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Pre-congress workshops

From 7–10 September 1988, workshops were held on the following subjects: Immunology; Chemotherapy; Epidemiology; Leprosy control, evaluation and integration; Information systems; Diagnosis and clinical aspects; The role of the ILA in training; Prevention and management of impairment; Vaccine trials; Social aspects; Health and education; Recommendations on rehabilitation; and Microbiology. As on the occasion of previous congresses, the reports were prepared by the chairmen and rapporteurs and distributed to all delegates.

Immunology

In the last 5 years it is clear that advances in basic immunology are rapidly expanding our understanding of the immunology of leprosy. The workshop arbitrarily divided the field into five general areas which we have attempted to summarize:

IMMUNOGENETICS

Additional evidence has accumulated that HLA-genes control the type of leprosy that develops in infected, susceptible individuals. Different HLA-alleles are associated with the respective leprosy types but susceptibility to leprosy *per se* is not under HLA control. No association has been found between HLA and reversal reactions and no studies have been done with respect to HLA and ENL. The mechanisms of the HLA influence in leprosy may be via differential binding of processed antigenic peptides by the polymorphic domains of HLA molecules. As a possible example, helper-T cell clones recognize different epitopes on the ML 65 KD protein that are segregated according to the class II restrictor element used (DR1, 2, 3 and 5 but not DR 4, 6, 7 or 8). It is not clear yet how antigen epitope specificity is related to protective or pathological responses. Future studies should include a search for a human counterpart to the murine Bcg R/S phenotype/gene and understanding the mechanism of the association between epitope specificity and MHC restriction element specificity and their relationship with protection, immunopathology and vaccine efficacy.

MYCOBACTERIUM LEPRAE (ML) ANTIGENS AND MOLECULAR BIOLOGY

In recent years, 7 protein (10, 65, 36, 35, 28, 18 and 12 kD) and 2 glycolipid (PGL-1, LAM-B) antigens have been identified from ML. Much detail is now available. In general a large number of ML-specific and cross-reactive epitopes have been identified, many down to the molecular level. One of the most studied, for example, is the 65 kD protein. It has now been shown to contain 1 specific and 10 cross-reactive antibody epitopes and at least 1 specific and 10 cross-reactive T cell epitopes. Virtually all of these proteins are being expressed from recombinant DNA libraries. The gene (and amino acid) sequences are now complete for the 65 kD protein as well as the 18 kD protein and major portions of the 10 kD protein. In addition to the ML antigenic epitopes which have been identified by these techniques, there is evidence that many more T cell epitopes exist on other ML proteins. Goals in the study of molecular biology of ML continue to be production and

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identification of ML antigens for: 1, the development of immunodiagnostic tests (serology and skin tests); 2, dissection of the immunoresponse to ML (*e.g.* identify antigens important in protective cell-mediated immunity and hypersensitivity, pathologic immune responses, reactions or autoimmunity); 3, understanding the structure and function of ML which may shed light on how the organism resists killing by the immune system by some individuals; and 4, development of a subunit antileprosy vaccine.

MACROPHAGES (M)

Evidence is lacking that failure in macrophage (M) function is the basis for host susceptibility to leprosy. Examples in which activated M successfully cope with ML were discussed and contrasted with experimental models where ML-infected M became defective in afferent and efferent function. The anatomical source of M being studied was emphasized. Caution was expressed about solely studying readily obtainable (blood, peritoneal cavity) M. Interest should be focused more on M from the leprosy lesions themselves. Collectively *in vivo* and *in vitro* mouse studies and clinical trials of local immunotherapy in LL patients suggest that killing and clearance of ML from lepromatous lesions likely depends on the influx of new M into the lesions rather than activation of resident ML-burdened M. Future studies should address: 1, the importance of antibody in the phagocytosis of ML by M; 2, clarification of early events in phagocytosis (phagosome acidification, fusion with lysosomes); 3, whether ML *do* escape from the phagosome into the cytoplasm; 4, kinetics of M traffic into the lepromatous lesion; and 5, importance of infected M as target cells for cytotoxic T cell lysis or destruction by new M. Finally the mechanisms of ML entry into nonphagocytic cells should be studied and the importance of these infected host cells in pathogenesis explored.

CELL MEDIATED IMMUNITY (CMI)

Lymphocytes can be divided functionally into helper, cytolytic, and suppressor subclasses and by phenotype and genetic (MHC) restriction into CD4+, Class II restricted and CD8+, Class I restricted subgroups. Generally CD4+ T cells are helpers and CD8+ are cytotoxic. Exogenous antigens preferentially induce CD4+ T cells while newly synthesized or endogenous antigens induce CD8+ T cells. Killed ML should induce CD4+ helper T cells. Intracellular bacteria, including ML, can activate CD8+ T cells to lyse antigen primed M. CD4+ T cells as well as CD8+ T cells may express cytolytic activity that could result in the release of ML from host cells of low microbicidal potential (ineffective M, Schwann cells, somatic cells) and thus could function in protection. Reversal reaction-type phenomena occur locally after PPD, interferon gamma or IL-2 are infected into the skin lesions of LL patients. ML-specific suppressor T cell clones have been described. In TT skin lesions, CD8+ cells appear to be cytolytic and in LL lesions, suppressive. The role of distinct suppressor T cells in the pathogenesis of unresponsiveness in LL is not clear. Different T cells both produce and respond to different interleukins. The types, quantities and interactions of these different interleukins may play a role in the development of an individual's type of leprosy. Future studies should continue to explore: 1, the mechanisms of ineffective CMI in LL; 2, which immunomechanisms contribute to protection and which to disease; 3, the traffic of mononuclear cells into leprosy lesions; and 4, the characteristics of the cellular infiltrate in leprosy lesions including (a) functional studies on cells isolated from these lesions, (b) studies using CD4+ cell markers of maturity and antigen exposure (CD45R and CD45), and (c) studies using CD8+ cell markers for cytolytic capability (CD28].

SEROLOGY

Over the past 5 years, four types of antigens have been evaluated in leprosy serology: 1, PGL-1; 2, ML-specific epitope monoclonal antibody inhibition assays; 3, antibody assays to synthetic

peptides of specific and cross-reactive epitopes on ML proteins; and 4, the cross-reactive LAM-B of ML. Assays utilizing PGL-1 and its synthetic analogues have had the most widespread application. With these assays virtually 100% of LL patients but only approximately 30% of paucibacillary (PB) patients are positive. Antibody levels are positively correlated with BI in untreated multibacillary (MB) patients and fall (together with BI) in treated MB patients. Anti-LAM-B and monoclonal antibody inhibition assays fall more sharply. Antibody assays are not helpful in predicting reactions. Several prospective studies of contacts of MB patients have identified an increased relative risk of developing clinical leprosy in seropositive individuals. Future studies should include: 1, further exploration of synthetic peptides; 2, refinement of techniques for monitoring patients on chemotherapy; and 3, further evaluation of antigen detection systems in clinical specimens using both immunological and DNA probe techniques such as the polymerase chain reaction.

THE FUTURE

In addition to a number of specific areas requiring attention which have been mentioned, there are several broad recommendations for the next 5 years. At present there does not seem to be enough basic knowledge to suggest new field trials of new potential vaccines. Effort should continue to integrate leprosy into general scientific research to increase the number of researchers and the variety of skills working on a leprosy vaccine. In the shorter term the immunopathology of possible autoimmunity in leprosy, and the pathogenesis and possible immunomodulation of ENL and reversal reactions, particularly neural reactions, deserve high priorities.

R HASTINGS, *Chairman*

Chemotherapy

The 5 years since the Delhi Congress have seen a number of important advances in the chemotherapy of leprosy. Studies have continued to demonstrate a high frequency of relapse with secondary dapsone resistance during dapsone monotherapy, and a high prevalence of primary dapsone resistance, further emphasizing the need for multidrug therapy (MDT). On the other hand, primary resistance to rifampicin has not yet been recognized, even in those areas in which secondary resistance to rifampicin has occurred as a consequence of rifampicin monotherapy. Most importantly, implementation of MDT has expanded, so that, by this time, more than 2 million patients have completed MDT. MDT has been implemented in most endemic countries, although, in the majority of countries, only a proportion of patients has been covered. MDT has been widely accepted, both by patients and by leprosy control personnel; the three components—rifampicin, dapsone and clofazimine—have been extremely well tolerated, and patient compliance has been at least as good as in the days of dapsone monotherapy. The main difficulties have been in the reliable delivery of the drugs to the patients by the leprosy control infrastructure; however, MDT has proved to be operationally feasible where the infrastructure is adequate. Relapses have been remarkably few in the short term—fewer than 1% per year, despite the persistence of viable *Mycobacterium leprae* in a significant proportion of patients after MDT for 1 or more years, and caseloads have been substantially reduced in many areas.

Drugs of 2 additional classes exhibited bactericidal activity against *M. leprae*. Two fluoroquinolones—pefloxacin and ofloxacin—are fully active against *M. leprae* in mice, pefloxacin is rapidly bactericidal in patients with previously untreated lepromatous leprosy, and ofloxacin is currently in clinical trial. Minocycline, a lipid soluble tetracycline, is also fully active against *M. leprae* in mice, and is soon to be tested in men.

At this time, a number of important problems await resolution. A few patient paucibacillary leprosy appear to be more appropriately treated by the regimen for multibacillary leprosy, but we

are as yet unable to recognize these patients before treatment. The slow resolution of some paucibacillary lesions makes patients and staff unwilling to stop therapy. And it has been difficult to distinguish some late reversal reactions from relapse. The most effective way of using the new fluoroquinolones and minocycline to strengthen MDT had not yet been established, and the potential role of immunotherapy remains unclear. The potential role in leprosy control of rifampicin as chemoprophylaxis has not yet been assessed, and measurement of the impact of MDT upon transmission of *M. leprae* in the community is made much more difficult by the lack of a reliable test for latent infection. There is a continuing need for new bactericidal drugs that are well tolerated and not prohibitively expensive, especially if they are suitable for intermittent, supervisable administration. Sensitive and reliable *in vitro* methods of detecting viable *M. leprae* and measuring their susceptibility to drugs are needed to aid the assessment of treatment—outcome, and to facilitate the screening of new compounds. It is hoped that application of the techniques of molecular biology will assist in the achievement of these goals, and suggest new, potentially useful approaches to the cultivation of *M. leprae*. During the next 5 years, MDT should be implemented in all countries for all patients. Simultaneously the effectiveness of MDT over the long term must be assessed as precisely as possible. Special efforts should be undertaken to facilitate the distinction between reversal reaction and relapse, and relapse of multibacillary leprosy must be documented whenever possible by inoculation of mice and drug-susceptibility testing. Trials ofloxacin and minocycline should be mounted to measure the potential of these drugs for strengthening MDT. Work should be continued in the areas of the biology of *M. leprae*, to understand better the action of the presently available drugs, and to discover new targets of drug action. The search for additional new drugs should continue. The development of immunomodulating agents, including vaccines, should be pursued, both to strengthen chemotherapy and for immunoprophylaxis.

Efforts to cultivate *M. leprae* to assess the potential role for chemoprophylaxis and to develop means of detecting subclinical infection with *M. leprae* should be encouraged. And operational studies should be undertaken, particularly to find the most effective methods of delivering MDT in a variety of geographical and socioeconomic environments.

L LEVY, *Chairman*

Epidemiology

MAGNITUDE OF THE PROBLEM

The estimate of the global magnitude of leprosy has changed little for more than 20 years. Moreover such estimates are often based on unsystematic criteria and reports. Therefore in order to make a realistic projection of the global problem, the workshop recommends:

1 Acceptance of the *definition* of a *case* of *leprosy* as recommended by the WHO Expert Committee, *i.e.* 'A case of leprosy is a person showing clinical signs with or without bacteriological confirmation and requiring chemotherapy.'
2 That prevalence rates should be based on *registered* cases as per the above definition.

As per present data, the total number of registered cases world-wide is approximately 5 million. Eighty-two percent of the registered cases are from 6 countries. Since 1985, the number of patients who completed treatment appears to be higher than the newly detected cases. It must however be noted that even in countries of low or medium prevalence, there can be pockets of high prevalence.

TRENDS OF LEPROSY

Some countries have reported well-documented declining trends of leprosy; some areas and some countries still show increasing trends. Thus in general there is a great need to carefully evaluate the work done during the last decades. This calls for the collection of reliable data on the patients and on the populations to which they belong. These data should be analysed separately by age, sex and type of disease. Trends in relation to factors such as BCG coverage must also be analysed.

While criteria for classification can differ to some extent country-wise, there is need for *standard criteria* of classification, taking into account clinical, bacteriological and immunological status of the patient.

URBAN LEPROSY

Trends in urban leprosy have not been sufficiently analysed so far. This is partly due to the operational difficulties in the control programmes and the fact that most of the urban programmes are of recent origin. It is recommended to have studies to evaluate the pattern and trend of leprosy in urban areas, in order to investigate whether epidemiological factors and trends differ in urban areas compared to rural areas and to know whether there are unique epidemiological features in urban areas.

SOCIOECONOMIC DETERMINANTS

Though the relationship between leprosy and poor socioeconomic conditions is widely recognized, the factors that contribute to the transmission of infection and/or the development of the disease under such conditions are not established. Ideally there is a need to collectively study factors such as overcrowding, migration, hygiene, nutritional state, intercurrent infection, ethnic variations, BCG coverage, housing etc., and to separate them in the analysis.

SEROEPIDEMIOLOGICAL TOOLS FOR LEPROSY

Almost all data and reports on leprosy are based on clinical disease. There is very little indication of subclinical infection. None of the available tests to detect subclinical infection is sufficiently specific or reliable for use under field conditions. Therefore there is need for development of a reliable test appropriate for field use. Skin tests used during immunoprophylactic trials have demonstrated the usefulness of detecting individual susceptability and to study the immunological conversion induced by potential vaccines. Such studies need to be encouraged.

RECENT PROGRESS IN EPIDEMIOLOGICAL WORK AND RESEARCH

1 Epidemiological applications of serological tests in the context of prevalence and incidence studies.
2 Confirmation of HLA-linked determinants for lepromatous as well as tuberculoid leprosy.
3 Discovery of natural *M. leprae* (or *M. leprae*-like) infections in armadillos and monkeys.
4 Institution of large-scale vaccine trials providing population laboratories for leprosy research.
5 Application of case control study methodology to identify risk factors, *e.g.* armadillo contact and absence of BCG vaccination.
6 Shift to MDT regimens and initial studies aimed at measuring reaction and relapse rates after different regimens.

PRIORITY ISSUES FOR THE FUTURE

1 Clarification and application of rigorous case definition.

2 Studies of the implications of HIV infections for leprosy risk and type.
3 Application of new genetic tools (*e.g.* restriction fragment length polymorphisms) in family segregation analysis studies.
4 Application of new serological tools to study sources, modes of *M. leprae* transmission and risk factors.
5 Cohort and case control studies of resistance, and relapse rates with new drug regimens.
6 Descriptive and analytical studies of the epidemiology of reactions and disabilities.
7 Longitudinal and cohort analyses to describe trends in leprosy incidence, and to identify the determinants of any changes.

M ZUNIGA, *Chairman*

Leprosy control, evaluation and integration

The strategy for leprosy control continues to be based on secondary prevention, that is early detection and chemotherapy for all cases of leprosy. Today the most effective chemotherapy is multidrug therapy (MDT) and already 40% of the Worlds 5 million registered cases have benefited. There is urgent need to speed up MDT implementation, to make it accessible to at least 80% of the estimated cases, in a phased, time bound, target-oriented programme as part of national health plans.

To achieve this end, in many circumstances, the advantages of integration within a well functioning health service should be recognized. Primary health care can provide a comprehensive, continuous and adequate leprosy service, with specialized training, technical support, referral services, treatment delivery, supervision and evaluation.

Many issues pertinent to leprosy control have been discussed in other workshops, and hence are not included in this report (Epidemiology, Health Education, etc.) The recommendations of the 6th WHO expert committee were generally endorsed, taking special note of the definition of the case of leprosy and of the prevalence rate in operational terms. There was a full discussion of a number of important operational points:

1 It is recommended that MDT be implemented as a country-wide, community-based service. Reports received suggest that, with proper implementation, MDT cannot only reduce the caseload, but also constitute an important factor in the decline of leprosy.
2 The effectiveness of MDT suggest that no deviation from the present recommended PB and MB regimes (adapted as necessary for operational reasons) are needed. Reports indicate that the acceptance and compliance are good, therapeutic problems during and after therapy, including reactive episodes, relapse and persistence of active lesions do not hamper the programme. On the other hand, injunctions use of MDT, without proper supervision or not in the correct combinations, must be avoided, because of the risk of drug resistance. The use of thiomides is not recommended under field conditions.
3 The suggestion by the 6th WHO expert committee is that all smear positive patients be treated as MB was endorsed. The need for greatly improved quality for skin smears was recognized. It was recommended in MB cases smears should be taken at least once at the start of MDT and again on completion of treatment. Although in some circumstances it may be necessary to start MDT based on clinical judgement alone, efforts must be to carry out bacteriological examination as soon as possible.
4 The operational problems of continuing surveillance after stopping chemotherapy, and continuing treatment in MB cases after 2 years if they are still positive were recognized. At the moment, however, there is insufficient evidence to deviate from the original WHO guidelines.
5 Skills in the prevention of management of disability should be strengthened. The training of appropriate staff in the recognition and treatment of reactive episodes, involving nerves (and eyes)

with steroids in the field is essential. Adequate referral facilities for each case, as well as the correction and care of established deformity needs the urgent attention it deserves.

6 The cost-effectiveness of different types of surveys for case detection need further evaluation. It is suggested that contact examinations be done systematically at least once at registration of a new case. The importance of health education in case detection was emphasized.

7 Greater attention has to be paid to monitoring and evaluation. There is an urgent need to apply the established indicators and to develop new ones to help programme managers in decision making. Such monitoring and evaluation is not only needed at every level of programme implementation but should include all the components of leprosy control. Management information systems should be designed with this in view in order to improve the effectiveness of the programme implementation.

8 The rapidly increasing urban population, slums, shanty towns and their related leprosy problems, threatens all the achievements of the leprosy control today. Though in both urban and rural areas the methodology is similar, urban leprosy control has to be recognized as a specialized area, varied and complex calling for an imaginative and an unconventional approach, within the framework of urban health care system. All programme managers should recognize that involvement of all medical personnel, the community, the use of health education, selective surveys and emphasis on rehabilitation are needed.

9 Multidisciplinary action oriented health systems research will go a long way to clarifying operational problems. Research at selected regional centres is needed to evaluate the impact of MDT. Operational research in key result areas needs to be carried out to improve efficiency of the programme.

10 Tests for the detection of the subclinical infection, when applicable in the field will greatly assist in the control of leprosy. The results of vaccine trials in progress are not yet available. Till the availability of the field-tested vaccine, the strategy for leprosy control will have to rely on secondary prevention.

11 The rapidly increasing prevalence of human immunodeficiency virus infection and increasing concern of governments should not result in lowering of the priority given to leprosy control. Relationship between HIV infection and leprosy needs investigation. Suitable precautions should be taken by leprosy control staff dealing with patients possibly infected with HIV, Hepatitis B and other such infections.

12 The assistance already given by nongovernmental organizations and contributing agencies was fully recognized. In view of the need for the governments of endemic countries to increase MDT coverage, even greater efforts are called for to mobilize resources. Governments should strengthen their cooperation with the NGOs and coordinate their activities, within the national health plans, so that no leprosy patient is denied MDT for want of resources. In conclusion there is renewed optimism that with increased MDT coverage, integration, mobilization of resources, human resources development, training, increase participation by the NGOs, enhanced monitoring, evaluation and health systems research leprosy control will become a reality.

H SANSARRICQ, *Chairman*

Information systems

The terms of reference were:

1 To deliberate on major issues confronting information systems, including the lack of reliable indicators and possible solutions.

2 To identify serious gaps in present knowledge that affect information systems so as to suggest priorities for research.

1 The meeting, having reviewed various information systems as reported by participants and considering difficulties experienced in implementation, reaffirmed that OMSLEP forms the base for developing systems in all countries with appropriate modifications to suit the requirements of the country. It recommended that: 1.1, Clarification should be made on WHO regimen and on definitions used, specifically with regard to case, adequacy of MDT, and application of reporting system in urban areas. 1.2, The system should give due priority to the needs of field workers; only appropriate data should be collected for analysis, interpretation and programme assessment at the district/state and national level. 1.3, Any system should provide adequate and timely feedback to field workers.

2 The meeting recognizing that the indicators suggested in OMSLEP do not cover the needs of promotional activities and that proxi indicators give only an indirect assessment, recommended that: 1, Promotional programme should specify the exact aims and objectives of various activities, so as to build in evaluation. 2, Research be conducted into developing appropriate indicators for such purposes. The meeting appreciated that appropriate indicators are needed to meet not only scientific concern but also to satisfy political needs.

3 The meeting recognized that there was insufficient information not specific to leprosy, which is important in assessing programme effectiveness, e.g. coverage of the population by the programme or health services, equal accessibility to health care services by all individuals in a country and therefore, recommended: That such indicators for health service accessibility and equity be developed through health systems research.

4 The meeting highlighted various other problems that affect information systems and recommended that: a, a centralized register be maintained in each country to prevent duplication of recording of case; b, each country ensure that patients under the care of private doctors are also reported to the national system; c, NGO's (Non Governmental Organization) maintain information systems in line with national systems; d, the workshop on chemotherapy considers developing clearer definitions for the terms regularity, irregularity and defaulters which do not require such complex calculations; e, research be carried out to ascertain the cost in terms of time and human resources for information systems so as to provide the most appropriate approach for maintaining and developing this system; and f, any information system should report on all activities within a unified system.

5 The meeting considered the suitability of computerization for information systems; but it recognized that computers may not be the appropriate solution in all circumstances, and reaffirmed the need for each country to consider all the pros and cons of such computerization as detailed in the document.

6 Training prior to the implementation of any information system is a fundamental requirement.

LIM KUAN JOO, *Chairman*

Diagnosis and clinical aspects

DIAGNOSIS

In a great number of highly endemic countries, case-finding is undertaken by health workers, who in integrated programmes and in primary health care should be able to make the diagnosis, treatment and follow-up not only of leprosy patients but also of cases of other diseases. Consequently, diagnostic methods should be simple and easily applied in the field. When necessary and wherever possible more elaborative methods should be employed.

Leprous neuropathy (new approaches)

The diagnosis of early neural involvement (especially as for indeterminate or tuberculoid cases) may be achieved in skin biopsies by identifying the antigen in the nerve, with the use of monoclonal antibodies and the presence of the Schwann cell using S-100 protein (immunoperoxidase techniques).

Neurophysiological examinations (electromyogram, nerve conduction velocity, Hoffmann reflex, F wave, and cerebral evoked potentials) may be useful for early leprosy diagnosis.

However, these examinations can only be performed by trained specialists and cannot be undertaken in the field.

Subclinical infection diagnosis

FLA abs, ELISA test, and SACT (serum antibody competition test) may detect subclinical infection. Household contacts were found to have positive reactions and a proportion of them became seronegative.

Further investigations in areas of different endemicity are required to throw light on this subject. Dot-ELISA methods (micromethod) easily applied in villages, and inexpensive, should be preferentially employed.

Household contacts with positive reactions should be tested with lepromin, and the nonreactors (more prone to acquire leprosy and develop the L type) kept under strict surveillance. Although it is not mandatory, for many lepromin negative contacts to develop clinical manifestations, an attempt could be made to prevent their appearance by appropriate intervention.

Probe for M. leprae *identification—recombinant DNA technology*

Cloning of mycobacterial proteins by recombinant DNA technology might offer interesting possibilities for identifying *M. leprae* in suspected specimens (viable and non-viable ones) in addition to the study of the mechanisms of drug-resistance, screening drugs, etc.

CLINICAL ASPECTS

Early manifestations of leprosy

The first signs are cutaneous and occasionally neurological ones. The earliest skin lesion (indeterminate form) appears as one or as a few hypopigmented and sometimes erythematous macules. They are flat, without infiltration, with rather ill-defined margins, and some sensory loss. Most often they are distributed on the extremities. Sometimes there may be a hair loss on the lesions. These are often transient and self-healing. Leprosy bacilli are not found or are extremely scanty, by the routine methods.

The lepromin response is positive in a very high proportion of indeterminate cases. Most of the cases evolve towards the tuberculoid type and only in a small proportion towards the lepromatous type.

Occasionally, neurological symptoms and signs precede the onset of skin lesions. Tuberculoid lesions are very often an early manifestation.

Reactional episodes

Reactional episodes represent acute or subacute phenomena, with local and/or general involvement and occurring in the chronic course of leprosy. Following studies on cellular and humoral immunity, the reactional states have been divided into 2 groups:

Reaction type 1: associated to cell-mediated immunity, may result in improvement (up-grading or reversal reaction) or worsening (down-grading) of the disease.

Reaction type 2: is an immunocomplex syndrome characteristic of the lepromatous type. Cutaneous manifestations may consist of: 'Erythema Nodosum' (EN), and less frequently 'Erythema Multiforme' and 'Erythema Necrosans', often accompanied by constitutional symptoms and systemic involvement.

The correct diagnosis of reactional episodes is important for the appropriate treatment. Differentiation of reversal reaction and relapse is also important in cases who have completed MDT.

The study of the reactional states is recommended with regard to: lysosomal activity, immune-complexes, autoantibodies, use of immunoperoxidase techniques, cell-mediated immunity and ultra structure of the nerve particularly to identify the sites of involvement.

The silent nerve paralysis

While in reactional states painful neuritis is easily recognized in a large number of cases, worsening of the disease process in the nerve is not heralded by pain or paresthesia. Sensory and motor deficit occur insidiously. This may occur in the early stages of the disease or later. Diagnosis of this condition in the early stages, by routine sensory and motor assessments, is necessary to institute treatment and avoid irreversible deformities.

Lucio's leprosy—Lucio's Phenomenon

Lucio's leprosy is a variety of lepromatous type, characterized by a diffuse and generalized skin infiltration which never presents nodules and with a special kind of lepra reaction: 'Erythema Necrosans' (Lucio's Phenomenon). It is mainly seen in Mexico. A few cases have been reported from some other countries.

J C GATTI, *Chairman*

The role of the ILA in training

INTRODUCTION

There are two principal roles for professional associations in training. The first is to provide opportunities for continuing education for members and other professionals and the second, to recruit and train additional professionals. It is generally agreed that there is a great unmet need for training in leprosy, particularly amongst people responsible for the clinical care of leprosy patients in countries where the disease is endemic, especially where integration has been adopted as a national policy. With these presuppositions in mind the members of the workshop considered the topic in 5 aspects: 1, The *International Journal of Leprosy* and other journals; 2, Associations of leprosy professionals; 3, Teaching and learning materials; 4, Undergraduate medical education; and 5, Possibilities for a resource information network.

THE *INTERNATIONAL JOURNAL OF LEPROSY* AND OTHER JOURNALS

Initially the very existence of journals devoted to leprosy must be justified. As long as there is a need for a specialized body of knowledge which makes up leprology there will need to be an International Leprosy Association and its Journal. This need will exist as long as leprosy remains a health problem, *i.e.* for as long as the disease is not 'adequately' controlled.

Given that leprosy journals are still needed, to whom should these journals be directed? Certainly the relatively small group of full-time leprosy researchers and leprosy physicians (2000?) should be served. As well as the significant numbers of physicians and surgeons, who must care for leprosy patients in specialist or general medical practice. Many paraprofessionals working in leprosy should find at least some parts of leprosy journals of interest. As a practical matter it is most unlikely that leprosy journals can be of value to much larger but nonprofessional groups such as community health workers. A leprosy journal should provide leprosy professionals with a focus for their discipline, a means of exchanging information, and a constant motivation to perform better. A focused, well-informed, and well-motivated professional leprosy worker—in a laboratory, at the bedside or teaching—is our greatest asset in caring for today's leprosy patients and in preventing tomorrow's. For the membership of the association the journal should foster a sense of pride in belonging to a group with a high professional standard as well as being a convenient, reliable and readable source of accurate, timely and stimulating information through original articles, editorials, review articles and current literature summaries. For writers including those who fill the correspondence columns and especially for the younger professionals the Journal provides not only motivation and an opportunity to share their work with others, but with exposure to the disciplines that publication in a reputable Journal entails and with exposure to free, critical and kindly advice from experienced reviewers.

ASSOCIATIONS OF LEPROSY PROFESSIONALS

Leprosy associations are defined as being those composed primarily of professional workers with a serious interest in this disease. Such professionals need not be leprosy workers exclusively, but will include any recognized medically oriented discipline. In providing training opportunities to those actively or potentially engaged in leprosy work control activities, it is important that the private sector is not overlooked, as in many parts of the world private practitioners are becoming more involved in such activities. It is essential for the ILA to identify local or national associations (or appropriate institutions) with actual or potential ability and willingness to provide training for those with a need, and to design mechanisms by which whatever support required is provided to these associations so as to enable them to conduct effective training programmes.

Although not defined at present, there needs to be a focus on specific targeted actions which will enhance these efforts, but it is deemed important to at least first identify ILA members who can and will collaborate in training activities; determining the mechanisms of their support, including financial support, is of prime importance.

Finally, the ILA and its individual members should strongly consider making serious efforts to convince governments of various nations that leprosy continues to be a serious global problem, and that support of leprosy control activities remains extremely important.

TEACHING AND LEARNING MATERIALS

It is recognized that there is a very great unmet need for teaching and learning materials especially for general medical workers at all levels involved in integrated leprosy programmes. However apart from once again drawing attention to the need it was agreed that no specific role for the ILA could be identified in this area. The possibilities for the provision of material specifically designed for self-assessment and self-instruction were also captured—again it was emphasized that the greatest needs are to be found amongst those working in general health services who have limited numbers of patients to care for. However it was considered questionable whether self-instructional material would be of greater utility to this group than basic handbooks or manuals and the matter was referred for further study.

UNDERGRADUATE MEDICAL EDUCATION

Leprosy is either not included at all or is allocated insufficient time in the curriculum of many medical schools. The ILA should emphasize the importance and value of teaching leprosy patient management and disease control in medical schools especially in leprosy endemic countries. The following approaches were discussed: Interdisciplinary teaching in conjunction with dermatology, infectious diseases, neurology, epidemiology, ophthalmology and rehabilitation medicine. The involvement of disciplines outside the clinical medical field including sociology and psychology in order to increase the understanding of and eventually reduce the stigma associated with the disease. The preparation and distribution of leprosy training material. The identification and encouragement of individual teaching staff who are interested in leprosy.

RESOURCE INFORMATION NETWORKS

There is a need for a resource information network to identify leprosy information materials and leprosy specialists worldwide, particularly in the field of training. Such a resource would be especially helpful to persons working in remote areas without access to good libraries and computer-search facilities. Because of the practical difficulties and costs inherent in the development and maintenance of these networks it was proposed to proceed with caution and possibly begin with a relatively small network linking individuals working in training institutions.

W F ROSS, *Chairman*

Prevention and management of impairment in leprosy

Great strides have been made in the chemotherapy of leprosy, but despite adequate treatment, including MDT, patients continue to develop incapacities. Limited and unreliable information is available about the disability pattern in this new group of patients either active or discharged from treatment.

Where leprosy is common, it is identified as deformity and disability by the public. The failure of control programmes to master the problem of deformity is seen by the public as failure to cure the disease. Discharge of patients from the register of MDT removes the stigma of deformity only from statistics. It remains and accumulates in the sight of the public and of new patients who need treatment. Only if disability is controlled will leprosy control programmes win and maintain the confidence that is essential to success.

Treating and preventing disability should be an integral part of any control programme. We also strongly support the long-term follow-up of patients released from MDT programmes with regard to appearance or worsening of disabilities in spite of 'bacterial cure'. Regular testing should include accurate measurement of nerve function in the eyes, hands and feet and recording of other disabling or stigmatizing physical signs in the face like nose collapse and loss of eyebrows. Every effort should be made at this stage to ensure that treatment and preventive measures are available to the disabled patients that are no longer on the active register.

Training of personnel working in leprosy, but specifically in the areas of prevention and rehabilitation is of utmost importance. Too big a gap continues to exist between available knowledge and implementation. For this we need support and funding. Education in rehabilitation and prevention should start at the top with health care and government officials, administrators and also reach the heart of medical schools and allied health training centres. The well-known training centres should be better supported and probably a few secondary ones developed. Cooperation and communication among the major training centres should be stimulated.

More time devoted to presentations on disability, rehabilitation and prevention should be made available at leprosy congresses.

In spite of past efforts in education and training there is still stigma in the disease, even among health care personnel and we should continue on all fronts in our education programme. No special status or financial benefits (like automatic pensions) should be given to the patient solely on the basis of the diagnosis of leprosy. Doing so only adds to the problems already present in trying to rehabilitate these patients especially in the social and vocational areas.

There is a need for a more workable disability grading system for control programmes. We recommend that the modified grading system presented at the March 1987 WHO Consultation on Disability Prevention and Rehabilitation in Geneva be implemented. This grading system only uses grades 0, 1 and 2, eliminating the existing confusion about grades 2 and 3. We would like to suggest that the term anaesthesia should be replaced by an objective measurement representing protective sensation. However, specifically for control, prevention and management of disability we need more detailed testing systems. Control programme records should have provision for initial and follow-up nerve function examination. It is recommended that a range of filaments be used to identify levels of normal, diminished and lost protective sensation. Successful treatment of peripheral nerve impairment requires the early recognition of changes in nerve function. This will allow treatment for the nerve before the damage becomes irreversible. Only regular and accurate testing of nerve function will alert us in cases of nerve impairment without symptoms. The role that physical and occupational therapists could have in all these areas needs to be stressed.

A programme, treating and preventing disability successfully, as a back-up to the control team, will give credibility to that control programme. Foot care in particular is an aspect of treatment that patients notice and can help to promote compliance and confidence in the programme.

The loss of sight is the most devastating disability in leprosy because it most often is associated with loss of sensation in hands and feet. Basic screening of eye function and status is easy and quickly done. Every leprosy worker, at all levels, should be trained in the basic examination of the eye. Every patient has to have his eyes examined initially and all multibacillary patients at regular intervals. Routine prevention and treatment is possible in the vast majority of cases by specially trained paramedical workers. Medical officers can be adequately trained to deal with the more complex problems and supervise the eye programme by training in special centres.

We would like to emphasize again that leprosy is not a disease of just the skin, but also of nerves and that it produces social, emotional and physical disabilities. These can be prevented in many cases by appropriate measures at the appropriate time. When already established, rehabilitation is more difficult, but these cases must also be treated. No patient should be denied his right to these modalities of treatment, but he also must be made an active and responsible participant in his treatment and prevention programme. Many patients can be taught to recognize 'reportable events' like changes in eye, sensory or motor function and nerve pain and look for help as indicated, but monitoring is still necessary in most cases because many patients are not aware of ongoing changes as in the 'silent neuritis'.

F DUERKSEN, *Chairman*

Vaccine trials

The participants for the workshop came from a wide range of disciplines which included epidemiologists, statisticians, and immunologists. The participants had rich experience in large-scale vaccine trials. The group discussed the results from the 4 major BCG vaccine trials to generate information that could be useful to the ongoing and future leprosy vaccine trials.

1 BCG TRIALS

1.1 Burma

Some 26,000 healthy children were included in the trial and one half of them received BCG, the other half served as controls. Two batches of Glaxo freeze-dried vaccine were used. Very little protection (10%) was observed with the first batch, and as much as 30% with the second batch. Although the secondary batch was a little more potent, both batches had acceptable potency. Combining the results from both batches, it was concluded that the protection conferred by BCG was of a very modest level.

1.2 Uganda

A trial of BCG vaccine against leprosy among 19,000 children in Uganda, all contacts or relations of known cases, began in 1960, using the Glaxo strain of BCG. The efficacy of BCG against early forms of tuberculoid leprosy during the first 8 years was 80%, with evidence of continued protection up to 23 years. The degree of protection was independent of age, sex, and the child's exposure to infection.

1.3 South India

BCG prophylaxis study against tuberculosis in South India included the leprosy component, 5 years after the large-scale study (intake 1968–71) began, involving 200,000 persons. An overall 25% protection against all forms of leprosy has been recorded in 5–12·5 year period. Two different strains of BCG (French and Danish) gave similar results. With a lower dose of BCG (0·01 mg) there was a lower level of protection, and with the higher dose (0·1 mg), there was a higher level of protection seen against different types of leprosy in all age and sex groups.

1.4 Papua New Guinea

The intake period for the trial was about 1 year in 1963–64 and involved about 5000 persons. At the end of 9 years of follow-up, the efficacy rate of BCG was 46%. This trial was carried out in an area virtually free of tuberculosis and environmental mycobacteria.

1.5 Reasons for the differences

The differing results of the trials of BCG vaccine in leprosy were similar to the experiences with BCG against tuberculosis. Possible explanations include, (a) differential exposure of the population to *M. leprae* and other mycobacteria, (b) differences in immunogenetic characteristics of the population, (c) different strains of *M. leprae*, and (d) BCG strains could vary with respect to their protective effect.

2 ANIMAL MODELS

The limitations of the mouse model in experimental situations to judge vaccine efficacy were highlighted. Conflicting results have been reported by different investigators. The participants suggested that additional animal models should be developed.

3 ONGOING TRIALS

3.1 Venezuela

A large-scale trial was started in Venezuela in 1985, to test the ability of a vaccine based on a mixture

of killed *M. leprae* and live BCG to protect against leprosy. Participants in the trial were selected from among the household contacts and other close contacts of prevalent leprosy patients in three states of Venezuela. After initial skin testing with PPD and leprosy soluble antigens (LSA), about 30,000 contacts, aged 6–64 years were randomized in a double-blind fashion to receive either BCG or BCG plus *M. leprae*. The trial population is being followed through annual surveys for the occurrence of leprosy, each year a sample of participants are skin tested with PPD and LSA. To date, the incidence of leprosy in the trial population has been about 0·75 cases per 1000 per year, and no side-effects to vaccination have been observed other than those normally associated with BCG. The skin test studies show no differences in response to PPD between the 2 randomized groups, but large and significant differences in responses to LSA up to 3 years postvaccination (the maximum follow-up time to date). It is expected that sufficient cases will have occurred within the next 2 years to evaluate the initial protective effect against leprosy.

3.2 Malawi

The Karonga Prevention Trial is a randomized controlled trial of BCG and BCG plus killed *M. leprae* vaccine against leprosy (and tuberculosis). Among individuals without a BCG scar prior to entry into the trial, the protective efficacy of BCG plus killed *M. leprae* will be assessed against vaccination with BCG alone. In individuals with a BCG scar, the protective efficacy of repeat vaccination with either BCG or BCG plus killed *M. leprae* vaccine will be assessed. The initial vaccination with prior BCG, was mostly given several years ago. The intake phase started in December, 1985 and is expected to be completed at the end of 1989. The first follow-up survey will take place from 1991 to 1994. First results can be anticipated by 1995.

3.3 ICRC Vaccine

ICRC bacilli, a group of leprosy-derived cultivable mycobacteria exhibit cross-reactivity with *M. leprae* with reference to both B and T cell antigens, this forms the basis of their use in the vaccine preparation. It has been demonstrated that the ICRC vaccine brings about lepromin conversion in a proportion of lepromatous leprosy patients and in 95% of contacts, as well it possesses immunotherapeutic potential. The vaccine is currently undergoing a large scale immunoprophylactic trial in Maharashtra, India, from February 1987. It is a randomized, double-blind and controlled trial. The target population consists of 40,000 healthy household contacts of leprosy patients (all forms) between 1 and 65 years old and both sexes. The trial has 2 arms, receiving, (a) 1×10^9 radiation attenuated ICRC bacilli, and (b) one fifth the standard dose of BCG which is the control arm. Lowering the incidence of the disease (all forms of leprosy) will be used as the criterion of the vaccine efficacy. The trial is expected to last 10 years. To date, about 20,000 contacts have been vaccinated. In addition, a separate large-scale study on the immunotherapeutic efficacy is underway. Simultaneously, a vaccine containing a very high molecular weight (approx. 10^6) cell wall component of ICRC bacilli is now undergoing phase I and phase II clinical studies.

3.4 M.welchii *(L.) Vaccine*

M.w is a non-pathogenic, fast-growing soil mycobacterium, similar, but not identical, to mycobacteria listed in Runyon's group IV. It shares several antigens with *M. leprae*, but has also additional CMI-reactive antigens not present in *M. leprae*. An immunotherapeutic trial with this vaccine was initiated in December 1986 in 2 hospitals in Delhi. The patients belong to LL, BL and BB type of leprosy, and are bacillary positive, lepromin negative. All 89 patients reported to date received MDT, with 52 of them given, in addition, immunotherapy with *M.w* vaccine. The first dose consisted of 10^9 autoclaved *M.w.* bacilli. Repeat doses of 5×10^9 bacilli are to be given at 3-month intervals, up to 8 injections. Preliminary results are promising.

4 PROPOSED TRIAL

South India

CJIL Field Unit, ICMR, Madras proposes to carry out a vaccine trial against leprosy to test the efficacy of 3 candidate vaccines: (a) BCG plus armadillo-derived killed *M. leprae*, (b) ICRG vaccine, and (c) *M.w* vaccine. This trial would include 260,000 individuals from the Chingleput district, an area known to be hyperendemic for leprosy.

5 LABORATORY SUPPORT

Presently there are no proxy indicators available to judge the efficacy of a vaccine. The only method available would be measure the protective efficacy in terms of reduction in the incidence of clinical disease. Recently several *M. leprae* specific antigens/epitopes have been studied as candidates for tools for the detection of infection with *M. leprae*. The ongoing large-scale leprosy vaccine trials provide ideal, well characterized 'population laboratories' for the evaluation of candidate assays. The initial observations suggest that several assays may have epidemiological value.

5.1 PGL-1 Antibody

Findings from Venezuela indicate the high relative risk of developing clinical disease in individuals with high levels of antibodies for the phenolic glycolipid. However this type of survey would not be useful as a screening test to identify high risk individuals, as a large proportion of cases came from individuals with low levels of antibody response. Findings from Malaŵi, which are of cross-sectional nature, do not indicate any predictive value for the PGL antibodies. The levels are similar in contacts as well as noncontacts.

6 Skin test antigens

M. leprae derived soluble antigens, particularly the Rees and the Convit antigens, are being used for research purposes. Results from Venezuela show that the Convit antigen indurations are positively and strongly correlated to the Mitsuda antigen late reactions. However, results from Malaŵi and India bring out the deficiencies with these antigens in terms of reproducibility, sensitivity and specificity.

7 Development of second generation subunit vaccines

The recent application of recombinant DNA technologies, together with the availability of *M. leprae*-specific monoclonal antibodies and the ability to derive *M. leprae*-specific T cell clones, has led to the identification and characterization of at least 6 major protein antigens from *M. leprae*. Based on this approach, the identification of those antigens which are capable of evoking an appropriate cellular immune response in man should contribute to the development of a new generation of leprosy vaccines. Several groups are actively engaged in attempts to introduce genes coding for mycobacterial antigens into various potential vaccine vehicles, including vaccinia virus, BCG, and salmonella. In addition, several recent reports suggest that *M. leprae* cell wall-associated antigens may be candidates for a subunit vaccine.

8 Methodological and design issues

Like most vaccine trials, those for leprosy should in general include, (a) prior evidence of protection as for example from animal studies, sensitization studies, etc., (b) selection of trial area, trial groups

and determination of sample size, (c) choice and definition of 'control' and vaccine groups and dose of vaccine, (d) revaccination criteria, when indicated, (e) procedures for avoiding bias such as randomization, coding, ('blinding' etc.), (f) exclusion criteria, (g) standardization of leprosy diagnosis, (h) quality control of vaccines and field procedures, (i) resurveys and provision to monitor adverse effects, (j) information system including data processing, and (k) duration of trial and rules for stopping.

9 Additional epidemiological information from vaccine trials

While the trial should, in principle, concentrate on its specific objectives, the population base and the resources deployed permit, in general, the gathering of critical epidemiological information, such as trends in incidence rates, with very little additional effort. Such information is generally of value in interpreting the trial results. Care should be taken that this extra effort is kept separate and does not interfere with the conduct of the vaccine trial.

10 Conclusions

(a) Vaccine trials should be carried out simultaneously in different areas of the world with uniform methodology which includes procedures, vaccines and doses.

(b) At least one large-scale trial should compare the 3 candidate vaccines currently available: BCG + killed *M. leprae*, ICRC bacillus, and *M.w* bacillus.

(c) Serious consideration should be given to immunotherapeutic and immunoprophylactic trials in view of their importance to control programmes.

M D GUPTE, *Chairman*

Social aspects

INTRODUCTION

The group composed of social scientists, clinicians and leprosy programmers deliberated on the comprehensive meaning of the social aspects of leprosy. After reviewing reports of earlier workshops on the social aspects of leprosy and taking into consideration the concurrent workshops on Health Education Rehabilitation. At this Congress the group identified the role of social sciences in leprosy as the focus on the workshop.

The contribution of the social sciences extends to all aspects of leprosy control including transmission, treatment, training and health services delivery. The group reaffirms that leprosy control also includes the prevention of associated deformities (WHO TRS 675).

For the purpose of leprosy control, the social sciences include disciplines of anthropology, economics, psychology, history, sociology, philosophy, linguistics, political science and law.

The workshop reviewed the social science publications related to leprosy and noted the theoretical and methodological limitations of many of these studies. Therefore the research results have been of little practical significance. Furthermore, it was also noted that majority of passed research on the social aspects of leprosy had not been conducted by trained social scientists.

The group strongly advocated a need for scientific rigour in terms of research design, methodology, data collection and analysis of research data. This would result in increased scientific reliability and validity, thus facilitating effective use of research results in leprosy control.

The role of a multidisciplinary research team was emphasized. This team should include social science researchers and leprosy programmers at all levels from field leprosy workers to policy planners.

The dissemination of research results was identified as a critical issue. These results need to be (a), clear; (b), easily accessible; and (c), translatable to be of value in leprosy control.

Research in other areas of health, disease and illness is a valuable source from which social scientists in the field of leprosy could benefit. For example, extensive research on compliance improving strategies to hypertension and diabetic regimens would be of importance. The group agreed for the need of detailed background papers from sources. These 'state of art' papers would include an annotated bibliography and would form the basis of further leprosy related scientific enquiries.

The group recommended that a centralized documentation centre of social science and leprosy be established as part of the WHO Leprosy Archives in Geneva.

RESEARCH

The priorities of social science research on leprosy include the following:

1 Those having an immediate relevance to better leprosy control, e.g. improved patient treatment compliance.
2 The differential impact of monotherapy and multidrug therapy on patients, community and health workers concept of cure.
3 The study of social epidemiological factors related to the transmission of leprosy should be conducted by multidisciplinary teams of social scientists, epidemiologists and other researchers.
4 The study of social environment which creates fear on account of prevalence of ulcers and deformity resulting in nonparticipation of community in leprosy control programmes.

RESEARCH PROGRAMMES

1 Studies in health beliefs, behaviour and practices of the community, health providers and patients.
2 Impact of multidrug therapy on the community and health services.
3 Impact of existing health systems (vertical and integrated) on the health functionaries and their relative efficiency.
4 The diagnosis, treatment and rehabilitation problems of women.
5 Studies on patients' and families' self-stigmatization and low self-esteem.
6 The status of leprosy health personnel in the entire health care system.
7 Effective communication between health providers and patients.
8 Legislation regarding leprosy.
9 Cost-effectiveness of various approaches in leprosy control programmes.
10 Concept of 'cure' amongst patients, community and health providers under monotherapy and multidrug therapy.
11 Semantic problems associated with various aspects of leprosy.

TRAINING

The training for social scientists needs to include an orientation to the various problems of leprosy control. The group also emphasized the need for special training in social science research methodology for other leprosy workers who may form part of the multidisciplinary research team. Special funding should be made available for training to attract social scientists to the field.

CONCLUSION

Social science insights aim to provide scientific understanding of the process of change that is brought about in the behaviour, attitudes and practices of various sectors of society towards leprosy.

R K MUTATKAR, *Chairperson*

Health education

RECOMMENDATIONS ON PUBLIC AWARENESS ACTIVITIES IN LEPROSY

Members of the workshop recommend that:

1 There be someone in the leprosy programme with the task of liason with media personnel, who can provide access to media expertise, channels etc. The liason person should have experience and skills or benefit from extra training in communication methods.
2 Awareness activities be continuous throughout the year, not only on World Leprosy Day.
3 Simple studies be conducted locally (including information from experienced workers) to provide background information about current beliefs, practice and attitudes towards leprosy among different groups. Information from these studies should be used in public awareness activities.

RECOMMENDATIONS FOR PATIENT EDUCATION

1 That health workers try to understand the reasons for noncompliance, rather than labelling a patient 'uncooperative'.
2 The major emphasis in leprosy care be on educating the patients to want to be treated. Effective patient education should remove the need for defaulter tracing.
3 All health workers should receive training in patient education skills. Having acquired these skills, they need time to talk with patients. This may require adjustment in the programming of clinics and workload.
4 Guidelines be agreed upon, whereby patient education is carried out in small steps and in a progressive manner according to the patients needs. Written records to monitor progress in patient education and to obtain feedback could be used.

RECOMMENDATIONS ON TRAINING HEALTH WORKERS

1 A course or module on health education in leprosy be included in the training programme of all leprosy training centres, i.e. regional, national, local. Where courses do not exist they should be developed; where there are courses but their content is not adequate, they should be revised.
2 The following strategy be adopted for in-service training; a, an initial workshop on health education/communication skills to demonstrate the approach and to identify potential trainers; b, a second workshop to train the trainers; and c, a third visit to assist the trainees in implementing in their own area what they have learned. This strategy had budgetary implications, and should cover a minimum period of 3 years.
3 The main learning objectives for the leprosy workers will be: a, to learn to look at leprosy through the eyes of patients, their families and public; b, to acquire skill in translating ideas into language which the patient, family and public can easily understand; and c, to learn interpersonal skills to ensure that their communication is effective; and, d, to apply what they have learned, using guidelines for specific situations.

4 In the evaluation of training, the emphasis should be on assessing through follow-up and supervision, how trainees use the health education guidelines in patient and community care.
5 Training of teams of leprosy workers in an area is preferable to training just one level of health worker.
6 A list be drawn up of available resource persons to provide such training. The list should be made available to countries through ILA member associations and the ILA coordinating bureau.

RECOMMENDATIONS ON HEALTH EDUCATION IN LEPROSY

1 Development of materials be at local level, so as to be consistent with local language and culture, but production could be done centrally.
2 Priority should be on pictorial materials used by field workers for patient and community education. Every field worker should have a set of flash cards and be trained to use them.
3 Separate materials should be designed for different target groups.
4 Materials should be pre-tested before production, evaluated and then revised. When possible, advice from a communication specialist should be obtained.
5 ILA takes initiative in identifying agencies to help with material production in various regions, and provides funds to implement the above recommendations.

RECOMMENDATIONS ON IMPLICATIONS FOR HEALTH EDUCATION RELATED TO THE INTRODUCTION OF MULTIDRUG THERAPY (MDT)

1 Prior to the implementation of MDT: a, all health workers involved in leprosy care be trained in appropriate managerial, clinical and health educational aspects of the MDT programme; and b, all patients receive adequate education concerning MDT. The initial preparatory training of staff and education of patients should be reinforced periodically.
2 The objective of leprosy control includes the prevention of disability as well as interrupting transmission of infection. Therefore, health education in all aspects of self care remains a high priority.
3 Where appropriate, the general population should be informed about MDT prior to its implementation.

RECOMMENDATIONS FOR THE EDUCATIONAL TASKS OF THE PERIPHERAL HEALTH WORKER IN LEPROSY CONTROL

1 A variety of types of peripheral health worker be recognized in different places. They range from the informal contact person in the community to the trained health worker. They all influence community opinion about leprosy, and are able to help patients emotionally and socially.
2 The informal contact person or villagers should be identified and listened to. They will devise their own activities, and the health worker gives support when requested.
3 The trained peripheral health worker encourages members of the community to carry out activities like drama, puppet shows, small group discussions to inform the community about leprosy. Other tasks can include: a, explaining to the patient and his family about treatment of leprosy; b, how to prevent deformity; c, about reactions; and d, possible side-effects of the drugs.

J NEVILLE, *Chairwoman*

Recommendations on rehabilitation

1 INTRODUCTION

Any leprosy programme which fails to address the patients disability and dislocation from society, is, especially from his perspective, a failure.

2 DEFINITION

Rehabilitation is the process of maintaining in, or restoring the individual to, his/her rightful place in society.

3 OBJECTIVES

Rehabilitation may be implemented by the achievement of the following objectives:

1 Encourage early treatment of the disease, and perseverance until cure.
2 Recognize early signs of damage to eyes and nerves, and apply appropriate preventive measures and treatment.
3 Develop reconstructive surgery and ophthalmology programmes, including the providing of specialist training in these fields.
4 Find (or create) for the individual job opportunities appropriate to his/her ability. This may involve vocational/other training, and encouragement towards achieving independence, and the ability to compete for employment in the community.
5 For the severely disabled, make life possible with dignity and fellowship, regardless of their physical condition.

4 SPECIFIC RECOMMENDATIONS

While many aspects of rehabilitation have been discussed before, at earlier congresses and elsewhere, and by other groups at this Congress, our group would like to emphasize the following points:

1 Disability control. It is the responsibility of staff at all levels, peripheral, regional, and central, to: a, set measurable disability control and rehabilitation objectives, and evaluate progress towards them; and b, enable patients to minimize their own disability problem. Patients and families are often even more motivated than paramedical workers, and maybe quick to learn simple techniques testing for levels of risk, and following up by preventive care. They must be used.
2 Disability recording. The WHO system for grading of disability is for statistical purposes, and not for recording the progress in individual patients. Detailed records are necessary to monitor changes in eye and nerve status. However these will be too complicated for routine assessments. Hence it is essential that there be, in addition, a *simple* disability record for field use, from which changes in eye status and sensation, strength, and secondary problems can be immediately identified, and appropriate action taken on a priority basis.
3 Implications of multidrug therapy (MDT). Careful record keeping has particular significance now, with the implementation of MDT, where there is an increased threat of nerve damage, especially in borderline patients.

Field personnel must be trained in early recognition and active treatment of eye/nerve damage at the peripheral level. It is imperative that they be able to prevent damage/deterioration, otherwise the compliance and confidence of patients and others will be adversely affected. This intensive surveillance must be continued even after the completion of MDT in the patient. Care must also be taken to be aware of nerve damage in patients with silent neuritis.

4 SURGERY

a Nerve involvement. In the management of neuritis, when medical treatment alone has been shown to be ineffective, the addition of a nerve decompression procedure will relieve pain, and may give good functional recovery. This has special significance with regard to decompression of the posterior tibial nerve, which may restore plantar sensation, and prevent ulceration. To prevent permanent paralysis, the procedure must be done before the nerve is irreversibly damaged, and may be done by any surgeon with appropriate training.

b Reconstructive surgery. Surgery in patients with established paralysis is not of an emergency nature. As long as proper care is taken to prevent the development of secondary deformity, such surgery may be delayed, until a competent surgeon is available.

c Eyelid surgery. Patients who have *lagophthalmus*, especially if corneal sensation too is impaired, are at risk of corneal breakdown. Some type of tarsorraphy should be done as soon as possible.

In those patients with corneal sensation, other sophisticated procedures (such as temporalis transfer) may be done, after proper evaluation. If ulceration is already present, a temporary tarsorraphy using a 'matrass' suture to close the lid should be done as an emergency procedure. Facilities and personnel with appropriate training should be available, at field level, in all control programmes.

d Intraocular surgery. Intraocular procedures may be essential for controlling glaucoma, or for restoring visual function, as in cataract extraction. Some of these patients are at risk for serious post-operative complications. They include those with impaired corneal sensitivity, and those with a recent history of iritis. They should be referred for surgery to a skilled ophthalmologist experienced in ocular leprosy.

e Ulcer and foot care. In anaesthetic feet, ulcers can often be prevented by daily care, careful examination, and the use of appropriate footwear. The patient should be trained and encouraged to take responsibility for this.

Ulcers, once they have occurred, need rest. In uncomplicated cases this need not be neccessarily in bed: some simple ulcers may be managed by wearing protective footwear and minimizing walking; others will need the use of established procedures for ulcer healing. We emphasize that the provision of footwear, and other disability preventing activities, must be an integral part of any leprosy control programme.

5 CONCLUSION

Rehabilitation is not an additional service to leprosy control, that can be left out if funds are limited. It is *fundamental* to the success of control, which may be a waste of money without it.

M BRAND, *Chairman*

Microbiology

SOURCES

The nine-banded armadillo still provides bulk quantities of *M. leprae* of acceptible microbiological quality, so long as protocols for controlling contamination are followed. Smaller quantities of *M. leprae* of high quality (high viability, low chance of contamination) are available from nu/nu mice. In some regions of the world, adequate supplies for research are not available.

PURIFICATION

The 'IMMLEP 1/79' procedure yields suspensions comparable in viability with unpurified

suspensions. Other satisfactory methods involving density-gradient centrifugation exist; one appears to fractionate *M. leprae* cells according to density (possibly related to intactness). A small-scale method for purifying *M. leprae* from human biopsies needs to be developed.

STRUCTURE AND COMPOSITION

Evidence is emerging for the presence in *M. leprae* of a 30 kDa protein like that secreted by *M. bovis*. Capsular material can be observed electron-microscopically and may form the electron-transparent zone of intracellular mycobacteria. 'Buried' proteins linked to the peptidoglycan of *M. leprae* apparently exist. Most components of the envelope (some unique to *M. leprae*) have been identified and MoABs, potentially useful in studying ultrastructure, raised to most. *M. leprae* (like *M. tuberculosis*) inhibits phagosome-lysosome fusion in phagocytic cells.

MOLECULAR BIOLOGY

Five immunodominant antigens were cloned and 2 have been sequenced. As SDS-denatured proteins they are recognized by antibodies and by some T cells. A repeated sequence of DNA has been discovered in *M. leprae*; probes for this may be useful for detection and identification. Expression of *M. leprae* genes has been obtained in *E. coli* and *Streptomyces*. There are encouraging prospects of cloning *M. leprae* genes in cultivable mycobacteria. An immunomodulatory fusion protein has been reported. Genes cloning for identifiable enzymes have been expressed: citrate synthetase and biotinylated proteins (probably acyl-CoA carboxylases, involved in lipid synthesis). Analysis of the sequence of 16S rNA placed *M. leprae* phylogenetically in the group of slow-growing mycobacteria; analysis of the sequence of the ribosomal RNA gene gave preliminary indications of strain differences in *M. leprae*.

BIOCHEMISTRY

M. leprae apparently depends on the host for purines, but is able to synthesize its own pyrimidines. It can synthesize fatty acids de novo and can use the glycoxylate shunt. However, phosphotransacetylase seems deficient; acetate is incorporated into lipids only in intracellular *M. leprae*. Palmitate is incorporated into PGL-I and is readily oxidized. Iron-chelating molecules have not been detected but those from *M. neoaurum* can be utilized. Cytochrome B1, but no others, has been identified. Catalase levels are very low but can be detected by immunoprecipitation methods.

VIABILITY TESTING AND DRUG SCREENS

Systems were described for assessing viability and drug susceptibility *in vitro*. Different systems might be optimal for each purpose. It was noted that compounds have different relative activities in different systems. It is essential to use good quality bacteria for drug screening. Assays for viability varied greatly in sensitivity. Palmitate catabolism appeared to be a particularly promising assay for drug screening; assays based on synthesis of macromolecules will probably be useful. No results of comparisons by double-blind trial of existing *in vitro* drug screens are available.

CULTIVATION

Two new tissue culture systems seem promising; *M. leprae* multiplied in mouse fibroblasts (but lost infectivity) and also in Schwann cell cultures. Axenic multiplication has been described: in the presence of 'adjuvant' mycobacteria; in conditioned medium; in a microaerophilic medium (coccoid forms); in normal media. Identification criteria (see below) should be applied to all these cultures with precautions to ensure that the initial inoculum is diluted out.

IDENTIFICATION

Use of several or all of the following are recommended for identification of cultures claimed to be *M. leprae*: mycolic acids (types by high-resolution chromatography after alkaline methanolysis; species by GC–MS); PGL-1 (using MoABs); G + C content of DNA (56%); DNA hybridization. Restriction fragment analysis will be valuable when fully developed. Reaction with specific MoABs to the 'famous five' antigens is suggested with the caveat that 3 of them appear to be stress proteins and may not be expressed in cultured *M. leprae*. Immunodiffusion analysis can rule out known, cultivable mycobacteria. Growth in normal mouse footpads, and nerve involvement, are characteristic (though not technically taxonomic tests).

P DRAPER, *Chairman*