformities	No.	%	No.	%	No.	%
FACE						
Eyelid weakness	11	2·7	34	17·6	45	7·46
Corneal insensitivity	7	1·7	1	0·5	8	1·33
Lagophthalmos	9	2·2	6	3·1	15	2·49
HAND						
Palmar insensitivity	73	17·8	31	16·1	104	17·24
Absorption	13	3·2	7	3·6	20	3·32
Contracture	18	4·4	4	2·1	22	3·65
Palmar ulcer	21	5·1	15	7·8	36	5·97
Wrist drop	6	1·5	2	1·0	8	1·33
Mobile claw hand	58	14·1	20	10·4	78	12·94
Weakness	17	4·1	12	6·2	29	4·81
FOOT						
Plantar insensitivity	76	18·5	32	16·6	108	17·91
Mobile claw toes	5	1·2	0	0·0	5	0·83
Plantar ulcer	50	12·2	15	7·8	65	10·78
Absorption	13	3·2	4	2·1	17	2·82
Foot drop	24	5·9	7	3·6	31	5·14
Contracture	3	0·7	2	1·0	5	0·83
Weakness	6	1·5	1	0·5	7	1·16
Total	410	100	193	100	603	100

Table 3. Summary of 603 deformities in face, hands and feet amongst 159 leprosy patients

	Male		Female		Total	
Types of deformity	No.	%	No.	%	No.	%
Face	27	6·6	41	21·20	68	11·28
Hand	206	50·2	91	47·20	297	49·25
Foot	177	43·20	61	31·60	238	39·47
Total	410	100	193	100	603	100

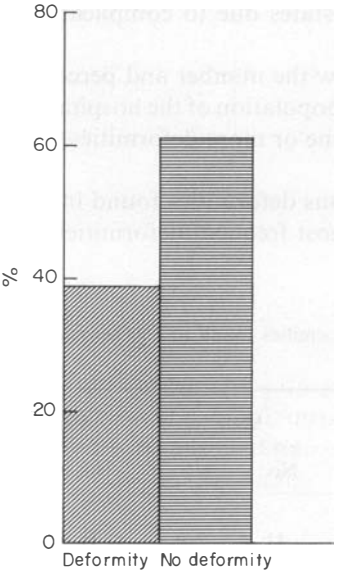

Figure 1. Percentage of patients with deformities amongst 410 leprosy patients.

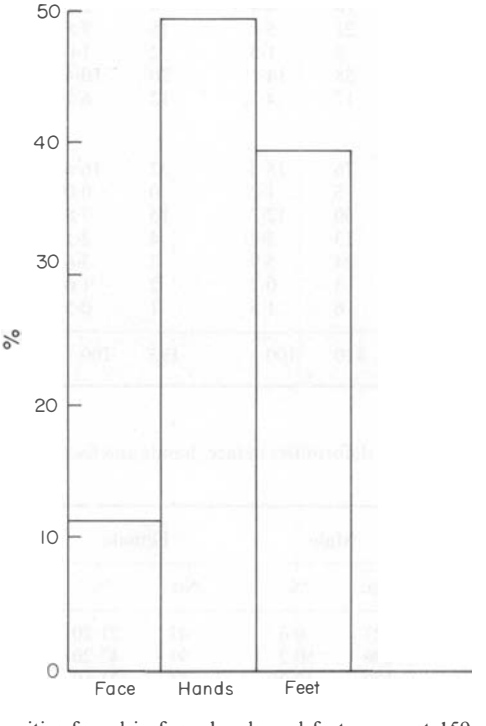

Figure 2. Percentage of deformities found in face, hands and feet amongst 159 patients with a total of 603 deformities.

17·91%), palmar insensitivity (104 or 17·24%), mobile claw hand (78 or 12·94%) and plantar ulcer (65 or 10·78%), of all deformities.

Table 2 also indicates that the two most common deformities of the face, hands and feet were eye weakness 45 (7·46%) and lagophthalmos 15 (2·49%); palmar insensitivity 104 (17·23%) and mobile claw hand 78 (12·94%); plantar insensitivity 108 (17·91%) and plantar ulcer 65 (10·78%) of all deformities.

Table 3 and Figure 2 show the total deformities found in face, hands and feet. Most patients presented with hand deformities, 297 (49·25%); 238 (39·47%) were foot deformities, while face deformities accounted for 68 (11·28%).

Figure 3 and Table 3 show the sex distribution of patients' deformities. They indicate that with the exception of face deformities, male patients presented with more deformities than female patients.

The total numbers and percentages in Tables 2 and 3 and Figures 2 and 3 respectively are expressed relative to the total 603 deformities found in the 159 leprosy patients with deformities. The 603 deformities (410 male, 193 female) is because some of the 159 patients with deformities had one or more deformities.

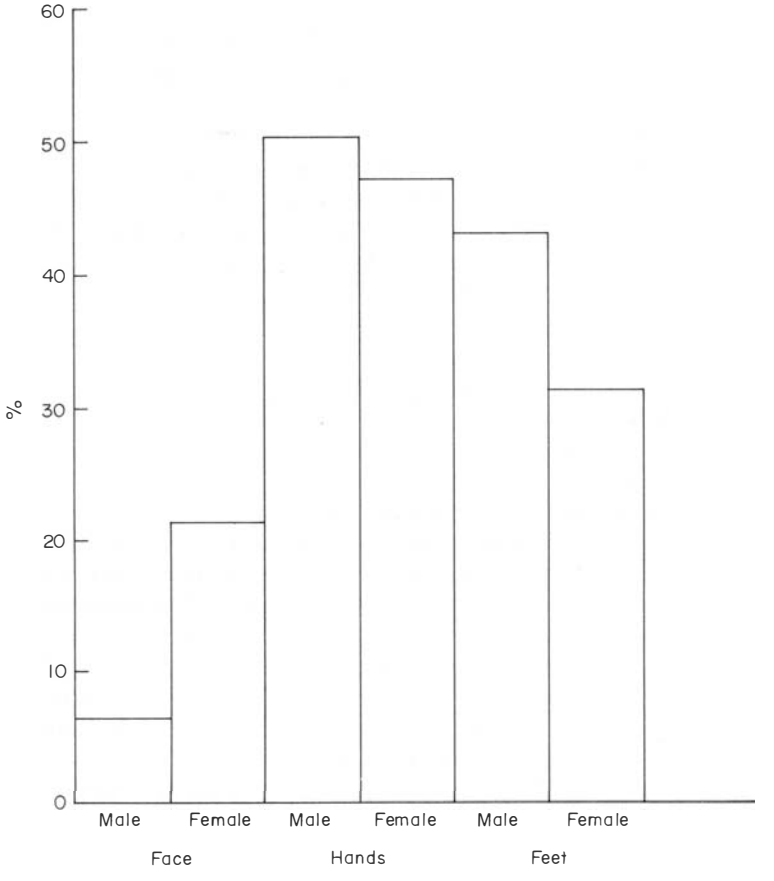

Figure 3. Percentage of male/female distribution of deformities in face, hands and feet amongst 159 leprosy patients with a total of 603 deformities.

Discussion

The need to know the prevalence of deformities and an estimate of the number of patients with such deformities in a leprosy population cannot be too strongly emphasized. Such data helps to assess and evaluate the success or failure of the leprosy control programme. The general public and the patients will find it hard to believe that leprosy can be cured if the disability rate remains high.

Deformities in leprosy are of two categories, one is related to the disease process and the other is due to preventable secondary complications related largely to the level of patient care.[3] Early detection and appropriate management remain the best way to help patients prevent irreversible damage and deformity.

In primary (direct) damage, the nerve may be damaged in the disease process. This can result in sensory loss, muscle paralysis or weakness and dry skin. Sensory loss makes the part of the patient affected very vulnerable to abuse and injuries such as burns and injuries from sharp objects, muscle paralysis could result in stiffness of joints, while dry skin could result in cracked skin and fissures that may eventually develop into ulcers. Burns and other injuries due to anaesthetic parts of the body, stiff joints and ulcers are all secondary complications of the disease. There could be primary damage without these secondary complications. This arrest of nerve and muscle damage at the primary level depends on the adequacy of the patient's management and meticulous self-care on the part of the patient.

This study showed that about 38·78% of the patients studied had one or more deformities. This figure is not as high as the nearly 50% reported in another study.[9] Hand deformities were the most common with 49·25% of all deformities, followed by foot, 39·47% and face, 11·28%. This sequence conforms with other studies.[10,11] Apart from sensory loss of the palms and soles, the three most frequent of all deformities were mobile claw hands, plantar and palmar ulcers.

Sehgal & Srivastava[2,11] citing another study[12] observed that hand deformities accounted for 29·1% of total patients with deformities, also citing further studies[13,14] claw hands were recorded as 19·7% and 8% and absorption of fingers 8·3% and 19·8% respectively. The present study however indicates that hand deformities account for 49·2% of all deformities, while claw hand and absorption of fingers account for 12·94% and 3·32% respectively.

The probable reasons for the ulcers could be traced to the nature of farming tools and the footwear of the patients. Most patients are subsistence farmers who use hoes and cutlasses, and trek long distances barefoot or with inappropriate footwear in search of pasture for their animals. Most of them refuse to use hospital handpads when out of sight of hospital workers on the grounds that they prevent an adequate grasp of their farming tools. They do not use protective footwear because they expose the feet of those without toes, and the sandals are well known and associated with leprosy patients.

Water is a major problem in most drought-stricken areas of the state, so foot and general selfcare constitute major problems to the patients.

The challenge now is to develop appropriate handpads for tools, and to design protective footwear that is fashionable and acceptable to patients.

The essence of adequate self-care has to be emphasized to the patients. There is also the need to reach out to patients, persuade and influence them at the earliest stage of the disease to avoid complications, or where they already exist, to avoid their worsening.

They should not be waited for in the hospitals, they should, where possible, be reached in their communities.

Acknowledgment

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Multiple cutaneous nerve abscesses on a healed tuberculoid patch

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Summary A case of healed tuberculoid leprosy (TT) with multiple superficial nerve abscesses involving the whole cutaneous network on the patch is reported. To the best of our knowledge multiple cutaneous nerve abscesses involving the entire subcutaneous plexus on a TT patch is a very uncommon observation.

Introduction

Nerve abscesses in leprosy are usually seen in paucibacillary leprosy particularly during reaction, but have rarely been reported in multibacillary leprosy.[1–4] A case of TT with multiple nerve abscesses involving the entire superficial cutaneous network over the lesion is reported.

CASE REPORT

A 58-year-old Indian male dairy worker and a resident of Haryana, India (a low endemic state) presented 6 years previously with an erythematous lesion on the posterolateral aspect of the left forearm of $2\frac{1}{2}$ months duration. The lesion gradually increased in size and within the next $1\frac{1}{2}$ months the patient noticed complete loss of sensation over the area. There was no history of similar lesions in the family or close contacts.

On examination of the skin there was an oval well-defined lesion, 10×5 cm in size, on the posterolateral aspect of left forearm. It was erythematous, rough, dry and with raised infiltrated borders. There was complete loss of sensation over the patch. Nerves leading to the patch were palpable and nontender. The ulnar nerve on the affected side was uniformly thickened and nontender. There was no other positive finding on cutaneous and systemic examination. A clinical diagnosis of TT leprosy was confirmed by histopathological examination and a strongly positive lepromin test. No acid-fast bacilli were seen in the section.

The patient received dapsone monotherapy 100 mg daily for one year. There was gradual improvement of the lesion. It became flattened, hypopigmented, slightly atrophic

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with loss of activity. Nerves to the patch were still palpable and nontender. A follow-up biopsy was taken after one year of treatment which showed chronic inflammatory infiltration and a few remnant granulomas with no evidence of active disease. In view of his clinical and histopathological inactivity and strong positive lepromin, dapsone was stopped and the patient was put under surveillance. Two months later the patient noticed some papulonodular lesions on the patch. These nodules persisted without any evidence of clinical activity. At the end of 4 years of discharge from treatment the cutaneous examination revealed a slightly hypopigmented atrophic patch studded with as many as 17 papulonodular swellings, which were superficial, firm, freely mobile and ranged from 0·5 to 1 cm in size (Figure 1). An X-ray of the forearm did not show any evidence of calcification in the nodules. Histopathological examination of a nodule revealed a central area of caseation lined by a zone of epithelioid and giant cells and a layer of compressed fibrous tissue. No residual nerve fibres were seen. These features were characteristic of a caseating nerve abscess with no histopathological evidence of calcification (Figure 2). The cutaneous biopsy taken simultaneously showed features of subsided disease. The patient was later put on paucibacillary MDT for 6 months, with no change in the nodular thickenings at the completion of the regimen.

Discussion

Thickened nerves are characteristic of tuberculoid leprosy. There may occasionally be a nerve abscess in association with active tuberculoid lesion, but the abscesses are a manifestation of the reactional state of tuberculoid leprosy, often in association with a thickened and tender nerve. They are of the nature of cold abscesses and may appear as fusiform fluctuant swellings along the course of the nerve, or as a globular swelling by the side of the nerve.[5] In most cases these abscesses persist after the reaction has subsided and eventually they may undergo calcification. The most common sites are the ulnar and

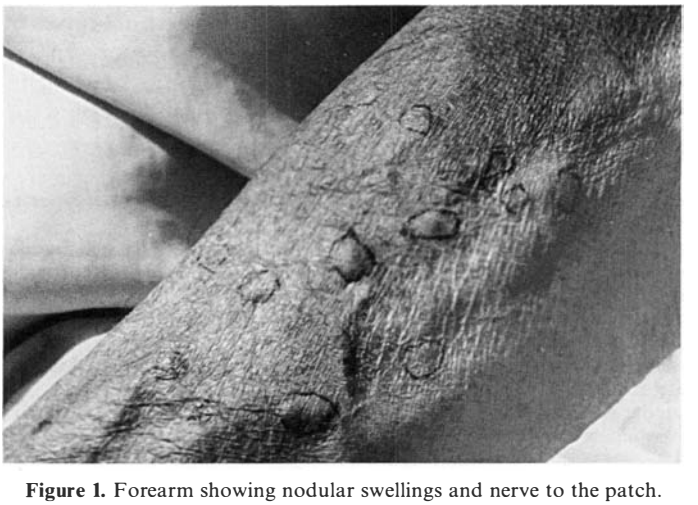

Figure 1. Forearm showing nodular swellings and nerve to the patch.

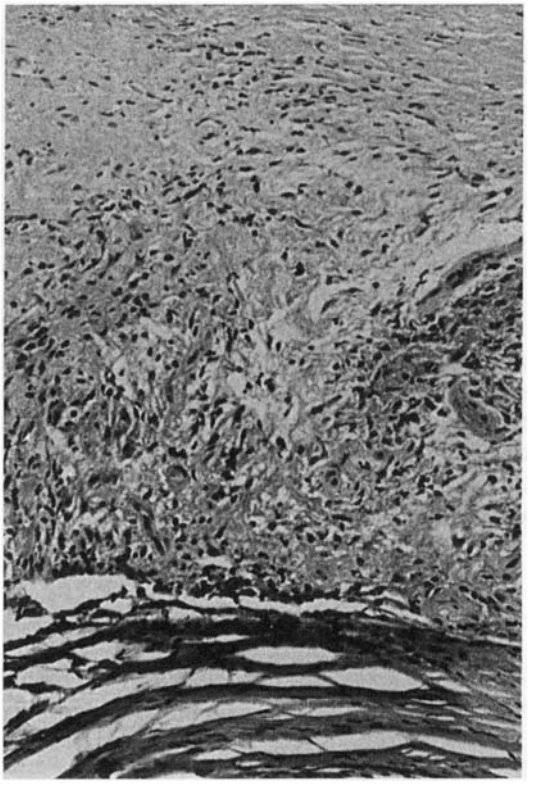

Figure 2. Section of a subcutaneous nodule showing caseation, epithelioid and giant cells in the centre, and peripheral fibrosis.

lateral popliteal nerve trunks,[6] although median and posterior tibial nerves are also involved. The present case is curious because of the involvement of the superficial cutaneous nerve plexus which was studded with multiple nerve abscesses over a healed TT patch.

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SPECIAL ARTICLE

Leprosy control in Zimbabwe: from a vertical to a horizontal programme

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Summary In Zimbabwe leprosy control services were re-established in 1983, following the war of independence. Its main objectives were the nation-wide implementation of multiple drug treatment (MDT) and the integration of leprosy control into the general health services.

The MDT regimens have led to a rapid reduction of the prevalence of leprosy. At the beginning of 1989 357 patients were on treatment and 1299 under follow-up. Six hundred and twenty-seven new cases have been detected since 1984, which represents an annual case detection rate of 1·6 per 100,000. This seems a fair reflection of the incidence rate, as the new cases are characterized by a minority of patients under the age of 15 (4%) and a lepromatous percentage of 50%.

As the budget of the programme has remained unchanged integration of leprosy control into the general health services has become imperative. However, this transition is now hindered by a number of obstacles that were not foreseen at the start of the programme, because they are in measure corollaries of the successful implementation of MDT.

Most of the problems that leprosy control is facing in Zimbabwe could have been avoided if instruction in leprosy had been introduced into the curricula of the (para) medical training schools 20 years ago.

Introduction

In Zimbabwe a very successful leprosy control programme based on MDT was established in 1983. It led to a rapid decrease in the prevalence of leprosy; however, the cost-effectiveness of the programme declined as well. Priority for leprosy control in Zimbabwe at present is therefore its full integration into the general health services. This paper discusses the problems attending that process.

Geography

Zimbabwe lies in southern Africa, bordered by Zambia, Mozambique, Botswana and South Africa. The country has an area of nearly 400,000 sq. km and is divided into eight

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provinces and 55 districts. It has a good infrastructure with regard to roads, public transport and telephone communication. The capital city is Harare.

The population of Zimbabwe is 8·7 million, with an annual growth rate of 2·8%. The population density varies from 10 to 60 per sq. km. Twenty per cent of the population live in the commercial farming areas, which comprises 42% of the country.

Zimbabwe became an independent republic in 1980.

History of leprosy control in Zimbabwe

Following the Leprosy Suppression Act of 1911, leprosy patients were 'arrested' and segregated from the community in two large leprosaria, where dapsone treatment was introduced in 1955. All patients, irrespective of their classification, were treated for life with dosages as low as 12·5 to 25 mg daily.

In 1964 the leprosaria were closed and mobile leprosy control services were started. These were well organized, with a defaulter rate of less than 25%. The treatment policy remained the same as in the leprosaria. Approximately 6000 patients were on register by the mid-seventies, while the prevalence was estimated at 10,000 cases (1·25 per thousand). The majority of the patients were living in the least developed parts of the country in the Zambezi valley, along the borders with Zambia and Mozambique.

During the war of liberation preceding Independence, leprosy control—like most of the medical services—collapsed as health centres were destroyed and rural health workers moved into the towns.

The leprosy control services were re-established in 1983 with the help of the Associzione Italiana 'Amici di Raoul Follereau'. It was to be based first, on nation-wide implementation of the WHO-recommended MDT regimens, and second, on the integration of leprosy control into the general health services. Since 1984 the latter are being organized according to primary health care principles.

As there was little leprosy-trained staff among the general health personnel, eight general health workers were given training in leprosy, both locally and at ALERT, and subsequently appointed as Provincial Leprosy Officers (PLOs). They were charged with the implementation of MDT in the provinces, and with the in-service training of general health staff. Additionally, a total of 24 leprosy 'scouts' were employed in areas of high endemicity for the detection of new cases and the follow-up of defaulters.

Table 1 summarizes the intake of patients since the start of the programme in 1984.

Table 1. It is shown that the intake of patients was greatest during the first two years when no distinction was made between previously treated patients and new cases. After 1986 the former were accepted for an additional course of MDT only if they showed clinical or bacteriological signs of activity of leprosy.

	1984		1985		1986		1987		1988		
	MB	PB	MB	PB	MB	PB	MB	PB	MB	PB	Total
New cases (never treated)	43	35	70	92	59	87	67	68	49	57	627
Previously treated with dapsone monotherapy	381	804	488	712	73	102	54	52	14	5	2685

Many of the 6000 patients who were on register in the seventies were found to have died, their disease had arrested, or they had returned to their home country Malawi or Zambia.

At present the majority of the patients have completed their six months or two years of treatment, and the paucibacillary patients among them also their two years of follow-up. At the beginning of 1989, 357 patients were still on treatment while 1299—mostly multibacillary cases—had not yet completed their five years of follow-up. The 627 new cases found since 1984 represent an average case detection rate of 1·6 per 100,000 inhabitants per year; this seems a fair reflection of the incidence, as the new cases are characterized by a minority of children below the age of 15 years (4%) and by a lepromatous fraction of 50%. Although the latter percentage includes all smear positive and BB cases, the explanation for this relatively high figure could be that only the most susceptible individuals will develop disease when the probability of infection decreases to very low levels.

While the size of the leprosy problem in Zimbabwe has decreased, and will be reduced further when over 1000 lepromatous patients will be discharged from follow-up during the next two years, the costs of running the programme have remained unchanged. In view of the ever-decreasing cost-effectiveness, the integration of the programme into the general health services has thus become imperative.

Impediments to decentralization of the leprosy control programme

In the decentralization process leprosy has to compete with a great number of other health problems, many of which are acute and extensive, killing rather than disabling, and far less costly and complicated to treat or prevent. Securing dedication to the leprosy patient and his problems is no doubt further impeded by the fact that little attention has been directed in the past to stimulating interest in leprosy among medical and paramedical health personnel.

A second obstacle to integration may be the leprosy patient himself, who is used to travelling by bus warrant to a clinic where a special leprosy officer has come from the provincial capital especially to see him and other leprosy patients. In the decentralized programme he will be attended by 'only' a nurse or health assistant. Given, in addition, the fragile ego of the average leprosy patient, it may be expected that decentralization will cause an increase in the defaulter rate.

The gravest impediments, however, lie in the domain of personnel and of its training. There is still a great shortage of health personnel in the country, and especially of staff trained in leprosy. The in-service training of general health staff has been going at a much slower rate than was anticipated. The Programme has been conducting one-month training courses at the Leprosy Hospital in Harare once or twice a year. As a result, two or three nurses or health assistants able to deal with leprosy patients can now be found in almost all districts. They are carrying out the leprosy work within the setting of their regular duties. Undeniably, the employment of such 'special' staff for leprosy control maintains a degree of verticality. It is questionable, however, whether any further integration is a commendable objective; given the present incidence of leprosy, the employment of two to three workers per district would mean each diagnosing, on average, one or two new cases annually. It seems implausible that health workers can maintain the necessary skills for recognizing, treating and following-up leprosy patients when these skills are addressed at such low rates.

An unfortunate sequel of the Programme's accomplishment in training a number of general health workers in almost every district is that many district medical officers, health inspectors and nursing officers cannot supervise and assess the leprosy work of their staff, as they were not trained in the subject themselves. This contributes to the situation being somewhat unstable. In addition, transfers, resignations and appointments to other duties of the leprosy staff regularly disrupt the continuity of the services. Instruction of the senior district health staff is now considered a priority of the training programme. However, most can ill-afford to leave the district for a training course at the Leprosy Hospital in Harare; besides, in view of the size of the problem in their district, many are little inclined to appreciate their training in leprosy as a matter of urgency. The best that can normally be achieved is a one-day or two-day workshop in the district, preferably including the local leprosy clinic day. As there are 55 districts in the country, this is a very time-consuming enterprise. Evidently, these training activities should be conducted especially in areas of high leprosy prevalence (see Figure 1).

The satisfactory integration of leprosy control into the general health services seems attainable only by transferring the theoretical and practical training in leprosy to the medical and paramedical training schools—a process that will take another 10 to 15 years. It has already been accomplished for the medical undergraduates, who have been receiving instruction in leprosy since 1984. For six mornings they are attached to the outpatient clinic of the Leprosy Hospital. Although not much, it seems sufficient to familiarize them with the problems of leprosy and leprosy control, and with the management of the most common complications of the disease, such as neuritis and foot

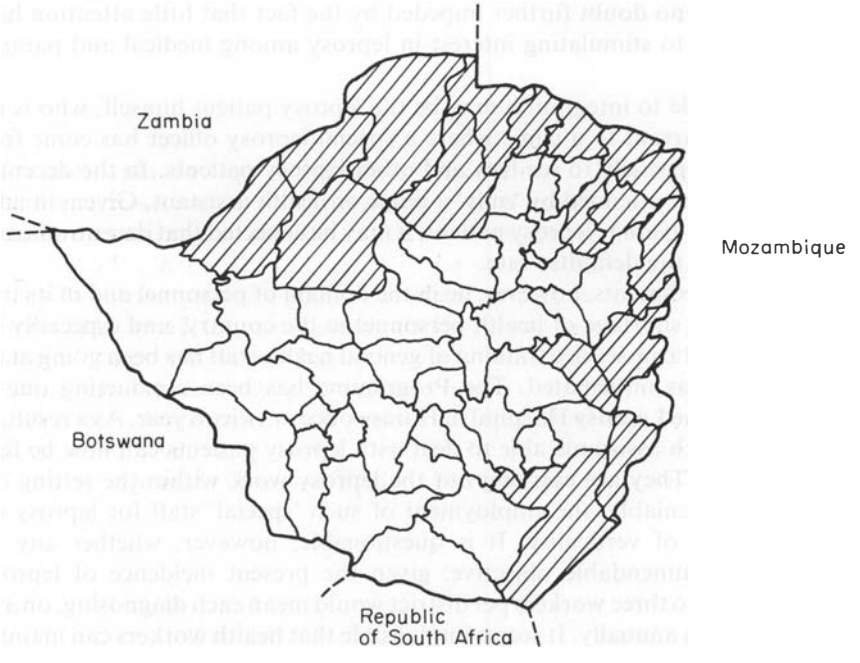

Figure 1. Zimbabwean administrative districts. Those districts in which the prevalence of leprosy is high are shaded.

ulcers. Therefore since 1985 all Zimbabwean doctors that have graduated should be able to participate in the care of leprosy patients.

In the paramedical training schools the time allocated to leprosy in the curriculum has been, until now, usually left unused or allocated to other subjects in the absence of tutors trained and experienced in leprosy. Some PLOs have already been assisting at schools in their province. In view of the declining patient load in all provinces, participation in the instruction of trainee general health staff has now been identified as the first priority of the PLOs. As they have ready access to patients, their tutoring offers the great advantage of permitting students to become involved in the practical examination and health education of the patients, the taking of skin smears, and in the execution of administrative aspects, e.g. registers, treatment cards.

However, the decline of the patient load is also beginning to show in the field of teaching, as fewer and fewer patients are becoming available for practical demonstrations, especially with respect to the early signs of the disease, and of complications such as reversal reaction and ENL. Photographic material cannot, on the whole, replace the living patient, and is of very restricted value if the student has not become familiar with the manifestations of leprosy at first hand. Consequently, it seems that it will gradually become more and more difficult for trainee health workers in Zimbabwe to acquire sufficient knowledge and skills for the early diagnosis of leprosy, of early stages of neuritis with loss of nerve function, and of other complications. That may well have its repercussions on the quality of future leprosy control in the country. The scope of this problem and its trend could be assessed by the careful monitoring of the disability proportion among the new cases registered during the following years. Therefore it will be vital to ensure that registration and reporting in the decentralized programme should continue to be reliable.

Conclusion

Clearly Zimbabwe finds itself in an enviable position having such a low rate of leprosy incidence. It appears to have been largely unforeseeable that the successful implementation of the MDT regimen would provoke the hindrances to decentralization discussed in this paper. It is open to speculation whether the transition from the vertical to an integrated leprosy control programme might have been less complicated if it had been given first priority at the outset. As it happened, the initial intake of large numbers of patients induced not only a great workload but tended to generate an attitude amongst leprosy control staff that left little room for efforts directed towards integration.

It seems indubitable that most of the problems that leprosy control in Zimbabwe is now facing would have been avoided if training in leprosy had been introduced in the curricula of the medical and paramedical training schools 20 years ago.

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Letters to the Editor

SEVERITY OF LEPROSY EYE LESIONS IN ARMADILLOS INFECTED WITH *MYCOBACTERIUM LEPRAE*

Sir,

Although leprosy as a cause of bindness is not mentioned in some leading books about blindness,[1,2] the scope of blindness due to leprosy has always been very large. It was estimated that up to 250,000 leprosy patients could be blind.[3] The importance of prevention and treatment of ocular leprosy and its consequent blindness is well recognized by some; and a meeting was held in 1987 to examine various aspects concerning eye leprosy, and the need of some basic biomedical research on ocular leprosy was emphasized, including histopathological and immunopathological examination of human ocular tissues taken from surgical procedures. Due to the paucity of human eye tissues at any stage of the disease, the use of animal models was also emphasized.[3]

The discovery that an armadillo could be experimentally infected *Mycobacterium leprae* made it a model for many in research purposes.[4] One of them is to gain some insight into the pathogenesis and pathology of eye lesions, even though this animal is not a primate and the severity of the lesions caused by the infection are not exactly like those in human beings. But the pathology of the eye of the *M. leprae* infected armadillos could serve as a ground for further investigations with different approaches.

During our study of the pathology of 127 eyes of 66 armadillos infected experimentally with *M. leprae* in 3 research institutes, we found that although these animals were infected with almost the same dose of the bacilli intravenously, the lesions in the eyes of different animals were not of the same severity. We examined the possible factors causing the variance in these lesions.

The experimental infection of armadillos with M. leprae

The armadillos (*Dasypus novemcinctus*) used for the experiments were all caught in Florida, USA. The animals were kept and infected in 3 institutes: Medical Research Institute in Melbourne, Florida, USA, Forschungsinstitut Borstel in Borstel, FRG and the Royal Tropical Institute, Amsterdam, Holland.

After capture in the wild, they were transported to the institutes. Within a period of 6 weeks of quarantine, examinations for acquired leprosy and treatment of parasitic infestations were carried out.

Then a dose of 10^8 *M. leprae* in 1 ml of saline was inoculated into the femoral vein of each animal. After the inoculation, the animals were kept at 25° $\pm$2°C, humidity of 50–60% and examined by experienced personnel till the death of the animal or until they were killed.

At the time of autopsy the liver and spleen of the animals were weighed and the amount of *M. leprae* in these tissues measured.

The eyes of the animals were removed, many with the eyelids and intra-orbital tissues, fixed in buffered formaldehyde or glutaraldehyde and histological preparations were made and examined.

Grading of eye lesions

We categorize the lesions of the eyes of these animals into 4 groups, according to the severity of the reactions. The group with the slightest lesions (the $\pm$group) included the eyes with a very small

amount of lymphocyte, plasma cell infiltrations, usually around the anterior chamber angle, in the ciliary body, and occasionally in the iris and choroid. If there were several macrophages present, the cytoplasm of these cells was not very abundant. The 1 plus (+) group included the eyes with some lymphocyte, plasma cell and large macrophage (with abundant cytoplasm) infiltrations around the anterior chamber angle and in the iris, ciliary body and choroid. The 2 plus (++) group included the cases with significant infiltrations of plump macrophages in the ciliary body, iris and choroid, with slight to moderate thickening of these structures. The 3 plus (+++) group included the cases with the whole uvea tract densely infiltrated with plump macrophages and the uvea was thickened significantly.

Besides each eye being categorized, each animal was also put into one of the four grades, making the higher grade of the two eyes its grade when the grades of their two eyes were not identical. The numbers of animals in the four grade groups from the three institutes are shown in Table 1.

Facts and discussions

The details of the pathology of the lesions of the eyes of these armadillos was reported in a separate article.[5]

No bacillus was found in the liver and spleen of 5 of the inoculated animals. The percentage of the inoculated but not infected (resistant) armadillos, 7·5% (5/66), was similar to other reports.[6] The eyes of these animals showed very slight cell infiltrations around the anterior chamber angle area, which made us put them in the ± group when we viewed the slides without knowing the AFB content in the liver, spleen and eyes of the animals. AFB were found in the eyes of 12 of the 20 ± group animals. In view of this finding in these uninfected and uninoculated normal control animals, the ± lesion could mean either a mild or early reaction to *M. leprae* or to some non-specific irritant.

In the great majority, 56/66 (85%), two eyes of the same animal had the same severity of lesion. In 6/66 (9%) the grades of the lesions in the two eyes were of adjacent grades, only in 4/66 (6%) were they of one or more grades apart. As our specimens were not serial sections and the lesions in the uvea sometimes segmental, the possibility of the chance manifestation in showing the lesions in different cutting planes of the same eyeball was considered, when the discrepancies of the grades of lesions in the two eyes of the same animal and of different animals was reviewed.

Since ± and 1+ groups were those with slight lesions and 2+ and 3+ groups were those with severe lesions, the ± and 1+ groups were combined as one group and the 2+ and 3+ as another in the following analysis.

In the Borstel and Florida experiments, the number of animals on the ±,+ group were of the great majority: 23/28 (82%) and 20/23 (87%), while those in the 2+,3+ group were 5/28 (18%) and 3/23 (13%) respectively. When the duration of infection and the total amount of the AFB in the spleen and liver of these two groups of animals were considered (Table 2), no meaningful relationship between these factors and the lesion severity was found.

Table 1. Number and percentage (in parenthesis) of animals from 3 institutes in different lesion grade groups

Eye lesions	±	+	++	+++	Total
Borstel	18 (64%)	5 (18%)	2 (7%)	3 (11%)	28 (100%)
Amsterdam	2 (13%)	1 (7%)	7 (47%)	5 (33%)	15 (100%)
Florida		20 (87%)	2 (8·7%)	1 (4·3%)	23 (100%)
Total	20 (30%)	26 (39%)	11 (17%)	9 (14%)	66 (100%)

Table 2. The duration of infection and the total amount of AFB in the spleen and liver of the Florida and Borstel armadillos

Number of animals (lesion grade)	Duration of infection (Mo), range (average)	No. of AFB in spleen (10^9) range (average)	No. of AFB in liver (10^9) range (average)
18* (±,+) Florida	13–37 (22·1)	30·42–3600·6 (495·67)	111·3–12676·0 (564·4)
20† (±,+) Borstel	15–60 (26)	0·5–24990·0 (2976·41)	1·2–1844700 (117698)
7† (2+,3+) Florida Borstel	15–49 (23·8)	3·04–810·0 (245·19)	6·8–4116·8 (1477·3)

* AFB in 2 additional animals were not known; † AFB in 3 additional animals were not known; ‡ AFB in 1 additional animal were not known.

But when the animals of the Amsterdam group was considered, the situation was different (Table 3).

But when the animals of the Amsterdam group was considered, the situation was different (Table 3).

Table 3. The duration of infection and the total amount of AFB in the spleen and liver of the Amsterdam armadillos

Number of animal (lesion grade)	Duration of infection (Mo), range (average)	No. of AFB in spleen (10^9) range (average)	No. of AFB in liver (10^9) range (average)
3 (±)	8–55* (26)	0·0–3·0† (1·77)	0·5–3810‡ (1270·6)
12 (2+, 3+)	12–15	112·5–3760 (1052·3)	128·0–5019 (2276·9)

* 8, 16, 55 in these 3 animals each; † 0·0, 2·1, and 3·0 in these 3 animals each; ‡ 0·5, 1·4, and 3810 in these 3 animals each.

In the Amsterdam group, although the duration of the infection in the ±,+ and 2+,3+ groups were not of significant difference, the amount of the AFB in the spleen of the animals of these groups were significantly different, as shown in Table 3, i.e. $0{\cdot}0–3{\cdot}0 \times 10^9$ in the ±,+ group *vs* $112{\cdot}5–3760 \times 10^9$ of the 2+,3+ group. These figures suggested that there seemed a parallel relationship between the eye lesion severity and the amount of AFB in the spleen of these animals. If the AFB amount of the spleen could be considered as representing something about the degree of bacteremia, the degree of generalization of the infection or the condition of the immunity of the infected animal, then the more severe lesions that occurred in the high spleen AFB concentration animals could be explained accordingly. But the differences of the amount of AFB in the liver of these two groups seemed to be of no meaningful significance.

The amounts of AFB in the spleen and liver of the infected armadillos seemed not always parallel to each other and there seemed to be no distinctive regular relationship between them. They randomly surpassed (or were similar to) each other without known reasons.

In contrast to the Borstel and Florida animals in which the animals with higher grade eye lesions were significantly less (8/51, 16%), the lesions in the animals from Amsterdam were more similar and mostly in the higher grade (12/15, 80%). There was some differences in performing the inoculations in these groups. In the Borstel and Florida animals, the inoculations of *M. leprae* were not done the same day, in the same month and or even the same year. That might mean that the

inoculated bacteria might not be of the same viability or virulence since different manipulations of the same batch, not mentioning different batches, of bacteria might occur. But the Amsterdam animals were inoculated on the same day with *M. leprae* of one Borstel armadillo's spleen (animal number 74, with ± eye lesion grade and $6{\cdot}9 \times 10^9$ AFB/g of spleen). The spleen was taken and held at soft ice temperature for 2 days before the experimental intravenous inoculation. The suspension for inoculation was prepared and dispersed by mild ultrasonic treatment for 5 minutes just before inoculation. This procedure would fragment the particles in the suspension and enhance the distribution of *M. leprae* in infected animals and lead to development of more lesions.[7] This may be one of the causes of the enhancement of the eye complication in the animals infected in Amsterdam. A higher viability of *M. leprae* in the suspension might also be considered, since the *M. leprae* in the suspension used in the Amsterdam group were not subjected to freezing and thawing during the preparation of the inoculum. These might be the reasons why the Amsterdam animals had more similar and severe eye lesions.

Since our present study is a retrospective one, we could not have the desired control over groups of animals included in the study as in a prospective one, for example a control group in the Amsterdam animals using the same batch of *M. leprae* but without sonication before the inoculation. The aforementioned possibilities should be examined when a prospective experiment is possible.

In inducing an eye leprosy animal model for further research, a method guaranteeing a higher rate of forming intra-ocular lesions and a more uniform intra-ocular infection, through systemic inoculation of *M. leprae*, would be very beneficial. We would like to see if the method used in the Amsterdam experiment could give a more constant result.

Acknowledgments

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SUGGESTED NEW METHODS OF TESTING THERMAL SENSATION DURING FIELD WORK

Sir,

It is well accepted that loss or impairment of thermal sensation is one of the earliest signs suggestive of leprosy. The World Health Organization is currently evaluating battery operated devices for testing thermal sensation in the field areas. But for most of the developing world, where the disease continues to be a public health problem, such devices would have to be imported and the dry cell batteries would have to be supplied regularly (a recurring expenditure) to the paramedical staff.

During house-to-house visits as part of antileprosy vaccine trials, we have tried the following methods to test thermal sensation (apart from conventional scientifically accepted methods):

1 Carefully focusing light from the morning sun with a magnifying glass on the suspected patch (or area) for a few seconds and comparing with normal surrounding skin. Since the morning sunlight is not strong (till about 0830 hours in summer and 0930 hours in winter in India), there is no fear of burning the skin. Adults and older children are able to say that they feel a 'warm' sensation. Children under 6 years demonstrate a withdrawal reflex, the absence of which may *suggest* sensory impairment.
2 Using small ice cubes from vaccine carriers; the ice cube is applied gently on the suspected part and compared with normal skin. Patients describe the difference in 'coldness' that they feel.
3 Applying a cotton swab soaked in ether/spirit/acetone/alcohol on the suspected part and comparing the 'coldness' felt by the subject with normal surrounding skin.

All the above-mentioned methods have been compared with the standard thermal testing technique using hot and cold test tubes.[1] In our field areas, hot water can be obtained at almost every house in the morning. Cold water is obtained from melted ice in the vaccine carriers in summer and ordinary water is used during winter. Our studies show reasonably consistent results. The main advantage of these suggested methods is that there is no need for imported instruments, the necessary items being locally available in the developing world.

However we feel that these suggested methods need to be scientifically evaluated.

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Reference

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COMMENT: OCULAR CHANGES IN REACTIONS IN LEPROSY

Sir,

I read with interest the paper by Shorey *et al.* 'Ocular changes in reactions in leprosy' (*Lepr Rev* 1989; **60:** 102–8) and would like to report my findings.

1457 cases of all types of leprosy were studied at random for ocular changes in 1983.[1] Among

them 237 multibacillary cases[2,3] were followed up for a period of 6 years. Fifty-one patients had moderate to severe reactions lasting from 6 months to 6 years with an average duration of 2·5 years. Out of these, eye complications were seen in 9 patients.

Episcleritis/scleritis was seen in one eye in 2 patients and in both eyes in 2 other patients. In all except one, it subsided at the end of the first year and in 1 patient it continued for 4 years. Signs of insidious anterior uveitis were seen in 9 patients on routine examination. Acute iritis was seen in 2 patients, and in one it persisted for 4 years and in the other, after the initial attack, the eyes became quiscent. Posterior polar sub-capsular polychromatic cataracts were found in 4 patients as a result of corticosteroid therapy.

Madarosis, superficial punctate keratitis, corneal hypoaesthesia and lagophthalmos in Type II reactions were not encountered in any of these 51 patients.

Examination of the eye prior to reaction, during reaction and periodic follow-up are essential to say that these changes are due to reactions. Single examination during reaction may not show the true picture as to whether these changes are due to leprosy *per se* or to reactions. Moreover when reactions (Type I and Type II) are properly managed, with periodic ocular examination and appropriate treatment, eye complications can be prevented and ocular morbidity diminished to almost nil. Ocular status did not worsen in any of the patients, though some of them had recurrent reactions for as long as 6 years.

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COMMENT: DO WE NEED TRIALS OF AGENTS ALLEGED TO IMPROVE HEALING OF PLANTAR ULCERS?

Sir,

I fully support Dr Srinivasan in his article (*Lepr Rev* 1989; **60:** 278–82), that it is useless to carry out trials of agents proposed to improve healing of plantar ulcers.

The basis for almost all wounds in anaesthetic extremities is insensitivity. Excessive trauma of some sort is permitted to damage the foot. Since this trauma depends upon some type of mechanical force, prevention is simply not to allow the force to occur. The management of such ulceration is to remove the source of injury, and to prevent its recurrence, all the while protecting the injured structures in order to allow healing.

There are two things that do help the normal healing process. Usually of most importance is immobilization of the part so that movement will not produce cellular disruption. Also of significance is the prevention of secondary infection. There are many ways in which this can be done. The method I have found most effective is the use of 0·5% silver nitrate solution as a wet dressing.[1]

The advantage that I feel this technique has over others is that no bacteria can adapt to growth in the presence of silver nitrate. I began using this technique after reading articles recommending it, in the *Archives of Surgery* Vol. 90, June 1965, Vol. 91, July 1965, and Vol. 93, Sept 1966 by Carl Moyer *et al.*, as it was used in burn wound care.

Also, I strongly support the use of skin grafting to speed the healing process and have used it in hundreds of instances.

The technique I refer to here is also dramatically effective in extraplantar ulcers (like stasis ulcers) referred to by Dr Srinivasan.

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R E PFALTZGRAFF

REPLY: LEPROSY IN CHILDREN

Sir,

Leprosy in children is now a well-established entity.[1–3] It is characterized by well-defined hypopigmented macule(s). Their border may either be regular or serrated. Usually they are few in number and erythema and loss of hair may also be present. The sensations in the macules are invariably impaired or lost. The nerves feeding or supplying the lesions may be enlarged and tender. The macules are largely disposed over body areas susceptable to trauma or injury. Occasionally, plaque(s) may also be encountered. The morphology of the lesions usually corresponds to either indeterminate or tuberculoid (TT) or borderline–tuberculoid (BT).[4] Occasionally, however, borderline–borderline (BB), borderline–lepromatous (BL) or lepromatous (LL) may be seen, indicating clearly that the spectrum in the 0–14 year age group is incomplete. The reactions and deformities are infrequent.[3] Because of the relative innocuous nature of the clinical manifestation, leprosy in children is seen rarely. During the last decade (1981–89) 127 children had leprosy amongst 2513 new leprosy patients attending an urban leprosy centre.

Furthermore, the parameters, namely bacterial index and microscopic pathology are largely unhelpful in this group. Nevertheless, it is imperative that they are performed in each case.[5–7] The early features of leprosy in children have been reported recently.[7–9] It is to be appreciated that the contrasting clinical features observed certainly warrant further attention. In a recent work[10] an endeavour has been made to unfold this aspect by instituting the estimation of total T-lymphocytes, their subsets CD_4 (inducer) and CD_8 (cytotoxic) and their ratio in the peripheral blood, with equivocal results. Whereas *in vivo* lepromin (Mitsuda) and epicutaneous sensitization with dinitrochlorobenzene (DNCB) were significantly poor in mid-borderline (BB) leprosy. B-lymphocytes serum immunoglobulin and C_3 pivotal complement component were found to be normal in all leprosy groups.

The preceding account, therefore, comprehensively shows that the diagnosis of leprosy in children is not at all in doubt. This has been further confirmed by the favourable response to chemotherapy.[11] Therefore the conclusion drawn that the diagnosis should be clinical is well placed.

It is hard to subscribe to the contention that separate operational criteria for diagnosis from those used for leprosy research should be adopted because it may be difficult to compare the cumulative data of different studies. Hence the author has proposed a seven-group classification, which could be utilized for institutional and field work.[12,13]

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REPLY: HONEY AND PROPOLIS AS POSSIBLE PROMOTERS OF THE HEALING OF ULCERS IN LEPROSY

Sir,

Dr L A Wiseman has advocated a sugar paste for the treatment of ulcers in leprosy patients (*Lepr Rev*, 1989; **60:** 67). In this context two other substances merit consideration; namely, honey and propolis. The latter, also termed bee glue, is a related but more resinous plant-derived substance used by bees to seal defects in their hives. Honey has been shown in several studies to promote wound healing and to inhibit growth of bacteria.[1,2] Propolis has strong bactericidal properties, especially against Gram positive bacteria and *Mycobacterium tuberculosis* but also against pseudomonads and other Gram negative bacteria.[3] In addition, ethanolic extracts of propolis have been shown to promote the regeneration of connective tissue, cartilage and bone.[4]

It appears likely that the healing properties of honey and propolis are due, at least in part, to the presence of flavonoids—a class of molecules found in all photosynthesizing cells. Some flavonoids are known to be anti-inflammatory and to promote the regeneration of collagen.[5]

Honey is, of course, widely available. Propolis is also available in many regions and is prepared for use by dissolving it in ethanol to form a tincture. It is also commercially available, as a tincture, from Ainsworth's Pharmacy, London and from Boiron et Cie, Lyon, France. These substances may, in view of their claimed effects on connective tissue regeneration, be of particular benefit in cases where there is underlying damage to cartilage and bone.

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Book Review

Leprosy, Racism and Public Health. Social Policy in Chronic Disease Control. **Zachary Gussow**

The author of this book is a retired American psychologist/anthropologist who became aware of leprosy when he moved South to the Louisiana State University, School of Medicine. He presents a detailed history of attitudes to leprosy and their causes in nineteenth-century America. He suggests that the stigma associated with leprosy in America and parts of Europe was not the product of a long tradition, but was reactivated in the nineteenth century. Colonial expansion took Europeans and Americans to countries where leprosy was endemic and the disease became associated in the public mind, and more importantly in the minds of public health administrators, with the dirt and depravity of 'uncivilized' and 'inferior' people. The fear that, with the immigration of foreign populations, the disease might contaminate the civilized world, resulted in intense leprophobia among the Western nations by the turn of the century. Norway 'the enlightened kingdom' was the exception and there is a chapter devoted to the humane way in which leprosy patients were regarded even after Armauer Hansen's studies suggested that leprosy was a contagious disease.

The author carried out field work at Carville in the 1960s and there are two chapters detailing the history of the leprosarium there. In his preface, he says that Stanley Browne told him that if he wanted to understand leprosy he should venture beyond Carville. He travelled through Tanzania, on a WHO grant, studying the delivery of leprosy services and visited ALERT, Ethiopia but no data from Africa appear in the text. Perhaps that is material for a future book.

This book is probably too long and there is a good deal of repetition, but I found it fascinating as a social history of a disease which people seemed to fear above all others.

Jill Curtis

Published by Westview Press, San Francisco and London.

Lepr Rev (1990) **61,** 197–202

Teaching Materials and Services

AIDS and tuberculosis

The following item by John Maurice is reproduced by permission of *The Guardian* (UK) where it was published in February 1990.

'Anxiety is growing among World Health Organization experts and other scientists about the potential for the Aids virus (HIV) to react with tropical infections in Africa and other Third World areas. The consequences, they say, could be "catastrophic".

The World Bank, for example, has just announced that it will provide $335,000 to WHO's Global Aids and Tropical Diseases Research programmes to support "high quality" research on HIV-tropical disease interactions. In an article soon to appear in the British journal Aids, epidemiologist Richard Morrow of WHO's Geneva-based Tropical Disease Research Programme, and Robert Colebunders of the Institute of Tropical Medicine in Antwerp, Belgium, say the interaction of HIV with tropical disease-producing microbes could be "disastrous". Two British scientists, Diana Lockwood and Jonathan Weber of the London School of Hygiene and Tropical Medicine have also drawn attention to tropical parasite infections in Aids patients.

Morrow and Colebunder describe four possible tropical disease-HIV interactions. (1) An HIV infection, by lowering immunity to invading organisms, could make a person more vulnerable to a tropical disease. (2) A person infected with a tropical parasite could be more vulnerable to HIV infection and could possibly spread the Aids virus more easily. (3) HIV could upset the uneasy "peace" between parasite and human "host" and by tipping the balance against the host allow a dormant or latent tropical infection to become a full-blown disease or a hitherto mild disease to attain life-threatening proportions. (4) Conversely, a tropical parasite attacking a person with dormant or latent HIV infection could trigger HIV-infected cells into viral activity and so hasten the onset of full-blown Aids.

Diagnosis of tropical diseases could also be affected by HIV. Many tests of tropical infection are based on detection of an immune response to the parasite. As HIV inhibits the immune system, such tests could give "false" negative results on a person infected with a tropical parasite. Treatment of tropical diseases could also be affected by HIV infection. In a person with an HIV-depressed immune system, drugs may not work as effectively as they were designed to do and might allow drug-resistant parasite strains to emerge.

One reason why there is so little documented evidence of interaction could be that tropical diseases are mainly rural whereas HIV infection is mainly urban. HIV, however, is beginning to spread outside the cities and cities are attracting more and more people from rural areas thereby increasing the risk of an explosive encounter.

Morrow gives a second reason: not enough researchers are actually looking for an HIV-tropical disease interaction. The few studies that have been done, he said in an interview, have not had strictly designed protocols. "They have not taken sufficient care, for example, in making sure control subjects were really not infected with a tropical disease or HIV." He believes reports of interactions will increase. "HIV may lead to a significant jump in the number of cases of tropical diseases generally. We should begin to prepare for this new situation, before it gets out of hand."

The growing anxiety about an HIV-tropical disease interaction is based more on knowledge of how the respective causitive agents do their damage and how they spread rather than actual evidence of an interaction. HIV homes onto any cells carrying the "CD4" molecule. Helper T-

lymphocytes, the white blood cells responsible for orchestrating the immune response, all have CD4 molecules on them. About 20 per cent of macrophages, the immune cells that "present" an infecting agent to the T-helper cells and ultimately destroy it, are also CD4 positive. As are five per cent of B lymphocytes, the antibody producing white blood cells.

Any infection, therefore, tropical or otherwise, involving CD-bearing immune cells could theoretically clash with HIV. The parasites that cause malaria, for example, elicit an immune response involving B-lymphocytes, T-lymphocytes and macrophages. Macrophages are home to the organisms causing tuberculosis, leprosy, leishmaniasis (a disease that can cause leprosy-like tissue changes), Chagas disease and sleeping sickness (which also elicits a strong B-lymphocytes antibody response). Worms, such as those responsible for lymphatic filariasis (elephantiasis), onchocerciasis (river blindness) and schistosomiasis (or biharziasis) generally provoke a B-lymphocyte antibody response. So these tropical diseases are the first to watch for any HIV interaction.'

Reagents available for leprosy research

The Immunology of Leprosy Steering Committee (IMMLEP) has established several reagent banks for the purpose of supplying various biological materials free of charge to interested, qualified investigators for research related to the immunological aspects of leprosy.

The IMMLEP *M. leprae* tissue bank (National Institute for Medical Research, London) supplies killed *M. leprae*, soluble *M. leprae* preparations and phenolic glycolipid-I (PGL-I; native and synthetic forms). The IMMLEP Monoclonal Antibody Bank (Centers for Disease Control, Atlanta, Georgia, USA) supplies various *M. leprae*-specific monoclonal antibodies for research. The IMMLEP Recombinant DNA Bank (Whitehead Institute for Biomedical Research, Cambridge, Massachusetts, USA) makes available various rDNA clones, libraries, sequences, and vaccinia virus-*M. leprae* gene constructs to qualified investigators. And finally, the IMMLEP Recombinant Protein/Peptide Bank (National Institute of Public Health, Bilthoven, Netherlands) can supply a limited number of mycobacteria-derived recombinant proteins in milligram amounts for further characterization of their immunological and biological properties.

Interested investigators should send their inquiries and/or requests for any of the above-mentioned reagents, together with a brief one-half to one page summary of experiments to be conducted with the requested reagents to: Dr H D Engers, Secretary, IMMLEP, World Health Organization, 1211 Geneva 27, Switzerland.

In addition to the above-mentioned reagents, limited quantities of armadillo-derived Lepromin (Lepromin A; produced at the Gillis W Long Hansen's Disease Center, Carville, Louisiana, USA) can be obtained by writing to: Dr S K Noordeen, Chief Leprosy Unit, World Health Organization, 1211 Geneva 27, Switzerland.

(Source: *TDR News*, No. 30, December 1989.)

Tropical Health and Education Trust

Dr Roger Harman, President of the British Association of Dermatologists, has supplied the following extracted information on the Tropical Health and Education Trust, recently formed in the UK. The trustees are Professor Eldryd H O Parry OBE MD FRCP (Chairman), Professor Keith P W J McAdam FRCP, Professor David A Warrell DM FRCP, Helen M Parry MA and Richard C Southwell QC.

The Aims of the Trust

The aims of the Trust are to get low cost text books to students, to promote their work in the community, and to develop links in teaching and research between British Medical Schools and African Universities.

Background

The idea for this Charitable Trust grew out of our experience of the plight of students in African Universities and the policies of the Overseas Development Administration in concentrating the dwindling resources for overseas aid for health largely on primary health care.

Quite simply, tropical African Medical Schools have so little foreign exchange that libraries lack books and journals, and students can not get their own books. Governments are cutting back severely on the funding of Universities. Restructuring of African economies will inevitably lead to students having to pay fees for tuition and accommodation which will hit the poor very hard indeed.

Work in the community by students, which is complex and costly, and is essential if they are to learn about the needs of the rural poor, is underfunded because Medical Schools are hard hit by lack of government funding.

Long standing links in medical research and training between Britain and Africa, potentially of great importance to both sides, are being weakened by policies in London.

Target Countries

We shall work at first with Ethiopia, Ghana, Tanzania and Zambia but we plan to include other countries in Africa as soon as our systems are tested and efficient.

Methods of Work

We shall buy books in bulk from a core list of 20: nearly all have the British Council subsidized imprint. We have negotiated discounted prices with publishers. The assembly and shipping of books will be done by the Ranfurly Library Service.

The Deans of the recipient Medical Schools, whom the Trustees know personally, are most enthusiastic. They have agreed to handle the books and to get them to senior students. The students will thus be equipped for their final examinations and, more importantly, for their subsequent 2 or 3 compulsory years of rural service. Poor students identified by the Dean will pay nothing: those who are better able to afford books will pay towards their costs. Any money received from students will be used to give students wider opportunity in community health and field research. When our funds allow, we shall get key journals to libraries. Later we hope to develop collaborative field and clinical research. This is seriously lacking but offers rich opportunities for identifying and solving major health problems, for developing the skills of younger African doctors and for maintaining continuing links with British academic medicine. Must support for the Third World at present is directed not towards long-term development but towards short-term help in emergencies and disasters. The Tropical Health and Education Trust is directing its urgently needed work to long-term goals, in supporting the training of those who will be responsible, in the years ahead, for health services in the poorer countries of the tropics.

Further information is available from: Secretary, Tropical Health and Education Trust, 24 Stephenson Way, London NW1 2BQ.

Technical Guide for Smear Examination, Portuguese edition

The second revised edition of a *Technical Guide for Smear Examination for Leprosy*, 1987 is now available in Portuguese from CERPHA, (Comisao Evangelica de Reabilitacao de Pacientes de Hanseniase), Rua Guanpeni 54/101—CEP 20.520, Caixa Postal 24046, Rio de Janeiro, Brasil. A description of the publication's contents was published in *Lepr Rev*, 1989; **60:** 333.

Implementing Multiple Drug Therapy for Leprosy, Bengali edition

This booklet, published by OXFAM, 274 Banbury Road, Oxford OX2 7DZ, England, was translated into Bengali by Dr and Mrs D S Chaudhury of the Greater Calcutta Leprosy Treatment and Health Education Scheme, 35/1/A Old Ballygunge 1st Lane, Calcutta, 700 019, India. The first printing was widely distributed in India and Bangladesh. A further 1000 are now being printed with assistance from OXFAM in Calcutta.

Centre for Medical Education, Dundee, Scotland—*Newsletter*

The format of the *Newsletter* for the Centre for Medical Education has recently been revised and will now highlight the activities of the Centre and may be of interest to local medical teachers and staff outside Dundee and overseas. The areas covered by this newsletter will include regular updates on the current research projects within the Centre and provide information on the services we have on offer and the expertise of the staff of the Centre. It will also give details of the courses and other staff development activities which are run regularly by the Centre and information on what is currently available in our medical education library. The Centre newsletter will be published in February, May and November each year.

The newsletter is available from Ninewells Hospital and Medical School, Dundee DD1 9SY, Scotland, UK.

Directory of International Grants and Fellowships

The Fogarty International Center of the US National Institutes of Health has compiled a 74-page directory of sources of grants and fellowships in the health sciences. Its purpose is to help biomedical and behavioural scientists identify fellowships for training outside their home countries and locate grants for research projects in their home countries. Published in April 1989, it contains information as of August 1988 on eligibility requirements, financial provisions, and application deadlines set by over 180 organizations and agencies worldwide. The directory is available free of charge. To order, send a self-addressed label to: Public Affairs Office, Fogarty International Center, Building 16, Room 306, National Institutes of Health, Bethesda, MD 20892, USA.

Health Technology Directions: issue on leprosy

Health Technology Directions, 1989; **9:** No. 3, is devoted entirely to leprosy. Following a general introduction, it reviews current approaches to diagnosis; treatment; prevention; programme management; national programme strategies. Technical advice on content was provided by P Feenstra (Amsterdam), R Jacobson (USA), A C McDougall (UK), S K Noordeen (Geneva), W F Ross (USA) and T Ramasoota (Thailand). There is a short but valuable list of materials available for further information and reading. Published by PATH, 4 Nickerson Street, Seattle, WA 98109-1699, USA. Single copies are free to health programme managers in developing countries and others interested in health care programmes.

TALC, England; books for community health workers

TALC (Teaching Aids at Low Cost) now have a colour poster, which shows both the front cover and price of all low-cost books handled by TALC. Fifty-six books are illustrated and the range is comprehensive and probably every one of them should be on the shelves of every developing country library, including the district hospital level.

Apply: TALC, PO Box 49, St Albans, Hertfordshire AL1 4AX, England. FAX: (0727). 46852.

Leprosy in childhood; TALC, London

This set of colour transparencies and written text has been fully revised and brought up to date (1989) and now includes a section describing the regimens of multiple drug therapy recommended for all cases by the World Health Organization in 1982. It is intended as a general introduction to leprosy, with particular reference to the disease as it occurs in children. It is suitable for all health workers in areas where leprosy is endemic and who may have to care for patients with leprosy, including non-specialized doctors, medical students, nurses, physiotherapists, clinical officers, auxiliary health workers and health educationists. The set of 24 slides covers: definition, prevalence, clinical types of leprosy, transmission, natural, history of the disease, nerve damage, classification, foot ulcers, differential diagnosis, reactions, prevention and multiple drug therapy.

Cost of transparencies for self-mounting, with text: £3.50 (£2.75 to developing countries); cost of mounted slides in plastic folder, with text: £4.90 (£4.40 to developing countries).

Apply: TALC, PO Box 49, St Albans, Hertfordshire AL1 4AX, England.

Reconstructive surgery: leprosy (hand), Poona, India—best film award

At the 36th National Film Festival (1989) held in New Delhi 'Reconstructive surgery: leprosy (hand)' was chosen as the Best Scientific Film (including the environment and ecology). Produced by Dr Jal Mehta, Department of Surgery, Dr Bandorawalla Hospital, the film shows two reconstructive surgery operations. One, lumbrical replacement under measured tension is an innovation devised in the Department by Dr P V Joshi (surgeon) and Mr Walter Jennings (physiotherapist). The production team also included Dr Sanjay Sane, Mr Vivek Kulkarni (medical team), Anil Revankar, Bharat Nerkar and S Phansalkar (technical team). Further details are available from Dr Jan Mehta, Honorary President, Poona District Leprosy Committee, 35 Manisha, 2-A Moledina Road, Pune 411 001, India.

99 Ideas for volunteers in leprosy awareness work, GMLF

Shri G Ranga Rao, Director, The Bharat Scouts and Guides, 16 Mahatma Gandhi Marg, 1.p. Estate, New Delhi 110002, India, has produced a small booklet listing 99 ways in which young people can help improve awareness about leprosy in their communities, in a practical manner. The idea arose out of discussions and exchanges of views at the International Youth Workshop on Leprosy and Health, held in Germany, May 1989, organized by the Leprosy Relief Organization, Munich. A report of this meeting was published in *Lepr Rev*, 1989; **60,** 255.

Management courses for people working in voluntary organizations

The Open University, 1 Cofferidge Close, Stony Stratford, Milton Keynes MK11, 1BY, England.

The Open University's School of Management is one of the largest providers of management education in the country. It is now planning a series of courses designed specifically to meet the needs of people working in the voluntary sector—for example, charities and community projects, housing associations, or independent agencies working in cultural, welfare, environmental, religious, health or other fields. It will be possible to take these courses separately, or as modules building towards the Open University Professional Diploma in Management.

The courses are designed for:

- People who have management responsibilities in the voluntary sector but who have received little or no formal training or those who have trained but wish to update their knowledge and skills.

They will also be useful for:

- Professionals or specialists from other fields who have recently acquired management responsibilities.
- Newly appointed managers who need to acquire knowledge and skills quickly.
- Staff who are seconded from the private sector to work in voluntary organizations.

The unquiet eye; a diagnostic guide

Produced by Glaxo Laboratories Ltd, Greenford, Middlesex UB6 0HE, England and written by A J Bron, Reader in Ophthalmology, The University of Oxford and Honorary Consultant, Oxford Eye Hospital. This Booklet has 98 pages with 83 excellent colour plates.

The main headings include: a guide to techniques, interpretation of symptoms and signs, dry eye, ocular trauma, subconjunctival haemorrhage, conjunctivitis, keratitis, anterior uveitis, angel-closure glaucoma, episceleritis and scleritis, the red eye with proptosis, the red lid, summary of treatment, ocular screening by the general practitioner, anatomy and useful diagnostic equipment. There is also a full glossary.

Although written to some extent with UK general practitioners in mind, this publication, which can be obtained without charge from the above Glaxo address, deserves wider circulation and could be of considerable value to those working with leprosy patients in developing countries.

The Leprosy Mission (Southern Africa)—history

The Reverend L Wiseman has sent details on the history of the The Leprosy Mission (Southern Africa) which are as follows:

1874 Dr Hansen identifies the leprosy bacillus.
1874 The Mission is founded by Wellesley Bailey.
1949 The Leprosy Mission commences in Southern Africa.
1976 Multi Drug Therapy introduced and offers healing to leprosy patients.*
1976 In conjunction with TLM International, a Leprosy Control Programme is initiated in Lesotho.
1981 TLM Southern Africa starts its own field work. Leprosy Control Programmes commenced in Swaziland and Transkei. Rehabilitation programme is based at Westfort.
1984 New Life Centre in Transkei is opened.
1985 Kwa Zulu project commences.
1987 Ciskei project commences.
1988 Project RSA commences in Transvaal and Orange Free State.
1989 Projects commence in Kangwane, Lebowa, Kwa Ndebele, Qwa Qwa, Bophutatswana and in the refugee camps in Gazankulu.

*Case detection, multidrug therapy and management are proceeding extremely well on an outpatient basis. For details of the locally produced blister-calendar pack for MDT see *Lepr Rev* (1987), **58,** 85–87, Letter to the Editor by L Wiseman.

Voluntary Service Overseas

The explanatory brochure of the Voluntary Service Overseas organization begins:

'VSO is a registered charity dedicated to assisting less developed countries. More specifically, we are a recruitment agency which finds, selects and places volunteers in answer to Third World requests. This work makes us distinctive among other charities and organizatons in the UK. We send people, not money, so that our services are, in effect, entirely complementary to the efforts being made by agencies like Oxfam, Christian Aid and Save the Children Fund with whom we often work directly. VSO tries to respond to requests from overseas that include a strong training element. Our bias is firmly towards the poorest members of the community and we take great care to avoid undermining job opportunities for local people. Both staff and volunteers also pay special attention to women's role in development projects. This is because women's roles in child-rearing, in education and community cohesion underpin any healthy process of change.

Over the past 30 years, more than 30,000 volunteers have worked abroad with VSO. There are now over 1000 volunteers working in 40 of the less developed countries in Africa, Asia, the Pacific and the Caribbean. The application of each volunteer is carefully considered in order to select and interview candidates against each job request from the field, to seek the person with the right blend of skills and personality. An applicant may not wish to be considered immediately. VSO therefore keeps a register of interested people who receive job lists and other information at regular intervals.'

For further details contact: VSO, Enquiries Unit, FG 33, 317 Putney Bridge Road, London SW15 2PN.

Erwin Stindl Oration 1989, India

Dr D S Chaudhury, Director, Greater Calcutta Leprosy Treatment and Health Education Scheme, 35/1/A Old Ballygunge First Lane, Calcutta 700 019, West Bengal, India has kindly sent a copy of the 1989 Memorial Oration in memory of Mr Erwin Stindl, entitled 'Vaccines for leprosy; present status and future prospects', given by Dr Rama Mukherjee. There are 50 references and the text includes a most useful account of the various vaccine preparations currently under trial in India. Copies are available from the above address.

Lepr Rev (1990) **61,** 203–208

News and Notes

Research needs, new tools and methodologies reviewed, WHO Working Group

The Chemotherapy of Leprosy (THELEP) and Immunology of Leprosy (IMMLEP) Scientific Working Groups (SWG) held a joint meeting on 4 September 1989 at WHO headquarters in Geneva.

The meeting, whose main objective was to identify research needs for leprosy control, dealt with research activities and the need for new research tools and methodologies. The goals of leprosy control were defined as (1) interruption of transmission; (2) cure of the patient; (3) prevention of dehabilitation; (4) rehabilitation. Meeting participants agreed that to achieve these goals, it is important to establish links between basic research, development of new monitoring tools, and disease control programmes.

A surge of interest in immunodiagnostic tools has followed the identification of a variety of monoclonal antibodies, native bacterial antigens, T-cell lines and clones, and host-derived (nerve) antigens. Dr Brennan, who reviewed these recent developments, described the powerful antigenic nature of the mycobacterial cell wall. Dr Gupte described the current status of serological and skin tests, and how the development of molecular biological tools can help in understanding the epidemiology and dynamics of disease development.

Dr Pannikar reported the results of two field trials in southern India involving the use of the WHO-recommended multi-drug regimens, and a trial of limited duration therapy. There have been no relapses after more than 3000 person-years follow-up, which would suggest relapse rates considerably lower than those previously observed using dapsone alone.

Demonstration of very rapid bactericidal activity against *M. leprae* in man represents a major development in new antileprosy drug development, reported Dr Grosset. In addition, two other drugs—minocycline and clarithromycin—have been shown to be bactericidal in mouse experiments and are undergoing clinical trials.

Large-scale leprosy vaccine trials are underway in Venezuela (30,000 participants) and Malawi (125,000 participants). In south India a proposed vaccine trial (300,000 participants) would compared the killed *M. leprae* plus BCG vaccine with two other vaccines based on cultivable mycobacteria which have been developed in India.

Recent progress in the molecular biology of mycobacteria

The production of libraries of mycobacterial DNA in cosmid or expression systems has allowed the isolation of major antigenic proteins of *M. leprae*, and the cellular functions of several of these have been identified. More recently, genetic systems for working in mycobacteria have been developed, and should promote understanding of pathogenicity and immunogenicity. The insertion of *M. leprae*-specific genes into potential vaccine vehicles, including BCG and vaccinia virus, was also described.

In reviewing the difficulties of vaccine development, Dr Bloom stressed the importance of understanding the relationship between immunity and protection against infection. Non-human primates, such as the rhesus monkey, develop disease which is more similar to that seen in humans than other animal models, and may be useful for studying immunopathological aspects of leprosy (including nerve damage), immunity and protection against disease, reported Dr Modlin.

The testing of new compounds for antileprosy activity using rapid, *in vitro* systems was described by Dr Hastings. The incorporation of radiolabelled palmitate into *M. leprae* and measurement of CO_2 appears to be particularly valuable, he said, and has already led to the discovery of drugs, with potential antileprosy activity.

Dr Srinivasan drew attention to the inadequacy of research into the involvement of and damage to peripheral nerves. *M. leprae* are found within neural elements, especially Schwann cells, where they can persist and multiply. This induces a tissue response which subsequently leads to nerve thickening and possible damage, whereupon a functional deficit becomes apparent. These multifactorial and complex phenomena require a much greater understanding both at the clinical and the basic levels.

In conclusion, Dr Feenstra emphasized the importance of health systems research in leprosy control. The aim of such research should be to improve the effectiveness of leprosy control programmes. While basic research and new tools are important, research aimed at developing a model for health systems research would also be of great value to control programmes.

(Source: *TDR News*, No. 30, December 1989.)

Leprosy in Ceausescu's Romania

The following is extracted from *The Guardian* (UK), 15 March 1990: A dirt road leading to the Tichilesti Leper Colony is unmarked. The colony is 4 miles from the nearest village and does not appear on any map. It is the legacy of the former Romanian dictator, Nicolae Ceausescu, who wanted its existence kept secret and who told the World Health Organization that the disease had been eradicated. The colony was opened in 1877 with a capacity of 100, but the numbers have shrunk in recent years as standards of hygiene have improved. The 54 patients—27 men and 27 women—are mostly elderly. Only two are in a contagious state, medical treatment having stabilized the rest, though they have to live with their disfigurement. New admissions are down to a trickle—the most recent was 4 years ago. The director of the colony, Dr Gheorghie Popa, expects a few more admissions now that medical information is freely available in Romania, because he thinks new patients will be discovered.

World Congress on AIDS, Bombay, December 1990

Arranged by the Indian Health Organization this World Congress on AIDS is to be held in Bombay, India on 7–9 December 1990. It has a sub-title, 'HIV: the future of an epidemic'. The closing date for abstracts is 1 October 1990. For further information for submission of abstracts, registration etc, contact: Chairman: Organizing Committee, World Congress on AIDS, 1/F, Tulsi Bhuvan, Block 1, 23 Bhulabhai Desai Road, Bombay 400 026, India. Telephone: 851 90 20; Telex: 11-75656 MKAYIN; Fax: 91-22-356957.

Damien Centenary Workshop, Bhubaneswar, Orissa, India, August 1989

A workshop marking the Centenary of the death of Father Damien of Molokai, Hawaii, was held in Bhubaneswar, Orissa, India, 11–15 August 1989. The Meeting was organized by the Damien Institute in collaboration with the Government of Orissa and the Hind Kusht Nivaran Sangh, Orissa. Grants were received from OXFAM (India), UNICEF and the Damien Foundation. Its main objective was the presentation of up-to-date knowledge about leprosy to doctors in the State of Orissa and the delegates included all those working in leprosy eradication units, district leprosy officers and zonal leprosy officers, specialists in skin and venereology departments and medical officers in special leprosy hospitals, together with representatives from non-government agencies such as HKNS, DANIDA and the Damien Foundation.

A team of 23 resource people, all from India with the exception of Niwat Montrewasuwat (Thailand), Tulip Tan (Singapore) and Colin McDougall (UK), gave brief presentations of the

salient features of leprosy, followed by questions and discussions. The Workshop ran for 3 days and was attended by more than 150 people, including senior representatives of the Ministry of Health. Mr Philippe Falisse, Cultural Attaché, Belgian Embassy, New Delhi, joined the Meeting and contributed a stimulating account of the life and work of Father Damien for the leprosy patients of Molokai. Dr P C Roy, Deputy Director, General Health Services, New Delhi, summarized the present state of leprosy control in India and the remarkable extent to which multiple drug therapy has been implemented. Progress is impressive and it is aimed to have all hyper-endemic States under MDT by the year 1992. The State of Orissa already has 9 out of its total of 13 districts under MDT; 2 more (Koraput and Balangir) will soon be included with support from LEPRA (British Leprosy Relief Association), leaving only 2 districts, which will be covered within the next 2 to 3 years.

Following the Workshop, some of the delegates, including Dr R Ganapati, President of the Indian Association of Leprologists, took part in a 'shared meal' at the Cuttack Leprosy Home & Hospital, attended by over 2000 patients.

The Workshop certainly achieved its main objective of transmitting up-to-date information about leprosy and its control to a considerable number of doctors in the State of Orissa and discussions are already taking place about a possible meeting in Bhubaneswar or Puri, in January 1990, to establish a 'Chapter' of the Indian Association of Leprologists, with a core membership of dermatologists, giving emphasis to the even wider implementation of multiple drug therapy in Orissa.

Further information: Father William Petrie, Damien Institute, 1 Satyanagar, Bhubaneswar 751 007, Orissa, India.

Maharashtra Lokahita Seva Mandal—Anti-leprosy Week Celebration 1989

We are grateful to Mr Jayadas for supplying the following report on the Maharashtra Lokahita Seva Mandal Anti-leprosy Week Celebration:

'"*Towards the 21st Century Without Leprosy*" is the goal of every leprosy worker/institution. Their day-to-day activities fall nowhere short of their desire to root out leprosy. However, special emphasis is made to reach much closer to the community through the celebration of Anti-Leprosy Week. The week commencing 30 January, International Leprosy Day (also being the anniversary of the death of the late Shri M K alias Mahatma Gandhi), is observed upto 5 February each year.

Maharashtra Lokahita Seva Mandal (MLSM), a non-sectarian organization formed by Mrs Florie Freitas in 1970, with the help of Bishop Longinus Pereira and Dr Noel Lewis, has taken up the challenge and work hard with a zeal towards the goal. A team of dedicated medical and non-medical workers, which had only 3 members to start with and has now grown to over 40, is its main power. In 1976, MLSM adopted the SET (Survey, Education and Treatment) working pattern of National Leprosy Eradication Programme as its working policy under the aegis of the German Leprosy Relief Association. In over a decade of sincere efforts, MLSM has detected and treated over 11,000 leprosy patients of which over 5200 patients have been declared cured. Thirty-nine dispensaries are run in the project area ('H') East and 'P' wards of Bombay Municipal Corporation with a population of 11 lakhs). Besides treatment and medical care, patients of leprosy have also benefited by the availability of multiple community welfare schemes run by MLSM, such as the Tuberculosis Control Project, job placement, community development, housing, loan scheme, creche, children's sponsorship, typing and tailoring classes and last but not the least, the Box Project-cum-Rehabilitation Centre.

MLSM, as a real fighter against leprosy, also had a large share in the Anti-Leprosy Week Celebration of 1989. Although health education on leprosy is a regular working feature, this week was considered as an opportunity to accelerate it. All possible efforts were taken up to reach each and every corner of the community, in and outside of the project area. This was to motivate and ensure the people's participation in its struggle against leprosy.

The preparatory work was started as early as November 1988. The week was marked by

multiple programmes involving different sections of the community. The main attraction was the use of video shows on leprosy. The main function was organized by the Western Railway at their headquarters at Churchgate on 30 January 1989. MLSM was the most active participant. A new set of exhibition material on leprosy was displayed. Over 1000 railway employees were physically examined for leprosy in this camp which was conducted till the end of the week. An eye-catching poster '*Towards 2000 AD Without Leprosy*' designed and produced by MLSM was released at this inaugural function by Shri E Sreedharan, General Manager of Western Railway. These posters were put on Western Railway Suburban trains as a part of leprosy propaganda, and were much appreciated by the masses. This programme would not have been a great success without the initiative and inspiration of Dr M P Garg of Western Railway. The response of this programme was so encouraging that the exhibition had to be extended to the Churchgate main station the following week. Besides the exhibition, video shows together with other routine educative measures were used. For the first time in the city of Bombay MLSM introduced the use of a "*Moving Message Machine*" and "*A Model of the Globe*" with messages and leprosy statistics on it. The Moving Message Machine was filled with many informative messages about leprosy. Its use will be a regular feature in MLSM's Health Activities in the future.

Similarly, a motivating slogan "*Want to do Something Noble? Help Us Eradicate Leprosy*" was printed on the reverse of BEST city bus tickets. Over 16 lakhs of such tickets have been circulated since then. It was a new experience for the Mandal to reach out to more people through these efforts. There is a continuous flow of enquiries following these attempts. People were eager to know how they could contribute in the struggle against leprosy.

There were two big ambitious Seminars, one for doctors and the other for high school teachers, organized at the Hotel Holiday Inn and JDT High School Complex respectively. Over 150 doctors and 200 teachers participated in them. Dr M S Nilakanta Rao, WHO Consultant, was the guest speaker, his lectures on leprosy enriched participant's knowledge about leprosy, there was an active response from the audience during discussion. Dr K C Mohanty, Professor & Head of Dept. of TB & Chest Diseases, Grant Medical College, Bombay gave a talk on tuberculosis in the doctor's seminar. Hon. Shri K A Bastiwala, Municipal Councillor and Member of the BEST Committee was the Chief Guest while the Hon. Shri Subhash Sawant, Chairman Improvements Committee was the Guest of Honour at the Holiday Inn function. At the teachers' seminar Dr P B Shetty, Chief Medical Officer for Schools of Bombay Municipal Corporation, was the chairperson.

A '*Quiz Competition*' for the 10th standard school students was also one of the features during this week. Over 4300 students entered the competition from over 34 schools in the project area. Slide shows on leprosy were conducted in each school before the competition. At a special function 2 students with the highest marks from every school were awarded trophies. A special Rotating Trophy was awarded to Fatimadevi High School, Malad for its outstanding performance, and the outstanding student, who came from St Thomas Academy, was also suitably rewarded.

Special slide shows were held at C.W.C. Homoeopathy College and Cooper Hospital for medical students and nurses respectively. Over 250 medical students and 300 nurses benefited through this. Their active participation in the post-slide-show discussion was indeed encouraging.

Leprosy transparencies were supplied to cinema theatres for regular projection. Slide and film shows for slum residents and the displaying of banners on leprosy at different corners of the project area were among other activities carried out to mark the week-long celebration.

The team spirit and collective efforts of MLSM staff made the Anti-Leprosy Week a great success. MLSM is contributing its mite towards a world without leprosy in the 21st century.'

Subsequently a report of Anti-Leprosy Week Celebration 1990 has been received. Similar activities were carried out to those in 1989. The public response was very encouraging. The organizers now believe that though regular health education in their SET programme is a must, the impact of this intensive and exclusive focus on leprosy during anti-leprosy week is very impressive, positive and hence influential.

Leprosy in India—a statistical compendium. GMLF

The Gandhi Memorial Leprosy Foundation (GMLF) has produced *Leprosy in India—a statistical compendium* in the belief that 'it would fulfil a long-felt need. Health related social and economic statistics included in the volume add to its utility; so does the international comparison. The few charts and maps are of great help in comprehending the global status of leprosy in India.' This publication is comprised of 153 pp of typewritten tables plus 13 figures. The nine chapters are headed: Selected population statistics; Selected socio-economic indicators; Leprosy profile; Leprosy and five-year plans; Leprosy profile and infrastructure under NLEP; Leprosy training; Voluntary efforts in leprosy work; International leprosy scene; Appendices. It is intended as the first of a series and GMLF are wanting to regularly update it. To this end they would be grateful for any critical evaluation, comments and suggestions.

Leprosy in India brings together the available statistical data on leprosy to be used as a reference volume by those interested in issues related to the diseases. e.g. programme managers, administrators, researchers and epidemiologists. Copies are available from: Gandhi Memorial Leprosy Foundation, Hindinagar, Wardha-442103 Maharashtra, India. Price Rs. 50 plus postage.

Handbook of leprosy; 600 copies for India

One hundred copies of the fourth edition of the *Handbook of Leprosy* (International, lower price format) have been safely received by Dr Nilkanta Rao, 'Anupama', Number 4, 11th Main 4th Block East, Jayanagar, Bangalore 560011, India and distribution has already started to selected people working in leprosy and to institutions. Bone fide applicants should write for a copy to Dr Rao. This consignment has been made possible due to a grant from the St Francis Leprosy Guild, London.

In addition, Dass Media Private Ltd, 207 Bhandari House, 91 Nehru Place, New Delhi 110019, India have arranged for 500 copies to be sold to CBS Publishers and Distributors of Delhi for exclusive distribution in India and Bangladesh. CBS are supplying retailers all over India.

Stocks of both the international and hardback editions are now low and the publishers, William Heinemann Medical Books, Jordan Hill, Oxford, UK, will reprint both in the near future.

The prevention of blindness in Africa

The following is extracted from the International Agency for the Prevention of Blindness (IAPB) *Newsletter*, August 1989, No. 12:

The prevalence of blindness in the African Region has been estimated to be 1·2%. Therefore, there are about 5 million blind Africans and another 5 million who have severe visual deprivation. The major causes of blindness in Africa are cataract, onchocerciasis, trachoma, glaucoma and vitamin A deficiency. There are over 2·9 million Africans who are blind from cataract; this represents 58% of all of those who are blind on that continent.

Blindness can be prevented or cured through proper hygiene, adequate food, vector control, adequate safety measures, and early detection and treatment of eye diseases. However, in Africa the paucity of ophthalmologists and auxiliary ophthalmic personnel constitutes a major constraint in these endeavours. The available number of ophthalmologists in Africa is estimated to be one per million population. Only 12 countries have established training institutes for ophthalmic manpower.

The Auxiliary Training Institute at Lilongwe, Malaŵi, continues to train ophthalmic medical assistants from different parts of the region. At present 114 auxiliary eye personnel have undergone training in the Institute, some through the WHO fellowships programme.

These joint efforts of the World Health Organization and non-governmental organization are stimulating programme development in the member states. To date, 16 countries have already established national programmes for the prevention of blindness.

IAPB News is published twice-yearly and can be obtained from:
IAPB, National Eye Institute, National Institutes of Health Building 31, Room 6A03, Bethesda, Maryland 20892, USA.

The Alexander von Humboldt Institute of Tropical Medicine, Lima, Peru

The following is extracted from *Tropical Diseases. Progress in International Research, 1987–1988. Ninth Programme Report.* UNDP/World Bank/WHO, Special Programme for Research and Training (TDR) 1989.

The Instituto de Medicina Tropical 'Alexander von Humboldt' of the Universidad Peruana Cayetano Heredia in Lima was created in 1968 with help from the Alexander von Humboldt Foundation of the Federal Republic of Germany and from the British Council. From the outset its research activities, both clinical and field research, focused on four diseases: leishmaniasis, malaria, Chagas disease and leprosy.

In 1980 a long-term TDR grant was awarded, and a vigorous programme of research and staff development could begin. Teaching was added to the Institute's functions, and in 1983 it became the Peruvian Ministry of Health's Reference Centre for Infectious and Tropical Diseases.

Over the 5 years of the US$ 454,000 TDR grant, the Institute had conducted locally and internationally significant research on leishmaniasis, of which two forms, uta (cutaneous Andean leishmaniasis) and espundia (jungle mucocutaneous leishmaniasis), are endemic in many areas of Peru. The Institute developed and applied laboratory methods, including isoenzyme analysis, monoclonal-antibody-based assays and DNA probes, for identifying and differentiating these two forms of the disease. Its research staff have recently devised an extremely sensitive test, which, if confirmed by the results of current field trials, could provide a simple, rapid, highly accurate means of diagnosing infection with common strains of *Leishmania* species.

The Institute's work on leishmaniasis has achieved wide recognition in the region and has been the basis of strong links with institutions in other countries, notably the Tropical Medicine Unit of the Federal University of Brasilia. Steps are also being taken to designate the Institute as a PAHO/WHO Collaborating Centre for Research on Leishmaniasis.

Although the Institute's research activities have not been as intensive in other areas, work on leprosy was stimulated by the establishment in 1983 of a small armadillo colony for the local production of *Mycobacterium leprae* and soluble skin-test antigens. Attempts to achieve *in vitro* viability of *M. leprae* and application of the mouse footpad model to the development of drug sensitivity tests have been the main thrusts of the Institute's leprosy work over the past few years.

With a current staff of 24 scientists and 21 technical and support staff, the Alexander von Humboldt Institute now appears to have the basic facilities to develop its potential as a resource centre for tropical disease research in Latin America.

Further enquiries: Professor Humberto Guerra, Universidad Peruana Cayetano Heredio, Instituto de Medecina Tropical, Alexander von Humboldt, AP 5045, Lima 100, Peru.

Blister–calendar packs for MDT: price reduction by Ciba-Geigy

As from 1 January 1990 Ciba-Geigy Ltd, Pharma International, CH 4002, Basle, Switzerland has considerably reduced the price of both paucibacillary and multibacillary packs for MDT in leprosy. Compared with previous prices, monthly treatment will now be 19% cheaper for multibacillary and 17·6% cheaper for paucibacillary leprosy. Particularly with regard to the multibacillary pack carrying three drugs, the company point out that it is difficult to reduce prices any further at this stage in view of the expensive and complicated technical machinery involved.

VII Congrès International des Leprologues de Langue Francaise, Bamako, Mali, February 1991

Details of this Congress, which is to be held 3–6 February 1991 and will be in French, are available from: Association Francaise Raoul Follereau, Commission Médicale, 29 rue de Dantzig, 75015 Paris, France. Telephone 48 28 72 42. The closing date is 1 September 1990.

Instructions to Authors

Papers submitted for publication in *Leprosy Review* should be sent to the Editor, Professor J. L. Turk, 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 clearly indicated below the title of the paper. Degrees and diplomas are not to be included.

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

Units and Abbreviations. The Journal recognizes the adoption of the Système International d'Unitès (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.

Proofs are submitted to authors for immediate return by air.

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