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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.

1994 DAMIEN-DUTTON AWARD RECIPIENT

Dr. Robert C. Hastings, IJL Editor, (left) accepts 1994 Damien-Dutton Award from Mr. Howard Crouch.

We are extremely proud to announce that the winner of the Damien-Dutton Award for 1994 is the INTERNATIONAL JOURNAL OF LEPROSY. The presentation was made at the Carville Centennial in November 1994 at the U.S. Public Health Service Hospital in Carville, Louisiana, U.S.A. The Award was presented by Mr. Howard Crouch to Robert C. Hastings, M.D., Ph.D., Editor of the JOURNAL, who was asked to accept the Award on behalf of the JOURNAL, the official organ of the ILA, by Dr. Yo Yuasa, ILA President.

The plaque reads: "1994 Damien-Dutton Award presented to the INTERNATIONAL JOURNAL OF LEPROSY for more than 60 years of disseminating scientific information to those engaged in the treatment and care of leprosy patients in all parts of the world. Through the JOURNAL scientists and paramedical workers have shared their findings and views leading to the conquest of leprosy."

Dr. Hastings' acceptance speech follows.

The Damien-Dutton Award is the most prestigious recognition in the field of leprosy. The list of recipients since 1953 reads like a Who's Who of leprosy. There have been three previous recipients which have been organizations rather than individuals. These were: the U.S. Peace Corps in 1966, American Leprosy Mission in 1981, and Catholic Medical Mission Board in 1989. It

is a great honor that the INTERNATIONAL JOURNAL OF LEPROSY has been chosen by the distinguished Board of the Damien-Dutton Society to receive this honor this year, 1994, coinciding with the 100th year anniversary of this hospital at Carville.

It is a great personal honor for me to have been asked by Dr. Yo Yuasa, President of the International Leprosy Association, to accept this Damien-Dutton Award on behalf of the INTERNATIONAL JOURNAL OF LEPROSY, the official organ of the International Leprosy Association (ILA).

It has been my privilege to serve as Editor of the JOURNAL since 1979, following in the footsteps of giants in the field of leprosy, beginning in 1933 with Dr. H. Windsor Wade, then Dr. Esmond Long, and then Dr. Olaf Skinsnes. Theirs have been formidable footsteps to attempt to follow. They created a sound format and they created sound traditions for our JOURNAL. Without the pioneering work done by these Editors, there would be no JOURNAL today.

For almost the entire time I have been Editor, I have been privileged to work with Mrs. Dee Goodman as Assistant Editor. Dee is the only full-time employee of the JOURNAL and that makes her the only full-time employee of the ILA. She meticulously minds the store, patiently correcting the spelling and grammar of authors and editor alike, tracking down obscure references, tracking manuscripts, working with the printer, and seamlessly integrates the regular mass confusion into issue after issue. If I would only follow her instructions our JOURNAL would be timely as well as virtually error-free. Without Dee there would be no JOURNAL.

The JOURNAL operates by the grace of volunteers. The foremost volunteer is the Executive Officer of the JOURNAL and Treasurer of the ILA, Dr. Felton Ross. Each year, year in and year out, Felton manages to keep track of subscriptions, to collect dues from members, and to raise the additional money from voluntary organizations to make the payroll and to pay for the printing and distribution of our JOURNAL. Without Felton there would be no JOURNAL.

The paid subscriptions to the JOURNAL are paid by individuals and by voluntary organizations on behalf of individuals. From both sources the paid subscriptions are not sufficient to support the JOURNAL's costs of production and printing. Contributions from voluntary organizations make up the shortfall year after year. Special Grantors include the Swiss Leprosy Relief Organization, American Leprosy Mission International, the Italian Friends of Leprosy Foundation, the Damien-Dutton Society, the Damien Foundation of Belgium, the German Leprosy Relief Organization, the Canadian Leprosy Relief Organization, the Netherlands Leprosy Relief Association, the Pacific Leprosy Foundation, the Sasakawa Memorial Health Foundation of Japan, The Leprosy Mission International of the U.K., and the Order of Charity in England. Sustaining Members include the Foundation Follereau of France and the Japanese Leprosy Association. Without these voluntary organizations there would be no JOURNAL.

Obviously, what appears in our JOURNAL depends entirely on what is submitted to it for publication. Each year, as an average, over 70 original articles are submitted, and each averages some four authors. Since 1979, approximately 1075 original articles, written by approximately 4300 authors, have been entrusted to the JOURNAL for publication. Clearly, without these authors there would be no JOURNAL.

Each original article submitted for publication is subjected to peer review. At least two referees review each original article for its suitability for publication. This means that, since 1979, over 2150 reviews have been made of manuscripts submitted to the JOURNAL. These referees are chosen on the basis of their knowledge and expertise in the subject area of the manuscript. These individuals are extremely busy in their own work. As expert biomedical consultants, their time is very valuable. As an average, perhaps four hours are spent by these individuals on each review. A guess of the value of reviewers to the JOURNAL would be between US$500,000 to $1 million since 1979. They volunteer their time and expertise, time after time, to evaluate manuscripts and sometimes, even more importantly, they offer their expertise in suggestions for revisions of the manuscript to improve it. This takes many forms. Sometimes it is simply a better use of the language. Sometimes it is an error that is pointed out in statistical analysis. There have been times

when it amounted to suggesting additional experiments or additional clinical observations and advising that the paper could be improved if those findings were submitted in a revised manuscript. Peer review makes the JOURNAL a teaching tool for all of us. Without these reviewers there would be no JOURNAL as we know it.

Since its founding in 1933, the JOURNAL has served the membership of the ILA in many ways. In the early days it served as a means of communication for a small group of individuals concerned about leprosy who were widely scattered over usually remote parts of the world with primitive communications. Opinions of colleagues about leprosy and how it manifested itself in different countries, different climates, and different societies, were important. Epidemiological studies gave some clues as to how the disease was transmitted. Histopathology served to clarify the types of disease and their clinical manifestations. But perhaps mainly the JOURNAL was a tool to identify a field of work, a field of concentration, a diverse field called leprosy. In the early years of the JOURNAL, leprosy was clearly outside the mainstream of medicine and science, and so was the JOURNAL.

Far-sighted leprologists realized that rapid progress in leprosy required participation from more than leprologists themselves. The call was made repeatedly that leprosy should be brought into the mainstream of medicine. But this was not to be for many years. Leprologists here at this hospital (Carville) developed the first effective treatment for leprosy. The findings were presented to their fellow leprologists as a reprinted article in the JOURNAL after the end or World War II. This was not a double-blind, controlled clinical trial with all sorts of laboratory surrogate end-points. This was a group of leprologists trying out something new in their patients and reporting what happened.

In the coming decades the JOURNAL continued to serve as a link among leprologists around the world. It is the only official activity of the ILA other than the International Leprosy Congresses held every 5 years. It continued to serve as a bulletin board of sorts for the members of the ILA, providing news and notes of the happenings in the world of leprosy, providing abstracts of current literature which might prove useful for members working in remote areas, and noting the deaths of colleagues through obituaries.

At some point the JOURNAL became more than a bulletin board for the members of the ILA. It became a scientific journal as well. It is difficult to pinpoint that transition. It came as more and more information became known about leprosy, information that frequently was published first, not in our JOURNAL, but in a journal of a scientific society representing the discipline and training of the author. Subtly leprologists found themselves acknowledging the contributions of nonleprologists to their field of leprosy. Orthopedic surgeons began to publish articles about rehabilitation of leprosy patients. Microbiologists published papers on the growth of the leprosy bacillus in the foot pads of mice. Pharmacologists measured blood levels of sulfones in patients and discussed compliance with treatment regimens. Immunologists began to discuss leprosy as a model of an infectious disease with immunodeficiency. Social scientists contributed to understanding the stigma of leprosy and how patients cope with it.

To be sure, professional leprologists continued to make their contributions. The final proof of the value of any new drug rested on clinical trials supervised by a leprologist, supplemented perhaps with tests of bacterial viability in the laboratory. Many leprologists developed expertise in a specialized area and continued to make contributions in that specialized area. But the field of leprosy changed. It changed from primarily being an association of leprologists to a field open to any and all disciplines. It changed from a general practice of leprosy into a collection of contributions from specialists, some leprologists, but more significantly perhaps, many nonleprologists.

Our JOURNAL has moved with the times. Many of the articles now appearing in the JOURNAL are of superb quality and reflect the very latest technology. For that, leprologists have to take pride. Leprosy has attracted very talented and dedicated people over time. It continues to attract very talented and dedicated professional leprologists. Now it is also attracting very talented and dedicated people who are not professional leprologists. If leprosy is not yet in the mainstream of medicine, it is close.

Our JOURNAL is a living collection of efforts by authors, referees, the assistant editor, the executive officer, the Board of Directors, the Contributing Editors, the subscribers, the members of the ILA, and the voluntary organizations which support it. I am proud that our JOURNAL has played a part in the progress we have made in leprosy, and I hope that our JOURNAL can continue to serve the readers and members of the ILA for generations to come.

Thank you very much, Mr. Crouch, for the honor that you and the Damien-Dutton Society have bestowed on the INTERNATIONAL JOURNAL OF LEPROSY.

Previous Recipients of the Damien-Dutton Award

1953 Stanley Stein, U.S.A.
1954 Rev. Joseph Sweeney, KOREA
1955 Sister Marie Suzanne, FRANCE
1956 Perry Burgess, U.S.A.
1957 John Farrow, U.S.A.
1958 Sister Hilary Ross, U.S.A.
1959 Dr. H. Windsor Wade, PHILIPPINES
1960 Mgr. Louis Joseph Mendelis, U.S.A.
1961 Dr. Kensuke Mitsuda, JAPAN
1962 Rev. Pierre de Orgeval, FRANCE
1963 Eunice Weaver, BRAZIL
1964 Dr. Robert G. Cochrane, U.K.
1965 John F. Kennedy, U.S.A. (Posthumous)
1966 Peace Corps, U.S.A.
1967 Dr. Howard A. Rusk, U.S.A.
1968 Dr. Franz Hemerijckx, BELGIUM
1969 Dr. Victor George Heiser, U.S.A.
1970 Dr. Dharmendra, INDIA
1971 Dr. Chapman H. Binford, U.S.A.
1972 Dr. Patricia Smith, VIETNAM
1973 Dr. Jacinto Convit, VENEZUELA
1974 Dr. José N. Rodriguez, PHILIPPINES
1975 Dr. Oliver Hasselblad, U.S.A.
1976 Dr. Yoshio Yoshie, JAPAN
1977 Drs. Paul and Margaret Brand, U.S.A.
1978 Dr. Fernando Latapi, MEXICO
1979 Dr. Stanley G. Browne, U.K.
1980 Robert Watelet, ZAIRE
1981 American Leprosy Missions, U.S.A.
1982 Dr. Ma Haide, CHINA
1983 Murlidhar D. Amte (Baba Amte), INDIA
1984 Mother Tereza, INDIA
1985 Dr. John H. Hanks, U.S.A.
1986 Samuel J. Butcher, U.S.A.
1987 Dr. W. Felton Ross, U.S.A.
1988 Hermann Kober, WEST GERMANY
1989 Catholic Medical Mission Board
1990 Dr. Wayne M. Meyers, U.S.A.
1991 Dr. Ruth K. M. Pfau, GERMANY
1992 Anwei Skinsnes-Law, U.S.A.
1993 Dr. Charles K. Job, INDIA

Cameroon. *VIII Congrès International des Léprologues de Langue Française.* Le prochain Congrès International des Léprologues de Langue Française aura Lieu à Yaoundé dans un peu plus d'un an (28–31 janvier 1996).

Nous sommes reconnaissants au gouvernement du Cameroun d'avoir bien voulu accepter de recevoir notre Congrès et à Monsieur le Ministre de la Santé publique d'avoir bien voulu nous accorder son haut patronage.

Le Comité exécutif de l'Association des Léprologues de Langue Française et l'Association française Raoul Follereau ont établi leur collaboration pour la préparation de ce Congrès. Le Comité exécutif de l'ALLF a tenu, en octobre 1994, une première réunion sur les aspects scientifiques de cette manifestation dont le Comité scientifique se réunira en janvier prochain.

Ce VIII[e] Congrès débutera comme à l'habitude à la fin de la Journée mondiale des Lépreux, le dimanche 28 janvier 1996.

Les thèmes qui nous semblent s'imposer à l'heure actuelle (sans que la liste ci-dessous soit encore définitive) sont, bien sûr, le traitement antibactérien de la lèpre, les problèmes opérationnels dans la lutte antilépreuse, les névrites et réactions lépreuses, la prévention des invalidités et la réadaptation et les perspectives en immunologie et en biologie moléculaire, mais également deux sujets rarement traités, les complications oculaires de la lèpre et l'apport de l'histopathologie.

Ce Congrès devrait avoir un réel intérêt pour tous ceux qui, dans les pays francophones, s'intéressent à la lèpre. Ceci, au moins pour trois raisons:

1. Au Congrès d'Orlando (14[e] Congrès international de la Lèpre) les participants

des pays francophones étaient en nombre très faible et tout le monde l'a regretté.

2. La stratégie d'elimination de la lèpre en tant que problème de santé publique d'ici l'an 2000 s'est développée jusqu'ici dans pratiquement tous les pays d'endémie. La PCT a rèduit le nombre des malades de manière impressionnante mais il est nécessaire de continuer à améliorer les méthodes permettant de prendre en charge au moindre coût la "prévalence inconnue." L'expérience acquise a continué de s'accroître depuis Orlando et on devrait pouvoir en tirer des enseignements significatifs.

3. Enfin, le problème de la prévention des invalidités et de la réadaptation, dont on a depuis toujours reconnu la priorité, continue de rester généralement négligé. On devrait, dit-on, pouvoir s'en occuper après que le nombre des malades eut beaucoup diminué à la suite de l'application de la PCT. Et pourquoi ne commencerait-on pas par organiser la prise en charge des névrites et réactions au niveau périphérique?

Bien entendu, nous demandons à tous les futurs participants qui le souhaitent de nous faire connaître leurs vues sur le contenu et l'organisation de ce Congrès. De notre côté, nous donnerons dans les prochains numéros d'Acta Leprologica toutes les précisions utiles sur les modalités de participation.—Dr. Hubert Sansarricq, President de l'Association des Léprologues de Langue Française

Germany. *1995 European Conference on Tropical Medicine.* For the first time Europe's tropical medicine societies are holding a joint conference. It will be held at Hamburg's CCH (Congress Centrum) from 22–26 October 1995. At this conference the various societies will join up to form a European Federation; at the same time several national trade publications will merge to create a single European magazine.

The aim of the Conference is to improve the treatment of global health problems by encouraging pan-European cooperation and partnership between Europe and the tropical regions of the world. To this end, numerous doctors, health experts and scientists from Europe, Africa, South America and Asia have been invited to attend.

The program will cover every subject within the field of tropical medicine—a spectrum ranging from basic research through questions of clinical practice to the organization of health services. The main emphases include, for example, new epidemics, family planning, the provision of health care to refugees, the tie-up between research and caring for the sick, computer simulation of the spread of diseases, travel medicine, immunology and the development of vaccine.

Information on the scientific program is available from the Congress Secretariat at the Bernhard Nocht Institute for Tropical Medicine, Bernhard-Nocht-Str. 74, 20359 Hamburg, Germany. Phone (+49 40) 31182-511. Fax (+49 40) 31182-512. Registration forms will be mailed by the Congress Secretariat at CCH (Congress Centrum Hamburg). Phone (+49 40) 3569-2245. Fax (+49 40) 3569-2343.—From press release/first announcement

India. *1994 ILEF Awards for Excellence.* Eminent persons distinguished for their contributions in the field of leprosy in the national scene received Indian Leprosy Foundation (ILEF) Awards for Excellence for 1994 at the National Conference of Voluntary Organizations in Delhi. The recipients were: Dr. A. K. Mukherjee, Director General of Health Services (DGHS); Dr. S. K. Noordeen, Chief of Leprosy Division, WHO, Geneva; Dr. B. N. Mittal, Dy. DGHS (Lep); Mr. Hermann Kober, Executive Director, GLRA; Dr. R. Ganapati, Director, Bombay Leprosy Project; Dr. C. K. Rao, Former Dy. DGHS; Dr. H. Srinivasan, Former Director of Central JALMA Institute; Dr. B. Kameswara Rao, Former Director of Health Services, AP; Dr. V. Ekambaram, Special Representative, Amici di Follreau; Mr. S. P. Tare, Director, Gandhi Memorial Leprosy Foundation; Dr. G. Ramu, Former Dy. Director, Central JALMA Institute.

They were each given a citation and a silver salver in appreciation of their contribution for leprosy work in India. The Awards, instituted by the Indian Leprosy Foundation, have now become a regular feature.

Dr. R. Ganapati, Director, Bombay Leprosy Project, who could not go to Delhi due to health reasons, received the ILEF Award and citation at the hands of Mr. A. B. Maduskar, Dy. Municipal Commissioner,

Greater Bombay, at a simple function organized by the Indian Leprosy Foundation at the L.T.M. Medical College, Sion, Bombay on Thursday, 24 November 1994. Dr. (Mrs.) S. S. Deshmukh, Dean of the College; Dr. A. P. Potdar, Asst. Director of Health Services (Leprosy), and the heads of various voluntary organizations attended the Award function.

An audio-visual presentation titled "Communication Strategies for Elimination of Leprosy" was presented by Dr. A. R. K. Pillai, President, Indian Leprosy Foundation, for the benefit of the audience. Dr. C. R. Revankar, Dy. Director, Bombay Leprosy Project, proposed a vote of thanks.—From Dr. K. V. Gupte

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ICMR Annual Report. The 1992–1993 Annual Report of the Director-General of the Indian Council of Medical Research (ICMR) contains the following section on leprosy:

The Council's Central JALMA Institute for Leprosy (CJIL) at Agra is engaged in studies to assess the current methods of diagnosis and treatment, to develop newer methods and tools which may serve to improve upon the available ones, and to improve an understanding of the disease process and the complications that add to the morbidity in leprosy. Other investigations in progress include studies on (a) *Mycobacterium leprae* for developing better methods to destroy the organism, (b) to improve understanding of the disease dynamics in the community, and (c) comparative trials on candidate vaccine preparations. Research in leprosy is also being done through extramural projects in various institutes of the country.

Clinical Studies

A need is felt for differentiating indeterminate leprosy from nonspecific dermatitis. The extended morphometric study carried out earlier, however, did not lead to any conclusive results. Hence, a prospective study using gene probes, gene amplification techniques, immunohistology and histology to analyze these cases better was initiated at CJIL, Agra. Intake of patients was started during the year and pilot experiments using these newer approaches were conducted. Immunohistological techniques for demonstration of mycobacterial antigen (using anti-BCG antibodies) were established. The antigens could be demonstrated in 30% of patients by direct staining; whereas up to 70% positivity was seen with indirect techniques in the paraffin sections.

Calcification of peripheral nerves in leprosy is being studied. Initial screening showed that nearly 10% of patients with thickened nerves had radiological evidence of calcification. Ulnar nerve followed by lateral popliteal nerve were the common nerves which showed calcification.

A study to understand the significance of cellular morphology of Mitsuda lepromin response was completed during the year. Results indicate that the histology of lepromin reaction using Mitsuda antigen has a fair degree of correlation with clinical and histopathological classification of patients. However, the degree of positivity was not always found to correlate with the underlying morphology.

At the Safdarjang Hospital, New Delhi, attempt is being made to study the fine structure of the nerves, the vascular and lymphatic capillaries and dermal appendages in biopsies taken from early lesions of leprosy. Ultrastructural examination of patients with negative histological findings on light microscopy did not show any specific change in 20 of the 25 patients studied. It is thus felt that ultrastructural studies on early lesions in leprosy may not contribute much to confirmation of the diagnosis.

Pathology and Immuno-pathology

Ultrastructural studies to characterize the cells in granuloma of the nerves due to leprosy were continued at CJIL, Agra, during the year. Initial results had shown good correlation between the cellular characteristics in the skin and nerve lesions. Studies are in progress on a larger number of patients.

Ultracytochemical studies of lysosomal morphology and function in sequential biopsies of patients in reaction have shown that the membranes stabilize after control of reactions by means of antireaction treatment.

Immunology of Leprosy

To determine the immune responses to the antigens of *M. leprae* and related mycobacteria, a technique targeting crossreactive antigens of BCG was standardized last year and this is now being evaluated. During the year, skin smears have been collected from patients for detection of antigens using ELISA and dot-blot assays.

During last year, a study had shown that most patients with erythema nodosum leprosum (ENL) had significant increase in the levels of lactoferrin. Further studies on the lactoferrin levels in leprosy patients indicated a positive correlation between the bacterial index and serum lactoferrin levels. Follow-up study is in progress to find out if continued rise of lactoferrin in patients with lepromatous leprosy could be useful for the prediction of occurrence of reactions.

Studies were carried out on complement and immune complexes (ICs) in leprosy. The terminal complement complexes (TCC) were studied by double antibody sandwich ELISA. Results have shown that there is no elevation of TCC in the sera of leprosy patients as compared to healthy volunteers.

M. leprae and Related Mycobacteria

Studies have been continuing at CJIL, Agra, to understand the metabolic requirements of *M. leprae* which may help in development of rapid *in vitro* drug screening system or the eventual cultivation of *M. leprae*. Based on the results of the experiments, an improved *in vitro* system had been standardized earlier at the Institute. During the year, this method was tried in bacilli derived from patients of multibacillary leprosy and results indicate that the technique can be used to study the energy synthesis of various human isolates of *M. leprae*.

Efforts have been made to develop methods for rapid determination of viability of *M. leprae* in patients with multibacillary and paucibacillary leprosy. During the year, three gene amplification techniques along with highly sensitive ATP bioluminescent assay system (earlier standardized and tried at CJIL) were applied to frozen specimens from patients of multibacillary leprosy who were under different phases of treatment. Preliminary analysis of the results shows that positivity with polymerase chain reaction (PCR) decreases during the course of treatment. However, weak signals were observed to persist for a longer time than ATP assays. Studies to assess the applicability of these methods to patients of paucibacillary leprosy have been initiated.

Molecular Biology of Mycobacteria including *M. leprae*

Studies are being undertaken at CJIL, Agra, to design and evaluate various diagnostic probes. The techniques for analysis of restriction fragment length polymorphism (RFLP) of rRNA gene region which were earlier standardized and found useful to characterize various pathogenic mycobacteria, are being applied to large numbers of strains including leprosy-derived isolates from Foundation for Medical Research, Bombay, and Postgraduate Institute of Basic Medical Sciences (PGIBMS), Calcutta. To make these applicable to *M. leprae*, an amplified rDNA-RFLP analysis method has been standardized during the year.

As reported earlier, the cloning and sequencing of rRNA genes and flanking sequences of 12 species of mycobacteria had led to identification of 9 variable regions within rRNA gene and flanking regions of ribosomal genes of *M. leprae* and other mycobacteria. Further evaluation/modification of probes/primers designed last year continued during the year. Extended studies confirm the potential usefulness of four of these probes. Methodological studies for their application are in progress.

Studies aiming at optimizing the conditions for the application of gene amplification techniques like PCR, using primers based on 18-kDa and 36-kDA antigen genes and reverse PCR being standardized at CJIL, on the basis of their rRNA gene sequencing work, continued during the year. The enzymatic technique for isolating the mycobacterial nucleic acids from biopsies, reported last year, was applied to specimens from patients of multibacillary and paucibacillary leprosy. Initial results show that technique is an improvement over the earlier known techniques. Attempts to improve the protocol for reverse PCR from biopsies continued during year. Efforts are being made to obtain better amplification by this method, as compared to DNA-based amplifications.

Studies to elicit the expression of enzymes which are metabolically or immunologically important are continuing. Using polyclonal antibodies raised at CJIL, Agra, against superoxide dismutases and other enzymes of mycobacteria as well as with oligonucleotide probes against malate synthase, gene libraries are being screened to elicit their expression. The initial results are promising.

Studies to characterize the DNA-dependent RNA polymerase of *M. leprae* continued during the year at CJIL, Agra. Experiments to raise antibodies against these subunits were initiated during this period which would be used to screen the libraries for their expression.

Pharmacology (including Immunopharmacology)

Pharmacological (including immunopharmacological) studies were continued to help in better understanding the penetration of drugs across the cell membranes of macrophages and mycobacteria. The results of work carried out during the year indicate that the penetration of dapsone into macrophages is enhanced in the presence of primaquine, dexamethasone and calcium ionophores.

Gamma interferons are believed to play an important role in clinical healing and clearing of bacilli from the skin of patients of lepromatous leprosy. Efficacy of intradermal injections of gamma interferons in leprosy is being investigated at AIIMS, New Delhi.

The drug screening system based on *M. leprae* ATP synthesis and decay profile was further improved last year. During the year, more *M. leprae* isolates from patients of multibacillary leprosy were included. Trends of the results confirm that the modified system appears to be more sensitive than the earlier technique in determining the drug susceptibility of human isolates of *M. leprae*. Studies are continuing in patients under different stages of treatment.

Studies to assess the effect of various anti-mycobacterial drugs on mycolic acid levels are in progress during the year. Extended studies confirmed that rifampin affects the mycolic acid levels of various mycobacteria including *M. leprae*. Various aminoglycosides were observed to affect the mycolic acid content in a concentration dependent manner. INH—a drug believed to primarily affect mycolic acid biosynthesis—showed varied responses in different sensitive strains. These results and the earlier experience with various quinolones suggest that it may not be proper to draw general conclusions about mechanisms of a particular compound against various mycobacteria. Studies to understand the therapeutic relevance of these findings are being continued.

Therapeutic Trials

Several studies have been in progress at CJIL, Agra, to assess the clinical and bacteriological responses of leprosy patients, relapse rates, and complications due to various drug regimens.

Multibacillary leprosy

Various studies to investigate the efficacy of different regimens of multidrug therapy (MDT) in patients of multibacillary leprosy continued during the year.

Highly bacillated (4 to 6+) BL/LL patients who were treated with a modified WHO regimen and who became smear negative within 3–6 years of treatment, have completed a follow up of 2–5 years after smear negativity. No relapses have been observed so far.

Multibacillary patients who have been treated for 1 year with a MDT regimen which includes pyrazinamide have completed a follow up of 3 years. Earlier, no persisters were detectable in these patients after 2 years of treatment. Further follow up indicates that the fall in the borderline indeterminates is faster among the patients treated with the pyrazinamide-containing regimen.

Studies for assessing the usefulness of immunotherapy with *M.w.* vaccine were continued. The highly bacillated BL/LL patients included in the pilot trial have completed 36–42 months of treatment. All the cases in the immunotherapy groups became smear negative by 36 months of treatment while most of patients on MDT alone were still smear positive. Follow-up studies confirm the earlier tentative conclusion that chemotherapy combined with immunotherapy may be useful in reducing the duration of treatment. These trials are being expanded to include larger numbers of patients across the spectrum of leprosy.

Paucibacillary leprosy

With an aim to further reduce the duration of treatment, a regiment comprising dapsone, rifampin and prothionamide is being tried. Results of 18–24 months of follow up after stopping the MDT are available. With the addition of prothionamide to the WHO regimen, the inactivity rates are better, late reactions/early relapses are significantly lower than those reported using WHO regimens. No relapses have been recorded during the last year. Further follow up is being continued.

Corrective Surgery

At CJIL, Agra, studies were contined for assessing the sensory impairment in normal and anesthetic hands and feet, finger dynamography and correction of ulnar palsy.

An Indo-Dutch project aiming at the development of foot model and pressure monitoring system for better understanding and management of tarsal disintegration and plantar ulcers continued to make significant progress at CJIL, Agra. Analysis of X-rays of the foot from patients with plantar ulcers showed that the small bones of the foot and corresponding joints are affected in advanced stages of the lesion. The intake of patients for monitoring of foot pressure as well as radiographic investigations was started during the year.

Immunoprophylaxis and Immunotherapy

The main emphasis in research on leprosy hinges on the ultimate aim to reduce the infection load in the community by introducing effective MDT and developing an effective vaccine against leprosy. Presently three such vaccines are being evaluated under the aegis of the Council. The ICRC antileprosy vaccine which is undergoing phase III trial was developed by the Cancer Research Institute, Bombay. The study was initiated in Maharashtra on the comparative evaluation of the immunoprophylactic efficacy of two vaccines, ICRC and BCG, in the prevention of leprosy. The intake of the vaccines is now complete. The procedure and proforma for re-survey has been finalized and the resurvey is expected to start shortly.

The Cancer Research Institute, Bombay, is also carrying out immunotherapeutic trials in patients of leprosy. Most of the leprosy patients who were clinically resistant to MDT showed clinical improvement, progressive decline in bacillary index and marked increase in lymphocyte transformation. Various laboratory studies were carried out to investigate the immunoreactivity of lymphocytes in leprosy patients to antigens of ICRC and *M. leprae* before and after administration of ICRC vaccine. The procedure for extracting T lymphocytes from skin lesions of TT patients and establishing *M. leprae*-specific T-cell clones has been standardized. With the use of the same methodology, the T-cell repertoire in skin lesions of vaccinated patients is being analyzed.

Apart from the ICRC vaccine, two other antileprosy vaccines are undergoing clinical trials at the CJIL field unit at Avadi (Tamil Nadu) to identify the best of the available vaccines for Indian situations. A controlled five-arm prophylactic vaccine trial against leprosy involving ICRC, *M.w.* (developed by the National Institute of Immunology, New Delhi) killed *M. leprae* + BCG (WHO), BCG and normal saline was launched in Chingleput district of Tamil Nadu. Of the 269,702 persons enumerated, 162,983 have been vaccinated. Intake for this study is expected to be completed by July 1993. The results of analysis of postvaccination sensitization induced by ICRC vaccine showed that sensitization effect with ICRC vaccine was substantially lower than that observed with the combination vaccine comprising BCG + *M. leprae*. Resurvey of the vaccinated individuals is to start from middle of 1993.

Immunopathological studies have been undertaken at the Institute of Pathology (IOP), New Delhi, on the resolving granuloma in leprosy patients treated with standard MDT and MDT plus *M.w.* vaccine. The results suggest that patients should be followed up until mycobacterial antigen is cleared from the lesions; the nature of persisting antigen should be studied, and that morphometry along with immunohistology should be used for assessing response to therapy.

Results of certain basic studies supported at the Foundation for Medical Research, Bombay, have raised hopes of the development of yet another vaccine against leprosy. Delipidified cell component of *M. leprae* has been demonstrated to possess very powerful immunomodulatory potentiality with blood cells of leprosy patients to qualify itself as a potential vaccine. Monoclonal antibodies were obtained against delipidified cell component of *M. leprae*. This antibody helps in identifying a 65-kDa protein as part of the immunomodulatory component in the delipidified cell of *M. leprae*. Further studies are necessary for developing a new vaccine.

Field Studies

Clinico-epidemiological studies on the incidence, prevalence rates, quiet nerve paralysis, as well as related aspects continued to progress during the year. After 2188 person-years of follow up patients of paucibacillary leprosy, a relapse rate of 5.03/1000 person years has been observed.

Analysis of data of studies on the possible association of HLA and different types of leprosy in progress at Vishakhapatnam, has shown that TT patients are associated with A26, B8; A29, C2; B22, C2; A30, DR3; B27, DR1 and C2, DR3; B27, DR1 and C2, DR3. BT patients were found to be associated with A25, B21; A2, C1; A2, C5; B28, C2; A28, DR8; B27, DR4 and C2, DR4. When TT/BT patients were combined an association was observed with A32; B49; A29, C2; B22, C2; A28, DR8; B27, D4 and C2, DR3.

Other Studies

Studies on anthropological and social causes of the stigma associated with leprosy and treatment compliance continued during the year. The protocols for assessing the stigma and its causes were standardized and pretested during the year.

In studies at the IOP, New Delhi, attempts have been made to generate information on biologically important elements in mycobacterial infections, leprosy and cutaneous tuberculosis. Preliminary results have shown that dermal granulomas and inflammatory cells in different forms of leprosy are poor in copper, zinc and calcium while levels of magnesium, phosphorus, sulfur and potassium are higher.—From the Report

Senegal. *5th Annual course offered by Institut de Leprologie Appliquee de Dakar.* Le Cinquieme Cours Annuel organize par l'Institut de Leprologie Appliquee de Dakar, Fondation de l'Ordre de Malte, en collaboration avec la DAHW-Senegal "Formation Pratique pour la Prevention des Invalidites et la Readaptation dans la Lepre":

Dates: Module 1.=26 Octobre–25 Novembre 1995; Module 2.=27 Novembre–9 Décembre 1995.

Nombre de participants: 8.

Objectifs: Module 1: Former des responsables pour la mise en oeuvre, l'organisation et le développement des techniques de Réadaptation fonctionnelle, d'Education sanitaire et de Prévention des invalidités dans le cadre d'un Programme National de Lutte contre la lèpre. Module 2. Formation à la rééducation pré et post-opératoire des handicapés de la lèpre opérés.

Type d'enseignement: Participatif et pratique.

Contenu: Module 1: Généralités sur la lèpre; prévention et prise en charge des atteintes nerveuses; chirurgie de la lèpre: indications; prescription et fabrication de chaussures adaptées; éducation sanitaire, conception, organisation, application et évaluation d'un Programme de Réadaptation; techniques de communication et formation des auxiliaires. Module 2: Rééducation fonctionnelle d'une paralysie récente et des paralysies opérées. Amputation et appareillage.

Langue: Français parlé couramment et écrit.

Mode d'admission: Sur dossier, après analyse des objectifs professionnels.

Date limite de depot des candidatures: 15 Juillet 1995.

Condition d'admission: Ne seront retenus que les dossiers des candidats bénéficiaires d'une bourse couvrant les frais de voyage et de séjour.

Niveau requis: Kinésithérapeutes, ergothérapeutes et infirmiers-rééducateurs pour les modules 1 et 2. Infirmiers spécialistes-lèpre pour le module 1.

Pour tout renseignement, s'adresser a: Dr. J. L. Cartel, Directeur, INSTITUT DE LEPROLOGIE APPLIQUEE DE DAKAR, BP 11023, DAKAR-CD, Sénégal. Fax: (221) 24.18.18.—From the Announcement

Spain. *1995 Fontilles' cursos.* XXXII Curso Internacional de Leprología Para Médicos organizado por el Sanatorio San Francisco de Borja de Fontilles y patrocinado por la Asamblea Española de la Soberana Orden de Malta con la colaboración de la Conselleria de Sanidad y Consumo de la Generalidad Valenciana Servicio Dermatología del Hospital Universitario de Valencia Profesores de Dermatología de las Facultades de Medicina. El XXXII Curso tendrá lugar en el Sanatorio de Fontilles

desde el 12 al 18 de noviembre de 1995, dirigido por el doctor J. Terencio de las Aguas, Director Médico del Sanatorio.

XXXVIII Curso Internacional de Leprología Para Misioneros, Diplomados en Enfermería y Trabajadores Sociales organizado por el Sanatorio San Francisco de Borja de Fontilles y patrocinado por la Asamblea Española de la Soberana Orden de Malta con la colaboración de la Conselleria de Sanidad y Consumo de la Generalidad Valenciana Profesores de Dermatología de las Facultades de Medicina. El XXXVIII Curso tendrá lugar en el Sanatorio de Fontilles desde el 8 al 21 de octubre de 1995, dirigido por el doctor J. Terencio de Aguas, Director Médico, Sanatorio San Francisco de Borja, 03791 Fontilles (Alicante), Espana.

Switzerland. *TDR faces no-growth budget.* Dr. Tore Godal, Director of TDR, turned prophet at the June 1994 (17th) session of the TDR top management body, the Joint Coordinating Board (JCB). "Before the end of the century there will be many changes in international health research," he said, referring especially to the likely effect of the WHO *Ad Hoc* Health Research and Development Review, which is to report in 1995. The Review's analytical approach to disease burden, to the promise of research and development, and to institutional arrangements, will help rationalize decision-making in health research, Godal said.

TDR's 20 years of experience and its recent streamlining will put it in an excellent position both to contribute and respond to these analyses—at least intellectually—but the Program must also take on board the current shortfall in contributions, which is reducing its room for creative changes. Approximately 10% had had to be lopped from every Research and Development component in 1994. TDR was about to embark on developing the Program budget for the 1996–1997 biennium, which would be presented to the JCB in 1995, said Godal. If budgetary pressures were to continue, JCB should consider the options:

- Should research resources be reduced in diseases where substantial progress had already been made in controlling them, such as leprosy, onchocerciasis and Chagas disease? (This would risk poor capacity to respond to any resurgence of the disease, as had happened with tuberculosis.)
- Should the argument be turned around and resources only be invested in activities where there was a chance of lasting impact on a disease?
- In terms of comparative advantage, should the Program eliminate its Strategic Research area, bearing in mind that this was the most difficult area for donors to support? But it was important for the Program to be in close touch with strategic research activities in order for it to pick up leads for product development and to establish links for research capability strengthening.
- Should the Program reduce its Applied Field Research area and leave more of the responsibility for this type of research to disease control programs? But if TDR abandoned it, would this important research in fact be carried out? Until now, TDR had only moved into unattended areas.
- Should research capability strengthening activities be reduced?
- Should the Program focus on a specific region of the world? As the problems were greatest in Africa, should TDR focus on Africa and assume that the other regions would be able to cope with their own problems? But international activities were important and the Program could operate in the most cost-effective way by investing selectively in global research. Many tools were applicable in all endemic regions of the world. In addition, focusing on where the problem was greatest might not necessarily give the best value for money.

Godal asked JCB participants to consider which—if any—of these options they would like to apply. The Board liked none of them, and stressed in particular that TDR must deal with *all* endemic areas. JCB agreed with the present balance of resources among strategic research, product research and development and applied field research—and stressed that no further cuts should be made in strategic research, particularly considering the dangers of increasing drug resistance in some parasites.—TDR news **46** (1994) 4, 8