

# TRC annual report

April 2003 – March 2004

Tuberculosis Research Centre  
Chennai



WHO Collaborating Centre for Tuberculosis Research & Training





# Tuberculosis Research Centre Chennai

## Annual Report

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# Preface

The year under review was an eventful one with significant advances being made in the various research activities of TRC and the establishment of new facilities. During the year, construction of the long-awaited patient care and clinical research facility was inaugurated and is rapidly progressing. A notable landmark was achieved with the establishment of an International Centre of Excellence in Research (ICER) in collaboration with the National Institutes of Health, USA. This singular honour is the fruit of many years of very high quality work carried out by TRC in the fields of clinical and epidemiological research. The establishment of the ICER, apart from enhancing the reputation of TRC, will facilitate upgradation of facilities and open up opportunities for collaborative research and training in priority areas.

In the area of clinical trials, we made steady progress in recruiting subjects to two very important randomised clinical trials in HIV-infected persons. The first is a study of the efficacy of the RNTCP recommended 6-month regimen for treatment of pulmonary tuberculosis in HIV-seropositive patients as compared to an extended 9-month regimen. The second is a chemoprophylaxis study of the efficacy of two regimens for the prevention of active tuberculosis in HIV-seropositive subjects. Both these are crucial studies, which will help to answer very important questions for the nation's health policies. We should have broad indicators about the efficacy of these regimens by next year.

The results of the intermittent ofloxacin study, in which the efficacy of a 4-month thrice-weekly ofloxacin-containing regimen was compared to a control thrice-weekly 6-month regimen for the treatment of patients with sputum-positive pulmonary tuberculosis, belied our expectations. The relapse rate in the test regimen cohort was unacceptably high and the study was closed prematurely in keeping with our reputation of maintaining high ethical standards. We are now embarking upon another randomized clinical trial with the newer generation of fluoroquinolones, gatifloxacin and moxifloxacin, which we are optimistic, will result in an effective 4-month thrice-weekly regimen in the near future.

The Model DOTS Project has entered its fifth year with many targets being reached earlier than planned. Following the baseline surveys of tuberculosis disease and infection in a community in Tiruvallur district, the first re-survey of tuberculosis disease has been completed. The results are being analysed. We now also have information for a five-year period on programme performance (case detection, sputum conversion and treatment outcome) of the RNTCP in one tuberculosis unit of Tiruvallur district, and the results are presented in this report. Many operational research questions are also being addressed in this field laboratory.

Good quality training is essential for successful implementation of the programme. TRC has been identified as a nodal centre for training in RNTCP by Central TB Division (CTD). TRC, though basically a research centre, accepted the challenge and started the training programme since 1999. All levels of health personnel are being trained at national and

international levels. During the period (April 2003-March 2004), we trained 48 medical officers in five batches, 28 medical officers in two batches, 83 senior treatment supervisors in five batches, 39 senior tuberculosis laboratory supervisors in six batches, 14 laboratory technicians in three batches and 49 field workers in four batches. A sensitisation programme on RNTCP was organised for Deputy Directors of Health Services (DDHS) and 21 officers participated in it. We also trained 14 programme managers—from DPR Korea (7), Myanmar (4), Bangladesh (2) and East Timor (1) – and one microbiologist from Bangladesh. Scientists from TRC were also invited as facilitators for training at national level to other states and international training programmes (SEARO).

Research in basic science progressed substantially in the reporting year. The regulatory role of vitamin D receptor gene variants, on vitamin D<sub>3</sub> modulated immune functions in pulmonary tuberculosis, suggested that normal subjects with BB, tt and FF genotypes may have down regulated immune functions and such individuals may be susceptible to tuberculosis. The ongoing project on construction of rBCG based HIV-1 epitope delivery system was completed. Cpn10-PND chimeric antigen was constructed and expressed in BCG. The role of PknI protein, which plays a key role in cell growth and development, was further studied to explain the slow growth of *M. tuberculosis* and its ability to persist in the dormant state. The search for a sensitive and specific diagnostic test for early diagnosis of tuberculosis is still on. Studies on cell proliferation and apoptosis induced by mycobacterial antigens in tuberculous pleuritis are in progress.

The recently formed Division of HIV/AIDS has initiated a number of laboratory studies aimed at understanding the immune responses in the HIV/TB co-infected patients. TRC is planning a randomised clinical trial with antiretroviral agents. In this context the laboratory has also taken up pharmacokinetic studies to identify drug interactions and assessment of the quality of antiretroviral agents. Using molecular typing methods to compare the genotypes of pretreatment and relapse isolates of *M. tuberculosis* from tuberculosis patients, we observed that exogenous

re-infection was more common among patients with HIV/TB and endogenous reactivation commoner in HIV-seronegative patients with tuberculosis.

It is heartening to inform you that as in the past, in the reporting year also, TRC has shared its expertise with local, national, regional and international agencies, institutions and individuals in various ways. Many of the scientists and technical staff have served as collaborators, consultants, coordinators, discussants, experts, partners and temporary advisors in tuberculosis control and research.

Several young students who have recently joined (and the number is increasing year after year) and registered with University of Madras to work for their Ph.D. at TRC will ensure that the laboratory infrastructure being developed will be used optimally.

In summary, while clinical trials and epidemiology continue to be our forte, we are also making special efforts to strengthen our presence in basic science research. We are hopeful that these efforts will yield results in the near future. I thank all the staff of TRC for their outstanding efforts in continuing to keep the status of TRC “high” in the TB research world. I would like to acknowledge the timely funding received by TRC from USAID, WHO, NIAID and UCLA that supported research projects relevant to the health needs of our country. I thank Prof. N.K. Ganguly, our Director General, and ICMR for continued encouragement and unstinted support. We realise that the DG, by posing challenge after challenge to TRC, is striving to make us leaders in TB research, control and training. I take this occasion to thank the Ministry of Health, Government of India, in general and the CTD in particular for according us the status of one of the “most favoured partners” in all aspects of TB control and research. Finally I thank the Corporation of Chennai and the Government of Tamil Nadu for their continued support and providing valuable feedback on our efforts in TB control, research and training.

Dr.P.R. Narayanan  
Director



Tuberculosis  
Research Centre  
2003-2004

# Scientific Advisory Committee

## Chairperson

**Dr. C.M. Gupta**

Director  
Central Drug Research Institute  
Lucknow

## Members

**Prof. K.V. Thiruvengadam**

Former Professor of Medicine  
Madras Medical College  
Chennai

**Dr. S.P. Tripathy**

Former Director General, ICMR  
Pune

**Dr. S. Radhakrishna**

Former Director, IRMS  
Hyderabad

**Prof. V.I. Mathan**

Consultant to ICMR  
National Institute of Epidemiology  
Chennai

**Dr. Lalji Singh**

Director  
Centre for Cellular and Molecular Biology (CCMB)  
Hyderabad

**Dr. L.S. Chauhan**

Deputy Director General (TB)  
Directorate General of Health Services  
New Delhi

**Dr. M.K. Bhan**

Professor of Paediatrics  
All India Institute of Medical Sciences  
New Delhi

**Prof. V. Nagaraja**

Professor  
Indian Institute of Science  
Bangalore

**Prof. Anil K. Tyagi**

Professor of Biochemistry  
University of Delhi  
(South Campus)  
New Delhi

**Dr. Dipali Mukherji**

Chief, Division of ECD  
Indian Council of Medical Research  
New Delhi

## Special Invitees

**Dr. P. Vijayalakshmi**

Director of Medical Education  
Government of Tamil Nadu  
Chennai

**Dr. P. Krishnamurthy**

Director of Public Health  
& Preventive Medicine  
Chennai

**Dr. J.R. Vijayalakshmi**

Director of Medical  
& Rural Health Services  
Chennai

**Dr. M. Perumal**

State TB Officer &  
Joint Director of Medical & Rural Health Services  
(TM)  
Directorate of Medical & Rural Health Services  
Chennai

**Prof. A.S. Natarajan**  
Director  
Institute of Thoracic Medicine  
Chennai

**Dr. Prahlad Kumar**  
Director  
National Tuberculosis Institute  
Bangalore

**Dr. Seyed E. Hasnain**  
(DG's Nominee)  
Director  
Centre for DNA Fingerprinting and Diagnostics  
Hyderabad

**Prof. S.C. Sehgal**  
Chief, International Health Division  
Indian Council of Medical Research  
New Delhi

**Dr. M.D. Gupte**  
Director  
National Institute of Epidemiology  
Chennai

**Dr. P.K. Das**  
Director  
Vector Control Research Centre  
Pondicherry

**Dr. V.M. Katoch**  
Director  
Central Jalma Institute for Leprosy  
Agra

**Dr. P.R. Narayanan (Member-Secretary)**  
Tuberculosis Research Centre  
Chennai



# Ethics Committee

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Dr. Jacob Abraham  
Consultant Neurosurgeon  
Chennai

## Members

Dr. H. Srinivasan  
Honorary Editor  
Indian Journal of Leprosy  
Chennai

Mr. Mohan Alagappan  
Industrialist  
Chennai

Dr. Usha Sriram  
Clinical Endocrinologist  
E.V. Kalyani Medical Centre  
Chennai

Dr. Vijayalakshmi Thanasekaraan  
Consultant Pulmonologist  
Sri Ramachandra Medical College  
& Research Institute  
Chennai

Dr. Uma Krishnaswamy  
Consultant General Surgeon  
Chennai

Dr. V.R. Muraleedharan  
Professor of Economics  
Indian Institute of Technology  
Chennai

Ms. Shyamala Nataraj  
Programme Director  
South India AIDS Action Programme (NGO)  
Chennai

Dr. V. Vijayasekaran  
Professor and Head  
Department of Pharmacology  
Vinayaka Mission Medical College  
Salem

Dr. Rema Mathew (Member-Secretary)  
Deputy Director  
Tuberculosis Research Centre  
Chennai



# Animal Ethics Committee

1. Mrs. Prema Veeraraghavan, No.172 (Old No. 94), 13, Kala Flats, Habibullah Road, T. Nagar, Chennai – 600 017
2. Dr. P. Krishnamoorthy, No.40, Third Street, V.R. Puram, Saligramam, Chennai – 600 093
3. Dr. Rama Rajaram, Scientist E, CLRI, Adyar, Chennai – 600 020



# Institutional Committees

## Abstract Committee

Dr. Rani Balasubramanian (Chairperson)  
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Mrs. Fathima Rahman  
Dr. T. Santha Devi  
Dr. Sujatha Narayanan  
Dr. P. Venkatesan (Member-Secretary)

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Dr. Sulochana Das  
Dr. K. Jayasankar  
Dr. P. Kannan (Member-Secretary)

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Dr. Geetha Ramachandran  
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Dr. P. Paul Kumaran

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Mr. V. Adikesavan (Member-Secretary)

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Dr. Sulochana Das  
Dr. V.D. Ramanathan  
Dr. M. Kannapiran (Member-Secretary)

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Dr. V.D. Ramanathan  
Dr. P. Venkatesan  
Mr. M. Subramanian (Member-Secretary)

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Ms. Nazeema Beevi  
Ms. Arumaikannu Anbalagan  
Ms. Beena Elizabeth Thomas  
Ms. M. Vijayalakshmi  
Dr. K. Jayasankar  
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Mr. E. Raman  
Mr. P.B. Madhavan  
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Dr. Rajeswari Ramachandran  
Dr. V.D. Ramanathan  
Dr. Soumya Swaminathan  
Dr. C. Kolappan  
Dr. M. Kannapiran  
Mr. P.G. Gopi  
Mr. R. Subramani  
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Mr. K. Jayarajan (Member-Secretary)

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Dr. K. Rajaram  
Dr. C. Kolappan  
Ms. Padma Balasubramanian  
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Mr. R. Manoharan  
Mr. E. Money  
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Mr. D. Shanmugam  
Mr. R.S. Somasundaram  
Mr. S.N. Sankaralingam (Member-Secretary)

## Infection Control Committee

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Mr. M. Subramanian  
Mr. S. Ramanujam  
Ms. S. Padma  
Mr. D. Shanmugam  
Dr. Ranjani Ramachandran  
(Member-Secretary)

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Dr. K. Sadacharam  
Dr. Rani Balasubramanian  
Dr. Pauline Joseph (Member-Secretary)

## Library Committee

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Dr. V.D. Ramanathan  
Dr. Sujatha Narayanan  
Dr. Pauline Joseph  
Mr. R. Rathinasabapati (Member-Secretary)

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Dr. Aleyamma Thomas  
Dr. M. Kannapiran (Member-Secretary)

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Mrs. Fathima Rahman  
Dr. Geetha Ramachandran  
Dr. A.K. Hemanth Kumar  
Dr. G. Kubendiran  
Dr. Luke Elizabeth Hanna

Dr. Ranjani Ramachandran  
Dr. P. Selvaraj  
Mr. R. Selvaraj  
Dr. Sujatha Narayanan  
Dr. Sulochana Das  
Dr. Vanaja Kumar  
Dr. Alamelu Raja (Member-Secretary)

### **Sr. Technical Officers and Technical Officers Committee**

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Mr. S.N. Sankaralingam  
Mr. K.J. Illampurnam  
Mrs. Lalitha Victor  
Mrs. Nalini Sundar Mohan  
Mrs. S. Sudhamathi  
Mr. E. Money  
Mr. S. Ramanujam (Member-Secretary)

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Mr. E. Money  
Ms. Jayalakshmi Vadivel  
Mr. V. Adikesavan (Member-Secretary)

### **Vigilance Committee**

Dr. V.D. Ramanathan (Chairperson)  
Dr. P. Selvaraj  
Ms. Sudha Ganapathy  
Mr. T.M. Kasinathan (Member-Secretary)



# Distinguished Visitors

Dr. Martien Borgdoff	Epidemiologist KNCV	The Netherlands
Dr. Christopher Dye	Division of Communicable Diseases Control and Prevention World Health Organization	Switzerland
Dr. Fabio Luelmo	TB Consultant Division of Communicable Diseases Control and Prevention World Health Organization	Switzerland
Dr. Brian Williams	Division of Communicable Diseases Control and Prevention World Health Organization	Switzerland
Dr. Eric Chamot	Assistant Professor University of Alabama at Birmingham	USA
Mr. Jack C. Chow	Ambassador Deputy Assistant Secretary for Health and Science U.S. Department of State	USA
Dr. Jose A Caminero Luna	Consultant International Union Against Tuberculosis and Lung Diseases	Spain
Mr. Jonathan Folkers	Computer Specialist National Institutes of Health	USA
Ms. Sibylle Kristensen	Program Director University of Alabama at Birmingham	USA
Dr. Marion E Broom	Professor/ Associate Dean University of Alabama at Birmingham	USA
Dr. Polly Sager	International Research Support & Training National Institutes of Health	USA
Dr. Anette Haller	Programme Advisor Regional Bureau of Asia UN World Food Programme	Thailand
Ms. Caroling Legros	World Food Programme	India



# Distinguished Visitors

Dr. Charles Wells	Chief International Activity Centers for Disease Control (CDC) and Prevention	USA
Dr. Marguerite Pappannaoui	Centers for Disease Control (CDC) and Prevention	USA
Dr. Michael Boom	Centers for Disease Control (CDC) and Prevention	USA
Dr. Rodrigo L.C. Romulo	Chairman Philippine TB initiative for the private sector	Philippines
Dr. Richard M. Krause	Senior Investigator NIAID National Institutes of Health	USA
Dr. Kathy DeRiemer	Division of Infectious Diseases and Geographic Medicine Stanford University	USA
Dr. Cristina Coutierret	Institut Pasteur at Paris	France
Dr. Philip Supply	Institut Pasteur at Paris	France
Dr. Bess Miller	Associate Director for TB/HIV Prevention and Care Centers for Disease Control (CDC) and Prevention	USA
Dr. Naomi Bock	Global AIDS program Centers for Disease Control (CDC) and Prevention	USA
Dr. Jamie Da Costa Sarmiento	Director NTP of East Timor	East Timor
Dr. Harold Jaffe	Centers for Disease Control (CDC) and Prevention	USA
Dr. Susan M. Bacheller	Senior Infectious Disease Advisor Office of the HIV/AIDS Bureau for Global Health, USAID	USA
Dr. Amy Bloom	Senior Technical Advisor USAID	USA
Dr. Irene Kolk	Chief, Infectious Diseases Division, Bureau for Global Health, USAID	USA



# Guest lectures during the year

Name	Institution	Topic
Dr. Christine Wanke	Tufts University School of Medicine, USA	HIV, nutrition and metabolism
Dr. Jose A Caminero	International Union against Tuberculosis and Lung Diseases, France	Standardised vs individualised treatment for MDR-TB
Dr. Vaidehi	Sundaram Medical Foundation, Chennai	Waste management
Ms. Sumathi Sundaram	London School of Tropical Medicine and Hygiene, UK	Tracking financial flows of health research and development in India
Dr. Kathy DeRiemer	Stanford University School of Medicine, USA	Comparative genomics of <i>M. tuberculosis</i>
Dr. Nalini Sathiakumar	University of Alabama at Birmingham, USA	Epidemiological research tools in control of infectious diseases
Dr. Mathur S. Kannan	Professor, Dept. of Veterinary Pathobiology, College of Veterinary Medicine, USA	Calcium regulation in airway cell: signaling mechanism
Dr. S. Jambunathan	Physician, St. Johns Hospital, Asst. Professor of Medicine, Wayne State University, USA	Community acquired pneumonias
Dr. Richard M. Krause	Senior Investigator, National Institutes of Health, USA	Reflections on the discovery of group A streptococci as a cause of rheumatic fever
Dr. Kenneth Mayer	Professor of Medicine, Brown University School of Medicine, USA	HIV prevention research



# Abbreviations

AFB	Acid Fast Bacilli	LRP	Luciferase Reporter Phage
AIDS	Acquired Immunodeficiency Syndrome	LT	Laboratory Technician
AP	Auramine Phenol	MABA	Microplate Alamar Blue Assay
ATT	Anti-TB treatment	MAC	<i>M. avium</i> Complex
AUDIT	Alcohol Use Disorders Identification Test	MBL	Mannose Binding Lectin
BCG	Bacillus Calmette Guerin	MDR-TB	Multidrug Resistant Tuberculosis
CF	Cystic Fibrosis	MGIT	Mycobacterial Growth Indicator Tube
CFA	Culture Filtrate Antigen	MIP	Macrophage Inflammatory Protein
CFU	Colony Forming Unit	MX	Moxifloxacin
CPC	Cetyl Pyridinium Chloride	NaCl	Sodium Chloride
CTD	Central TB Division	NHS	Normal Healthy Subjects
DOTS	Directly Observed Treatment Short Course	NPV	Negative Predictive Value
EMB	Ethambutol	NTM	Non-Tuberculous Mycobacteria
ELISpot	Enzyme Linked Immunosorbent Spot	OFX	Ofloxacin
FEV	Forced Expiratory Volume	PBMC	Peripheral Blood Mononuclear Cells
FVC	Forced Vital Capacity	PF	Pleural Fluid
GAT	Gatifloxacin	PFGE	Pulsed Field Gel Electrophoresis
HAART	Highly Active Antiretroviral Therapy	PFMC	Pleural Fluid Mononuclear Cells
HIV	Human Immunodeficiency Virus	PGRS	Polymorphic GC Repeat Sequence
HLA	Human Leucocyte Antigen	PHA	Phytohaemagglutinin
HPLC	High Performance Liquid Chromatography	PMN	Polymorphonuclear
IEC	Information, Education and Communication	PND	Principal Neutralizing Determinant
IFN	Interferon	PPV	Positive Predictive Value
IL	Interleukin	PZA	Pyrazinamide
INH	Isoniazid	QRDR	Quinolone Resistance Determining Region
IPTG	Isopropyl thiogalactopyranoside	RFLP	Restriction Fragment Length Polymorphism
IU	International Unit	RLU	Relative Light Unit
LQAS	Lot Quality Assurance Sampling	RMP	Rifampicin

RNTCP	Revised National Tuberculosis Control Programme	TLC	Total Lymphocyte Count
SCC	Short Course Chemotherapy	TLR	Toll-like Receptor
SM	Streptomycin	TNF	Tumor Necrosis Factor
SMR	Standardised Mortality Ratio	TU	Tuberculosis Unit
STD	Sexually Transmitted Disease	VCTC	Voluntary Counselling and Testing Centre
STLS	Senior Tuberculosis Laboratory Supervisor	VDR	Vitamin D Receptor
TB	Tuberculosis	VHN	Village Health Nurse
		ZN	Ziehl-Neelsen