

NEWS and NOTES

This department furnishes information concerning institutions, organizations, and individuals engaged in work on leprosy and other mycobacterial diseases, and makes note of scientific meetings and other matters of interest.

India. *ICMR Annual Report of the Director-General.* The following is the Leprosy Section of the ICMR Annual Report for 1997–1998.

The load of leprosy cases in India has been reduced through the successful implementation of multidrug therapy (MDT) under the National Leprosy Eradication Programme (NLEP). The total estimated leprosy population of 4 million in 1981 has been brought down to 0.62 million and a target has been fixed for attainment of prevalence less than 1 case per 1000 population by 2000 A.D. However, the new case detection rate has not shown much change indicating that the incidence of the disease has remained almost unchanged. Several problems such as specificity of diagnosis, and complications like nerve damage and disabilities still persist. The Council's Central JALMA Institute for Leprosy (CJIL), Agra, continues to focus on various clinical, therapeutic and laboratory studies aimed at a better understanding of leprosy, its causative organism and improved methods of diagnosis, treatment and prevention.

Clinical Studies

Investigations on early forms of leprosy were continued during the year at CJIL, Agra. The techniques for *in situ* hybridization of *Mycobacterium leprae*-specific sequences have been standardized and further studies are in progress.

Immunology of Leprosy

The results of a study undertaken at CJIL to determine whether lepromatous leprosy (LL) patients could overcome their anergy toward *M. leprae* after long treatment showed that the lymphocytes were capable of producing more IL-2 and IFN-gamma and less IL-10, indicating thereby the tendency for upregulation of CMI responsiveness. In another study higher IgG levels to heat shock protein antigens in BT/TT pa-

tients as compared to LL cases (with and without reactions) were observed.

Analysis of reactivity of samples from tuberculosis and leprosy patients to synthetic peptides has led to the identification of several immunologically relevant epitopes. In the case of leprosy, the identification of one 35-kDa peptide as a candidate for the immunodiagnosis of leprosy and a species-specific CD4 T-cell epitope of the same antigen were important new observations.

Studies on local immunity by using full thickness biopsy cultures are progressing at CJIL. Different classes of IgG antibodies produced in tissue cultures are being analyzed. IgG₃ antibody to *M. leprae* antigens has been found to be the main antibody in precipitation of ENL reactions.

M. leprae and Related Mycobacteria

During the year studies on the detection of persisters in patients treated with MDT for different durations continued at CJIL. By using combined application of mouse foot pad and ATP bioluminescence, persisters have been observed in a significant number of cases.

Experiments have been continuing to establish rRNA-based systems for viability determination. Techniques have been standardized and tested in a limited number of specimens. Follow-up results of quantitative hybridization with an rRNA probe in multibacillary cases being treated with ofloxacin, minocycline and standard MDT showed potential usefulness of this assay in monitoring therapy. While the trends are encouraging, more work is being carried out to establish such methods.

Studies to investigate multiple drug resistance in pathogenic mycobacteria were continued. The results revealed association of rifampin resistance with certain earlier known and new mutations of Indian strains of *M. tuberculosis*. These observations have

relevance in the development of probes for clinical application. The techniques could be subsequently applied to *M. leprae*.

A project on the role of leprosy sera reactive (LSR)/A15 kDa recombinant protein of *M. leprae* in reactional states of leprosy is ongoing at AIIMS, New Delhi. Peptides synthesized on the basis of the sequence of LSR/A15 distinguished overt and subclinical forms of ENL reactions of leprosy. Preliminary analysis of data showed that one-fifth of the patients suspected to have relapsed had evidence of *M. leprae* DNA in the skin on PCR analysis.

Mycobacterial Repository Center/Mycobacterial Referral Center

During the year the CJIL, Agra, continued to function as a DBT-funded Mycobacterial Repository Center for collection, characterization and supply of reference and well-characterized Indian strains. CJIL is also serving as a Referral Center for Mycobacterial Diseases for the purpose of validation of immunodiagnostics as well as biotechnology products developed in India.

Pharmacology

In vitro studies on drug permeability showed that rifampin and dapsone did not influence the permeation of each other, suggesting different permeability mechanisms of these drugs. Permeation of rifampin was observed to be temperature dependent. In experiments with mycobacteria other than *M. tuberculosis*, synergism among rifampin, clarithromycin and minocycline was recorded.

Therapeutic Trials

Follow up of various therapeutic trials in paucibacillary (PB) and multibacillary (MB) leprosy patients continued during the year at CJIL, Agra.

Multibacillary Leprosy

Multibacillary patients treated with the WHO regimen (both fixed-duration treatment as well as treatment till smear negativity) are being followed up to determine the therapeutic cure (as assessed by relapse rates). Further analysis of the follow-up results has reconfirmed that highly bacilliferous leprosy cases are at a much higher risk of relapse in spite of 2 years of MDT.

Though the relapses are lower in patients treated up to smear negativity, their occurrence suggests the presence of drug-sensitive persisters even after prolonged treatment.

Follow-up studies on patients treated with a 1 year MDT regimen for multibacillary cases (comprising rifampin, ofloxacin, minocycline, clofazimine and dapsone) were continued at CJIL. Episodes of ENL requiring the use of steroids were observed in the highly bacillated group. The follow up is continuing.

Paucibacillary Leprosy

Paucibacillary leprosy cases treated with a 6-month regimen comprising dapsone, clofazimine and rifampin were followed up during the year. This regimen is being evaluated to determine whether the complications/limitations of WHO/MDT (in terms of residual persisting activity, late reactions and relapses) could be reduced. Less residual activity, lower reaction rates and no relapses during the first 2 years of follow up have been observed in patients treated with this regimen.

Corrective Surgery

During the year, several studies using newer/improved surgical procedures such as use of abductor hallucis muscle transfer for closure of heel ulcer and posterior tibial artery neurovascular decompression for the management of plantar ulcers were continued at CJIL, Agra. While the initial results with closure of heel ulcers with abductor hallucis transfer are encouraging, some recurrences have been observed during follow up. Efforts are being made to improve/supplement the technique. Studies are continuing to improve and adapt the model established earlier for studying the foot pressure in patients with tarsal disintegration. It is planned to develop a scoring system for making these techniques workable at the field level. Encouraging results have been observed in the neurophysiology of various leprosy-afflicted nerves after decompression. These studies are being expanded and follow up is continuing.

A new adipo-subcutaneous flap (named as JALMA flap) taken from the forearm and used in the restoration of volume of the first web space in muscle atrophy associ-

ated with ulnar palsy in leprosy has been standardized, and a study to assess its application has been initiated.

Immunoprophylaxis and Immunotherapy

Comparative trials of various candidate leprosy vaccines *viz.* ICRC, *M. w* and a combination of BCG and armadillo-derived killed *M. leprae* (along with BCG and normal saline used as control) were continued at the CJIL Field Unit, Avadi. As per the protocol, the second resurvey which started in January 1997 has, till the end of March 1998, registered 295,827 persons, 195,502 of whom were clinically examined. A total of 567 "active" cases of leprosy diagnosed in the second resurvey were referred for MDT. The study is in progress.

A randomized, controlled clinical trial is ongoing at the Cancer Research Institute (CRI), Mumbai, for a comparative evaluation of the immunoprophylactic efficacy of the two vaccines containing ICRC and BCG by measuring the incidence of all forms of leprosy in the vaccinated healthy household contacts of active leprosy patients. The third and final follow up of the vaccinees would be undertaken during the year.

The immunotherapeutic efficacy of the ICRC vaccine has also been investigated in MDT-resistant LL patients. The interim results indicate marked improvement in BI. Laboratory investigations in these patients before and after immunotherapy with ICRC vaccine have also been conducted.

The Netherlands. *22nd International Congress of Chemotherapy.* The First Announcement for the 22nd International Congress of Chemotherapy indicates that the Congress will be held at the RAI International Congress Center, Europaplein, Amsterdam, and will take place 29 June–4 July 2001. The official Congress language is English. For details, contact: Eurocongress Conference Management, Jan van Goyenkade 11, 1075 HP Amsterdam, The Netherlands. Tel: 31-20-679-3411; FAX: 31-20-673-7306; e-mail: ice@eurocongres.com or visit their website for the latest information: <http://www.eurocongres.com/ice>

Switzerland. *Special LEAG meeting.* The following is the Executive Summary of the Report of a Special Meeting of the Leprosy Elimination Advisory Group (LEAG) with Potential Partners held in Geneva on 12 and 13 April 1999.

"In 1991, the World Health Organization (WHO) and its Member States committed themselves to eliminate leprosy as a public health problem by the year 2000, elimination being defined as prevalence below 1 case per 10,000 population. At the beginning of 1999, out of 122 countries which were considered endemic in 1985, 94 had reached the elimination target, and the leprosy prevalence had been reduced by 85% over the past 15 years.

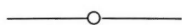
"While at the global level the progress made so far is impressive, in the 13 most endemic countries the leprosy prevalence, despite the enormous reduction already taking place, remains at four times the elimination level. It is likely that some of those countries will not attain elimination by the target date, even at the national level. Consequently, it was felt that the time had come to critically review the global elimination strategy and the tasks remaining to be accomplished.

"A meeting of the Leprosy Elimination Advisory Group (LEAG) with Potential Partners was held at WHO headquarters in Geneva on 12–13 April 1999. The most important recommendation from the meeting was that the elimination strategy remains valid but needs to be focused and intensified. Core activities of the Focused Strategy include active promotion of integration of multidrug therapy (MDT) services within primary health care to bring them as close as possible to the patients, research to further enhance control efforts, and the forging of new and strengthened partnerships at all levels to make the strategy as effective as possible. Partners should also be sought from other health disciplines and from sectors other than health.

"The Focused Strategy will thus have a twofold aim: a) In each of the countries which have not yet reached the elimination stage, to undertake an in-depth review of the situation, to be carried out as soon as possible, so as to step up the activities and put into place the mechanisms and resources that will be required to achieve the specified goal by the year 2000 or shortly thereafter;

and b) In those many countries that have achieved the elimination goal nationally, to ensure the sustainability of the gains that have been made and to initiate activities aimed at reaching the target figure at the appropriate subnational level.

"The LEAG considered that Leprosy Elimination Campaigns (LECs) have proved their worth and should continue to serve as useful tools during the next phase of elimination. Leprosy research remains essential, and among the core activities of the Focused Strategy will be improved monitoring and surveillance at all levels, and the deployment of such innovative measures as Special Action Projects (SAPEL) to reach particularly difficult-to-access population groups. These and other recommendations proposed by the LEAG appear at the end of this document."



U.K. *International Congress on Evolution and Paleoepidemiology of Infectious Diseases.* As a third in a series of bi-annual "International Congresses on the Evolution and Paleoepidemiology of Infectious Diseases" (ICEPID-3), a meeting on the "Past and Present of Leprosy" took place in Bradford, U.K., 26–31 July 1999. It was organized jointly by the Calvin Wells Laboratory, Bradford University's Department of Archeological Sciences (Dr. C. A. Roberts), the Department of Anthropology, Jozsef Attila University, Szeged, Hungary (Dr. G. Pálffy), and the Department of Anthropology, Université de la Méditerranée, Marseille, France (Prof. O. Dutour). Previous meetings were organized by the same group on syphilis in France in 1995 and tuberculosis in Hungary in 1997.

Some 80 participants attended, belonging to various disciplines, from paleopathology and the history of medicine to molecular biology and clinical leprosy. The work and legacy of Dr. V. Møller-Chris-

tensen, the recognized pioneer in the field of the osteology of leprosy, was magisterially reviewed by Dr. P. Bennike, who is in charge of the skeletal collection at the Museum of Medical History in Copenhagen, Denmark. The pathogenesis of bone change in leprosy was extensively discussed. The utilization of polymerase chain reaction to identify DNA in skeletal remains was illustrated by several examples from Bavaria, Hungary, Poland and Israel, as well as in soft tissues from old museum specimens.

Methods for studying paleodemography (prevalence rates of mycobacterial diseases) and paleogenetics (biological relationships of individuals) data in Egyptian burial sites were presented (Dr. J. E. Molto). The myth of the Crusades as having caused an epidemic of leprosy in Medieval Europe was critically reviewed (Dr. P. Mitchell).

In spite of this meeting being a multidisciplinary gathering of scientists, most of them more concerned with the past than with the present, and perhaps more directly interested in leprosy than in leprosy patients, special attention was given to current issues, such as the achievements of the World Health Organization (WHO) Leprosy Elimination Programme (A. C. McDougall), historic patterns in the spread of leprosy (M. F. Lechat), social concerns (J. M. Mehta, A. S. Law), and the ILA Global Project on the History of Leprosy (P. Sommerfeld).

The remarkable collection of skeletal material from the Chichester leprosy cemetery was on display.

It is expected that the papers presented at the Congress will be published. If the volume is the same quality as the one on tuberculosis issued after the Szeged 1997 meeting, it will constitute a most valuable work of reference for all interested.—M. F. Lechat

