TRC

ANNUAL REPORT

APRIL 2004 - MARCH 2005

TUBERCULOSIS RESEARCH CENTRE
CHENNAI

WHO Collaborating Centre for
Tuberculosis Research & Training

CONTENTS

Preface	2
Committees	4
Distinguished Visitors	10
Guest Lectures	12
Abbreviations	13

Research Activities

Clinical Research	14
Sociological Research	20
Epidemiological Research	23
Operational Research	25
Applied Research	30
Basic Research	36
Statistical Research	54
Information Services	58
Electronic Data Processing	61
Service Oriented Activities	62

Appendices

Publications	65
Awards	70
Technical Support	71
Capacity Building	74
Conferences organized	75
Conferences attended	76
Special Assignments	85
Ph.D. Scholars - Students	87
Ph.D. Scholars - Staff	89

PREFACE

In keeping with our mission of conducting scientific research and applying science for the benefit of the community, we at Tuberculosis Research Centre (TRC), have continued to make significant contributions in clinical, operational, applied and basic research. At TRC, we value the contributions made by our scientific and research staff and are aware of our responsibility towards the patients approaching our clinical facility. In order to ensure that we remain effective and to help us serve our patients better, various infrastructure-strengthening activities are currently in progress. This includes the construction of a "state of the art" patient care and clinical research facility.

Recently, the outstanding field research by the staff of the Epidemiology Division of TRC, presented the evidence that implementation of the Directly Observed Treatment Short-course (DOTS) strategy is associated with a rapid reduction in tuberculosis prevalence. This is in contrast to the gradual decline in TB prevalence over the preceding 30 years reported earlier by TRC. These observations emphasize the necessity for sustaining quality DOTS in the coming years by all sectors of the government, as well as non-governmental agencies if India wants to achieve the millennium development target of 50% reduction in TB prevalence by 2015.

Last year, a notable landmark was achieved with the establishment of an International Centre for Excellence in Research (ICER) in collaboration with the National Institutes of Health (NIH), USA. Up gradation of research facilities that include immunology and molecular biology laboratories as well as a BSL-3 facility are under way and are expected to be ready by the end of 2005.

The major new initiative during the reporting period has been the establishment of the HIV Vaccine Trial site. In October 2004, preparation for a randomized, placebo-controlled, dose-escalating phase I double-blinded study to evaluate the safety and immunogenicity of TBC-M4 [Modified Vaccinia Ankara (MVA) HIV-1 multigenic subtype C] vaccine in HIV-uninfected, healthy volunteers was initiated. This is a trial overseen by the Government of India, and is being conducted as a collaborative effort between the Indian Council of Medical Research (ICMR) and National AIDS Control Organization (NACO), in partnership with the not-for-profit International AIDS Vaccine Initiative (IAVI). The trial will be carried out by TRC, with collaboration from YRG Care, Chennai, Tamil Nadu State AIDS Control Society (TNSACS) and the Government of Tamil Nadu. During the period under review, renovation of the trial site has been completed to accommodate a state-of-the-art Vaccine Trial Centre (VTC).

The HIV/AIDS division will shortly initiate a randomized controlled clinical trial for TB-HIV patients, which will combine anti-retroviral therapy (ART) and anti-TB therapy in order to reduce mortality and improve TB treatment outcomes. The trial will test two different once-daily anti-retroviral regimens as well as the feasibility of providing ART by DOT. The trial has been funded by the NACO and will provide information that will be useful to both the National TB and AIDS control programmes.

The clinical trial on the efficacy and tolerability of the newer fluoroquinolones, moxifloxacin and gatifloxacin containing regimens in the treatment of patients with sputum positive pulmonary tuberculosis is continuing. The other two major trials that were initiated three years ago on the efficacy of RNTCP regimens in HIV-infected persons as well as chemoprophylaxis for TB among HIV positive individuals are also continuing. Patient intake has been completed and follow-up is in progress.

TRC continued its support for the TB Control programme of the Govt. of India by providing RNTCP training, carrying out disease and Annual Risk of Infection (ARI) surveys as well as drug resistance surveillance and establishing External Quality Assurance (EQA) of smear microscopy, for laboratories around the country.

TRC continues to offer plentiful opportunities for motivated and innovative minds to pursue research in various disciplines of life science including microbiology, biochemistry, biostatistics, immunology, molecular and cellular biology. A perfect blend of extremely focused faculty together with the high-tech laboratory facilities offered at this Centre provides the ideal ambience to foster a true spirit of enquiry and scientific acumen in young minds. Students are encouraged to participate in paper presentations and scientific debates to ensure interdisciplinary exchange of thoughts and to hone their communication skills. Currently, 26 brilliant and dexterous youngsters are pursuing their Ph. D. programme at TRC.

The pages to follow will elaborate on the major research and service activities undertaken by the Centre for the reporting time period.

Dr. P.R. Narayanan
Director

COMMITTEES

SCIENTIFIC ADVISORY COMMITTEE

Chairman

Prof. C.M. Gupta
Director
Central Drug Research Institute
Lucknow

Members

Dr. S.P. Thyagarajan
Vice Chancellor
University of Madras
Chennai

Dr. S.P. Tripathy
Former Director General – ICMR
Pune

Prof. Jaya S. Tyagi
Additional Professor
Department of Biotechnology
All India Institute of Medical Sciences
New Delhi

Prof. K. Ramachandran
Retd. Prof. of Statistics
Chennai

Dr. V.M. Katoch
Director
Central JALMA Institute of Leprosy
Agra

Prof. K.V. Thiruvengadam
Former Prof. of Medicine
Madras Medical College
Chennai

Dr. Sandip K. Basu
Director
National Institute of Immunology
New Delhi

Dr. Syed Hasnain
Director
Centre for DNA Fingerprinting and Diagnostics
Hyderabad

Lt.Gen.D. Raghunath
Sir Dorabji Tata Centre for
Research in Troical Diseases
Innovation Centre, Bangalore
Bangalore

Prof. Vimla V. Nadkarni
Head of Medical and Psychiatric
Social Work
Tata Institute of Social Sciences
Mumbai

Dr. Lalit Kant
Sr. Deputy Director General
Indian Council of Medical Research
New Delhi

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

ETHICS COMMITTEE

Chairperson

Dr. Jacob Abraham	Consultant Neurosurgeon Chennai

Members

Dr. H. Srinivasan	Honorary Editor Indian Journal of Leprosy Chennai
Mr. Mohan Alagappan	Industrialist 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 (SIAAP) 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)
Dr. Vanaja Kumar
Mrs. Fathima Rahman
Dr. T. Santha Devi
Dr. Sujatha Narayanan
Dr. P. Venkatesan (Member-Secretary)

Animal House Committee

Dr. Rajeswari Ramachandran (Chairperson)
Dr. K.V. Kuppu Rao
Dr. Sulochana Das
Dr. K. Jayasankar
Dr. P. Kannan (Member-Secretary)

Annual Report Committee

Dr. Alamelu Raja (Chairperson)
Dr. Paulin Joseph
Mr. K. Thyagarajan
Ms. Shanthi Viswanathan
Ms. Beena E. Thomas (Member-Secretary)

Anti-Women Harassment Committee

Dr. Soumya Swaminathan (Chairperson)
Mr. M. Mani
Dr. Geetharamani Shanmugam
Mr. V. Adikesavan (Member-Secretary)

Bio-safety Committee

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

Building Committee

Dr. C.N. Paramasivan (Chairperson)
Dr. M.S. Jawahar
Dr. V.D. Ramanathan
Dr. P. Venkatesan
Mr. M. Subramanian (Member-Secretary)

Canteen Committee

Mr. R. Subramani (Chairperson)
Mr. V. Venkatesh Prasad
Mr. R. Balakrishnan
Ms. Nazeema Beevi
Ms. Arumaikannu Anbalagan
Ms. Beena Elizabeth Thomas
Ms. M. Vijayalakshmi
Dr. K. Jayasankar
Mr. K. Krishnan
Mr. E. Raman
Mr. P.B. Madhavan
Mr. N.C. Sridharan (Member-Secretary)

Celebration Committee

Dr. V. Kumaraswami (Chairperson)
Mr. M. Subramanian
Mr. E. Money
Mr. D. Shanmugam
Mr. P.B. Madhavan
Mr. S.N. Sankaralingam
Mr. V. Adikesavan (Member-Secretary)

Committee of Heads of Departments

Dr. P.R. Narayanan (Chairperson)
Dr. C.N. Paramasivan
Dr. Aleyamma Thomas
Dr. V. Kumaraswami
Dr. Rajeswari Ramachandran
Dr. V.D. Ramanathan
Dr. Soumya Swaminathan
Dr. C. Kolappan
Dr. M. Kannapiran
Mr. P.G. Gopi
Mr. R. Subramani
Dr. K. Jayasankar
Mr. M. Subramanian
Mr. V. Adikesavan
Mr. N.C. Sridharan
Dr. P. Venkatesan (Member-Secretary)

Condemnation Committee

Dr. P. Venkatesan (Chairperson)
Mr. S.N. Sankaralingam
Mr. E. Money
Mr. K. Jayarajan (Member-Secretary)

Drug Committee

Dr. Rajeswari Ramachandran (Chairperson)
Dr. Rema Mathew
Dr. K. Rajaram
Dr. C. Kolappan
Ms. Padma Balasubramanian
(Member- Secretary)

Essential Services Committee

Dr. K. Jayasankar (Chairperson)
Ms. K.S. Anusuya
Mr. Balakrishna Sharma
Mr. B. Madhavan
Mr. R. Manoharan
Mr. E. Money
Mr. J. Ravi
Mr. D. Shanmugam
Mr. R.S. Somasundaram
Mr. S.N. Sankaralingam (Member-Secretary)

Infection Control Committee

Dr. V. Kumaraswami (Chairperson)
Dr. Soumya Swaminathan
Mr. M. Subramanian
Mr. S. Ramanujam
Ms. S. Padma
Mr. D. Shanmugam
Dr. Ranjani Ramachandran (Member-Secretary)

Internal Ethics Committee

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

Library Committee

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

Purchase Committee

Dr. N. Selva Kumar (Chairperson)
Dr. Aleyamma Thomas
Dr. M. Kannapiran (Member-Secretary)

Research Committee

Dr. N. Selvakumar (Chairperson)
Dr. V. Chandrasekaran
Ms. 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)

Senior Technical Officer and Technical Officers Committee

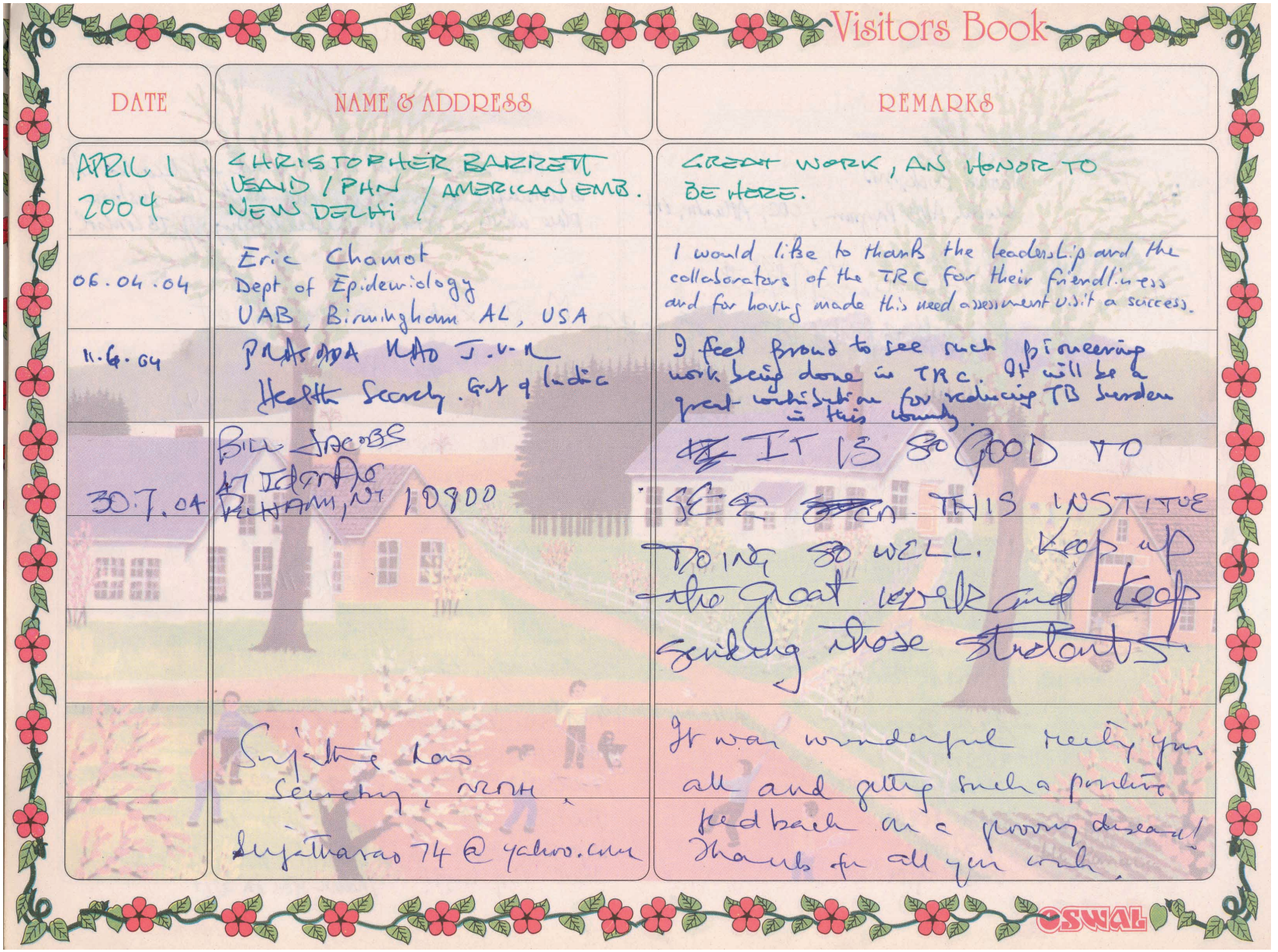
Dr. K. Jayasankar (Chairperson)
Ms. Jaya Gopinath
Mr. S.N. Sankaralingam
Mr. K.J. Illampurnam
Ms. Lalitha Victor
Ms. Nalini Sundar Mohan
Ms. S. Sudhamathi
Mr.E. Money
Mr. S. Ramanujam (Member-Secretary)

Transport Committee

Dr.M.S. Jawahar (Chairperson)
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)



Visitors Book

DATE	NAME & ADDRESS	REMARKS
APRIL 1 2004	CHRISTOPHER BARRETT USAID / PHN / AMERICAN EMB. NEW DELHI	GREAT WORK, AN HONOR TO BE HERE.
06.04.04	Eric Chamot Dept of Epidemiology UAB, Birmingham AL, USA	I would like to thank the leadership and the collaborators of the TRC for their friendliness and for having made this need assessment visit a success.
11.6.04	PRADIPA PATO J.V.R Health Security. Govt of India	I feel proud to see such pioneering work being done in TRC. It will be a great contribution for reducing TB burden in this country.
30.7.04	BILL JACOBS AT IDRAAS PUNJAB, INDIA 10900	IT IS SO GOOD TO SEE THIS INSTITUTE DOING SO WELL. Keep up the great work and keep guiding those students
	Sujatha Rao Security, MOHA. Sujatharao74@yahoo.com	It was wonderful meeting you all and getting such a positive feedback on a growing disease! Thanks for all your work.

Visitors Book

DATE	NAME & ADDRESS	REMARKS
Nov 10, 2004	MAMMO TESFAYE NIAID - NIH / Internation Technologies Support Bethesda, MD	Impressed with the dedication of TRC ICER staff for their work. Thank you for letting us work late & your hospitality during our stay. Looking forward to work with in the future.
10-11-04	Christopher Whalen International IT Projects NIAID - NIH Bethesda MD USA	It is an honor to be helping the TRC and all the ICER's with their data and communication needs. Thank you for the opportunity to work with you and for your hospitality.
6 JAN '05	COLIN BLAKEMORE MEDICAL RESEARCH COUNCIL 20 PARK CRESCENT LONDON W1B 1AL UK	Thank you for telling me about the history and excellent work of your institute. Colin Blakemore
24 Jan 05	AIME DE RUYNCK CTA DANTB, BHUBANESWAR ORISSA	I am very much impressed with the extend and variety of studies, with the concern for quality assurance and KNTCP policy implications
24 Jan 05	GEOFF SCOTT ROB THOMSON MIKE SHEMKO	A visit from Health Protection Agency & University College Londa Hospitals A link back through Wallace Fox, Denny Medina
	ALISON BOND CAROLINE PANKHURST BARRY COOKSON NANDINI SHETTY	and Bill Stott! Many thanks.

GUEST LECTURES

Name	Institution	Topic
Dr. Vishwanath Venkataraman	Asst. Professor, New Jersey Medical School, Newark, NJ, USA.	Glutathione and Tuberculosis
Mr.C. Sylendra Babu	Joint Commissioner of Police	Human Rights
Mrs.C. Padma Muralidharan	Account Manager, "Science Direct" Elsevier, India	Demonstration on "Science Direct"
Dr. Santhosh Babu	Additional Commissioner of Labour, Govt. of Tamil Nadu	Child labour elimination programme in Tamil Nadu
Mr. Ambuj Sharma	Managing Director, TNSCB, Chennai	Urban community development programmes in slum areas
Dr. Mukesh Doble	Associate Professor, Dept. of Biotechnology, IIT, Chennai	Natural products in drug development
Dr. David JM Lewis	St. George's Hospital Medical School, London, UK	Oral BCG as a booster vaccine against tuberculosis
Dr.George Chin – Shen Chou	General Manager & CEO Asian Corp., Taiwan	MTB-PCR test kit developed by Asiagen
Prof.Dr.HD. Klenk	Institute of Virology, Philips University, Marburg	Recent advances in hemorrhagic viral diseases
Dr. Salman Siddiqi	Becton-Dickinson, R & D, USA	The TB challenge-where do we stand today?
Mr. Murugan	Deputy Commissioner of Police, T.Nagar, Chennai .	Cyber Harassment
Dr. G.Thiry, Ph. D.	Director of Project Management Process & QA, IAVI	Development of AIDS Vaccine and activities of the" International AIDS Vaccine Initiative." (IAVI)

ABBREVIATIONS

AFB	Acid Fast Bacilli
ACT	Advocacy for Control of Tuberculosis
AIDS	Acquired Immuno Deficiency Syndrome
ATS	American Thoracic Society
ATT	Anti-TB treatment
BCG	Bacillus Calmette Guerin
BMI	Body Mass Index
CFA	Culture Filtrate Antigen
cfu	colony forming unit
Cpn10	Chaperonin-10
CLED	Cystine Lactose Electrolyte Deficient
DOTS	Directly Observed Treatment Short-course
DR	Direct Repeat
DRS	Drug Resistance Surveillance
DTC	District Tuberculosis Centre
DTH	Delayed Type Hypersensitivity
DST	Drug Susceptibility Testing
ECM	Expectation Conditional Maximization
EQA	External Quality Assurance
FGD	Focus Group Discussion
GEE	Generalized Estimating Equation
GFATM	Global Fund Against AIDS, Tuberculosis (TB) and Malaria (GFATM)
GLAS	Graphical Library Automation System
ICMR	Indian Council of Medical Research
IEF	Isoelectric Focusing
IFN-g	Interferon gamma
IL-4	Interleukin-4
LJ	Lowenstein-Jensen
LRP	Luciferase Reporter Phage
LT	Laboratory Technician
HIV	Human Immuno Deficiency Syndrome
HIVVT	HIV Vaccine Trials
HHC	Healthy Household Contacts
HLA	Human Leucocyte Antigen
MBL	Mannose Binding Lectin
MCMC	Markov Chain Monte Carlo
MDP	Model DOTS Project
MDR	Multi Drug Resistance
MDR-TB	Multi-Drug Resistant Tuberculosis
MOI	Multiplicity of Infection
NGO	Non-Governmental Organization
NHS	Normal Healthy Subjects
NIDDM	Non-insulin Dependent Diabetes Mellitus
NRA	Nitrate Reductase Assay
NRP2	Non Replicative Phase 2
NTM	Non Tuberculous Mycobacteria
OPC	Oropharyngeal Candidiasis
PBMC	Peripheral Blood Mononuclear Cells
PCR	Polymerase Chain Reaction
PFMC	Pleural Fluid Mononuclear Cells
PFT	Pulmonary Function Test
PGRS	Polymorphic GC Repeat Sequence
PMN	Polymorphonuclear Neutrophils
PPD	Purified Protein Derivative
PST	Proportional Sensitivity Test
PTB	Pulmonary Tuberculosis
QOL	Quality of life
rBCG	Recombinant BCG
RBC	Red Blood Cell
REACH	Resource group for Education and Advocacy for Community Health
RFLP	Restriction Fragment Length Polymorphism
RNTCP	Revised National Tuberculosis Control Programme
SDS	Sodium dodecyl sulphate
STD	Sexually Transmitted Disease
STDC	State TB Demonstration Centre
STI	Sexually Transmitted Infection
STLS	Senior Tuberculosis Laboratory Supervisor
STPKs	Serine/Threonine Protein Kinases
STS	Senior Treatment Supervisor
TB	Tuberculosis
TCS	Two Component Systems
TP	Tuberculosis Pleuritis
TU	Tuberculosis Unit
UTI	Urinary Tract Infection
USAID	United States Agency for International Development
VCTC	Voluntary Counseling and Testing Centre
VDR	Vitamin D Receptor
VHNs	Village Health Nurses
WGE	Whole Gel Elution
WHOQOL-BREF	WHO Quality of life Brief Scale
WHO	World Health Organization

RESEARCH ACTIVITIES

Clinical Research

Studies completed:

Lung function impairment in patients treated for pulmonary tuberculosis and the role of inhaled steroids – a double blind randomized controlled clinical trial

Background:

Recent studies have indicated that treated patients continue to have lung function abnormalities and inflammation even after 6 months of anti-TB treatment (ATT).

Aim:

To study the effect of inhaled steroids in reducing or reversing the residual lung function abnormalities after treatment for pulmonary TB.

Methods:

Patients who were aged 12 yrs and above, with at least one smear positive out of three for acid fast bacilli (AFB), no history of previous treatment, with no complicating illness and favourable sociological assessment were included for the study. These patients underwent pre treatment assessment, which included x-ray chest PA view and were then treated with Category-I regimen ($2EHRZ_3/4RH_3$) supervised as per RNTCP guidelines. Patients were followed up every month. The pulmonary function tests (PFT) were conducted at 3rd month or next earliest monthly that patient became smear negative. PFT included complete spirometry, lung volumes and carbon monoxide diffusion. Basic clinical and laboratory data were obtained from all patients.

Results:

Of the 318 patients assessed for the study, 145 patients were allocated to receive inhaled drugs as they had abnormal lung function at 3rd month. They were randomly assigned to receive either inhaled steroid by rotahaler

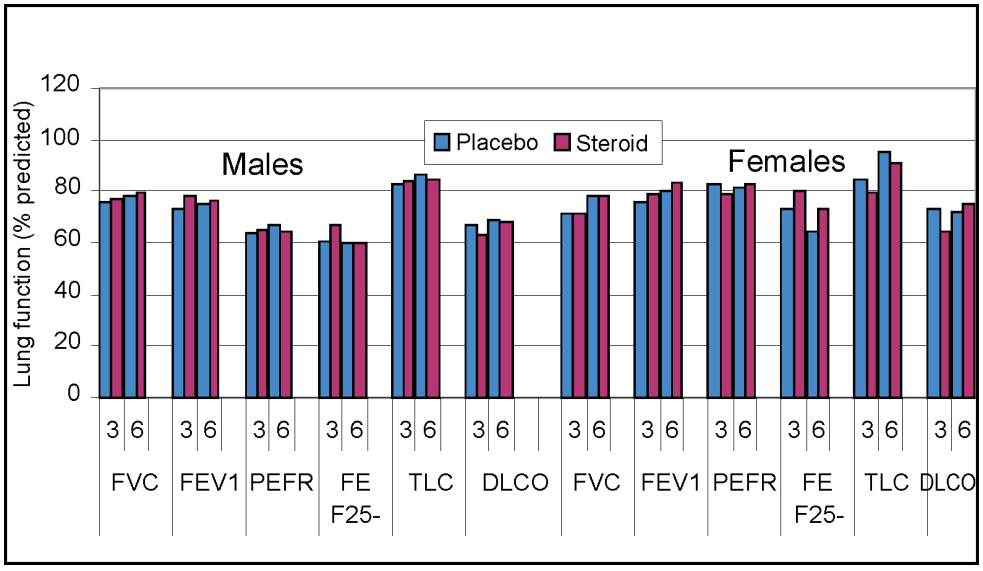


Fig. 1. Lung function in patients at 3rd and 6th month of treatment with inhaled steroid/placebo along with ATT

(Beclomethasone dipropionate 200 µg bid) or placebo. On completion of 6 months of anti-TB treatment (ATT) and 12 wks of inhaled drugs, the PFT tests were repeated. Twelve patients were excluded from the analysis based on insufficient clinical data, change of treatment due to adverse reactions, death in one patient for non-TB reasons, diabetes and cancer in one patient.

Conclusion:

There was no difference between the steroid and placebo groups in any of the lung function parameters studied. There was some improvement in FVC, FEV1% and TLC between the 3rd and 6th month but the improvement was similar in both groups (Fig. 1). Our results suggest that inhaled steroid given from the 3rd month of anti-TB therapy does not have a significant impact on lung function sequelae of TB. In general, males had poorer lung function at the end of therapy than females.

(Contact person: Dr.K.V. Kuppu Rao, e-mail: raokvk@icmr.org.in & Dr. Soumya Swaminathan, e-mail: soumyas@icmr.org.in)

Studies in progress:

A study of Category I regimen of Revised National Tuberculosis Control Programme (RNTCP) for the treatment of sputum-positive pulmonary tuberculosis associated with non-insulin dependent diabetes mellitus (NIDDM)

Background:

Tuberculosis is twice more common among patients suffering from diabetes mellitus. Presence of TB intensifies diabetes mellitus and vice versa. Under RNTCP Category I regimen is recommended for all sputum positive patients irrespective of the associated conditions.

Aim:

To study the efficacy of Category I regimen of the RNTCP for the treatment of patients with sputum positive pulmonary TB associated with NIDDM.

Methods:

Newly diagnosed patients with smear positive pulmonary TB and NIDDM, fulfilling the eligibility criteria were enrolled to the study. They were treated with isoniazid (H), rifampicin (R), ethambutol (E), pyrazinamide (Z) thrice-weekly for two months followed by isoniazid and rifampicin thrice-weekly for four months (2 $EHRZ_3/4HR_3$). Treatment was given under direct supervision. A total of 100 patients have been enrolled to the study.

Results:

Of 100 patients, 78% were males, 80% were aged 40 yrs or more and the mean weight was 51.5 kg. The culture conversion was 88% after 2 months of treatment and this increased to 97% by 3 months and remained the same till the end of treatment. A total of 90 patients received 75% or more of scheduled chemotherapy, 3 patients needed change of chemotherapy for drug toxicity and the remaining 7 patients received less than 75% of scheduled chemotherapy. These patients are being followed up for a period of 36 months after completion of treatment.

(Contact person: Dr. Rani Balasubramanian, e-mail: ranib@icmr.org.in)

A study of the efficacy and tolerability of moxifloxacin and gatifloxacin containing regimens in the treatment of patients with sputum positive pulmonary tuberculosis

Background:

A randomized clinical trial carried out by Tuberculosis Research Centre (TRC) had demonstrated that patients with sputum positive pulmonary TB can be successfully treated with a 4-month regimen that substituted ofloxacin for ethambutol in the 4-drug intensive phase given daily. However, a similar regimen administered thrice weekly was less successful. Meanwhile the newer generation of fluoroquinolones, moxifloxacin and gatifloxacin have been shown to have more potent anti-mycobacterial activity compared to ofloxacin.

Aim:

To study the efficacy and safety of thrice-weekly moxifloxacin and gatifloxacin containing regimens in the treatment of patients with smear positive pulmonary TB in a randomized clinical trial.

Methods:

Newly diagnosed sputum smear positive pulmonary TB patients, residing in or around Chennai and Madurai who fulfill the inclusion criteria are randomly allocated to one of the following three treatment regimens:

Regimen 1: Gatifloxacin, isoniazid and rifampicin thrice weekly for 4 months with pyrazinamide for the first 2 months $2GHRZ_3$ / $2GHR_3$.

Regimen 2: Moxifloxacin, isoniazid and rifampicin thrice weekly for 4 months with pyrazinamide for the first 2 months $2MHRZ_3$ / $2MHR_3$.

Regimen 3: As a control regimen. Isoniazid and rifampicin thrice weekly for 6 months with ethambutol and pyrazinamide for the first 2 months $2EHRZ_3/4HR_3$.

It is proposed to admit 300 patients to each arm. The study is being conducted in Chennai and Madurai. Since moxifloxacin was not available at the time of starting the study, patients are being allocated to regimens 1 and 3 only.

Results:

The study was started in May 2004 and 198 patients have been enrolled to date (98 in regimen 1 and 100 in regimen 3). The baseline characteristics are shown in the Table I.

Table I : Baseline characteristics of the study population

Baseline characteristics	Regimen	
	Regimen 1 (n=98)	Regimen 3 (n=100)
Sex:		
Male	73	72
Female	25	28
X-ray chest; extent of disease:		
1-2 zones	22	22
> 2 zones	76	78
Sputum examination:		
Smear: 1+	26	28
2+	53	53
3+	19	19
*Culture: 1+	3	1
2+	12	12
3+	64	65
@NTM	1	0

*culture results upto Dec. 2004
@NTM – Non-tuberculous mycobacteria

(Contact person: Dr. Rajeswari Ramachandran, e-mail: rajeswarir@icmr.org.in)

Long term status of sputum positive pulmonary tuberculosis patients successfully treated with short course chemotherapy

Background:

Information on the long-term clinical, radiological and bacteriological status of the patients successfully treated with SCC regimens both daily and intermittent remains, largely unknown. Also factors contributing to death among cured pulmonary TB patients and the impact of sequelae of the disease on the quality of life over a long period of time are not documented. Data on long term follow up of patients treated with SCC will be of great value in analyzing the long term impact related to disease and treatment.

Aim:

1. To do one time assessment of the clinical, bacteriological and radiological status including estimation of quality of life and pulmonary function of sputum positive pulmonary TB patients successfully treated with SCC regimen at 15-20 yrs after completion of treatment.
2. To find out the number of deaths and the cause of death.

Methods:

All sputum-positive pulmonary TB patients who were started on treatment during the period 1986-1990 at our centre and completed 60 months of follow up, form the study population. In this prospective study the following information was collected: detailed history on retreatment for TB, information on smoking, alcoholism, respiratory symptoms and co-morbid conditions like diabetes, hypertension, bronchial asthma, cardiac and renal problems. This was followed by clinical examination, X-ray chest - PA view, sputum examination by smear and culture for *M. tuberculosis*. Urine examination for albumin and sugar, relevant blood tests whenever necessary, pulmonary function test, ECG and to assess the quality of life St. George's respiratory questionnaire and the World Health Organization Disability Assessment Schedule II (WHODAS II) questionnaire were used.

It was planned to assess a total of 364 patients, which includes patients treated with daily regimen (163 patients) and intermittent Short Course Chemotheraphy regimen (201 patients). So far we have visited 80% of the study population and the information on long-term status of 291 patients is available.

(Contact person: Dr. Rajeswari Ramachandran, e-mail: rajeswarir@icmr.org.in)

Evaluation of chemotherapy regimens for tuberculosis in HIV-infected persons

Background:

The duration of anti-TB treatment among HIV+ve patients with TB is still a contentious issue. A 6-month intermittent (3 times/wk) regimen is the standard treatment for TB in the national programme in India and many countries.

Aim:

To compare the efficacy of a 6-month versus a 9-month intermittent anti-TB regimen among HIV+ve patients with TB.

Methods:

Prospective, randomized, controlled clinical

trial. Arm A: 6-month regimen $2EHRZ_3/4RH_3$. Arm B: 9-month regimen $2EHRZ_3/7RH_3$ (E: Ethambutol 1200mg, H: Isoniazid 600 mg, R: Rifampicin 450/600mg and Z: Pyrazinamide 1500mg with Pyridoxine 10mg, three days a week). Treatment was fully supervised for the first 2 months, then once a week. The intensive phase was extended by 4 weeks if sputum smears were positive at the 2nd month. Patients were followed every month with clinical examination, sputum AFB smear and culture for *M. tuberculosis*. Chest radiograph and CD4 counts were done at baseline and at the end of therapy. None of the patients were on antiretroviral therapy. End points of the study will be sputum culture negativity at the end of treatment and relapses during follow-up. Intent to treat analysis will be performed.

Results:

Three hundred and sixty patients have been admitted to the study, upto March 31, 2005. Of these, 226 had sputum culture-positive for *M. tuberculosis*, at baseline. One hundred and ninety five patients were randomized to the 6-month regimen (n =100) and 9-month regimen (n = 95) respectively. The Table II shows the baseline demographic and other characteristics of patients with sputum culture positive pulmonary tuberculosis admitted to the two treatment arms. At the end of the intensive phase, sputum smears were negative in 71% of patients while sputum cultures were negative in 86% of patients. 89% of the organisms isolated were susceptible to all anti-TB drugs while resistance to isoniazid and rifampicin (MDR-TB) was seen in 2.5% of patients.

(Contact person: Dr. Soumya Swaminathan, e-mail: soumyas@icmr.org.in)

Preventive therapy for tuberculosis in HIV-infected persons

Background:

Persons co-infected with *M. tuberculosis* and HIV have a 5-8% annual risk and a 50% or greater life time risk of developing active TB. The increased risk of developing TB disease among those infected with HIV has prompted a need to consider institution of preventive measures to enable HIV +ve patients to avoid the risk of progression to clinical TB.

Aim:

To compare the efficacy of two regimens (isoniazid 300 mg daily for 3 yrs vs ethambutol 800 mg with isoniazid 300 mg daily for 6 months) in reducing the incidence of TB and mortality among HIV-infected persons.

Table II : Baseline characteristics of patients admitted to the two treatment arms

Sl.No.	Baseline variables	6 months (n=100)	9 months (n=95)
1	Males (%)	78%	73%
2	Age (years)	35 ± 8	34 ± 7
3	Weight (kgs)	43 ± 7.6	43 ± 9.5
4	CD4 count (cells/mm3)	191 ± 181	211 ± 245
5	Sputum smear positives (%)	74%	77%

Methods:

HIV +ve individuals aged more than 15 yrs without evidence of active TB and willing for our terms were randomly allocated to receive either of the two regimens (stratification based on tuberculin test reaction of 5mm). Patients collect the drugs for self-administration once in 15 days and surprise home visits are done to check the pill count and also collect urine for acetyl INH measurements. All patients are given pyridoxine 10 mg daily. Clinical examination is done every 3 months while complete investigations including chest x-ray, sputum examination and CD4, CD8 counts are done every 6 months and at any time if clinical deterioration is present. Follow up is for 3 yrs and end points are development of TB or death.

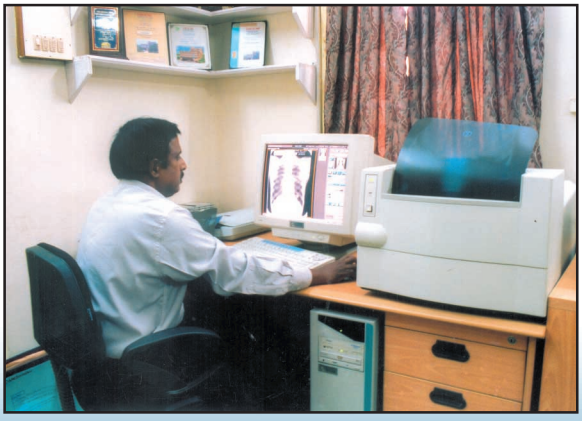
Results:

Six hundred and thirty three patients have been admitted to the study up to March 2005. Twenty seven patients were excluded because of baseline (pre-treatment) cultures being positive for *M. tuberculosis*. Of the 606 eligible cases, 303 were allocated to the EH regimen (6EH) and 303 to the INH regimen (36H). Table III shows the baseline characteristics of patients admitted to the 2 regimens. Ninety six patients in EH regimen and 96 patients in INH regimen have completed 36 months of follow-up. Ninety three percent of patients in the EH regimen and 92% in the INH regimen had taken >80% of the chemotherapy. Eight patients in each group have developed TB. There have been 5 deaths in the EH regimen and 5 in the INH regimen.

(Contact person: Dr. Pradeep Arvind Menon, e-mail: menonpa@icmr.org.in & Dr. Soumya Swaminathan, e-mail: soumyas@icmr.org.in)

Table III: Baseline characteristics of patients admitted to the two preventive therapy regimens

Sl.No.	Variables	EH regimen (n=303)	INH regimen (n=303)
1	Males (%)	37%	37%
2	Age (years)	30 ± 7.4	30 ± 6.7
3	Tuberculin reaction (mm)	8.7 ± 9.7	8.3 ± 9.3
4	CD4 cells/mm^3	377 ± 251	370 ± 236



Studies completed:

Gender differences in perceived health related quality of life among persons living with HIV

Background:

In the era of HIV/AIDS and in the context of the developing world HIV/AIDS has led to a pandemic. HIV antiretroviral drugs are inaccessible and unaffordable and the only choice that health care providers have is to work towards improving the quality of life of individuals, as long as they live with this dreaded disease.

Aim:

To find out the differences in the quality of life perceived by women and men living with HIV/AIDS.

Methods:

The study population included a cohort of 203 seropositive individuals, 102 women and 101 men, attending the Sexually Transmitted Disease (STD) out patient clinic of the Government General Hospital and the TRC. The WHOQOL-BREF scale was used to assess the quality of life.

Results:

The findings from this study revealed that men reported a poor quality of life in the psychological domain ($p<0.01$) while women in the sociological domain ($p=0.03$). The stage of illness did not seem to influence quality of life among women and men.

Conclusion:

The findings emphasize the need for health providers to assess the QOL among people living with HIV/AIDS. This information would be helpful in planning effective intervention strategies for men and women living with HIV/AIDS in order to be ensured of a quality of life.

(Contact person: Ms. Beena Thomas, e-mail: beenaelli@hotmail.com & Dr. Soumya Swaminathan, e-mail: soumyas@icmr.org.in)

Studies in progress:

Stress and coping strategy of women living with HIV/AIDS in relation to their marital status

Background:

Infection rates of HIV are becoming higher in women than men especially in the developing world. Studies have documented an increase of HIV among monogamous married women. Many women have become widows at a very early age losing their husbands to AIDS and having to look after the orphans on their own. Studies have also documented that individuals living with HIV/AIDS undergo enormous amounts of psychological stress. There is dearth of information from India on stress and coping strategies of women living with HIV/AIDS. It is against this background that this study was planned.

Aim:

1. To assess the stress experienced by women living with HIV/AIDS in relation to the marital status.
2. To evaluate the coping strategies adopted in order to cope with the stress.

Methods:

The respondents are recruited from a cohort of seropositive women patients attending the TRC Madurai unit between January 2004 to December 2004. Patients who are willing to participate in the study and give their informed consent are considered for the study. A semi structured interview schedule is being used to collect socio-demographic information. The Jalowiec & Powers coping scale, Dr Latha stress questionnaire and the WHOQOL-BREF scale was used to measure stress, coping and quality of life. So far 80 patients of whom 40 were widows have been interviewed.

The findings would help in innovating effective intervention strategies to help women living with HIV/AIDS cope with the disease and have a better quality of life.

(Contact person: Mr. Thiruvalluvan, e-mail: thispace@yahoo.com & Ms. Sudha Ganapathy, e-mail: esgee@hotmail.com)

A study on stigma related to tuberculosis among patients and community

Background:

Stigma associated with TB among patients, health providers and the community is an impediment in the control of tuberculosis. The health seeking behavior of patients can be influenced because of stigma. There is lack of documented information on stigma from south India. This study focuses on stigma related to TB in rural and urban areas in south India.

Aims:

To assess the

1. Stigma experienced by the TB patients
2. Community perception on stigma related to TB

Methods:

This study was conducted in two TB units (TUs), one in Kancheepuram (rural) and another in Chennai (urban), Tamil Nadu. Two hundred and seventy six patients registered during January - March 2004 formed the study population. The patients who were willing to participate in the study and give their informed consent were interviewed using a semi-structured interview schedule. In addition, Focus Group Discussions (FGD) was conducted among the DOT Providers and community.

The data collection has been complete and analysis in progress. Of the 276 patients, 110 were from rural and 166 from urban areas. Seventy three percent of the rural and 66% of urban respondents were males. The focus group discussions among the providers revealed that stigma was present more among female patients as compared to males. Patients were reluctant to disclose the diagnosis of tuberculosis to others.

(Contact person: Ms. Jaggarajamma, e-mail: jagannatharao2003@yahoo.com, & Ms. Sudha Ganapathy, e-mail: esgee@hotmail.com)

The impact of perceived social support on the treatment outcome of tuberculosis patients under DOTs

Background:

Tuberculosis is not only a medical disease but also a social disease. Compliance to the prescribed regimen is influenced by various factors like patient's social and economic background, his past health seeking behavior, and social support he /she gets from his family and community. Studies pertaining to the influence of social support on treatment compliance are limited.

Aim:

To study the influence of perceived social support on treatment outcome of TB patients under DOTS.

Methods:

This is a prospective study on TB patients registered at the Corporation clinics of Chennai and the District TB Centre Kancheepuram, Tamil Nadu. A semi-structured interview schedule was used to elicit information. So far 260 patients (100 from rural and 160 from urban) have been interviewed.

(Contact person: Ms. Niruparani Charles, e-mail: nijojach@yahoo.com & Ms. Sudha Gapanathy, e-mail: esgee@hotmail.com)

Knowledge, Attitude and Practice of Persons at risk in relation to a future HIV Vaccine Trial

Background:

In TRC, efforts are ongoing for conducting HIV Vaccine Trials (HIVVT). Prior to any HIV preventive vaccine trial, it is very important to assess the concerns, knowledge gaps, attitude toward HIV vaccines and willingness to participate in future HIVVTs among populations at high risk of HIV infection. To address these issues, a sociological study with two–phased qualitative–quantitative approach is being conducted to find out the HIV vaccine readiness among population at risk for HIV/AIDS.

Aims:

To elicit information on

1. Demographic characteristics of the study participants and their knowledge of and attitude towards HIV/AIDS and HIV vaccines.
2. Perceptions about willingness to participate in a future HIVVT and factors which enhance or diminish their willingness to participate.

Methods:

During phase-I from October 2004 to January 2005, 12 focus group discussions (8 from Chennai and 4 from Madurai) were conducted among the following sub groups: Injecting Drug Users, Men having Sex with Men, women in sex work, truckers and people who report recent Sexually Transmitted Infections (STIs). As there are indications that the HIV epidemic has moved into the general population, a representative sample of married women has been included for the study.

Results:

The participants were screened for their eligibility and written informed consent was obtained after giving the information about the purpose of the study and future HIVVTs. Focus group sessions were audio taped for subsequent transcription apart from the recorded observations. At the end, the participants were assessed using the CDC Vaccine Attitude Survey Scale. The analysis of qualitative data is being done on the basis of the study findings. Phase II will be conducted among 500 participants with the modified questionnaire. The information will help researchers to develop recommendations for encouraging participation of high-risk individuals in future HIVVTs.

(Contact person: Ms. Mohanarani Suhadev, e-mail: mohisuhadev@yahoo.com & Dr. Soumya Swaminathan, e-mail: soumyas@icmr.org.in)

Epidemiological Research

Directly Observed Treatment-Short course (DOTS), a global strategy for control of TB is being implemented in India in a phased manner since 1997. The epidemiological impact of this strategy in high burden countries is not known. To understand this, TRC is undertaking an epidemiological impact study in 5 blocks of Tiruvallur district, Tamil Nadu. This is the same area where the BCG trial was done and epidemiological data on TB is available in this area prior to DOTS implementation. Tamil Nadu government is implementing the programme and TRC is monitoring the same. The project has technical support from World Health Organization (WHO) and financial support from United States Agency for International Development (USAID). The project was started in May 1999. TRC is involved in:

a) Training
b) Monitoring of the programme
c) Epidemiological survey of tuberculous disease and infection
d) Bacteriological and molecular epidemiological studies and
e) Operational research

a. Training

Good quality training is essential for successful implementation of the programme. TRC has been identified as a nodal centre for training in RNTCP and during the period, we have trained 45 Medical Officers (Tr) in 4 batches, 7 Medical Officers in 1 batch, 63 Senior Treatment Supervisors (STS) in 4 batches, 39 Senior Tuberculosis Laboratory Supervisors (STLS) in 6 batches, 14 Lab Technicians (LTs) in 3 batches and 49 field workers in 4 batches.

b. Monitoring of the programme

During the reporting period, monitoring of the programme by TRC was done only upto December 2004. Six hundred and forty seven patients have been initiated on treatment for TB in the project area covering a population of 580,000. Of these, 336 were new sputum smear positive, 171 new smear negative, 83 extra pulmonary and 109 retreatment patients. Annualised case detection rate for new smear positive patients during the period was 92%.

c. Epidemiological Impact Study – Community survey of TB infection and disease

To assess the epidemiological impact of DOTS implementation, second resurvey to estimate the prevalence of TB disease and the third tuberculin survey to estimate the prevalence of infection in the project area were started.

Background:

DOTS was implemented in Tiruvallur district of Tamil Nadu in May 1999. To assess the epidemiological impact of DOTS strategy, TRC is carrying out a series of sample surveys to estimate the prevalence of TB infection and disease in Tiruvallur district, covering a population of 580,000.

Aim:

The aim of these surveys is to study the trends over time for both infection and disease and thereby to measure the epidemiological impact of DOTS implementation in this region.

Methods:

All adults ≥ 15 years included for the disease surveys were screened by two screening methods namely, elicitation of symptoms and x-ray examination. Two samples of sputum specimens were collected from those who were either symptomatics and/or x-ray abnormals suggestive of TB. These specimens were processed for smear and culture and those who became bacteriologically positive were referred for anti-TB treatment, if they satisfied the RNTCP guidelines. All children included in the tuberculin survey were tested with PPD 1TU RT23 and the reaction sizes were read after 72-96 hrs.

Results:

Two surveys have been completed and the second resurvey is in progress since January 2004. Of 41,670 subjects targeted for the disease survey, 38,225 (92%) were covered for symptom screening and 37,676 (90%) for x-ray screening. The coverage for sputum collection was 4645 (92%) of the 5027 that were eligible. For the tuberculin survey, of 17,306 subjects targeted the coverage was 16,647 (96%).

Conclusion:

The prevalence of disease from the two completed surveys have shown a decline of 9% among smear positive cases and 11.3% among culture positive cases, demonstrating that DOTS implementation was associated with a more rapid reduction in the prevalence of disease compared to that in the pre-DOTS period.

(Contact person: Dr. Aleyamma Thomas, e-mail: aleyammat@icmr.org.in & Mr. Gopi, e-mail: gopipg@icmr.org.in)

d. Molecular Epidemiology

Laboratory analysis of *M. tuberculosis* isolates by Restriction Fragment Length Polymorphism (RFLP):

Background:

TRC is undertaking RFLP studies on positive cultures obtained from patients. Sputum specimens have been collected from patients who were started on treatment and they have been set up for culture and sensitivity. RFLP typing is done on the positive cultures to understand the cluster effect.

Aim:

To understand the molecular epidemiology in the area and to monitor the same over time.

Methods:

M. tuberculosis clinical isolates were cultivated on LJ medium, harvested and killed by heating at 80^{o}C for 30 min. Genomic DNA was isolated and Pvu II-IS6110 RFLP analysis was performed according to standardized methods using a 245 bp right sided probe. In parallel, Alu I cleaved genomic DNA was probed with repetitive DR element isolated from *M. bovis* BCG according to standard protocols.

Results:

The RFLP analysis of *M. tuberculosis* isolates revealed that 40% of the TB isolates showed a single copy of IS6110. To overcome this limitation an additional probe Direct Repeat (DR) was used to fingerprint the isolates. During the last year, the same isolates were subjected to an additional typing method by using a third probe, called polymorphic GC repeat sequence (PGRS). Two thousand five hundred *M. tuberculosis* isolates from the MDP area have been processed for DNA extraction and RFLP has been performed on 1500 samples till June 2004. The PGRS typing has been completed for 500 IS6110 low copy isolates.

The DR probe RFLP has been replaced by an easier PCR based method called 'spoligotyping' and this newer method has been standardized and performed on 500 isolates upto December 2004.

(Contact person: Dr. Sujatha Narayanan, e-mail: sujathan@icmr.org.in)

Studies completed:

Timing and its significance in the diagnosis and treatment of tuberculosis in disease endemic countries: the interplay of health seeking and health systems

Background:

The impact of the DOTS strategy is limited by poor case detection in many settings, attributable both to the low sensitivity of smear microscopy and to multiple behavioral and health system factors. These obstacles lead to diagnostic delay and in some cases high rates of drop out from the diagnostic process, inevitably with the result of greater morbidity, higher cost, and ongoing transmission of infection as patients go undetected and untreated. This study was done in two parts.

Part I

Aim:

To quantify the delay in diagnosis and treatment of TB in all disease categories, at the levels of patient, health provider, laboratory and treatment stages.

Methods:

A cross sectional study was planned to quantify delay and drop-out in the TB diagnostic process, to identify factors associated with delay, and to evaluate its economic and health impact in four disease endemic countries (India, Peru, Thailand and Zambia). This study was conducted in Tiruvallur district, Chennai Corporation and Kancheepuram district. In order to collect qualitative data, we conducted 9 focus group discussions. The participants were LTs, STLS, Health Visitors, Lab Assistants, Village Health Nurses, Treatment Organisers and Health Inspectors. Based on the findings, a pre-coded structured interview schedule was developed. This was used to collect data from TB patients and chest symptomatics.

Results:

A total of 408 newly diagnosed adult TB patients were interviewed: 240 (59%) pulmonary smear-positive, 108 (26%) pulmonary smear-negative and 60 (15%) extra-pulmonary. Various delays (patient's delay, provider delay and total delay) and the mean, median cost of diagnosis for pulmonary and extrapulmonary cases were evaluated.

Part II

Aim:

To determine the frequency and timing of diagnostic drop-outs among pulmonary TB suspects.

Methods:

Subjects (≥15 years) presenting to government health centres with ≥3 weeks cough or haemoptysis were enrolled in a prospective observational study. All symptomatics who had been ordered smear microscopy were followed-up, for the presence and dates of i) serial laboratory sample registration, ii) patient notification and iii) treatment initiation. Interviews were undertaken for the following subjects who did not (a) deliver 3 sputum specimens, (b) collect results and (c) come for treatment initiation, within 2 weeks of request (drop-outs).

Results:

Out of the total of 1000 subjects recruited, 872 (87%) completed the diagnostic process. Among the 128 drop-outs, 92 (72%) drop-outs were tracked and interviewed, the main reasons for dropping out were analysed.

(Contact person: Dr. Rajeswari Ramachandran, e-mail: rajeswarir@icmr.org.in)

Studies in progress:

Drug resistance surveillance in Model DOTS Project (MDP) area

Background:

Drug resistance surveillance is considered as a useful tool to assess the effective functioning of tuberculosis control programmes. Drug resistance levels and its trends serve as an epidemiological indicator to assess the extent of resistant bacterial transmission in the community. The drug resistance levels among patients treated under TB control programmes are not available in many settings.

Aim:

To study the drug susceptibility pattern among patients admitted to treatment in the project area.

Methods:

The project area in Tiruvallur district has 17 peripheral health institutions where TB patients are diagnosed and started on treatment. Two additional sputum samples were collected from all types of patients started on treatment in these centers, preferably within a week and tested for culture and drug susceptibility to anti-TB drugs.

Results:

The collection of sputum samples was started in August 1999. Bacteriological results are available for 4647 patients. Of these, culture results were positive for 2547 patients and drug susceptibility pattern available for 2536 patients. Category wise distribution of the culture results and susceptibility pattern are given in Table IV.

Of the 2052 patients admitted to CAT I and III and for whom sensitivity results were available, 1740 (84.8%) were sensitive to all drugs, 98 (4.8%) resistant to streptomycin alone, 208 (10.1%) to isoniazid and only 27 (1.3%) had resistance to isoniazid and rifampicin (multi-drug resistant tuberculosis, MDR-TB). Among 484 CAT II patients, 279 (57.6%) were sensitive to all drugs, 184 (38.0%) had resistance to isoniazid and 57 (11.8%) had MDR-TB (Fig. 2).

Conclusion:

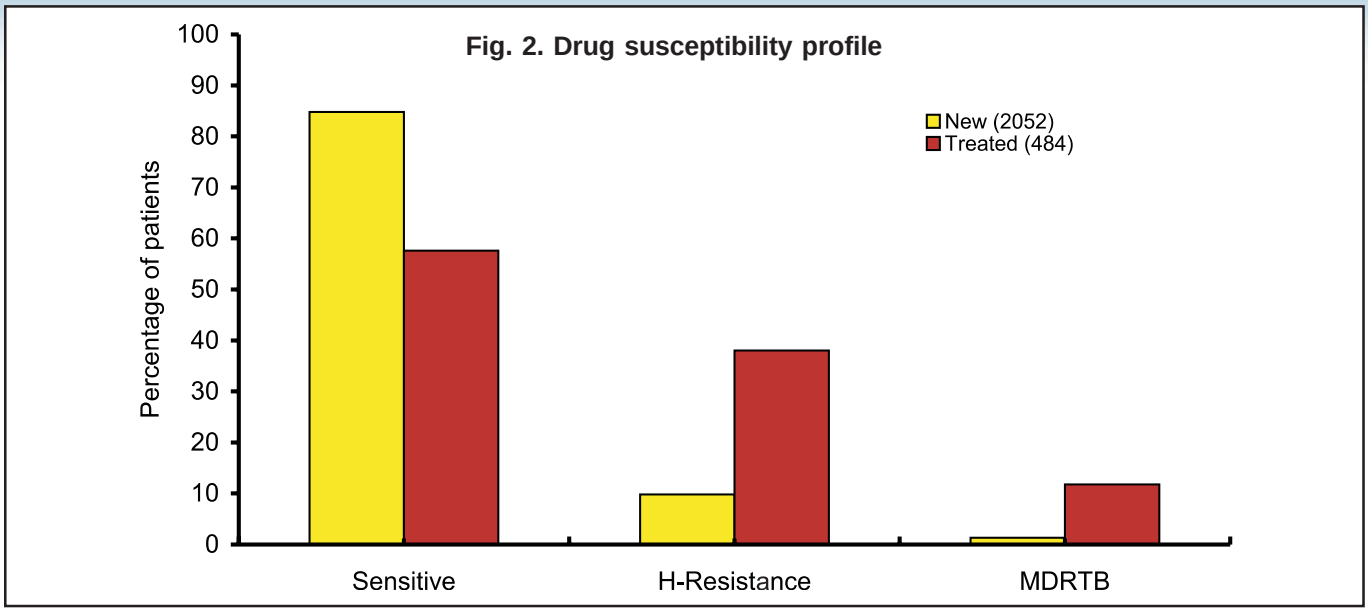
MDR-TB was observed in less than 2% in newly diagnosed patients

(Contact person: Dr. Aleyamma Thomas, e-mail: aleyammat@icmr.org.in & Mr.P.G. Gopi, e-mail:gopipg@icmr.org.in)

Table IV : Distribution of patients by category and bacteriological results

Category	Total patients admitted	Bact. Results available	S+C+	S-C-	S+C-	S-C-	Total S+	Total C+
I	2589	2350	1473	381	88	408	1561	1854
II	768	673	414	75	40	144	454	489
III	1822	1624	78	126	33	1387	111	204

S+C+ smear positive culture positive
S-C+ smear negative culture positive
S+C- smear positive culture negative
S-C- smear negative culture negative



Risk of tuberculosis infection and disease in different economic strata

Background:

Most researchers agree on the general association between TB and socio-economic conditions, but no direct cause and effect relationship has been demonstrated.

Aim:

To estimate TB infection and disease rates in the community and relate these to the economic status of the population.

Methods:

The study is being carried out in the same population where the disease survey is undertaken. All households in a village included for the survey will be visited and the head of the family/ informant identified. After explaining the purpose of the survey and obtaining consent a semi-structured interview schedule will be used to elicit the socio-economic status of the household.

Results:

The data collection was started in February 2004. Of the 11,926 households attempted, 11,374 (95%) were covered for the survey.

(Contact person: Dr. Aleyamma Thomas, e-mail: aleyammat@icmr.org.in & Mr.P.G. Gopi, e-mail: gopipg@icmr.org.in)

Assessment of Quality of life of TB patients treated under DOTS programme

Background:

The impact of a chronic disease like TB on individuals is often affecting not only physical health, but also social, economic and psychological well being. The economic costs incurred by TB patients are well studied. However very little information is available on patients' perceptions regarding health status and quality of life after completion of treatment.

Aim:

To assess perceptions of 'cured' or 'treatment completed' TB patients about their physical, mental and social well being.

Methods:

This study is being carried out in one TB unit (TU) of Tiruvallur district of Tamil Nadu, south India, with a population of 580,000. TB patients treated from July to December 2002 and January to June 2003 under the government health facilities of DOTS programme were visited at their residence after one year from the completion of treatment. Using a semi–structured (modified SF36) interview schedule to elicit data on physical and social functioning, role limitations due to physical or emotional problems, mental health, energy and vitality, pain and general health perceptions were collected.

So far, 567 patients were interviewed and data entry is in progress.

(Contact person: Mr. M. Muniyandi, e-mail: mmuniyandi@yahoo.com & Dr. Rajeswari Ramachandran, e-mail: rajeswarir@icmr.org.in

Management of MDR-TB patients from the field

Background:

Emergence of MDR-TB is a potential threat to the success of TB control. Patients diagnosed to have MDR-TB in the study area were managed by TRC under programme conditions.

Methods:

In the study area two additional sputum samples were collected for culture and sensitivity testing for *M. tuberculosis* from patients

1. Registered for treatment, within one week of admission
2. During follow up, if reported as positive by smear
3. Cured patients, at 12, 18 and 24 months from start of treatment to find the rate of relapse under RNTCP
4. All Cat II failure patients identified in the study area

Patients identified to have drug resistance to both isoniazid and rifampicin (MDR-TB), with or without resistance to other drugs, were treated with one of the following regimens.

Drug regimens	**No. Pts.**
S_3,Ofl_7,Eth_7,Emb_7,Z_7	31
K_3,Ofl_7,Eth_7,Emb_7,Z_7	20
Individually tailored	19
Total	**70**

Results:

So far 75 patients have been identified with multiple drug resistance. Five of them were not MDR-TB but had resistance to more than one drug. Of the remaining 70 MDR-TB patients, 48 were from study area and 22 referred by a Non-Governmental organization (NGO), Advocacy for control of tuberculosis (ACT) working in Chennai Corporation. Duration of treatment is a minimum period of 18 months and/or culture negativity for 12 months, whichever is later. Most of the patients are still on treatment.

(Contact person: Dr. Aleyamma Thomas, e-mail: aleyammat@icmr.org.in)

HIV seroprevalence in tuberculosis patients

Background:

The HIV seroprevalence among TB patients varies widely between different states in India and even between different districts in the same state.

The seroprevalence varies between 0.6% in certain areas to almost 24% in some regions. This wide variation is a reflection of the background seroprevalence among the high-risk groups and the general population. The TRC had undertaken 2 surveys previously. The findings of these surveys and other such studies show a trend towards increasing HIV prevalence among the new TB patients.

Aims:

1. To determine the HIV seroprevalence among persons with TB by age, sex, area of residence and site of disease.
2. To monitor trends of HIV infection among TB cases in 4 selected centres.
3. To study the feasibility of testing all TB patients for HIV, through Voluntary Counseling and Testing Centre (VCTC).

Methods:

All new TB patients are referred to the VCTC if willing and offered HIV testing after pretest counseling. Patients who are not willing are tested in an anonymous unlinked manner in order to get unbiased prevalence. Since, blood collection is not part of the routine for TB patients on treatment, the addition of this procedure will be explained to the patient.

- Purpose of the study, informed consent
- Referral to VCTC by TB Medical Officer, pretest counseling
- Retesting of all blood samples by ELISA at TRC (for confirmation of results)
- Results will be divulged after post test counseling
- Two sputum samples (bacteriology)

The study sites will include the 4 centres:

One rural	– Pennathur Sanatorium
One semi-urban	– Kancheepuram District Tuberculosis Centre (DTC)
One urban	– Vellore DTC
One Metropolitan	– Otteri TB Hospital, Chennai

These sites are the same as in the 2 surveys conducted by TRC earlier.

Outcome measures:

Prevalence of HIV among TB patients at these 4 centers in Tamil Nadu will be available.

Trend analysis can be done as this will be the third time point where the prevalence survey is being done in the same centres.

(Contact person: Dr. Ranjani Ramachandran, e-mail: ranjanir@icmr.org.in)

Studies completed:

Phagebiotics to process sputum specimens for Luciferase Reporter Phage assay

Background:

The mechanical pressure during centrifugation and the chemical pressure due to the alkali leave the tubercle bacilli in the sputum unsuitable for the phage to infect soon after processing sputum specimens by Petroff's procedure. It is mandatory that sputum specimens processed by 4% NaOH in Petroff's method have to be incubated overnight before subjecting it to any phage infection. Incubation overnight even with antibiotics yields heavy growth of normal flora that survives the action of 4% NaOH making it unsuitable for phage assay.

Aim:

To isolate normal flora that survives the action of 4% NaOH, isolate phages which infect all of them, add them to sputum deposits and assess their capacity to control the overgrowth of normal flora.

Methods:

The flora that survived the action of 4% NaOH was identified and 14 representative isolates were selected. Using them as bait, a total of 8 phages were isolated from soil and sewage samples. The host range of all these phages were assessed after preparing high titre phage lysates. Three of them inhibited 13/14 clinical isolates belonging to different genera including aerobic spore bearers excepting *Staphylococcus albus*. None of the other phages could control *Staphylococcus albus*. Screening more sewage samples is being attempted to get a suitable lytic phage infecting *Staphylococcus albus*.

Results:

Using the three phages with the wide host range as a cocktail, 100 sputum samples were analysed. Processed sputum samples when grown in liquid medium to facilitate rapid diagnosis of TB, yielded heavy growth of normal flora when subcultured onto blood agar plates. Addition of phage cocktail resulted in qualitative and quantitative reduction in commensal flora.

Conclusion:

The use of phagebiotics to control the overgrowth of normal flora when sputum specimens are incubated overnight is a biofriendly approach most suited for Luciferase Reporter Phage (LRP) diagnostic assay. However the present set of phagebiotics should be strengthened further to control *Staphylococcus albus* and *Bacillus sp.* (Table V).

(Contact person: Dr. Vanaja Kumar, e-mail: vanajakumar@icmr.org.in)

Table V: Growth of normal flora on blood agar from 100 sputum samples processed by Petroff's method as such (stage I) and after growing in liquid medium with (stage III) and without phagebiotics (stage II)

	Stage I	Stage II	Stage III
Hemolytic, Nonhemolytic Confluent	2	100	4
Nonhemolytic Confluent	11	0	0
Hemolytic, Single	4	0	17
Non hemolytic, Single	9	0	33
No Growth	74	0	46

Increasing nevirapine dose can overcome reduced bioavailability due to rifampicin co-administration

Background:

Majority of patients in the developing world who are receiving antiretroviral therapy are on 3-drug fixed dose combination pills that include nevirapine. Rifampicin, an integral part of anti-TB therapy, induces the cytochrome P-450 system, which is involved in the metabolism of nevirapine. This could lower the bioavailability of nevirapine when it is given along with rifampicin. Although it has been suggested that rifampicin could be administered along with nevirapine, supportive pharmacokinetic data of nevirapine in the presence of rifampicin are scarce.

Aim:

To study the effect of rifampicin on steady state pharmacokinetics of nevirapine and the impact of increasing the dose of nevirapine on its peak and trough levels.

Methods:

Thirteen HIV-infected patients (9 males and 4 females) with mean age of 34 yrs and body weight 58 kg and on regular antiretroviral therapy for a period of 1–8 months (stavudine 30/40 mg + lamivudine 150 mg + nevirapine 200 mg twice daily) participated in the study. A baseline pharmacokinetic study of nevirapine was conducted and repeated after one week of daily rifampicin 450/600 mg. The study was repeated in 7 out of 8 patients who had sub-therapeutic trough nevirapine levels, after increasing their nevirapine dose to 300 mg twice daily. Liver function was monitored.

Results:

The steady state pharmacokinetic parameters calculated based on plasma nevirapine concentrations alone and in combination with rifampicin are given in Table VI. Significant reductions in peak concentration (42%), trough concentration (53%) and exposure (46%) of nevirapine were observed when rifampicin was also administered ($p<0.01$). The trough concentration of nevirapine fell below the therapeutic range of 3.4 µg/ml in 8 out of 13 patients. An increase of nevirapine dose to 300 mg twice daily raised the trough concentration in all the 7 patients tested to above therapeutic levels and did not cross the toxic level of 12µg/ml. There were no clinical or laboratory adverse events.

Table VI : Steady state pharmacokinetics of nevirapine (n=13)

	Cmax µg/ml	Cmin µg/ml	AUC(0-12) µg/ml.hrs
Nevirapine	8.5 ± 2.7	5.5 ± 2.4	80.1 ± 30.3
Nevirapine + Rifampicin	4.9 ± 1.7	2.6 ± 1.4	43.2 ± 17.3
% Decrease	42	53	46

Cmax - peak concentration
Cmin - trough concentration
AUC - Area under time concentration curve
The above values are Mean ± SD

Conclusion:

Rifampicin significantly reduced the bioavailability of nevirapine, and the trough concentration to sub-therapeutic levels in a high proportion (62%) of patients. Prospective clinical trials are also required to determine the clinical implications of reduction in nevirapine blood concentrations and the optimal dose of nevirapine to be used in combination with rifampicin.

(Contact person: Dr. Geetha Ramachandran, e-mail: geethar@icmr.org.in)

Studies in progress

Absorption of nevirapine, lamivudine and stavudine (fixed dose combination) in patients with advanced HIV infection

Background:

The primary aim of antiretroviral treatment is to suppress viral replication. Despite treatment with potent antiretroviral drugs, therapeutic failure during HIV infection could occur due to several reasons. Adequate drug concentrations may not be reaching the virus due to reasons such as poor compliance to treatment, insufficient dosing, poor absorption or drug interactions. This could reduce efficacy and cause HIV resistance to antiretroviral agents. We have demonstrated a significant degree of malabsorption of anti-TB drugs in patients with advanced HIV infection. Information on absorption of generic antiretroviral drugs in HIV-infected patients in India and its relation to the degree of immunosuppression is lacking.

Aim:

To study the absorption of nevirapine, lamivudine and stavudine as a fixed dose combination in patients with varying degrees of immunosuppression, based on the blood concentrations of the drugs.

Methods:

The study participants comprise of HIV-infected patients undergoing regular antiretroviral treatment with nevirapine 200mg, lamivudine 150mg and stavudine 30/40mg twice daily for a minimum period of two weeks. They will be divided into three groups based on their CD4 lymphocyte counts, i.e. <100 cells, 100 to 200 cells and > 200 cells/mm^3. It has been planned to include 12 patients in each group. Steady state pharmacokinetics of nevirapine, lamivudine and stavudine will be determined in all the patients by estimating the drug concentrations in blood collected at different time points following drug administration.

(Contact person: Dr. Geetha Ramachandran, e-mail: geethar@icmr.org.in)

Nutritional assessment and supplementation in HIV-infected patients with and without tuberculosis

Background:

TB and HIV infection are known to be separately associated with malnutrition and TB might worsen the course of HIV associated immunosuppression and reduce survival among HIV-infected subjects. Despite the high prevalence of TB and malnutrition among HIV seropositive patients, data concerning the nutritional status of TB/HIV co-infected patients in developing countries like India are scarce.

Aims:

1. To document the occurrence of baseline macro and micronutrient deficiencies in HIV-

infected individuals in south India and correlate it with their immune status.

2. To test the efficacy of an intervention in the form of a nutritional supplement and to quantitate changes in nutritional, biochemical and immunological parameters over a period of one year.

Methods:

The study commenced in July 2003. The study population included (1) HIV-infected persons without TB and (2) HIV/TB patients who have completed anti-tuberculosis treatment. A baseline clinical, anthropometric and dietary assessment along with laboratory investigations (hematology, biochemistry and immunology) is done for all patients at the time of enrollment to the study. A high calorie, high protein supplement "Indiamix" supplied by the World Food Programme, New Delhi, is given to patients with the advice to consume 100gms per day which supplies an additional 400 Calories and 15 gms of protein. Patients are followed up clinically (including dietary assessment and anthropometric measurement) every 3 months and hematological, biochemical and immunological investigations are repeated every 6 months.

Results:

Five hundred and sixty six patients have been enrolled upto March 2005. This includes 422 asymptomatic HIV-infected individuals and 144 HIV+ve patients (42 females and 102 males) who have completed TB treatment. Two hundred and sixteen patients have completed 12 months of follow up. Ninety percent of our patients are from lower socio-economic strata. The mean age of patients in HIV-TB group was 31.5 $\pm$ 6 yrs and in HIV without TB group was 30 $\pm$ 7 yrs. Table VII shows the baseline anthropometry and laboratory parameters of the study population. Eighty seven HIV+ve patients have been enrolled as age, sex and socioeconomically matched controls. This group consisted of 48 females and 39 males with their mean age being 31.5 $\pm$ 7 yrs. These individuals were not given supplement for first 6 months. Ninety eight age, sex and socioeconomically matched individuals (53 females and 45 males) with mean age of 31 $\pm$ 8 yrs, from the community have also been enrolled as non-HIV controls. Table VIII shows the mean nutrient intake for patients in the different study groups.

Patients with HIV infection have lower body weight and Body Mass Index (BMI) than age, sex

Table VII : Baseline Anthropometric and Laboratory Parameters

S.No.	Variables	HIV+ves supplemented with 'Indiamix' (Mean ± S.D.)	
		Treated TB (n=144)	Without TB (n=422)
1)	Weight (kg)	48.0 ± 8.5	50.5 ± 9.9*
2)	BMI	18.7 ± 2.7	20.7 ± 3.6*
3)	Hemoglobin (gms%)	11.3 ± 2.2	11.9 ± 1.8*
4)	CD4 (cell/mm3)	243.3 ±173.8	355.7 ± 225.2*
5)	CD4 (%)	14.7 ± 9.7	18.3 ± 9.2*

* denotes P value <0.05

Table VIII : Mean nutrient intake based on dietary assessment

S.No.	Nutrients	HIV+ves supplemented with 'Indiamix' (Mean ± S.D.)	
		Treated TB (n=144)	Without TB (n=422)
1)	Calories (kcal)	2054.0 ± 665.7	2073.7 ± 664.6
2)	Carbohydrates	359.0 ± 122.3	352.0 ±_121.2
3)	Protein (gms)	67.0 ± 32.1	67.0 ± 32.1
4)	Fat (gms)	38.8 ± 30.9	44.0 ± 26.2

and socioeconomically matched controls. This cohort will be followed for one year to assess changes in anthropometric, immunological and hematological parameters after nutritional supplementation.

(Contact person: Dr. C. Padmapriyadarsini, e-mail: padmapriyadarsinic@icmr.org.in & Dr. Soumya Swaminathan, e-mail: soumyas@icmr.org.in)

Drug susceptibility testing of *M. tuberculosis* using nitrate reductase assay

Background:

Drug susceptibility testing for *M. tuberculosis* using conventional methods is time-consuming or expensive as is the newer BACTEC method. With the increasing prevalence of TB and MDR-TB in the HIV-infected and non-infected patients, the felt need of the hour is an alternative for the traditional susceptibility testing methods. A rapid and inexpensive method has been reported recently. The test is based on the ability of *M.tuberculosis* to reduce nitrate to nitrite, which is routinely used for the biochemical identification of mycobacteria. The reduction is detected by using specific reagents, which produce a colour change.

Aims:

1. To use Nitrate Reductase Assay (NRA) as a novel inexpensive and rapid method of drug susceptibility testing of first line drugs and ofloxacin.
2. To compare the method with BACTEC radiometric method and conventional Proportional Sensitivity Test (PST) method on Lowenstein-Jensen (LJ) medium.

Methods:

A panel of clinical isolates of *M. tuberculosis*, (25 susceptible and 75 drug-resistant) along with H37Rv will be tested. All strains were taken form the collection of strains available from all over India will be used. Strains will be sub-cultured and inoculated into various media, i.e. LJ with drugs (PST), LJ with potassium nitrate and drugs (NRA) and into the BACTEC 12 B medium for susceptibility testing. Appropriate controls will be used with all testing procedures.

Conventional Susceptibility Testing:

PST method standard LJ medium with antibiotics in critical concentrations will be used.

NRA Susceptibility Testing:

In this method the strains will be inoculated using the above method in LJ slopes containing

1000 µg/ml potassium nitrate and drugs in similar concentrations as in PST.

BACTEC Method:

The 12 B medium will be inoculated using the standard BACTEC radiometric method for drug susceptibility testing.

(Contact person: Ms. Nalini Sundar Mohan, e-mail: nalini@gawab.com & Dr. Ranjani Ramachandran, e-mail: ranjanir@icmr.org.in)

Bactericidal activity of PA 824, a nitroimidazopyran in various combinations with standard anti TB drugs against static culture of *M. tuberculosis*

Background:

PA 824, 5 nitroimidazole, a promising series of nitroimidazopyran, has been identified for the treatment of TB. This drug was found to show potent bactericidal activity against *M. tuberculosis* including MDR strains *in vitro* as well as in vivo in animal models (mice and guineapigs). It has comparable activity to isoniazid and isoniazid with combination of rifampicin, in the continuation phase of treatment tested in murine model. It was also shown that PA 824 (P) had activity under microaerophilic/anaerophic conditions thereby suggesting its potential sterilizing activity. This compound works by a novel mechanism inhibiting the protein and lipid synthesis. However, its activity in combination with other anti- TB drugs has not been fully evaluated, especially with potent sterilizing drug such as pyrazinamide. To study the activity of Z *in vitro*, it requires acidic medium as established earlier our laboratory.

Aim:

To study the bactericidal activity of PA 824 in various combinations with standard anti TB drugs against static culture of *M. tuberculosis.*

Method:

M. tuberculosis H37Rv is grown in Middlebrook 7H9 medium at a pH 5.9 for approximately 30 days as a static culture. Later, these cultures in turn will be exposed to the identified drugs, either alone or in combinations with other anti-TB drugs as follows.

1. No drug 2. P1 (3 µg/ml) 3. P2 (12.5 µg/ml) 4. H 5. R 6. Z 7. M 8. HR 9. HRZ 10. HRP1 11. HRZM 12. HRZP1 13. HRZMP1 14. RZM 15. RZMP1 16. RZMP2

M. tuberculosis H37Rv is grown to attain a non replicative phase 2 (NRP2) stage. The results will be interpreted based on the ability of reduction in colony forming unit (cfu) after exposure to the drug in combination with H, R and Z.

(Contact person: Ms. Sulochana Somasundaram, e-mail: sulochanasomu@yahoo.co.in& Dr.C.N. Paramasivan, e-mail: paramasivancn@icmr.org.in)

Studies completed

Role of Mannose binding Lectin (MBL) gene variants on immune functions in pulmonary tuberculosis

Background:

Mannose binding lectin is a calcium dependent serum lectin (protein) secreted by the liver. MBL binds mannose and N-acetyl glucosamine terminated glycoproteins of the pathogens and augments macrophage phagocytosis and plays an important role in innate immune functions against pathogens. Variant MBL genotypes have been shown to be associated with altered MBL level. Our earlier studies revealed the association of functional mutant homozygotes of MBL with susceptibility to TB.

Aim:

To assess the regulatory role of variant MBL genotypes on MBL level and immune functions.

Methods:

The study was carried out in 58 normal healthy subjects (NHS) and 48 pulmonary TB (PTB) patients. MBL genotyping was carried out by DNA based polymerase chain reaction (PCR) and dot-blotting technique. Macrophage phagocytosis with live *M. tuberculosis*, spontaneous and *M. tuberculosis* culture filtrate antigen (CFA) induced lymphoproliferative response, were studied.

Results

The study revealed a significant increase of MBL level in pulmonary TB patients than normal healthy subjects (p=0.008). A similar trend in MBL level was also observed irrespective of the MBL genotypes studied. However, the MBL genotype AA (MBL-52, 54 & 57 wild homozygotes), is associated with high level of MBL than AO (MBL-52, 54 & 57 heterozygotes) and OO genotype (MBL- 52, 54 & 57 functional mutant homozygotes). OO genotype is associated with very low level of MBL production in normal subjects and pulmonary TB patients.

(AA vs AO : NHS : $p = 2.46 \times 10^{-6}$, PTB : $p = 1.23 \times 10^{-5}$; AA vs OO : NHS : $p = 3.3 \times 10^{-9}$, PTB : $p = 3.11 \times 10^{-9;}$ AO vs OO : NHS : p = 0.00059, PTB : p = 0.0013) (Fig. 3)

The percentage phagocytosis of live *M. tuberculosis* by peripheral blood monocyte derived macrophage was significantly decreased in pulmonary TB patients as compared to normal subjects (p=0.005). Normal subjects with AA genotype showed a significantly lower phagocytosis than normals with AO (heterozygote) genotype (p=0.046). In pulmonary TB patients, no difference in phagocytosis was observed among different genotypes (Fig. 4). The spontaneous and CFA induced lymphoproliferative responses were not influenced by the variant MBL genotypes.

Conclusion

The present study suggests that pulmonary TB patients have higher level of MBL with decreased macrophage phagocytosis with live *M. tuberculosis* and an opposite effect in normals. Pulmonary TB patients and normal subjects with functional mutant homozygotes (OO genotype) showed very low MBL level.

(Contact person: Dr. P. Selvaraj, e-mail: selvarajp@icmr.org.in)

Fig. 3. Serum MBL level in NHS and PTB patients with variant MBL genotypes

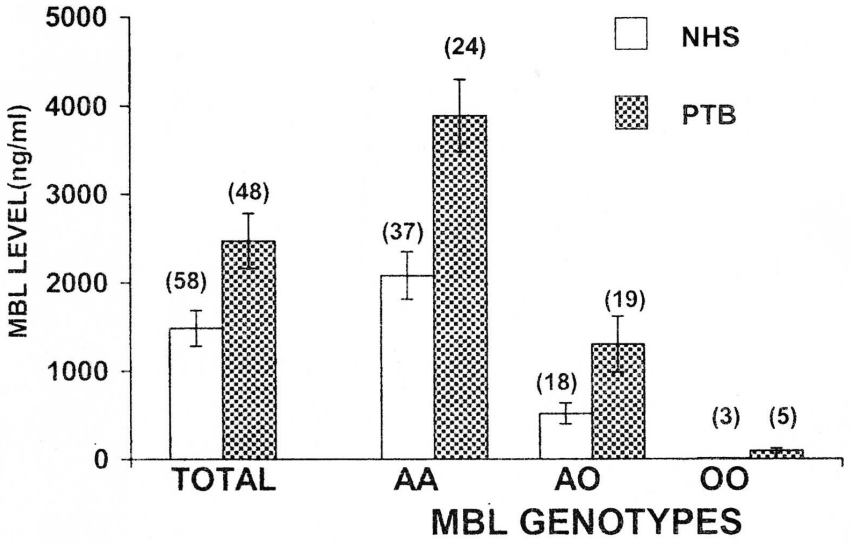
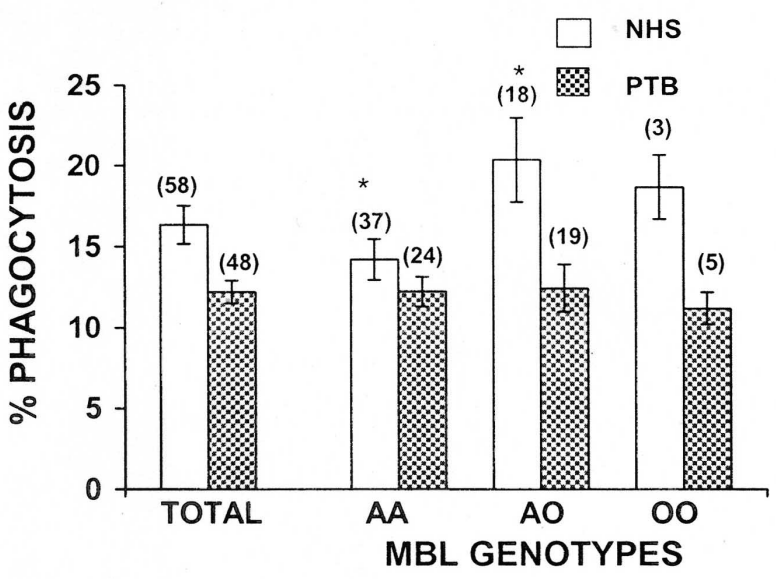


Fig. 4. Percentage phagocytosis in NHS PTB patients with variant MBL genotypes



Construction of recombinant BCG (rBCG) based HIV-1 epitope delivery system

Background:

AIDS is a global emergency. Reverse vaccinology is a fast emerging field which involves the identification of putative epitopes directly from the genomic sequences of the pathogens by *in silico* analysis. The lacunae in this novel approach is the lack of suitable "epitope-delivery vehicles" since the epitopes by themselves are poorly immunogenic. In this respect grafting an epitope from an immune unfriendly environment to an immune friendly environment enhances the immunogenicity of the epitopes and this forms the basic of 'epitope grafting'.

Aim:

In the present project an 'epitope-trap vector' was constructed using *M.tuberculosis* chaperonin-10 (Cpn10) antigen as a carrier. Using this vector the HIV-1 PND epitope was expressed in rBCG. The immunogenicity of the rBCG vaccine was tested in a murine model.

Methods:

The three-dimensional structure of the Cpn-10 antigen was analyzed using INSIGHT II software and an extended loop region was identified for grafting the foreign epitope. Using this information two versions of the Cpn10-PND chimeric antigen were constructed and expressed in *M. smegmatis*:

1. The replacement chimera where the PND epitope replaces the Cpn10 loop and
2. The insertion chimera where the PND epitope is inserted into the Cpn10 loop

Based on the expression profile, p306CRC (Cpn10-PND replacement chimera in an episomal vector with homologous promoter) was electroporated into BCG Pasteur. Sub-cellular localization studies showed the presence of the chimeric antigen in the cell wall, cytosol and culture filtrate but not in the cell membrane (Fig. 5). The immunogenicity of the recombinant BCG was evaluated in a murine model.

Results:

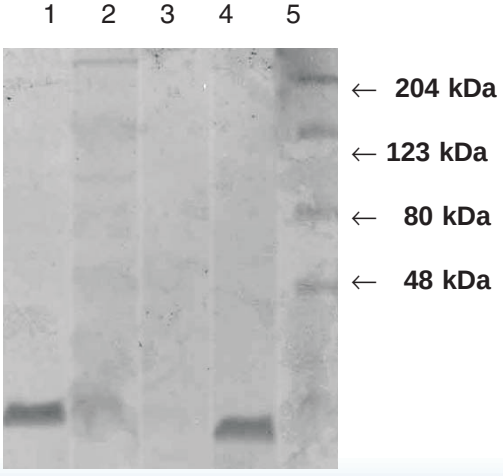
Vaccination with rBCG induced both cellular and humoral immune responses as measured by lymphocyte proliferation, delayed-type hypersensitivity (DTH) reaction and antibody production against the PND epitope (Fig 6). Isotype profiling of the serum anti-PND antibodies showed that all them were of IgG isotype with no IgA and IgM. Sub-isotype profiling showed the predominance of IgG2a and IgG2b sub-types indicating mixed response. The serum antibodies apart from recognizing the chimeric antigen also recognized other immunodominant antigens present in the culture supernatant of the rBCG.

Conclusion:

rBCG based epitope delivery systems was constructed and found to offer novel avenues in the field of reverse vaccinology.

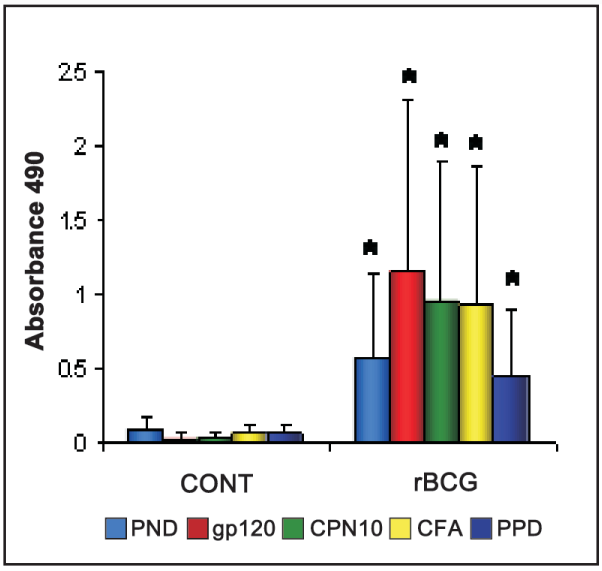
(Contact person: Mr.C.V. Aravindhan, e.mail: cvaravindhan@yahoo.co.uk)

Fig.5. Sub-cellular localization of Cpn10-PND chimeric antigen in rBCG



Lanes: 1-culture filtrate, 2-cell wall, 3-cell membrane, 4-cytosol and 5-Broad range marker.

Fig. 6. Humoral response induced by rBCG



Immune activation markers and their role in monitoring the course of HIV and tuberculosis

Background:

The association of HIV infection and TB is complex and bi-directional. Both HIV and TB via their actions on cell medicated immune responses, produce immune activation. We attempted to identify whether immune activation markers (neopterin, beta2-microglobulin, sTNFRI and sTNFRII) from serum samples obtained from clinically defined groups of patients could show relatively independent associations with TB or HIV disease in dually infected patients.

Methods:

The study population comprised of 42 HIV positive patients with active pulmonary tuberculosis (HIV+TB+), 37 HIV infected patients without tuberculosis (HIV+TB-), 38 HIV negative patients with pulmonary tuberculosis (HIV-TB+) and 62 healthy volunteers (HIV-TB-).

Concentration of immune markers in plasma stored at –80°C were measured using commercially available capture ELISA kits, the immune markers were beta-2 microglubulin, neopterin, sTNF-R I and sTNF-R II.

Total and differential white blood cell counts were determined for all study subjects using the automated hematology analyzer. Percentage and absolute number of CD3, CD4 and CD8 T lymphocytes were measured by dual colour flow cytometry on a FACSort Flow Cytometer using the Cell Quest software.

Results:

The mean CD4% of the HIV+TB+ group was 10.3 $\pm$ 0.8% while the HIV+TB- group was 16.7 $\pm$ 1.3%. Table IX shows the level of the four activation markers, at baseline. Levels of activation markers TNF-RI, TNF-RII, beta-2 microglobulin and serum neopterin were elevated in all the patient groups except in the HIV+TB- group with less advanced disease (CD4 cell counts > 200 cells/mm^3). There was a significant negative correlation between the CD4 count and the level of all the four immune activation markers. Table X shows the levels of immune activation markers before and at the completion of anti-TB treatment. Significant reduction of sTNF-RI and neopterin levels was seen in the HIV+TB+ group with advanced disease as well as in the TB group. The level of beta-2 microglobulin decreased significantly only in the HIV+TB+ group with advanced disease.

sTNF-R II levels did not show any significant changes after completion of anti-TB treatment in any of the patient groups studied.

Conclusion:

Although co-infection with TB and HIV produced a broad activation of the immune system, we have not been able to establish a definitive and independent marker for HIV and TB. None of the four markers studied was specific for disease progression of HIV and TB separately.

(Contact person : Dr. Sudha Subramanyam, e.mail: sudhas@icmr.org.in)

Studies in Progress:

Immune response in tuberculous pleuritis: Differential T-helper cell response in tuberculous pleuritis by intracellular cytokine studies

Background:

Among the many clinical manifestations of TB, tuberculous pleuritis (TP) is of particular interest, as it offers protective immune response. In our earlier studies with pleural fluid mononuclear cells (PFMC), both Th1 and Th2 types of cytokines could be measured, in response

Table IX : Concentration of plasma immune activation markers in the study population at baseline

	HIV+TB+		HIV+TB-		HIV-TB+	HIV-TB-
	CD4 <200 (N =24)	CD4 >200 (N= 18)	CD4 <200 (N= 17)	CD4>200 (N= 20)	(N = 38)	(N =62)
sTNFR-1	4.2 ± 0.6 *	3.4 ± 0.5 *	1.6 ± 0.4 *	0.6 ± 0.1	3.6 ± 0.5 *	0.4 ± 0.1
sTNFR-2	0.6 ± 0.1 *	0.5 ± 0.1 *	0.6 ± 0.1 *	0.4 ± 0 *	0.5 ± 0 *	0.2 ± 0
Neopterin	24.4 ± 5.9 *	12.5 + 2.7 *	14.9 ± 2.8 *	4.8 ± 2.1	13.8 ± 3.5 *	3.9 + 0.6
Beta-2 microglubulin	5241.3+ 1100.8 *	4642.8± 809.4 *	3664.1 ± 584.5	3393.6 ± 501.3	5979.2+ 1892. 9 *	1986.6+125.6

* $p \leq 0.05$ against control (HIV-TB-group)

Table X : Concentration of plasma immune activation markers in TB patients with or without HIV infection before start and after completion of ATT

	HIV+TB+				HIV-TB+	
	CD4 < 200 (N =24)		CD4 > 200 (N= 18)		(N = 8)	
	0	6	0	6	0	6
sTNFR-1	4.2 ± 0.6 *	2.2 ± 0.3	3.4 ± 0.5	2.7 ± 0.4	3.5 ± 0.4 *	2.0 ± 0.3
sTNFR-2	0.6 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0	0.2 ± 0.0	0.4 ± 0.1
neopterin	24.4 ± 5.9 *	15.0 ± 5.9	12.5 ± 2.7	13.7 ± 4.4	not assayed	not assayed
beta-2 M	5241.3 ± 1100.8 *	3699.6 ± 291.9	4642.8 ± 809.4	4775.6 ± 76.5	6330.3 ± 1467.9	6461.8 ± 835.9

to *M. tuberculosis* antigens. In order to study the source of the Th1 and Th2 cytokines in pleural fluid, CD4+ T cells were purified. E*x vivo* intracellular cytokine staining by flow cytometry was performed for interferon gamma (IFN-γ) and interleukin 4 (IL-4).

Aim:

To analyze the differential cytokine response in purified PFMC CD4+ T cells, by *ex vivo* and *in vitro* intracellular cytokine staining for IFN-γ and IL-4.

Methods:

The intracellular cytokine experiments were done in five TB pleuritis patients. The CD4+T cells were isolated from fresh peripheral blood mononuclear cells (PBMC) and PFMC and also from PFMC cultured with mycobacterial antigens [purified protein derivative (PPD), culture filtrate antigen (CFA), heat killed *M. tuberculosis* (MTB)]. The CD4+ T cells were positively selected using anti CD4 antibodies conjugated magnetic microbeads by MACS. Intracellular cytokine staining was done by fixing with paraformaldehyde and permeabilising the cells with 0.2% saponin. Fixed cells were stained with anti-human IFN-γ- FITC and anti-human IL-4 PE and analysed by FACS.

Results:

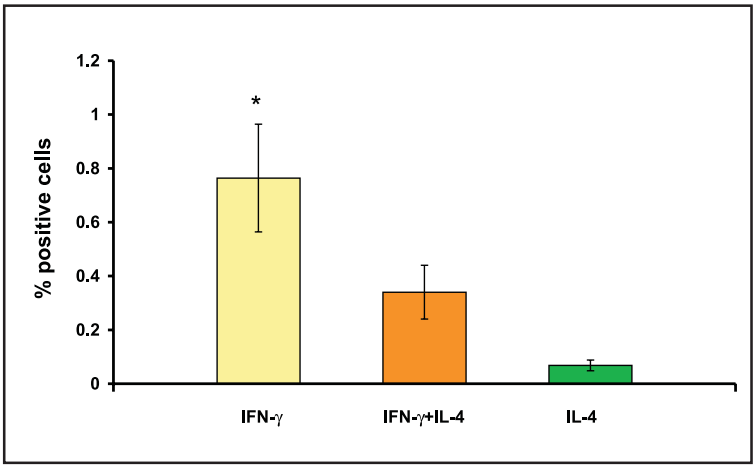
The *ex vivo* results on CD4+ T cells showed that there were cells producing IFN-γ alone, IL-4 alone or both. The percentage of IFN-γ producing cells were higher than the cells that secrete both IFN-γ and IL-4, and IL-4 alone (Fig. 7). Thus the pleural fluid T-helper cell response was predominantly of Th1 type. In contrast, *in vitro* stimulation of pleural fluid CD4+ T cells, with PPD, CF and heat killed MTB antigens, resulted in antigen specific increase in cells secreting IFN-γ alone and IL-4 alone. The double positive cells were also higher in all cultured conditions, more so for PPD indicating that the response was predominantly of Th0 type (Fig. 8).

Conclusion:

There is a differential T-helper cell response in TP suggestive of Th1 *ex vivo* and Th0/mixed response *in vitro*. This confirms our previous observation of differential cytokine profiles in TP.

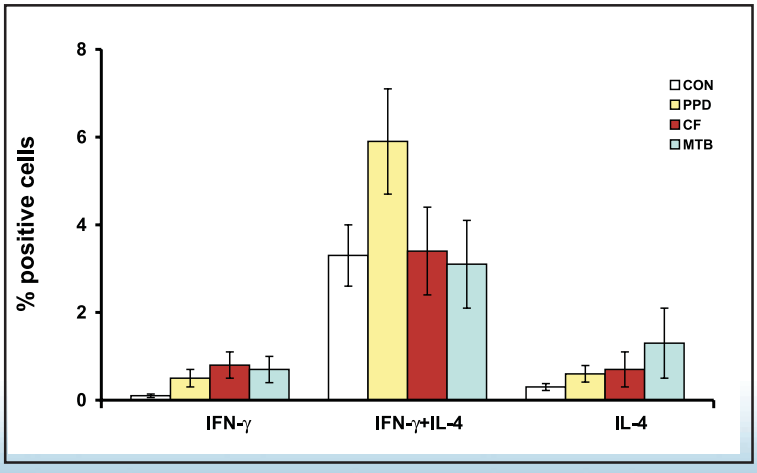
(Contact person : Ms.C. Prabha, e-mail: prabhapuffs@rediffmail.com & Dr. Sulochana D Das, e-mail: sulochanad@icmr.org.in)

Fig. 7. *Ex vivo* levels of intracellular cytokine in PFMC



*** P<0.05 compared to other two groups**

Fig. 8. *In vitro* levels of intracellular cytokine in PFMC



Molecular and immunological characterization of *M. tuberculosis* strains with single copy of IS6110: Th2 type of immune response observed in normal healthy individuals to S7 sonicate antigen

Background:

Different *M. tuberculosis* strains operate different immune evasion strategies for their survival in the host. This mainly depends on the virulence of the strain and the host immune responses. The most virulent strains are those actively involved in the transmission, are widely spread in the community and induce differential immune responses. The immune response was evaluated for sonicate antigen prepared from one such predominant strain (S7) of *M. tuberculosis* harboring single copy of IS6110 and actively involved in transmission.

Aim:

To evaluate the efficacy of the antigen S7 in modulating the immune response *in vitro* towards protection or otherwise in normal healthy PPD positive subjects.

Methods:

T-cell proliferative response to PPD, H37Rv and S7 antigens was studied. The cytokines IFN-γ, TNF-α, IL-12 and IL-4 in the culture supernatants and total IgG and IgA levels in the plasma of normal individuals were measured by ELISA.

Results:

Significant lymphoproliferative response and higher IFN-γ levels against PPD and H37Rv antigens were observed in PPD skin test positive normal individuals. The antigen S7 showed marginal T-cell proliferation, but did not induce IFN-γ secretion. Conversely, it induced significantly higher levels of IL-4 in normal subjects. The macrophage cytokines IL-12 and TNF-α did not show S7 antigen specific stimulation (Figs. 9 & 10). The intracellular cytokine assay further confirmed the increase in IL-4+/CD4+ T-cells and decrease in IFN-γ+/CD4+ T-cells after stimulation. The antibody response showed increase in IgG and IgA levels against this antigen in normal individuals.

Conclusion:

These observations suggest that antigen S7 modulates the *in vitro* immune response towards Th2 type by suppressing Th1 protective immune response in PPD skin test positive normal subjects. This leads to the speculation that some components of this sonicate antigen are associated with immunosuppressive response.

(Contact person : Ms.R. Priya, e.mail: pribya@yahoo.com & Dr. Sulochana D Das, e-mail: sulochanad@icmr.org.in)

Fig. 9. *In vitro* cytokine levels induced by MTB antigens in healthy PPD positive individuals

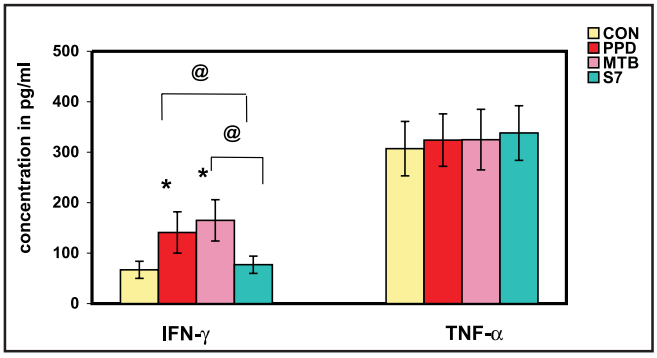
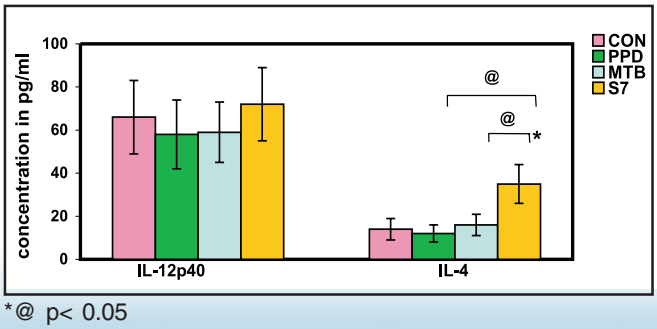


Fig. 10. *In vitro* cytokine levels induced by MTB antigens in healthy PPD positive individuals



*@ p< 0.05

Inflammatory response and apoptosis of polymorphonuclear neutrophils by prevalent strains of *M. tuberculosis*

Background:

Macrophages and polymorphonuclear neutrophils (PMN) are the professional phagocytes involved in antibacterial defense. The PMN influx, the first line of defense, occurs as the early response to curtail the mycobacterial infection. Chemokines stimulate the migration of PMN from circulation to the site of infection. *M. tuberculosis* induced activation leads to proinflammatory response and apoptosis of PMN.

Aim:

Two prevalent strains of *M. tuberculosis* (S7 and S10) showing differential immune response in PPD skin test positive subjects were selected for this study. The aim was to study the efficacy of these strains to induce apoptosis and modulate the expression of surface molecules and cytokine secretion in PMN of TB patients.

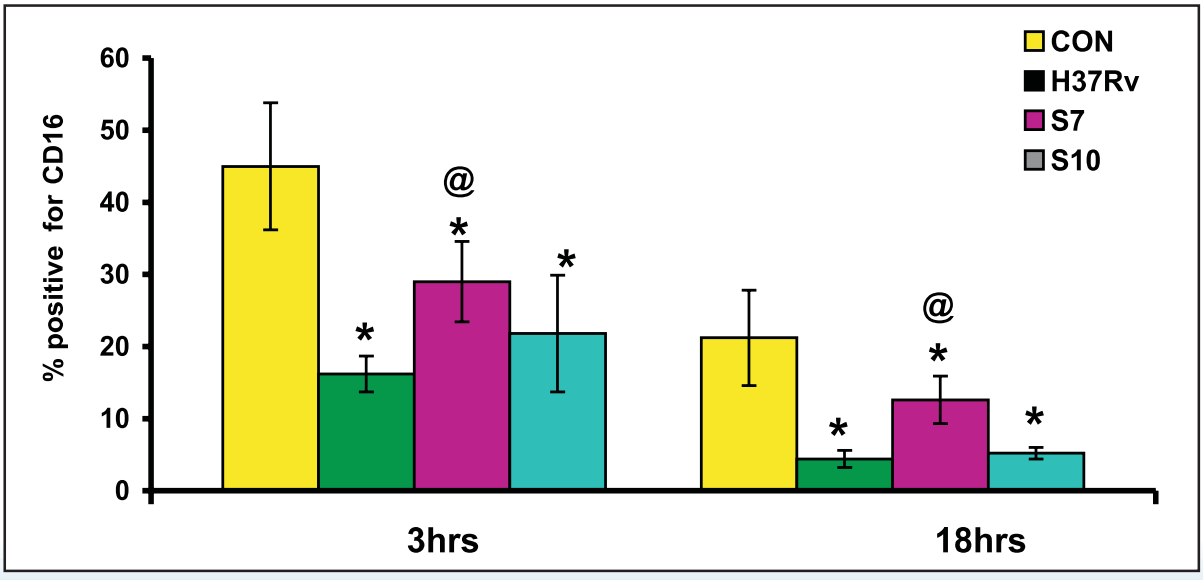
Methods:

PMN were isolated from red blood cell (RBC) pellet obtained from Ficoll-Hypaque gradient centrifugation and further subjected to sedimentation in 3% Dextran. PMN were infected with various mycobacterial strains (S7, S10, and H37Rv) at multiplicity of infection (MOI) of 3:1 and incubated for 3 and 18 hrs. The phagocytic index, percentage of apoptotic neutrophils (Annexin V positive), cell phenotypes (CD16 and CD69 by FACS) and cytokines (TNF-α and IL-1β by ELISA) were assessed.

Results:

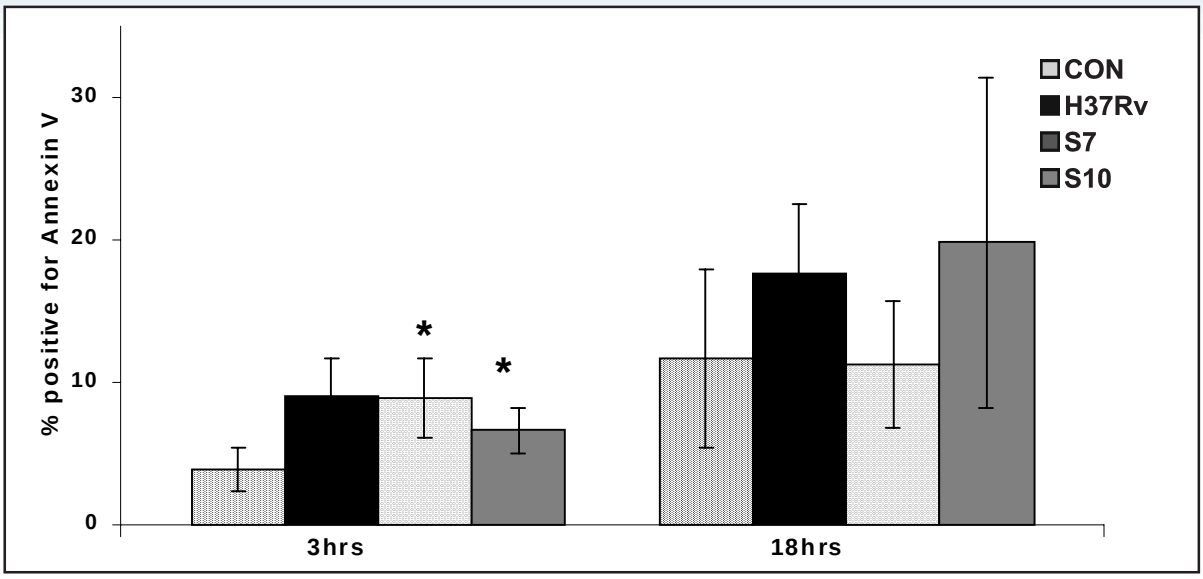
A significant increase in Annexin V positive cells with corresponding decrease in CD16 and CD69 expression was observed with S7 and S10 strains when compared to uninfected control after 3 hrs of infection. Further decrease in CD16 expression was observed at 18 hrs but no significant change in Annexin V positivity. When compared to H37Rv, S7 showed high CD16 expression at both the time points, but high CD69

Fig. 11. CD16 expression in TB-PMN after infection



. p < 0.05, compared to control
@ p <0.05, compared to H37Rv

Fig. 12. Differential induction of apoptosis in TB-PMN



* p < 0.05, compared to control
@ p <0.05, compared to H37Rv

expression only at 3hrs (Fig. 11 &12). There was no significant change in TNF-α production by the infected PMN at both the time points. Only S7, showed a significant increase in IL-1β at 18 hrs when compared with control.

Conclusion:

All *M. tuberculosis* strains showed apoptosis of TB-PMN in a pro-inflammatory cytokines dependent manner. Clinical strains down-regulated CD16 expression and inhibited *de novo* synthesis of an early activation marker, CD69 on TB-PMN. These strains also showed a significant increase in apoptosis after infection thereby reducing the number of phagocytes and escaping from the intracellular lytic microenvironment. Thus clinical isolates were able to inhibit the early activation of neutrophils and thin out the killing mechanisms for their own survival.

(Contact person : Ms.P. Supriya, e.mail: supriya_pokkali@gmail.com & Dr. Sulochana D Das, e-mail: sulochanad@icmr.org.in)

Identification of immunoreactive T-cell antigens of *M. tuberculosis* through proteomic techniques

Background:

Even though effective chemotherapy is available for treatment of TB, there are practical difficulties in ensuring the desired high cure rate, due to many factors. Immuno-prophylactic measures using vaccines is an alternative approach for control.

A limited number of attempts to screen human responses to separated antigens have demonstrated that there are still numerous uncharacterized antigens of various molecular masses to be evaluated. Moreover, a systematic approach to test the antigens purified by two-dimensional (2-D) preparative separations, in human subjects has not been attempted so far.

Aims:

The major aim of the proposed project is to identify a set of immunologically relevant T-cell

antigens and evaluate the response to these antigens in patients with TB and controls.

The main objectives are:

1. To carry out preparative 2-D electrophoresis and purify antigens of *M. tuberculosis*
2. To identify the immunologically relevant T cell antigens by comparing the *in vitro* proliferative response and cytokine (IFN-γ) response in tuberculous and control subjects.
3. To characterize the identified antigens using proteomics approaches.

Methods:

The study subjects are as follows:

1. Apparently healthy household contacts (HHC) from families where there is at least one case of sputum positive pulmonary TB living in the same household. TB will be ruled out in this group during the time of blood collection and hence considered "Protected".
2. Newly diagnosed adult pulmonary tuberculosis cases in the age group of 16-50 yrs. They form the "susceptible" group.

The methods to be followed are as follows:

1. 2-D Preparatory separation of antigenic fractions
2. Proliferative response and IFN-γ response will be studied using purified antigenic fractions.

Results:

The Culture Filtrate Antigen (CFA) has been subjected to First dimension Preparatory Isoelectric Focusing (IEF) in fluid phase and Second dimension Preparatory SDS-PAGE and Whole Gel Elution (WGE), for the preparation of antigenic fractions

Figure 13 shows the Sodium dodecyl sulphate – polyacrylamide gel electrophoresis (SDS-PAGE) pattern of one of the 20 fractions separated by IEF. The number of bands (1-D) seen in each fraction ranged from 10 to 20. The number of spots (2-D) seen in each fraction ranged from 20 to 260. The pI of the 20 fractions ranged from 3.0 to 12.5.

Each of the 20 IEF fractions were again separated by WGE into 30 fractions. A representative picture (Fig. 14) of one of the fractions is shown.

Since a large number of fraction will have to be tested in each blood sample, we have standardized a whole blood (1:10 dilution) assay, for proliferation and IFN-γ secretion.

(Contact person: Mr.D. Anbarasu, e-mail: harianbu@rediffmail.com & Dr. Alamelu Raja, e.mail: alamelur@icmr.org.in)

Fig. 13. Analysis of IEF fractions of CFA by 1D and 2D SDS-PAGE

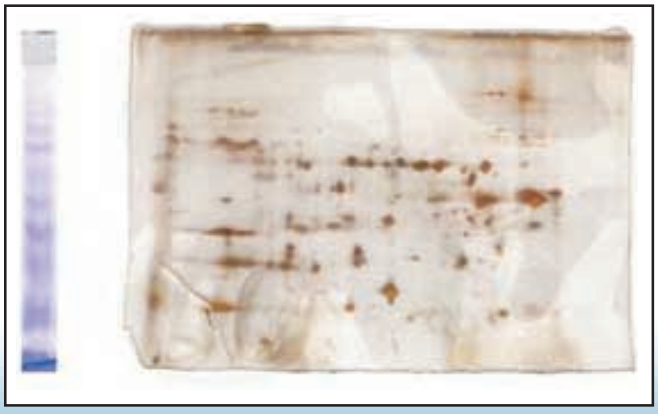
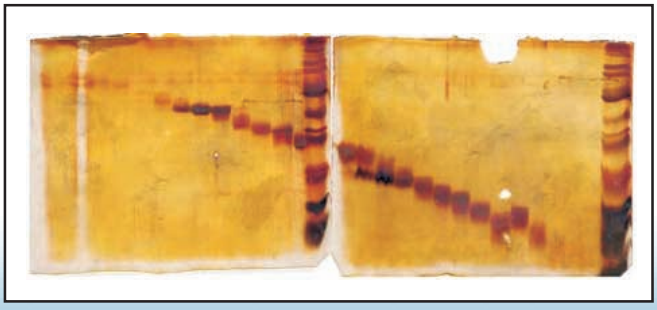


Fig. 14. Analysis of Whole Gel eluted IEF fraction by 1-D SDS-PAGE



Role of HLA-DR2 on immune functions in pulmonary tuberculosis

Background:

Earlier studies revealed the association of HLA-DR2 with susceptibility to pulmonary TB. In continuation, the present study has been planned.

Aim:

To understand the role of HLA-DR2 on the immune mechanism of TB susceptibility.

Methods:

The study will be carried out in 60 pulmonary TB patients and 60 normal healthy volunteers. DNA typing of HLA-DR, enumertion of perforin positive cells by flow cytometry, macrophage phagocytosis, *M. tuberculosis* antigen induced lymphoproliferation and cytokine production will be studied.

The above immune functions were carried out in 40 normal subjects and 40 pulmonary TB patients.

(Contact person : Dr.P. Selvaraj, e-mail: selvarajp@icmr.org.in)

Human Leucocyte Antigen (HLA) and non-HLA gene polymorphism studies in HIV and HIV-TB patients

Background:

In developing nations, HIV-1 infection has increased the burden of TB, especially in populations where the prevalence of TB infection is high among young adults. The importance of host genetic factors (HLA and non-HLA) on susceptibility or resistance and the variability of disease progression to HIV-1 infection has been emphasized by many studies.

Aim:

To find out whether HLA genes, HLA haplotypes and non-HLA genes are associated with the susceptibility or resistance to HIV and HIV-TB.

Methods:

The study will be carried out in HIV negative TB negative (HIV-TB-) (n=150), HIV negative TB positive (HIV-TB+) (n=150), HIV positive TB negative (HIV+TB-) (n-150) and HIV positive TB positive (HIV+TB+) (n=150) groups. HLA-A and B antigen will be serologically determined. HLA-DR and –DQ and various non-HLA gene polymorphism will be studied by PCR based DNA typing.

During the period, HLA-A, B, -DR and –DQ gene polymorphisms were studied in 50 HIV-TB+ patients and 50 HIV+TB- / HIV+TB+patients.

(Contact person: Dr. P. Selvaraj, e-mail: selvarajp@icmr.org.in)

Regulatory role of variant genotypes of vitamin D receptor and cytokine genes on cytokine response in pulmonary tuberculosis

Background

Our earlier studies revealed the regulatory role of vitamin D receptor (VDR) gene variants on vitamin D_3 modulated macrophage phagocytosis and lymphoproliferative responses.

Aim

To understand the regulatory role of VDR gene and cytokine gene variants on Th1 and Th2 type of cytokines in pulmonary TB.

Methods

The study will be carried out in 100 pulmonary TB patients and 100 normal healthy

volunteers. DNA typing of VDR gene and cytokine gene variants will be done using PCR-RFLP and dot-blotting techniques. Vitamin D_3 modulated antigen induced cytokines and granzyme positive cells will be studied.

During the year, 10 normal subjects and 10 pulmonary TB patients have been studied.

(Contact person: Dr. P. Selvaraj, e-mail: selvarajp@icmr.org.in)

Purification and characterization of a serine/threonine protein kinase-PknE of *M. tuberculosis* H37Rv

Background:

Serine/threonine protein kinases form important components of signal transduction elements along with the two-component systems in mycobacteria. They are "eukaryotic like", control important physiological processes in the cell and are involved in various aspects involving stress responses, development and pathogenicity. The biochemical characterization of these kinases would aid in better understanding of the ions required for autophosphorylation, kinase inhibition, substrate phosphorylation and cross reactivity with eukaryotic antibodies.

Aim:

To clone, express, purify and characterize the PknE protein of *M. tuberculosis* H37Rv.

Methods:

E.coli DH5α, GJ1158 and BL21 (DE3) were the strains that were used in the study. The *pkn*E gene was PCR amplified and cloned into pRSETb (full length gene) and into pGEX-5X3 (kinase domain). The recombinant proteins were purified using Nickel ion affinity chromatography and Glutathione affinity chromatography respectively. *In vitro* phosphorylation assays were carried out using γ-P32 labelled ATP and various divalent cations (Fig.15). Phosphoamino acid analysis and substrate phosphorylation were assessed using anti-phosphoserine and anti-phosphothreonine antibodies. Kinase inhibitors were used to generate the inhibition profile for the recombinant proteins. Antibodies against eukaryotic kinases were used to determine cross-reactivity with the purified protein (Fig. 16).

Results:

Recombinant proteins were expressed and purified either with a 6X histidine tag (full length enzyme) or a Glutathione-S-Transferase tag (kinase domain alone) and were found to correspond to a molecular weight of ~67kDa and ~68kDa respectively. PknE was found to be a magnesium or a manganese requiring enzyme. The purified proteins were found to autophosphorylate at serine and threonine residues and also phosphorylated the exogenous substrate, rabbit muscle enolase. They were capable of being inhibited by staurosporine and H7. The recombinant PknE protein cross-reacted with SAPK/JNK and phospho-SAPK/JNK antibody. Thus one of the eleven serine threonine protein kinases, PknE was cloned, expressed, purified and characterized biochemically. The purified protein showed a phosphorylation profile and kinase inhibition profile similar to the kinases of other bacteria.

(Contact person : Mr. Deepak Jayakumar, e-mail: deepakjayakumar@gmail.com & Dr. Sujatha Narayanan, e-mail: sujathan@icmr.org.in)

Fig. 15. *In vitro* autophosphorylation assays for the recombinant PknE proteins

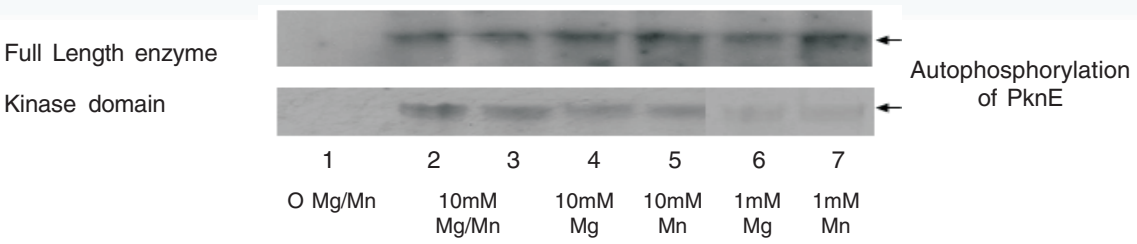
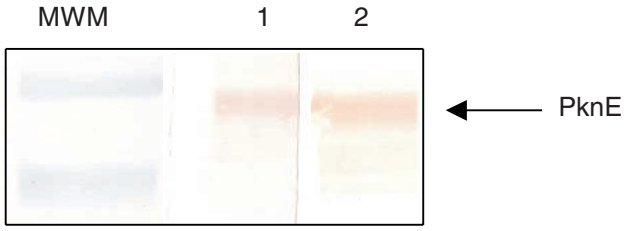


Fig. 16. Cross reactivity with eukaryotic protein kinase antibodies



1.Anti-SAPK/JNK antibody
2.Anti-Phospho SAPK/JNK antibody

Characterization of *cis* and *trans* acting factors regulating *M. smegmatis* acetamidase operon

Background:

Acetamidase was the first highly inducible gene found in *M. smegmatis*. The gene is part of an operon which has four open reading frames apart from the acetamidase gene and it has a complex regulation. By PCR mediated deletion mutagenesis we have identified several *cis* acting elements involved in the regulation of this operon. Specific binding of proteins to these upstream regulatory regions was observed in mobility shift assays. Further cold chase mobility shift experiments have been carried out to further confirm the specificity of binding.

Aim:

To identify the *trans*-acting factors that bind to these upstream *cis*-acting elements which controls acetamidase regulation.

Methods:

Whole cell lysate was obtained by bead beating. Ammonium sulfate fractionation was carried out using standard protocol Mobility Shift assay was carried out using the various fractions and the radiolabelled probes.

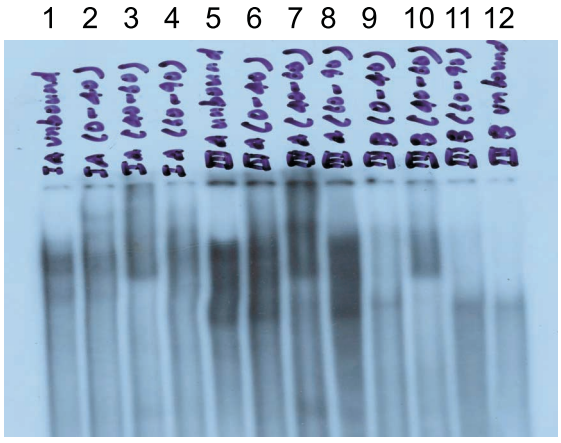
Results:

The fraction obtained between 40% and 60% was found to contain DNA binding activity based on mobility shift assays (Fig. 17). Figure 18 shows

the whole cell lysate fractionated by ammonium sulfate precipitation. An affinity chromatographic approach is being used to purify and characterize these DNA binding factors. As an alternate approach cloning of the four upstream open reading frames is also being carried out to find out whether these proteins are involved in regulation of acetamidase induction.

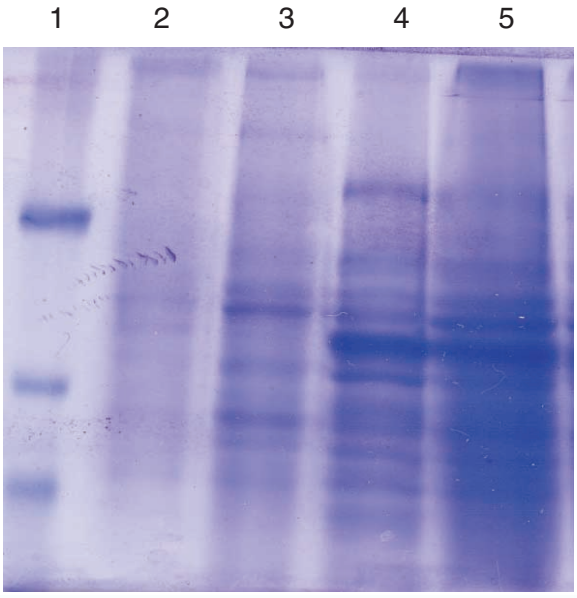
(Contact person : Mr.S. Dhinakaran, e-mail: dinakar_80@yahoo.co.in & Dr. Sujatha Narayanan, e-mail: sujathan@icmr.org.in)

Fig. 17. Mobility shift assay of ammonium sulfate fractions



Lanes 7 and 10 corresponding to ammonium sulfate fractions 40-60% showing shift in mobility.

Fig. 18. SDS-PAGE of fractions



Lane 1: Low Range marker

Lane 2: Fraction 0-40%

Lane 3: Fraction 40-60%

Lane 4: Fraction 60-90%

Lane 5: Whole Cell Lysate

Characterization of possible targets of Serine/ Threonine protein kinases of *M.tuberculosis*

Background:

Serine/ Threonine Protein Kinases (STPKs) are a novel class of mycobacterial proteins found to be involved in the signal transduction machinery in addition to the two component systems (TCS).These STPKs are being explored for the development of new drug targets and they have also been implicated in virulence and persistence of the pathogen. Two STPKs-PknI and PknE are being characterized in the laboratory.

Aim:

To identify the targets of the STPK-PknI.

Methods:

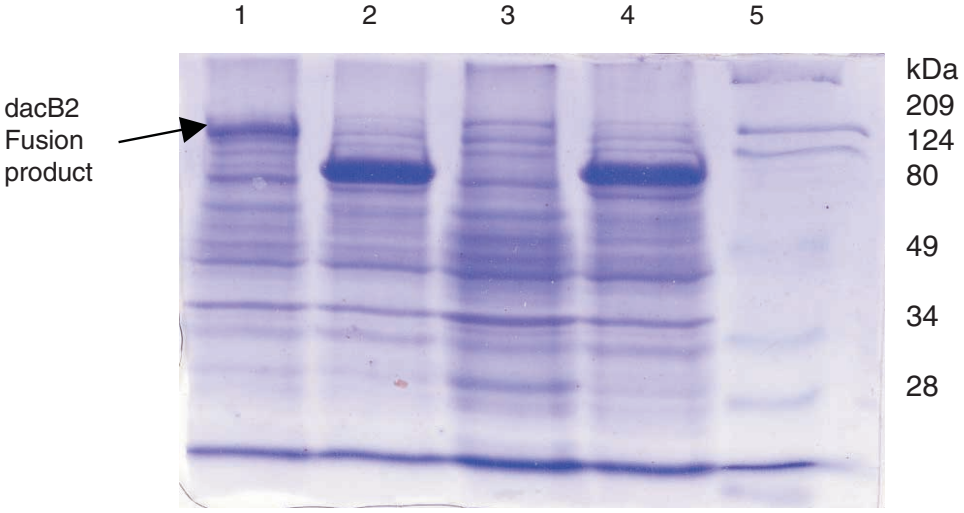
E.coli DH5α and BL21 (DE3) were the strains that were used in the study. Primers were designed using the genome sequence of *M. tuberculosis* H_{37}Rv for the three genes *dac*B2, *fts*Y and *ffh* (probable targets of *pkn*I).

Results:

PCR amplification was done for *dac*B2, *fts*Y and *ffh*. The three PCR products were cloned in a TA vector. Sub-cloning of *dac*B2 in an expression vector pET43.1a was done (Fig. 19). DNA sequencing of the cloned insert was carried out. Expression studies were performed following standard protocols. Purification of the recombinant protein is in progress.

(Contact person : Dr.T. Lakshmi Prasanth, e-mail: lptrc@yahoo.co.in & Dr. Sujatha Narayanan, e-mail: sujathan@icmr.org.in)

Fig. 19. SDS PAGE profile showing expression of dacB2



The role of complement activation and antibody in the early interaction between *M. tuberculosis* and macrophages

Background:

The complement system, which represents a chief component of innate immunity not only participates in inflammation but also act to enhance adaptive immune response. The initial interaction between host macrophage and *M. tuberculosis* is an important first step in the pathogenesis of tuberculosis and is mediated by specific macrophage receptors and ligands present on the surface of *M. tuberculosis*. The survival and replication of *M. tuberculosis* within the host macrophage are documented features of the pathogenesis of tuberculosis. However the means by which *M. tuberculosis* evades being killed by macrophages remain unclear. The phagocytosis, immune regulation, cytokine production, and effectors mechanism may all contribute innate immune responses. In the present study investigate that the antibody could modulate complement activation and determine the interaction of *M. tuberculosis* with the macrophage.

Aim:

To study whether antibodies could modulate complement activation and determine the interaction of *M. tuberculosis* with the macrophages.

Methods:

1. *M. tuberculosis* treated with complement (classical or alternative pathway) in the presence and absence of IgM or IgG antibodies against *M. tuberculosis.*
2. Investigate the receptor mediated route of entry of *M. tuberculosis* with in the macrophages.
3. Human macrophage will be used phagocytosis of tubercle bacilli and quantitative assessment of free radicals and different cytokine levels.
4. Intracellular viability of the tubercle bacilli will be assessed as cfu obtained from lysed macrophages.
5. The macrophage thus treated will be exposed to calcitriol and induction of apoptosis will be assed.

Results:

Methods to culture macrophages from peripheral blood monocytes, phagocytosis of *M. tuberculosis* by macrophages and estimation of viable counts of tubercle bacilli after phagocytosis by the macrophages have been standardized. Antibody purification and standardization of methods to estimate cytokines and free radicals are in progress.

(Contact person: Mr. S. Mannivannan, e-mail:smv_3677@yahoo.co.in & Dr.V.D. Ramanathan, e-mail: ramanathanvd@icmr.org.in)

Serum and tissue complement profile in *M. tuberculosis* infection

Background:

The complement system as part of the innate immune system influences the immune response to *Mycobacterium tuberculosis* by affecting both the cellular and humoral immune responses. This system is involved not only in the early interaction between the host and the pathogen but also plays an important role in the inflammatory reactions associated with the disease and acts as an acute phase reactant. Therefore, this exercise is designed to delineate the exact role of the complement system in tuberculosis.

Aim:

To study the complement profile in the patients with active and healed pulmonary tuberculosis and to observe the status of the complement system during treatment by sequential estimation of the complement proteins and their activated fragments.

Methods:

Participants

The study subjects will comprise of 25 patients with active,smear positive pulmonary tuberculosis, 25 subjects who have completed the full anti-tuberculosis treatment regimen and 25 normal healthy volunteers as controls.

1. The levels of complement proteins (C3, C4, C2, FactorB,MBL) and their activation fragments (C3d, iC3b, C4d, Bb, SC5b-9) will be measured by ELISA.
2. The functional efficiency of the activated complement cascade will be assessed by haemolytic complement through Classical Pathway (CH50) and the Alternative Pathway (AH50).
3. The altered expression of membrane bound complement effector proteins (CR1, CR2, CR3, CR4) in PBMC will be studied by Flow Cytometry.
4. The role of complement components in the clearance of circulating immune complexes will be measured by ELISA.
5. The expression of mRNA of complement proteins will be studied by PCR, RT-PCR
6. To study the relationship between the innate immune response and the individual susceptibility to tuberculosis, genotyping of the class III antigens (C2, C4, Factor B) will be performed by RFLP-PCR.

Results:

The above mentioned techniques are being standardized and samples are being collected.

(Contact person: Ms.G. Senbagavalli, e-mail: premasaki@yahoo.co.in & Dr.V.D. Ramanathan, e-mail: ramanathanvd@icmr.org.in)

Complement activation by strains of mycobacteria: Wild type and gene disrupted *M. tuberculosis*

Background:

Various pathogens and microbes including *M. tuberculosis* and *M. bovis* BCG are known to activate the complement system, which plays an essential role during the early interactions between *M. tuberculosis* and the human host. However, not much is known about the activating potential of various gene-disrupted *M. tuberculosis*. Hence, the present study is designed to investigate the interaction of the complement system with these genetically modified mycobacteria.

Aim:

To study the various effects triggered on the complement system by these strains and to study the changes induced in the protein component of the organisms by the complement system.

Following are the strains that are to be used: MptpA and MptpB (Tyrosine phosphatases A and B), a strain lacking both tyrosine phosphatases, VirS knockout, devR knockout and their respective complemented strains.

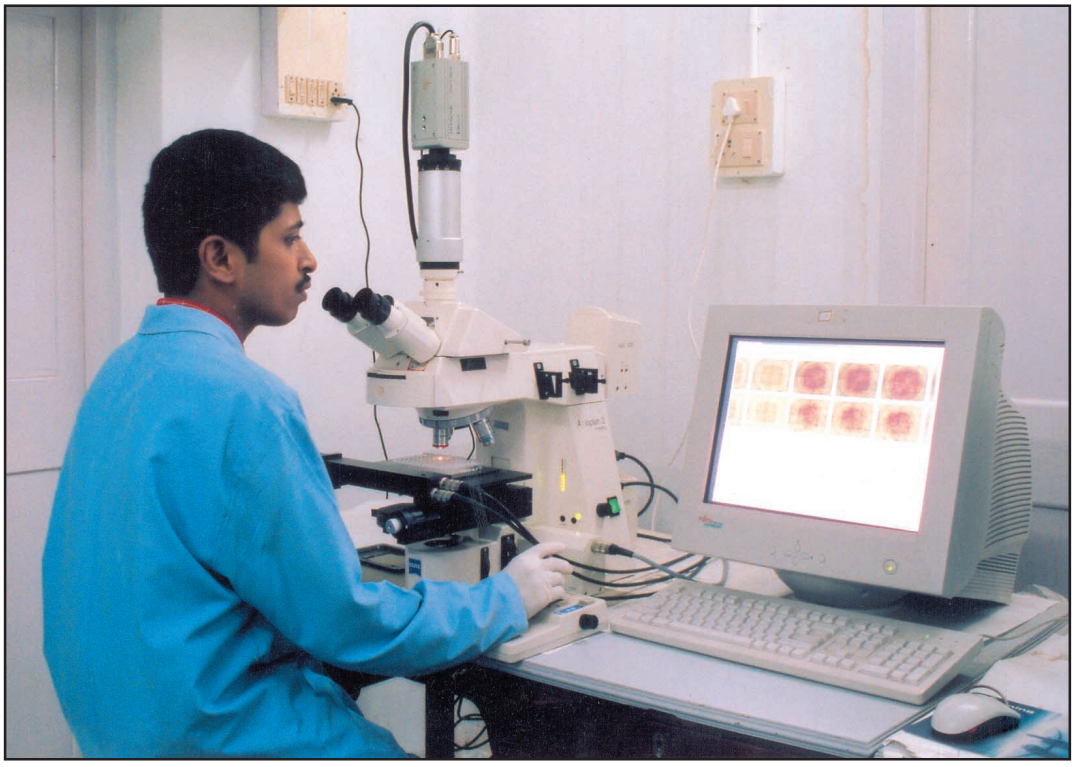
Methods:

1. Complement activation: Solid phase ELISA would be performed to assess the activating potential of complement by these strains.
2. Two dimensional electrophoresis and western blotting: Will be performed to assess the changes in the protein components of the bacteria after interacting with the complement system.

Results:

ELISA methods to assess complement activation by mycobacteria at the level of C3 and C4 have been carried out with MptpB and Erdman strains. Experiments with devR have been started.

(Contact person: Mr.V. Narayan Rao, e-mail: vnraoct177@yahoo.com & Dr.V.D. Ramanathan, e-mail: ramanathanvd@icmr.org.in)



Statistical Research

The Department of Statistics in collaboration with Center for Statistical Science, Brown University, USA is currently working on development and evaluation of "alternative markers for HIV staging in resource-limited settings: evaluation of TLC as a surrogate for CD4 counts". The Department of Statistics also in collaboration with Institute for Research in Medical Statistics, ICMR, New Delhi, undertaken a study entitled "Usage and Acceptability of ISM&H" in CGHS and private hospitals, dispensaries at Chennai city and its suburban areas. The study also covers both government (CGHS) and private allopathic hospitals. Separate schedules were used for hospitals, dispensaries, inpatients and outpatients.

Studies completed:

Mixed effects modeling of paraplegia data using Markov chain Monte Carlo method

Markov Chain Monte Carlo (MCMC) is a powerful technique for performing integration by simulation. In recent years MCMC has revolutionized the application of Bayesian statistics. Many high dimensional complex models, which were formally intractable, can now be handled routinely. MCMC has also been used in specialized non-Bayesian problems. The use of MCMC was first introduced in statistical mechanics to study the equation of the state of a two-dimensional rigid sphere system. The choice made by Metropolis was one of many other possibilities. Now this method has become a miraculous tool of Bayesian analysis and the flag of what has been called as the model liberation moment. Bayesian calculations not analytically tractable can be performed once a likelihood and prior are given. For non-Bayesian applications MCMC is considered as a very powerful numerical device in likelihood analysis or decision theory. MCMC methods have been successfully used to overcome problems caused by missing data when using small networks for conventional statistics. All MCMC methods are ways to produce a stochastic process, which has a desired distribution as its stationary distribution .The theory of stochastic processes tells as that the empirical average of a function of the stochastic process will converge to the expectation of that function under the desired distribution. MCMC is the idea of using simulations of the Markov Chain to approximate expectations by sample averages from the equilibrium distribution also called invariant distribution, stationary distribution or ergodic limit of the Markov Chain.

The two most commonly used MCMC algorithms that are applicable to both discrete and continuous systems are: (i) Gibbs Sampler and (ii) Metropolis Algorithm. The Gibbs sampler also known as the heatbath algorithm, is conceptually the simplest of the Markov chain sampling methods, but has come into prominence only recently. It is widely applicable to problems where the variables take on values from a small finite set,

or have conditional distributions of a parametric form that can easily be sampled from.

The basic operation used in the Gibbs sampling algorithm is the generation of a random value for some component of the state, X_i, from its conditional distribution given the current values of all the other components, X_j, for $j \neq i$. The speed of the algorithm depends crucially on whether this operation can be done quickly. For discrete components that take on values from a small set, the usual approach is to simply calculate the joint probabilities of all the states in which X_i takes on its various possible values, while the other X_j remain fixed at their current values. The conditional distribution for X_i is then found by normalizing these probabilities so they sum to one, and a new value for X_i is picked from this distribution. For complex and multimodal problems, the Metropolis algorithm is more appropriate. It has proved to be a flexible tool that is applicable to a wide range of problems. However when the required conditional distributions can be sampled from easily, the Gibbs sampler may be preferred, and when it is difficult to decompose the state into local components that are not too dependent, the dynamical algorithms may be more attractive.

Many problems such as generalized linear models and hierarchical models direct simulation is not possible even with two or more steps. Until recently approximating the desired distribution by normal or transformed normal distributions from which direct simulation can be drawn has attacked these problems. In recent years iterative simulation methods such as MCMC have been developed to draw from general distributions without any direct need for normal approximation. The advantage of these iterative methods is that they can be setup with virtually any model that can be setup in statistics. The main limitation is that they currently require extensive programming and debugging. In Bayesian posterior distribution, the goal of iterative simulation is the inference about the target distribution and not merely some moments of the target distribution. So it is desirable to choose starting points that widely dispersed in the target distribution over dispersed starting points are an important design feature of MCMC for two major reasons:

1. Starting far apart can make lack of convergence apparent.
2. Starting over dispersed can ensure that all major reasons of the target distributions are represented in the simulation.

The chain of the class of models where MCMC is easy to use, assessing the convergence, good guidelines for starting values. Many authors extensively discuss methods assessing the behavior of the chain and useful software.

An application to medical data

We illustrate the application of MCMC with a mixed model to data obtained from patients with Pott's paraplegia. This application is complicated with much observation on few patients that Markov Chain simulation methods are the most effective tool for exploring the posterior distribution. In this study 33 patients were admitted – 8 patients received only chemotherapy (streptomycin, rifampicin, isoniazid, pyrazinamide and ethambutol) and 21 received chemotherapy with surgery. Out of the 21 patients who received surgery, 5 received costotransversectomy and the remaining received modified Hong Kong surgery. Complete neurological assessments were done on admission, daily for 3 days and there after on

alternate days till 2 weeks, weekly till 3 months, monthly till 9 months and 3 monthly thereafter. We have considered a total of 32 measurements on each patient up to 24 months.

Finite Mixture Likelihood and Hierarchical Population Models

A brief review of the basic statistical approach is described in the following section. To address the problem of modeling the neurological responses, the following basic model was fit. The neurological score is described by random effect model in which the responses Y_{ij} (i= 1,2, .. 32) of chemotherapy regimen patients j (j = 1,2, ….8) are normally distributed with distinct mean α_j and common variance σy^2. To reflect the response of surgery regimen (j = 9 to 29), the scores are modeled as a two compartment mixture with probability (1-λ) for costotransversectomy patients which are assumed to be normally distributed with mean α_j and variance σy^2 and with probability λ for modified Hong Kong surgery patients with mean $\alpha_j + \tau$ and the same variance σy^2.

The comparison of the components of $\alpha = (\alpha_1, \alpha_2, \alpha_3, \ldots, \alpha_{29})$ for chemotherapy patients verses surgery patients addresses the magnitude of decrease in recovery period and increase the response score. A hierarchical parameter β measuring the activity was included. Specifically variation among the individuals is modeled by having the means α_j follow a normal distribution with mean μ for chemotherapy and $\mu + \beta$ for surgery patients with each distribution having variance σ_α^2. i.e. the mean of α_j in the population distribution is $\mu + \beta S_j$ where S_j is an indicator variable with 1 if the person j is surgery and 0 otherwise. The Bayesian model with an improper uniform prior distribution on the hyper parameters $\phi = (\sigma_y^2, \sigma_\alpha^2, \lambda, \mu, \beta, \tau)$ as given by Gelman and Rubin were followed.

A sample of 100 points were drawn at random from the distribution and used as a starting point for the Expectation Conditional Maximization (ECM) algorithm to search for modes as given by Gelman and Rubin. The posterior distribution was approximated by a multivariate t distribution centered at the major mode of ECM with covariance matrix as the inverse of negative of the second derivative matrix of the log posterior density. Another 1000 independent samples were drawn and importance resample subset of 10 was used as a starting point for independent Gibbs samplers.

Table XI : Posterior quantiles and estimated potential scale reduction factors for parameters.

Parameter	After 10 iterations				After 100 iterations			
	2.5%	50%	97.5%	√R	2.5%	50%	97.5%	√R
λ	0.10	0.29	0.58	2.4	0.21	0.22	0.31	1.01
τ	0.52	0.86	1.35	2.1	0.72	0.90	1.10	1.02
β	0.27	0.51	0.65	1.7	0.36	0.44	0.62	1.02

Table XI displays the posterior inferences and potential scale reduction factor for selected parameters after 10 iterations and 100 iterations. Only three-parameter estimate values are presented. After 100 iterations, the potential scale reduction factors were approximately 1 for all parameters in the model. The other hyper parameters were also estimated.

The MCMC methods provide a powerful statistical tool and have revolutionized statistical inference specifically Bayesian inference over the past few years. The ability to fit complicated models with little programming effort is in fact a key advantage of MCMC methods. The MCMC simulation should be undertaken after the problem has been approximated and explore using simple methods. There are a variety of methods of constructing efficient MCMC algorithms. However the implementation of many of these methods requires some expertise. Even though the recent works focus on construction of samples without this problem using exact samples, considerable work is still needed on the implementation issues to high dimensional databases. Comparison of different approaches for choosing initial values and convergence criteria needs further work.

(Contact person: Dr.P. Venkatesan, e-mail: venkatesanp@icmr.org.in)

Information Services

Information services

There has been remarkable progress in the library with regard to the services in general and in particular in its electronic resources.

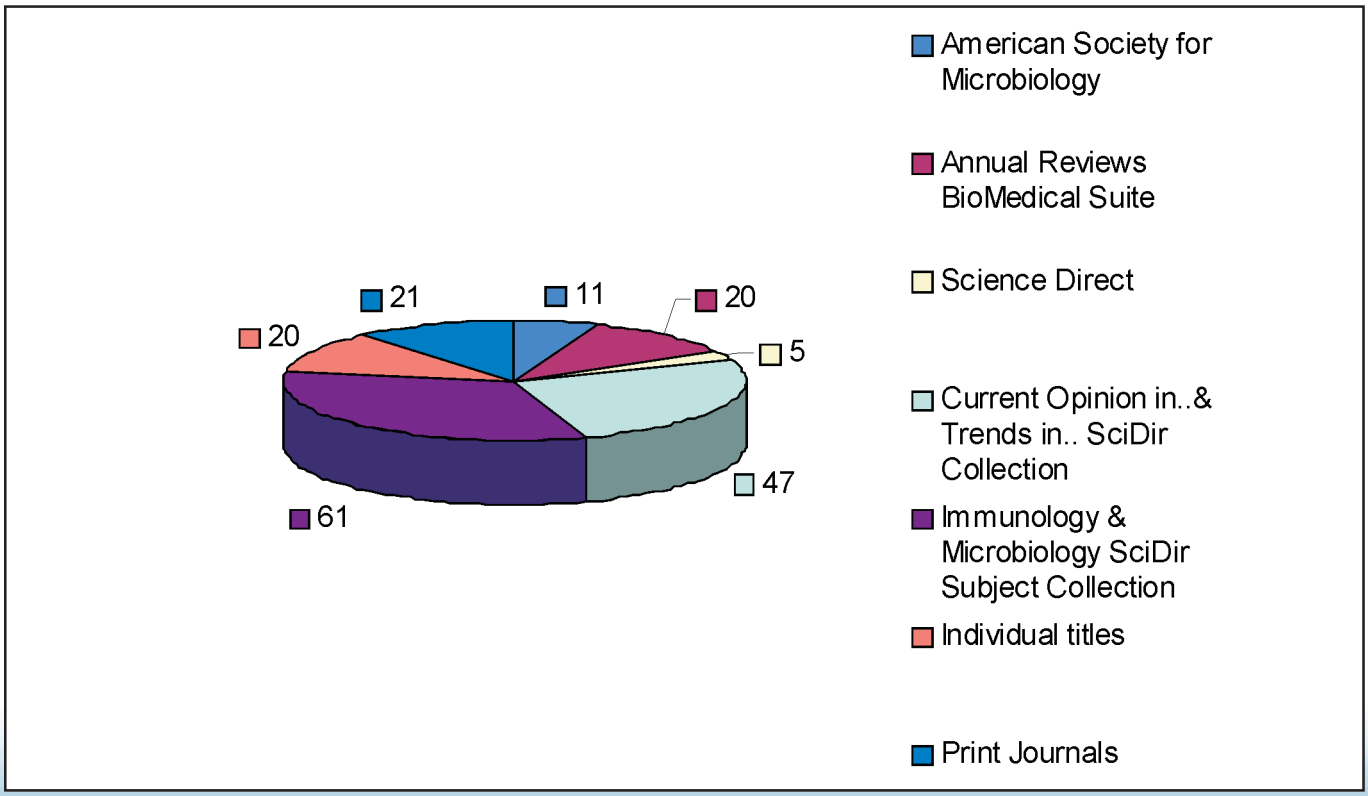
e-Collection development:

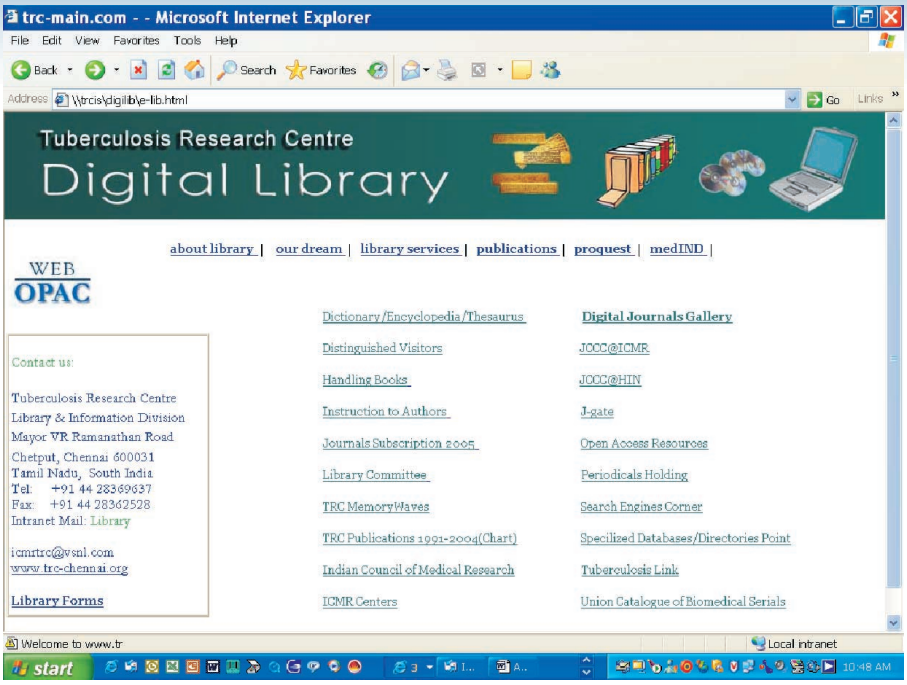
Our e-collection includes e-journals, e-databases, e-subject collection etc. The greatest health science e-collections like American Society for Microbiology cumulative collection, Annual Reviews Biomedical Suite, e-journals (individual titles), Science Direct Subject collections (Immunology & Microbiology; Current Opinions in.. & Trends in.. Journals) are the main resources of the library. The total subscribed e-resources covers nearly 85% of the library's regular collection.

Value Added Services:

Digital Library

The value added services are being extensively offered through digital library. The Digital Library has further been strengthened through interface with Journal Custom Content Consortia among ICMR institutes namely JCCC@ICMR, and Consortia among four major tuberculosis institutes in India viz., JCCC@HIN, as well as outside e-resources interface like International Tuberculosis Link, Open Access resources, medIND, J-gate, Meta Search Engines, Specialized Health Science Databases, Dictionaries, Thesaurus, etc. The interface for Library Web OPAC has also been established through digital library. The forms, which are used for regular library services are made available to the users through this digital library site.





Automation with Barcode ID

Retro conversion of card catalog has effectively been done and library automation system has been introduced with GLAS (Graphical Library Automation System, US) software, to integrate circulation and collection control. To make an effective functionality of the automation, Bar-code ID card has been issued to all the users of the library.

Web OPAC

TRC Library Online Public Access Catalog has been established through GLAS software and available through LAN. Current status of the library material(s) can be viewed by the users from their desk.

Multimedia Unit

Multimedia unit has been established with a view to expand the library services like pdf conversion of print documents of TRC publications; scanning and editing of print articles, and services like Geographical Information System (GIS).

Consortium

TRC library joined hands with JCCC for effective resource sharing of all the ICMR institutes. J-gate will be an added strength to maximize the utilization of Open Access resources.

Further JCCC has been established for 4 major TB institutes in India under the WHO project through NTI.

Resource Sharing

The Resource Sharing Is effectively being done through this consortium as well as through ICMR librarians' mail group. The institute retains its membership facility with British Council Library, Chennai. The databases like PROQUEST and OVID further strengthens the resource sharing facility among ICMR institutes.

Internet Browsing Lab

In order to maximize the utilization of the Internet services, the browsing lab gateway is being kept open to all the project staff and students from outside.

(Contact person: Mr.R. Rathinasabapati, e-mail: sabapatir@icmr.org.in)

Electronic Data Processing

The Electronic Data Processing (EDP) division provides computerized services for all departments in the TRC. TRC departments have direct access to the data with their personal computers (PC). The EDP division is continuing to give data management support including data entry/verification to various studies undertaken in the Centre. Also, this division generates reports and prepares pre-printed forms for field activity and supply data tabulations for monitoring the studies and publication of research work. Also, helps in preparation of employees' pay roll, income-tax sheets, loan schedules and central bills.

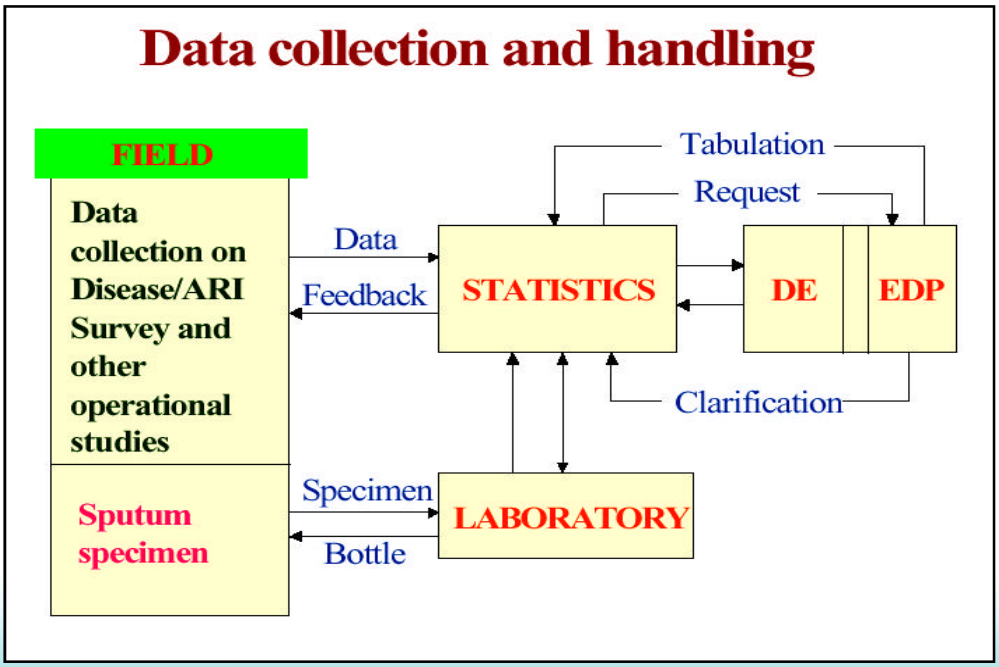
This division takes care to serve all the departments in their computing, data sharing and helps in accessing internet connection throughout. At present time the EDP division supports three server systems and four network printers and catering support for over 80 Pentium computers. The EDP division protects data through frequent backups. Apart from data processing and data management, this division is taking care of all the servers, PC's and printers by bringing under comprehensive maintenance contract service to avoid breakdown. Also, annual procurement for computer consumables is done by making indent through this division for user departments.

In this division, at present, six data entry/ verification operators, six data processing assistants and one EDP-In charge are working.

The quantum of documents entered and verified from April, 2004 to March, 2005 is shown below.

No. of documents entered:	2,01,011
No. of documents verified:	2,09,677

(Contact person: Mr.R. Subramani, e-mail: subramanir@icmr.org.in)



Drug Resistant Surveillance projects for TB drug susceptibility in India

Preliminary site visit training and on-site evaluation for undertaking the Drug Resistant Surveillance (DRS) for TB in the state of Gujarat has been completed. The pilot phase of this programme has been completed as planned and we have received sputum samples from 100 patients and processed. The results are being analysed. The concordance between TRC and State TB Demonstration Centre (STDC) Gujarat for smear microscopy is good.

(Contact person: Dr. C. N. Paramasivan, e-mail: paramasivancn@icmr.org.in)

DRS for TB drug susceptibility in two states

As per the global drug resistance surveillance programme, DRS in India is being undertaken in a phased manner. In this project, funded by the ICMR, two states in India, viz. Tamil Nadu and Sikkim have been selected. DRS for TB has already been undertaken in the state of Tamil Nadu in 1997, where the salient finding was a HR resistance of 3.4%. This was before the implementation of the RNTCP. Now the resurvey in Tami Nadu is planned. The other state will be Sikkim, where preparatory work is in progress and the protocol is being finalized in consultation with Central TB Division and the State TB Officer of Sikkim.

(Contact person: Dr. C. N. Paramasivan, e-mail: paramasivancn@icmr.org.in)

External Quality Assurance in TB drug susceptibility testing (DST) for the various national and international reference laboratories

TRC is involved in the Quality Assurance Programme in TB DST at the national level and the SAARC region. (Table XII).

The Centres involved in this program are:

- National Tuberculosis Institute, Bangalore,
- Lala Ram Swarup Institute of Tuberculosis and Chest Diseases, New Delhi,
- VP Chest Institute, New Delhi,

Table XII: Drug susceptibility testing

SITE	SM	INH	RIF	EMB
SEARO COUNTRIES				
National TB Reference Laboratory, Yangaon, Myanmar (2 rounds)	89 90	33 90	89 90	78 90
Mycobacteriology Laboratory ICDDRB, Bangladesh (2 rounds)	40 80	80 100	80 100	80 100
NATIONAL LABORATORIES				
National Tuberculosis Institute, Bangalore (3 rounds)	100 100 100	100 100 100	100 100 90	100 100 100

- New Delhi Tuberculosis Centre, New Delhi,

The SAARC countries involved at present are:

- The National Tuberculosis Laboratory, Yangon, Myanmar,
- The Tuberculosis Laboratory, International Centre for Diarrhoeal Diseases, Dhaka, Bangladesh.

(Contact person: Dr. C. N. Paramasivan, e-mail: paramasivancn@icmr.org.in)

Public-Private Partnership

The TRC in association with ACT, a division of Resource group for Education and Advocacy for Community Health (REACH), a Chennai-based NGO has undertaken the task of recruiting the private sector into TB control. During the year under review, several workshops were held for medical practitioners. At each of these workshops, which were well attended, private practitioners raised several issues regarding practical aspects of TB management and monitoring. Their questions were answered and innovative measures were employed to help them enlist more patients under the DOTS programme. A major feature of this year's activity was an attempt to enhance the awareness about TB diagnosis and treatment among the general public. In order to achieve this goal REACH enlisted the support of leading Tamil film and TV personalities to spread various messages regarding TB control. On the occasion of the World TB Day a walk/run for TB control was organized in which several schools and colleges participated. This project which is currently co-funded by the Global Fund Against AIDS, Tuberculosis (TB) and Malaria (GFATM) is now developing indicators to assess success and sustainability.

(Contact person: Dr. V. Kumaraswami, e-mail: kumaraswamiv@icmr.org.in)

Standardization of antiretroviral drugs in blood by HPLC

Background:

Pharmacokinetic studies of antiretroviral drugs are being carried out at the centre. These studies are aimed at studying interactions between anti-TB and antiretroviral drugs and assess the absorption of antiretroviral drugs in HIV-infected individuals. Pharmacokinetic studies require accurate and specific methods to estimate antiretroviral drugs in blood.

Aim:

To standardize the estimation of efavirenz, nevirapine, zidovudine, lamivudine, stavudine and didanosine in blood by HPLC.

Methods:

Simple and rapid methods to estimate efavirenz and simultaneously nevirapine and zidovudine in blood have been validated. Both the methods involved extraction of the drugs into ethyl acetate and analysis using a reversed-phase C_{18} column with UV detection. The mobile phase consisted of phosphate buffer (with varying pH and molarity) and acetonitrile in different proportions for both the methods. Internal standards were used in both the methods. The assays were linear from 0.0625-10.0 µg/ml for efavirenz, 0.05-10.0µg/ml for nevirapine and 0.025-10.0 µg/ml for zidovudine. The average recoveries of efavirenz, nevirapine and zidovudine were 98, 94 and 95% respectively. The methods

were sensitive, specific and reproducible and utilized a single step extraction. Due to the simplicity and small sample size, these methods can be used for pharmacokinetic studies and therapeutic drug monitoring.

Experiments are ongoing to validate a method that permits simultaneous estimation of lamivudine, stavudine and didanosine in blood.

(Contact person: Dr. Geetha Ramachandran, e-mail: geethar@icmr.org.in)

Mycolic acid analysis by HPLC for identification of Non Tuberculous Mycobacteria (NTM) species

Background:

Opportunistic infection due to *M. tuberculosis* is common among HIV +ve patients. However, infection due to NTM is on the increase in several parts of the world. Therefore, identification of NTM rapidly and accurately becomes important. HPLC offers a fast track method compared to other methods of identification.

Aim:

To identify the NTM species isolated from HIV infected and uninfected patients, selected as per the American Thoracic Society (ATS) criteria.

Method:

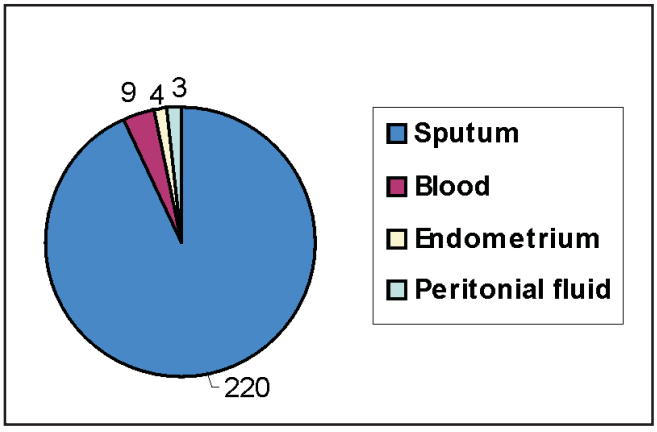
All the isolates were identified by standardized method for HPLC identification of mycobacteria developed by the U.S Department of Health and Human Services, CDC, Atlanta.

Results:

During the year April 2004 to March 2005, a total of 236 NTM cultures from patients repeatedly excreting were selected as per the ATS criteria and identified. Of the 236 NTM cultures, 9 cultures were isolated from blood sample, 3 from peritoneal fluid and 4 from endometrium. Rest of the 220 cultures isolates were from sputum (Fig. 20). Among the patients infected, infection due to *M.avium* and *M.intracellulare* predominates followed by *M.kansasii* and *M.chelonae/ M.abscessus*.

(Contact person: Dr. G. Kubendiran, e-mail: kubendirang@hotmail.com Dr.C.N. Paramasivan, e-mail: paramasivancn@icmr.org.in)

Fig. 20. Samplewise NTM identified



Appendices

Publications

Publications in	i)	International journals:	28
	ii)	National journals:	18
Accepted for publication in	i)	International journals:	14
	ii)	National journals:	7

Published

International

1. Raja A, Uma Devi KR, Ramalingam B, Brennan, PJ. Improved diagnosis of pulmonary tuberculosis by detection of free and immune complex-bound anti-30kDa antibodies. Diagn Microbiol Infect Dis. 2004 Dec;50(4):253-9.
2. Dube A, Jayasankar K, Prabakaran L, Kumar V, Gupta PK. Nitrogen laser irradiation (337 nm) causes temporary inactivation of clinical isolates of *Mycobacterium tuberculosis*. Lasers Med Sci. 2004;19(1):52-6.
3. Thomas BE, Rehman F, Malaisamy M, Dilip M, Suhadev M, Priyadarsini P, Purushotham NK, Swaminathan S. A study of condom acceptability among men in an urban population in South India. AIDS Behav. 2004 Jun;8(2):215-20.
4. Chandra C, Paramasivan S, Jawahar MS, Banurekha VV, Narayanan, PR. Effect of vitamin D_3 on phagocytic potential of macrophages with livess and lymphoproliferative response in pulmonary tuberculosis. J Clin Immunol. 2004 May;24(3):249-57.
5. Vanitha JD, Rehman F, Paramasivan CN. Evaluation of microplate alamar blue assay for drug susceptibility testing of *Mycobacterium avium* complex isolates. Diagn Microbiol Infect Dis. 2004 Jul; 49(3):179-82.
6. Ramachandran G, Perloff ES, von Moltke LL, Swaminathan S, Wanke CA, Greenblatt DJ. Analysis of generic antiretroviral formulations manufactured in India. AIDS. 2004 Jul 2;18(10):1482-4.
7. Gopi PG, Subramani R, Selvakumar N, Santha T, Eusuff SI, Narayanan PR. Smear examination of two specimens for diagnosis of pulmonary tuberculosis in Tiruvallur District, south India. Int J Tuberc Lung Dis. 2004 Jul;8(7):824-8.
8. Kolappan C, Gopi PG, Subramani R, Chadha VK, Kumar P, Prasad VV, Appegowda BN, Rao RS, Sasidharan R, Ganesan N, Santha T, Narayanan PR. Estimation of annual risk of tuberculosis infection (ARTI) among children aged 1-9 years in the south zone of India. Int J Tuberc Lung Dis. 2004 Apr;8(4):418-23.
9. Gurumurthy P, Ramachandran G, Hemanth Kumar AK, Rajasekaran S, Padmapriyadarsini C, Swaminathan S, Bhagavathy S, Venkatesan P, Sekar L, Mahilmaran A, Ravichandran N, Paramesh P. Decreased bioavailability of rifampin and other antituberculosis drugs in patients with advanced human immunodeficiency virus disease. Antimicrob Agents Chemother. 2004 Nov;48(11):4473-5.
10. Gopalaswamy R, Narayanan PR, Narayanan S. Cloning, overexpression, and characterization of a serine/threonine protein kinase pknI from *Mycobacterium tuberculosis*

H37Rv. Protein Expr Purif. 2004 Jul; 36(1):82-9.

11. Ramachandran G, Santha T, Garg R, Baskaran D, Iliayas SA, Venkatesan P, Fathima R, Narayanan PR. Vitamin A levels in sputum-positive pulmonary tuberculosis patients in comparison with household contacts and healthy 'normals'. Int J Tuberc Lung Dis. 2004 Sep;8(9):1130-3.
12. Ramalingam B, Baulard AR, Locht C, Narayanan PR, Raja A. Cloning, expression, and purification of the 27 kDa (MPT51, Rv3803c) protein of *Mycobacterium tuberculosis*. Protein Expr Purif. 2004 Jul; 36(1):53-60.
13. Selvaraj P, Chandra G, Jawahar MS, Rani MV, Rajeshwari DN, Narayanan PR. Regulatory role of vitamin D receptor gene variants of Bsm I, Apa I, Taq I, and Fok I polymorphisms on macrophage phagocytosis and lymphoproliferative response to *Mycobacterium tuberculosis* antigen in pulmonary tuberculosis. J Clin Immunol. 2004 Sep;24(5):523-32.
14. Sivakamasundari P, Varalakshmi P, Kannabiran M. Nuclear pore complex oxalate binding protein p62: its expression on oxalate exposure to VERO cells. J Cell Biochem. 2004 Dec 15;93(6):1099-106.
15. Swaminathan S, Paramasivan CN, Kumar SR, Mohan V, Venkatesan P. Unrecognised tuberculosis in HIV-infected patients: sputum culture is a useful tool. Int J Tuberc Lung Dis. 2004 Jul;8(7):896-8.
16. Swaminathan S. Tuberculosis in HIV-infected children. Paediatr Respir Rev. 2004 Sep;5(3):225-30.
17. Santha T, Rehman F, Mitchison DA, Sarma GR, Reetha AM, Prabhakar R; Tuberculosis Research Centre, Indian Council of Medical Research. Split-drug regimens for the treatment of patients with sputum smear-positive pulmonary tuberculosis—a unique approach. Trop Med Int Health. 2004 May;9(5):551-8.
18. Balasubramanian R. Operational research studies in tuberculosis control contributions in the last two decades from Tuberculosis Research Centre, south India. SAARC J TB L Dis. & HIV 2004 1 (1):1-13
19. Muniyandi M, Ramachandran R, Balasubramanian R. Tuberculosis Control Programme – Is it pro poor? SAARC J TB L Dis. & HIV 2004 1 (1):14-9.
20. Paramasivan CN, Sulochana S, Kubendiran G, Venkatesan P, Mitchison DA. Bactericidal action of gatifloxacin, rifampin, and isoniazid on logarithmic- and stationary-phase cultures of *Mycobacterium tuberculosis*. Antimicrob Agents Chemother. 2005 Feb;49(2):627-31.
21. Santha T, Garg R, Subramani R, Chandrasekaran V, Selvakumar N, Sisodia RS, Perumal M, Sinha SK, Singh RJ, Chavan R, Ali F, Sarma SK, Sharma KM, Jagtap RD, Frieden TR, Fabio L, Narayanan PR. Comparison of cough of 2 and 3 weeks to improve detection of smear-positive tuberculosis cases among out-patients in India. Int J Tuberc Lung Dis. 2005 Jan; 9(1):61-8.
22. Selvakumar N, Sekar MG, Ilampuranan KJ, Ponnuraja C, Narayanan PR. Increased detection by restaining of acid-fast bacilli in sputum samples transported in cetylpyridinium chloride solution. Int J Tuberc Lung Dis. 2005 Feb;9(2):195-9.
23. Selvakumar N, Sekar MG, Rahman F, Syamsunder A, Duraipandian M, Wares F, Narayanan PR. Comparison of variants of carbol-fuchsin solution in Ziehl-Neelsen for detection of acid-fast bacilli. Int J Tuberc Lung Dis. 2005 Feb;9(2):226-9.
24. Selvakumar N, Sivagamasundari S, Prabhakaran E, Govindaraju R, Perumal M,

Granich R, Wares F, Chauhan LS, Narayanan PR. Storage of heat-fixed unstained sputum AFB smears for panel testing in a tuberculosis unit in South India. Int J Tuberc Lung Dis. 2005 Feb;9(2):223-5.

25. Selvakumar N, Prabhakaran E, Murthy BN, Sivagamasundari S, Vasanthan S, Govindaraju R, Perumal M, Wares F, Chauhan LS, Santha T, Narayanan PR. Application of lot sampling of sputum AFB smears for the assessment of microscopy centres. Int J Tuberc Lung Dis. 2005 Mar;9(3):306-9.
26. Selvakumar N, Murthy BN, Prabhakaran E, Sivagamasundari S, Vasanthan S, Perumal M, Govindaraju R, Chauhan LS, Wares F, Santha T, Narayanan PR. Lot quality assurance sampling of sputum acid-fast bacillus smears for assessing sputum smear microscopy centers. J Clin Microbiol. 2005 Feb;43(2):913-5.
27. Das SD, Narayanan S, Hari L, Hoti SL, Thangathurai RK, Charles N, Jaggarajamma K, Narayanan PR. Differentiation of highly prevalent IS6110 single-copy strains of *Mycobacterium tuberculosis* from a rural community in South India with an ongoing DOTS programme. Infect Genet Evol. 2005 Jan;5(1):67-77.
28. Das SD, Hari L. My introduction to the Tsunami. The Lancet's Tsunami coverage – World report. Web publication. The Lancet 2005; 365:203.

National

1. Raja A. Immunology of tuberculosis. Indian J Med Res. 2004 Oct;120(4):213-32.
2. Balasubramanian R, Ramachandran R, Nayak AC, Duraipandian P, Karunakaran K, Narayanan PR. A double-blind study of oral salbutamol supplement and repeat sputum smear microscopy in enhancing diagnosis of smear-negative tuberculosis in south India. Indian J Tuberc. 2004 Oct;51(4):191-198.
3. Vadivel J, Gopu S. Role of health visitor for T.B. patients in the community. Nurses of India 2004;10-12.
4. Vadivel J. Nursing activities of (outpatients) TB patients in public health sector. Nurses of India 2004;4-7.
5. Jawahar MS. Current trends in chemotherapy of tuberculosis. Indian J Med Res. 2004 Oct;120(4):398-417.
6. S.M. Kurian, P. Selvaraj, A.M. Reetha, N. Charles, P.R. Narayanan. HLA-DR phenotypes and lymphocyte response to *M. tuberculosis* antigens in cured spinal tuberculosis patients and their contacts. Indian J Tuberc. 2004 Apr; 51(2):71-75.
7. Narayanan S. Molecular epidemiology of tuberculosis. Indian J Med Res. 2004 Oct;120(4):233-47.
8. Paramasivan CN. Two speedier phenotypic methods on drug susceptibility testing of *Mycobacterium tuberculosis*. Indian J Med Res. 2004 Nov;120(5):440-1.
9. Paramasivan CN, Venkataraman PV. Drug resistance in tuberculosis in India. Indian J Med Res. 2004 Oct;120(4):377-86.
10. Prabha C, Syed Abdul Khader K, Das SD. *In vitro* cytokine response in tuberculosis. J Imm Immunopath. 2004;6(s-1):62-63.
11. Selvaraj P, Raja A, Kurian SM, Uma Devi KR, Narayanan PR. HLA-DR phenotypes and IgG, IgA and IgM antibody responses to *Mycobacterium tuberculosis* culture filtrate and 30 kDa antigens in pulmonary tuberculosis. Curr Sci. 2004 Sept 87(6):771-775.
12. Swaminathan S, Rajasekaran S, Shibichakravarthy K, Amarendran VA, Raja K, Hari L, Narayanan, S. Multiple recurrences of tuberculosis in an HIV

infected individual. J Assoc Physicians India. 2004 Jun;52:513-4.
13. Swaminathan S. Protective efficacy of BCG. Indian J Pediatr. 2004 Dec;71(12):1083-4.
14. Hemanth Kumar AK, Immanuel C, Ramachandran G, Chelvi KS, Victor L, Gurumurthy P. A validated high-performance liquid chromatography method for the determination of rifampicin and desacetyl rifampicin in plasma and urine. Indian J Pharmacol. 2004 36:231-233.
15. Hemanth Kumar AK, Gurumurthy P. Ofloxacin pharmacokinetics in saliva. Indian J Pharmacol. 2004 36:80-83.
16. Selvakumar N, Kumar V, Gopi PG, Sivagamasundari S, Prabhakaran E, Samuel Vasanthan, Narayanan PR. Proficiency to read sputum AFB smears by senior tuberculosis laboratory supervisors under training at reference laboratory in India. Indian J Tuberc 2005 Jan;52(1):11-14.
17. Padmavathy L, Lakshmana Rao L, Ramanadhan, Shakila. Mycobacterial antigen in tissues in diagnosis of cutaneous tuberculosis. Indian J Tuberc 2005 Jan;52(1):31-35.
18. Swaminathan S, Raghavan A, Datta M, Paramasivan CN, Saravanan KC. Computerized tomography detects pulmonary lesions in children with normal radiographs diagnosed to have tuberculosis. Indian Pediatr. 2005 Mar;42(3):258-61.

Accepted for publication

International

1. Thomas A, Gopi PG, Santha Devi T, Chandrasekaran V, Subramani R, Selvakumar N, Eusuff SI, Sadacharam K, Narayanan PR. Predictors of relapse among pulmonary tuberculosis patients treated in a DOTS programme in South India. Int J Tuberc Lung Dis.
2. Khera A, Singh R, Shakila H, Rao V, Dhar N, Narayanan PR, Paramasivan CN, Ramanathan VD, Tyagi AK. Elicitation of efficiency, protective immune responses by using DNA vaccines against tuberculosis. Vaccine.
3. Thomas BE, Rehman F, Suryanarayanan D, Josephine K, Dilip M, Dorairaj VS, Swaminathan S. How stigmatizing is Stigma in the life of people living with HIV: A study on HIV positive individuals from Chennai, South India. AIDS Care, 2005, 17, 795-801.
4. Hanna LE, Bose JC, Nayak K, Subramanyam S, Swaminathan S. Influence of active tuberculosis on chemokine and chemokine receptor expression in HIV-infected persons. AIDS Res Hum Retroviruses.
5. Prabha C, Karthic S, Das SD, Swaminathan S, Subramanian S. Impact of tuberculous on serum leptin levels in patients with HIV infection. Horm Res.
6. Rajavelu P, Das SD. Th2 type of immune response observed in normal healthy individuals to sonicate antigen prepared from the most prevalent *Mycobacterium tuberculosis* strain with single copy of IS*6110*. FEMS Immunol Med Microbiol.
7. Rao V, Dhar N, Shakila H, Singh R, Khera A, Naseema M, Paramasivan CN, Narayanan PR, Ramanathan VD, Tyagi AK. Over-expression of the 19kDa lipoprotein of *Mycobacterium tuberculosis* obliterates the protective efficacy of BCG by polarizing the host immune responses to the Th2 phenotype. Scand J Immunol.
8. Singh A, Gupta R, Viswakarma RA, Narayanan PR, Paramasivan CN, Ramanathan VD, Tyagi AK. Requirement of *mymA* operon for appropriate cell wall

structure and persistence of *Mycobacterium tuberculosis* in the spleen of guinea pigs. J Bacteriol.

9. Swaminathan S, Raghavan A, Duraipandian M, Kripasankar AS, Ramachandran P. Short course chemotherapy for pediatric respiratory tuberculosis : Five year report. Int J Tuberc Lung Dis.
10. Swaminathan S, Paramasivan CN, Ponnuraja C. Anti-tuberculosis drug resistance in patients with HIV and tuberculosis in South India. Int J Tuberc Lung Dis.
11. Sulochana S, Rahman F, Paramasivan CN. *In vitro* activity of Quinolones against *Mycobacterium tuberculosis.* J Chemother.
12. Thomas BE. The sounds of the waves are frightening – Experiences of school children post Tsunami. Web publication. Lancet.
13. Thomas BE *et al*. Is awareness of HIV enough to alter high risk behaviour? What do HIV positive individuals have to say? A study from south India. SAARC J TB L Dis. & HIV.
14. Thomas BE *et al*. Gender differences in perceived health related quality of life among persons living with HIV – a study from Chennai, south India. SAARC J TB L Dis. & HIV.

National

1. Immanuel C, Victor L, Chelvi KS, Padmapriyadarsini C, Rehman F, Ilyas S, Swaminathan S. Serum neopterin levels in HIV infected patients with & without tuberculosis. Indian J Med Res.
2. Nirupa C, Sudha G, Santha T, Ponnuraja C, Fathima R, Chandrasekharan V, Jaggarajamma K, Thomas A, Gopi PG, Narayanan PR. Evaluation of directly observed treatment providers in the Revised National Tuberculosis Control Programme: A report from Tiruvallur District, South India. Indian J Tuberc.
3. Padmapriyadarsini C, Swaminathan S. Preventive therapy for tuberculosis in HIV infected individuals. Indian J Med Res.
4. Ramachandran R. Crytpcoccal Meningitis in HIV infected patients. J Assoc Physicians India.
5. Sibichakravarthy K, Swaminathan S, Paramasivan CN, Amarendran VA, Thomas B. A case of recurrent tuberculosis in an HIV infected individual. J Assoc Physicians India.
6. Swaminathan S, Padmapriyadarsini C, Narendan G, Thomas BE, Anand S, Aiswarya Rajyalaxmi. Immune reconstitution syndrome following invitation of antiretroviral therapy in HIV and multidrug resistant tuberculosis. Indian J Chest Dis Allied Sci.
7. Narayanan S. Reactivation of *Mycobacterium tuberculosis* as evidenced by DNA fingerprinting. Ranbaxy Science Foundation.

Books

1. G. Narendran and Soumya Swaminathan. Extrapulmonary tuberculosis. Medicine Update, 2005, edited by SB Gupta, Published by Diamond APICON.
2. A.R. Adhilakshmi and Soumya Swaminathan. Epidemiology to Tuberculosis in Children Common MDR Infections in Children- Typhoid, Tuberculosis, Malaria edited by Nurpur Ganguly, Ritabrata Kundu and Tapan Kr Ghosh, Published by CBS Publishers and Distributors, New Delhi, Bangalore – 2005.

Awards

- R.C. Garg Memorial Award for the best article published in the Indian Journal of Tuberculosis in 2002 at the 58th National Conference on Tuberculosis and Chest Diseases, Mumbai, Maharashtra, January 1-4th 2004. – **Tuberculosis Research Centre.**
- Prof. K.C. Mohanty award for the best paper publication in Indian Journal of Tuberculosis "Mycobacteremia in a HIV infected tuberculosis patient" – **Dr. Ranjani Ramachandran.**
- Prof. R.N. Srivastava award for young scientists at XXII ISMS conference, JIPMER, Pondicherry - 21-23 January, 2005 - **Dr.S. Anitha**.

Technical Support

Model DOTS Project

- Attended Medical College CME, programme held at Tiruvananthapuram on 30 June, 2004. Presented scientific basis of DOTS, extra pulmonary Tuberculosis and pediatric TB – **Dr. Aleyamma Thomas.**
- Participated in workshop for RNTCP Modules Revision organized by CTD at Bangalore during 5-10 July, 2004 – **Dr. Aleyamma Thomas**.
- Participated as panel member in CME programme on RNTCP held at PSG Medical College Coimbatore on 21 July, 2004 **– Dr. Aleyamma Thomas**.
- Participated in sensitization program in RNTCP for Medical College Hospital Staff and gave a lecture on "Evidences of effectiveness of DOTS Regimens" at PSG Medical College, Coimbatore, during 20-21 July, 2004 – **Dr. Paulin Joseph.**
- Attended the DTO review meeting conducted by Joint Secretary at DMS office, Chennai on July/August, 2004. Presented "MDR TB in Tamil Nadu" – **Dr. Aleyamma Thomas**.
- Attended the NGO workshop conducted by Government of Tamil Nadu, Chennai on 19 August, 2004. Presented the paper, "Role of TRC in RNTCP" – **Dr. Aleyamma Thomas.**
- Participated in the discussions on Research and Policy in RNTCP Meeting held at Nirman Bhavan, New Delhi on 18 September, 2004 – **Dr. Aleyamma Thomas.**
- Facilitated–RNTCP Training at Trivandrum STDC during 17-20 November, 2004 - **Dr. Paulin Joseph.**
- Attended 2 days Media Workshop conducted by Government of Tamil Nadu, Chennai on 16-17 December, 2004. Presented "Epidemiology of TB Global & Indian scenario" – **Dr. Aleyamma Thomas.**
- Attended CME programme organized by IMA, Government of Pondicherry, on19 December, 2004. Presented "Over view of RNTCP" – **Dr. Aleyamma Thomas**.
- Attended Awareness programme for CRRI in RNTCP conducted by Sri Ramachandra Medical College and Research institute, Porur, Chennai on 10 February, 2005. Presented –"Revised National Tuberculosis Control Programme an overview" – **Dr. Aleyamma Thomas.**
- Attended DTO review meeting conducted by Directorate of Medical Services, Chennai on 10 February, 2005 – **Dr. Aleyamma Thomas.**
- Nominated as the member of National Task Force constituted for involving all the Medical colleges in the country in RNTCP - **Dr Rani Balasubramanian.**

Social workers:

- Panelist for Viva voce examination for II year M.A. students at The Madras School of Social Work, 5 April, 2004 - **Dr. Geetharamani Shanmugam.**
- Talk on Fieldwork in a medical setting to II year M.A students of Madras School of Social Work, 24 June, 2004 - **Dr. Geetharamani Shanmugam.**
- Participated in the District Advisory Committee meeting on the implementation of ITACT at Police Commissioner's Office, 26 June, 2004 - **Dr. Geetharamani Shanmugam.**
- Resource person for the live telecast on information programme in Tamil in Podhigai Channel of Doordarshan – Theriyuma

Ungalukku – 6 August, 2004 – **Dr. Geetharamani Shanmugam.**

- Resource person for the workshop on "Counselling Skills in Sexual Health – Through Skill Enhancement Training" organized by the Department of Psychiatry, Madras Medical College, 10 August, 2004 - **Ms. Beena E. Thomas.**
- Awareness programme on Tuberculosis for the Community at Kothwalchavadi Street, Saidapet – organized by YRG Care and students of Social Work, Madras Christian College, Tambaram, 15 September, 2004 – **Ms. Kalaiselvi.**
- Panel member for the discussion on 'Trafficiking' organized on National Girl Child Day' by Mariyalaya at St. Mary's Anglo Indian Higher Secondary School, Chennai, 25 September, 2004 – **Dr. Geetharamani Shanmugam.**
- Dialogue on "Gender issues on TB and Private sector and TB" – broadcast programme by AIR –29 September, 2004 – **Ms. Sudha Ganapathy.**
- Awareness programme on Tuberculosis for the Community at Pulianthope organized by ARPANAM NGO, 2 October, 2004 – **Ms. Sheila Fredrick, Ms. Chandra Suresh**
- Being a visiting lecturer in Madras School of Social Work, Madras for Post graduate students in Social work, 12 October, 2004 to till date - **Ms. Beena E. Thomas.**
- Talk on "Sociological issues on TB with reference to women" – broadcast programme, 2 December, 2004 - **Dr. Geetharamani Shanmugam.**
- Guest Lecture on "What young girls need to do for HIV/AIDS?" at C.P.T. College for Women, Velachery, 12 December, 2004 - **Ms. Beena E. Thomas.**
- Awareness programme on Tuberculosis for the staff, students and their family members organized by the Johnson Nursery and Primary School, Chennai, 29 January 2005 - **Ms. Sheila Fredrick and Ms. Chandra Suresh.**
- State level Consultation Programme for policy formulation on street children organized by the Dept. of Social Defense, Chennai, 24 February 2005 – **Dr. Geetharamani Shanmugam.**
- Resource person for the workshop on Child line organized by ICCW and gave a talk on Child Welfare Committee for the NGOs and Govt. officials, 29 March, 2005 **– Dr. Geetharamani Shanmugam.**
- Talk on the "Role of ICMR in health" to II year MA (Social Work) students at the Madras School of Social Work, Chennai, 29 March, 2005 – **Ms. Sudha Ganapathy.**
- Served as the resource person for the workshop on "Child Line" organized by the ICCW and gave a talk on Child Welfare Committee" for the NGOs and Govt. officials, 29 March, 2005 – **Dr. Geetharamani Shanmugam.**

The Social Work department also provides support in the rehabilitation activities. Care and support services are offered to both tuberculosis and HIV patients. These include institutionalization, sponsorship for education, job opportunities, self employment and referral services.

Support Groups are organized for patients to ventilate and share their concerns and discuss solutions collectively.

Department of Statistics

The Department continued to provide academic support to basic medical sciences departments of universities and other colleges situated in and around the city. The Department conducts research programs leading to PhD in the following fields: Survival Analysis, Artificial Neural Networks, Computational Molecular Biology, HIV/AIDS Modeling, GEE, Markov Chain Monte Carlo (MCMC) and Casual Inference.

Departments of Bacteriology and Immunology

Batches of students from Medical Colleges (M.B.B.S., M.D.) and other educational institutions (M. Sc.) are regularly posted to these laboratories to learn microbiological and immunological techniques.

Capacity Building

- Undergone a short course on "Statistics for Micro array Data Analysis" organized jointly by the XXII International Biometric Conference and Australian Statistical Conference at Cairns, Australia – 10-11 July, 2004 – **Dr. P. Venkatesan.**
- Three months fellowship was availed to do Collaborative Research studies on Comparitive Genomics at the Department of Infectious diseases, August – October, 2004, University of Stanford. – **Dr. Sujatha Narayanan.**
- ICER funded training in HIV & TB vaccine projects in South Africa – 27 September – 3 October, 2004 – **Dr. Soumya Swaminathan, Dr. Ranjani Ramachandran.**
- ICER funded training in HIV & TB projects in Ugada – 16 – 23 October, 2004 – **Dr. Pradeep A. Meno, Ms. Beena E. Thomas.**
- **Mr. R. Selvaraj** was awarded Ph. D degree – thesis titled "Statistical considerations in modeling *Mycobacterium* infection with neural networks" – 4 October, 2004 – University of Madras.
- ICER funded training in Cellular Immunology at UMDNJ, NJ, USA – September -December, 2004 - **Ms. Priya Rajavelu.**
- Fifth Indo-US Workshop on Flow Cytometry organized by the Dept. of Biotechnology, Panjab University, Chandigarh, 16-19 February, 2005 - **Dr. Sudha Subramanyam, Ms. P. Supriya.**
- Certificate course on Bio-informatics tools for Life Sciences conducted by AU-KBC Research Centre, MIT Campus of Anna University, 22-25 February, 2005 – **Dr. A.K. Hemanth Kumar.**

Conferences/ seminars/ symposia/ workshops/ meetings etc. organized:

- Five days training programme on Basic aspects of Clinical Research Methodology - conducted jointly by TRC and University of Alabama under ICER programme at TRC, Chennai – 30 March – 3 April, 2004.

- Organisation of re-orientation course on EQA of sputum AFB microscopy for STOs, DTOs, STLSs, Directors and Microbiologists of STDCs. June-August 2004.

- AIDS in India: A Regional Symposium-Workshop on Research Trials and Treatment, 31 July-6 August, 2004.

Hands on training on isolation, propagation, maintenance of phages and luciferase reporter phage assay was provided for twenty participants of the workshop.

- National Seminar on HIV/TB at TRC, 11-12 September, 2004.

- Organised Research Dissemination Workshop –II on TB control Jointly orgainsed by WHO and Tuberculosis Research Center (ICMR) Chennai on 19th –20 January, 2005.

- Short course on "Qualitative Research Methodology" organized by the Tuberculosis Research Centre and University of Alabama (UAB), Birmingham USA at Chennai, 15-17 February, 2005.

Participation in conferences/ seminars/ symposia/ workshops/ meetings etc.

1. HIV/ AIDS counseling workshop, Christian Medical College, Vellore –29 March – 3 April, 2004 - **Ms. Niruparani Charles.**
2. HIV/AIDS Fellows and New Investigators Workshop on Grantsmanship and Career Development and HIV Vaccine Development: Progress and Prospects, organized by Keystone Symposia, Whistler, Canada - 11-18 April, 2004 - **Dr.M.S. Jawahar, Dr. Ranjani Ramachandran.**
3. Certificate course on ART in Resource Limited Settings – The Tamil Nadu Dr. M.G.R. Medical University, Chennai, 13-15 April, 2004 – **Dr. Rajeswari Ramachandran.**
4. Training faculty in the 'Trainers programme on Anti Retroviral therapy' at Tambaram Sanatorium, 14-17 April, 2004 – **Dr. Soumya Swaminathan.**
5. Comprehensive guidelines for laboratory support for HIV related tests - YRG Care organized by WHO SEARO, Chennai, 5-6 April and 1-2 May, 2004 – **Dr. Soumya Swaminathan.**
6. Workshop on 'Open Access' - M.S. Swaminathan Research Foundation, Chennai, 2-4 May, 2004 – **Dr.Paulin Joseph.**
7. Workshop on Grantsmanship for AIDS Researchers at the US National Institutes of Health, Bethesda, Maryland, 6-7 May, 2004 – **Dr. Soumya Swaminathan.**
8. "Recent statistical concepts in reliability theory" - seminar on Reliability, Chennai, 16 May, 2004 - **Dr. P. Venkatesan.**
9. 104th General meeting of American Society for Microbiology (ASM), New Orleans, Lousiana, USA, 23-27 May, 2004 – **Dr. Vanaja Kumar.**
10. 2nd International conference on Economics and Human Biology, Munich, Germany, 2-6 June, 2004

    Paper presented: "Economic impact of tuberculosis on patients and families in India"- **Mr. M. Muniyandi.**
11. Guest lectures – Workshop on Basic electrophoretic and immunological techniques – Jamal Mohamed College, Trichy, 7-8 June, 2004 -
    (i) "Cellular immunological techniques I & II" - **Dr.P. Selvaraj.**
    (ii) Humoral immune techniques" - **Dr. Alamelu Raja.**
12. RNTCP Central Steering Committee - New Delhi, 11 June, 2004 - **Dr. Rajeswari Ramachandran.**
13. Indo-French Conference on Physiopathology to the diagnosis of Tuberculosis organized by Biomerieux at Annecy, France, 1-2 July, 2004

    Papers presented:
    (i) "Four decades of experience in tuberculosis epidemiology"- **Dr.C. Kolappan**.
    (ii) "Genomics and genotyping of *M. tuberculosis*"- **Dr. Sujatha Narayanan.**
14. Participated in "Revision of RNTCP Modules for training of Medical Officers" - National Tuberculosis Institute, Bangalore from 6-15 July, 2004 - **Dr. Rani Balasubramanian.**
15. Dr.Sanjivi Centenary Celebration held at Voluntary Health Service, Chennai, 9 July, 2004.

    Papers presented:
    (i) "Review of studies on Extra-pulmonary

TB"- **Dr. Rani Balasubramanian.**

(ii) "Laboratory diagnosis of tuberculosis – Recent methods" – **Dr.C.N. Paramasivan.**

16. XV International AIDS conferene, Bangkok, Thailand, 11-16 July, 2004.

    Paper presented: "Reduced caloric intake, malnutrition and anemia in HIV positive south Indians" – **Dr. C. Padmapriyadarsini.**

17. International Biometric Society and Australian Statistical Association at Cairns, Australia, 11-16 July, 2004.

    Paper presented: "Evaluation of cost-effective biomarkers for HIV staging and monitoring" – **Dr. P. Venkatesan.**

18. INCLEN – CEU workshop on 'Anti-mycobacterial Drug Susceptibility assay, King George Medical University, Lucknow, 19 July, 2004.

    Paper presented: "Organisation of laboratory services for measuring drug resistance surveillance in tuberculosis" - **Dr.C.N. Paramasivan.**

19. AIDS in India: A Regional Symposium-Workshop on Research Trials and Treatment, organized by AIDS International training and research program (AITRP) of AECOM, New York - NNCASR and NIMHANS, Bangalore, 31 July - 6 August, 2004

    Paper presented: "New mycobacteriophage constructs to improve the sensitivity of LRP assay for TB diagnosis in AIDS patients" – **Dr. Vanaja Kumar.**

20. Regional workshop on Research, trials and treatment, Bangalore, 1-8 August, 2004 – **Dr. Soumya Swaminathan.**

21. Workshop on application of qualitative methodology to social work - Stella Marris College, Chennai, 5-8 August, 2004 - **Ms. Mohanarani Suhadev.**

22. Zonal Workshop – SMS Medical College, Jaipur, 7-8 August, 2004

    Paper presented: "Diagnosis and management of extra-pulmonary forms of TB" – **Dr. Rani Balasubramanian.**

23. Orientation programme on "Child Rights and Trafficking" organized by Department of Social Defence at Hotel Beverly on 17 August 2004 **– Dr. Geetharamani Shanmugam.**

24. "RNTCP NGO Workshop" organized by State TB Officer. The Residency Towers, Chennai, 19 August, 2004 - **Ms. Sudha Ganapathy.**

25. XXIX annual conference on IAP-TNSC at Kanyakumari, 20-22 August, 2004

    Delivered talk on: The changing phase of tuberculosis among children in developing countries" - **Dr. Soumya Swaminathan.**

26. Guest lecture given on "What more you can do in sputum AFB microscopy" at JJ College of Arts and Science, Pudukottai. 21 August, 2004 – **Dr.N. Selvakumar.**

27. Workshop on Data Cleaning and analysis, Chiang Mai, Thailand, 23-25 August 2004

    Paper presented: "WHO/TDR Multinational study on Timing and its significance in the diagnosis of tuberculosis" – **Dr. Rajeswari Ramachandran.**

28. Working group to review RNTCP and TB advocacy programme in Chennai city, meeting organised by Health Secretary at Secretariat, 23 August, 2004 - **Dr. Aleyamma Thomas.**

29. "Sociological issues related to TB" -

conducted at the Department of Social Work, Madras Christian College, Tambaram, 23 August, 2004 - **Ms. Sudha Ganapathy, Dr. Geetharamani Shanmugam, Ms. Nirupa Charles, Ms. Jagarajamma.**

30. Bidi Workshop – Tata Institute of Fundamental Research, New Delhi, 23-25 August, 2004 **– Dr.C. Kolappan.**

31. Meeting on "Experience sharing among the southern partners of the USAID, India", organised by AIDS Prevention and control project, New Delhi, 1 September, 2004 – **Dr. Soumya Swaminathan.**

32. Symposium held by the National Academy of Medical Sciences at Chennai, 9-10 September, 2004

    Paper presented: "HIV and MDR Tuberculosis" - **Dr.C.N. Paramasivan.**

33. National Seminar on HIV/TB, TRC, 11-12 September, 2004.

    Papers presented:

    (i) "Extra-pulmonary TB "- **Dr. Rani Balasubramanian.**

    (ii) "Monitoring the course of disease using surrogate markers: TLC as surrogate marker for CD4" - **Dr. P. Venkatesan.**

    Participants : - **Dr. Geetharamani Shanmugam, Ms. Sheila Fredrick, Ms. Chandra Suresh, Ms. Mohanarani Suhadev, Ms. Meenalochani Dilip.**

34. "Policy issues in RNTCP "- Meeting at Central TB division, Nirman Bhavan, New Delhi, 18 September, 2004 - **Dr. Rani Balasubramanian.**

35. International CME on Laboratory techniques and their utility in the diagnosis of tuberculosis, MGIMS, Wardha, 20 September, 2004 - **Dr.C.N. Paramasivan.**

    Papers presented:

    (i) "The true value of recent techniques in the laboratory diagnosis of tuberculosis".

    (ii) "Predicting the efficacy of newer drugs in the treatment of tuberculosis based on laboratory simulation studies".

36. District Level Advisory Board meeting on child line, organized by Dept. of Social Defense, Chennai, 8 October, 2004 – **Dr. Geetharamani Shanmugam.**

37. Workshop on "The present scenario in leprosy, tuberculosis, HIV/AIDS at Gremaltes Hospital, Chennai, 9 October, 2004 – **Dr. Soumya Swaminathan.**

38. "Urban Poverty alleviation programme" - State level convergence workshop organized by TNCDW/TNUDP at Chennai, 13 October, 2004 - **Ms. Sudha Ganapathy, Dr. Geetharamani Shanmugam.**

39. International conference on "Emerging viral infections: Frontiers and challenges", National Institute of Virology, Pune, 13-15 October, 2004 - **Dr. C. Padmapriyadarsini.**

40. "Human rights and health" International study conference - Madras Christian College, Tambaram, 14–16 October, 2004.

    Paper presented:

    "Child health right violation with a focus on child abuse" – **Dr. Geetharamani Shanmugam.**

    Participant **Ms. Chandra Suresh.**

41. 35th World Conference of the Lung Health (IUATLD), Paris, 29 October – 2 November, 2004.

Paper presented:

(i) "Is DST needed in NTPs in low and middle income countries" - **Dr.C.N. Paramasivan.**

(ii) "Assessment of epidemiological impact of DOTS programme in a district of south India - **Mr.P.G.Gopi.**

42. Chaired a session on infectious diseases - Indo-German Sci-Tech Forum, IIT-Madras, Chennai, 3 November, 2004

Paper presented: "Recent advances in the biotechnology of tuberculosis"– **Dr. V.D.Ramanathan.**

43. XXIV conference of Indian society for Probability and statistics and National conference on "Recent advances in statistical theory", Kottayam, 4-6 November, 2004

Invited presentation on "Markov chain Monte Carlo methods in Bayesian inference"- **Dr. P. Venkatesan.** .

44. Third National meeting on TB management in India: "Assessment, diagnosis and treatment", Bangalore, 4-6, November, 2004 – **Dr.K.C.Umapathy, Dr.R. Balambal.**

45. International symposium on Emerging trends in tuberculosis research. International Centre for Genetic Engineering & Biotechnology (ICGEB Campus), New Delhi – 15-17 November, 2004.

Invited plenary talk:

"Molecular epidemiology of *M. tuberculosis*" – **Dr. Sujatha Narayanan.**

Papers presented:

(i) "Induction of apoptosis in THP-1 monocytes by sonicate antigens prepared from the prevalent strains of *M. tuberculosis*" - **Dr. Sulochana Das.**

(ii) "Regulatory role of vitamin D receptor gene variants of *Bsm*I, *Apa*I, *Taq*I and *Fok*I polymorphisms on vitamin D3 modulated immune functions in pulmonary tuberculosis" – **Dr.P. Selvaraj.**

(iii) "Immunological characterization of 27 kDa (MPT51, Rv3803c) protein of *Mycobacterium tuberculosis*" – **Dr. Alamelu Raja.**

(iv) "Construction of recombinant BCG based HIV-1 epitope delivery system" – **Mr.V. Aravindhan.**

46. Workshop on "TB Training Focal Points from high burden countries" - National Institute of Tuberculosis, Bangalore, 16-18 November 2004 – **Dr. Aleyamma Thomas.**

47. CME on tuberculosis - National Academy of Chest Physicians Conference at the Tagore hall, Ahamedabad, 17 November 2004

Paper presented: "Diagnosis and management of extra-pulmonary forms of TB in RNTCP" – **Dr. Rani Balasubramanian.**

48. National Medical College Workshop - AIIMS, New Delhi, 23-24 November, 2004 - **Dr. Rani Balasubramanian.**

49. ICMR workshop in Clinical Pharmacology, by Dept. of Clinical Pharmacology, Seth G.S. Medical College & K.E.M. Hospital, Mumbai, Nov. - Dec. 2004 **– Dr.A.K. Hemanth Kumar.**

50. Royal Tropical Institute, Amsterdam, Netherlands, 29 November – 2 December, 2004

Paper presented: "Health Related Stigma and discrimination" - **Ms. Sudha Ganapathy.**

51. World AIDS day conference by Tamil Nadu AIDS Control Society at Kalaivanar Arangam, Chennai, 1 December, 2004 – **Ms. Mohanarani Suhadev.**

52. 8th international epidemiological association / South East Asia conference, Jhansi, 5-8 December, 2004 -

Papers presented: (i) "On the incubation time distribution and the Indian AIDS data" – **Dr.P. Venkatesan.**

(ii) "Adaptive subspace self-organizing maps in tuberculosis data – **Dr.R. Selvaraj.**

(iii) "Impact of external aid on tuberculosis control programme in India" – **Mr.M. Muniyandi.**

53. Seminar on 'Update on TB Management", Indonesia at Jakarta, 7 December, 2004 -

Paper presented: "The importance of instituting Quality Assurance Program in the laboratory services of TB" – **Dr.C.N. Paramasivan.**

54. 40th Anniversary meeting of US-Japan Co-operative Medical Science program at Kyoto, Japan - 7-10 December, 2004

Paper presented: "Clinical diagnostic algorithm for TB in HIV positive persons"– **Dr. Soumya Swaminathan.**

55. National seminar - Centre for security analysis – Health Security: Disease surveillance, Challenges and Responses in Peninsular India, Image conference hall, Chennai, 14 December, 2004 **– Dr. Rani Balasubramanian.**

56. Panel member for the sessions on Bacteriology and Pathology and Immunology of Leprosy of Post Graduate seminar in SRMC, organized by Damien Foundation India Trust, 14 December, 2004. – **Dr.V.D. Ramanathan.**

57. 31st Annual conference of Indian Immunology Society, Anna University, Chennai, 15-18 December, 2004.

Chairperson for session on Clinical Immunology – **Dr.V.D. Ramanathan.**

Chairperson for session on Oral presentation by young scientists/students **– Dr.P. Selvaraj.**

Papers presented:

(i) "Rationale of conducting simulation experiments with newer anti-TB drugs" – **Dr. C.N. Paramasivan.**

(ii) "Apoptosis of Polymorphonuclear Neutrophils (PMN) and its role in Tuberculosis" – **Ms.P. Supriya.**

(iii) "Modulation of apoptosis in THP-1 cells infected with prevalent strains of *M. tuberculosis*" – **Ms.Priya Rajavelu.**

(iv) "Differential immune response in tuberculous pleuritis" – **Ms.C. Prabha.**

(v) "Impact of HIV on immunology of tuberculosis" – **Dr. Soumya Swaminathan.**

(vi) "Regulatory role of variant genotypes of vitamin D receptor gene on vitamin D3 modulated macrophage and lymphocyte functions" – **Dr.P. Selvaraj.**

(vii) "Perforin positive cells and macrophage phagocytosis with live *Mycobacterium tuberculosis* in pulmonary tuberculosis" – **Ms.D. Nisha Rajeswari.**

(viii) "Interleukin-4 (IL-4) gene polymorphism and IL-4 levels in pulmonary tuberculosis" – **Ms.M. Vidyarani.**

(ix) "Circulating immune complexes in the pathogenesis of tuberculosis" **– Mr.S. Mannivannan.**

(x) "Activation of complement system by gene-disrupted *Mycobacterium tuberculosis*" – **Mr.V. Narayana Rao.**

(xi) "Immunohistochemical demonstration of mycobacterial antigen and complement proteins in tuberculous granulomas" – **Ms.G. Senbagavalli.**

(xii) "Improved diagnosis of pulmonary tuberculosis by detection of serum antibodies against multiple *M. tuberculosis* antigens" – **Mr.D. Anbarasu.**

(xiii) "Purification and biochemical characterization of a serine threonine protein kinase, pknE of *Mycobacterium tuberculosis*" – **Mr. Deepak Jayakumar.**

58. 87th Annual conference of the Indian Economic Association, Banaras Hindu University, Varanasi, 21-23 December, 2004

    Paper presented: "Indian population policy 1950-2000 with special reference to health care" - **Mr.M. Muniyandi.**

59. Attended workshop on R-programming" - Madras University, Chennai, 23 December, 2004 **- Dr. P. Venkatesan.**

60. International conference on recent developments in statistics and applications, Sri Venkateswara University, Tirupathi, 3-4 January, 2005.

    Paper presented: "Mixed effects modeling with Markov chain Monte Carlo methods" - **Dr. P. Venkatesan.**

61. 3rd National conference of Indian Association of Applied Microbiologists. 5-7 January, 2005

    Guest lecture : "Molecular biology of *M. tuberculosis*" - **Dr.N. Selvakumar.**

62. Ranbaxy science foundation, Delhi, 8 January, 2005

    Paper presented: "Reactivation of tuberculosis as evidenced by fingerprinting" – **Dr. Sujatha Narayanan.**.

63. 15th round table conference on "HIV and tuberculosis co-infections", New Delhi, 8 January, 2005

    Paper presented: "Chemoprophylaxis of TB in HIV positive persons"– **Dr. Soumya Swaminathan.**

64. National symposium, Indian Institute of Technology, Chennai, 9 January, 2005

    Paper presented: "Molecular basis of diseases" – **Dr. Sujatha Narayanan.**

65. National nursing congress at SRMC & RI, Chennai, 15-17 January, 2005

    Paper presented: "Plan for categorical data analysis" - **Dr. P. Venkatesan.**

66. Pre-conference workshop/seminar on "Recent advances in survival analysis", JIPMER, Pondicherry, 19-20 January 2005

    Invited presentation: "Non-parametric survival methods" and "Recent advances in survival analysis" – **Dr. P. Venkatesan.**

67. Research Dissemination Workshop –II, organised by World Health Organisation and Tuberculosis Research Centre (ICMR), Chennai during 19-20 January, 2005

    Paper presented : "Improving yield of smear positive pulmonary TB" **– Dr. Aleyamma Thomas**.

68. XXII Annual National Conference of Indian Society for Medical Statistics, JIPMER, Pondicherry - 21-23 January, 2005.

    Papers presented:

    (i) Hidden Markov modules in the analysis of heterogenous biological sequences – **Dr.P. Venkatesan**.

(ii) Quantifying statistical artifacts with neural networks - as a stimulation technique - **Dr. R. Selvaraj.**

(iii) Psychometric analysis of the HIV stigma scale: a south Indian scenario - **Mr. D. Suryanarayanan**.

(iv) Application of propensity scores in handling data with missing values - **Mr. N. Arun Kumar.**

(v) Artificial neural networks for spinal tuberculosis survival data - **Dr. S. Anitha.**

(vi) A logistic regression approach for estimating additional risk of relapse in cavitory TB patients - **Mr. B. Sukumar.**

(vii) Covariate analysis for Tuberculosis Response data – A proportional Hazard Model Approach - **Mr. C. Ponnuraja.**

Participant: **Mr.R. Srinivasan.**

69. Meeting to decide the strategies of the next phase of the World Bank assisted RNTCP at World Bank office, New Delhi, 24-25 January, 2005 – **Dr. Rajeswari Ramachandran.**

70. Seminar on "Responding to realities- Professional social work with a difference". The Institute of Research and Rehabilitation, Department of hand and plastic surgery, Govt. Stanley Hospital, Chennai, 25 January, 2005

Paper presented: "Professional social work with a difference – a research worker's perspective" – **Ms. Sudha Ganapathy.**

71. "Epidemiology of HIV" - Aravind Eye Hospitals, Madurai, 3 February, 2005 – **Dr. Soumya Swaminathan.**

72. 59th National Conference of Tuberculosis and Chest Diseases, LRS Institute of Tuberculosis and Respiratory Diseases, New Delhi, 4-6 February, 2005.

Invited talks : "Laboratory diagnosis of TB. Ensuring quality assurance" – **Dr.N. Selvakumar.**

"Role of serological / immunological assays in the diagnosis of tuberculosis" – **Dr. Alamelu Raja.**

Papers presented:

(i) "HIV-Drug Resistance TB: Global and Indian Scenario" – **Dr.C.N. Paramasivan.**

(ii) "Shortening Short Course Chemotherapy" – **Dr. Rajeswari Ramachandran.**

(iii) "Operational research studies in India" – **Dr. Rani Balasubramanian.**

(iv) "The burden of tuberculosis in India for the year 2000" – **Mr.P.G. Gopi.**

(vi) Feasibility of Community DOT providers for the tuberculosis treatment in HIV infected individuals – **Mrs. Mohanarani Suhadev.**

Participants : **Dr.R. Balambal, Dr. Paulin Joseph.**

73. International course in "Management, Finance and Logistics for TB Control" organized by IUATLD and Indian Institute of Health Management, Jaipur, 7-20 February, 2005.

Paper presented: "RNTCP in India" - **Mr.M. Muniyandi.**

74. International conference on Spectrophysics, Pachayappa's College, Chennai, 9-12 February, 2005 - **Dr. P. Venkatesan.**

Invited presentation:

(i) "Markov chain Monte Carlo methods for spectral data"

Paper presented:

(ii) "A comparative study of rank reduction multivariate calibration algorithms applied to classification of diabetic serum from normal based on Mid-IR spectral data"

75. International conference on Functional genomics for Novel Vaccine and drug design against mycobacterial infection (VDMI), IIT, Kharagpur, 11-12 February, 2005 – **Dr. Alamelu Raja, Mr. V. Aravindhan, Mr. Deepak Jayakumar, Mr. D. Anbarasu, Mr. S. Manivannan, Mr. V. N. Narayana Rao, Dr. Lakshmi Prashanth, Mr. Madhan Kumar, Mr. Ramana Rao, Mr. Dinakar.**

76. Annual Courses in Clinical Neurosciences meeting at ITC Hotel Park Sheraton and Towers, Chennai, 14 February, 2005

    Paper presented: "TBM – Indian perspective" - **Dr. Rajeswari Ramachandran.**

77. National Symposium on Emerging Infections in India - Current Perspectives, Vel's Colege of Science, Chennai, 14-15 February, 2005

    Invited talk : "Laboratory diagnosis of pulmonary tuberculosis" – **Dr.N. Selvakumar.** .

78. Short course on "Qualitative Research Methodology" organized by the Tuberculosis Research Centre and University of Alabama (UAB), Birmingham USA at Chennai, 15-17 February, 2005 - **Ms. Beena E. Thomas, Ms. Mohanarani Suhadev, Mr.D. Suryanarayanan, Mr.R. Srinivasan, Ms. Chandra Suresh, Ms. Niruparani Charles.**

79. Second Scientific conference of the Indian Society for Histocompatibility and Immunogenetics, AIIMS, New Delhi, 17-19 February, 2005 –

    (i) Invited talk : Vitamin D receptor gene variants and immunity to tuberculosis – **Dr.P. Selvaraj.**

    (ii) Presentation : Promoter region polymorphism of IL-8 gene and IL-8 production in pulmonary tuberculosis" – **Mr.S. Prabhu Anand.**

80. Dr. P.V. Benjamin Memorial Oration - 29th A.P.State Tuberculosis and Chest Diseases Conference organized by Department of Pulmonary Medicine, Govt. General & Chest Hospital, Hyderabad, 19-20 February, 2005

    Paper presented: "Problem of HIV and Tuberculosis – Indian perspective" - **Dr. Rajeswari Ramachandran.**

81. 12th conference on Retroviruses and Opportunistic infections, Boston, USA, 22-25 February, 2005

    Paper presented: "Randomised clinical trial of 6-month vs 9-month anti-tuberculosis treatment and HIV positive individuals with pulmonary tuberculosis.- **Dr. Soumya Swaminathan.**

82. Conference of North American Region of the International Union against TB and Lung Disease, Canada, 23-26 February, 2005

    Paper presented: "Stigma and barriers: Does a combined programme make matters better or worse in high HIV-prevalent countries"- **Dr. Soumya Swaminathan.**

83. AIDS awareness programme to Southern Railway employees women's wing in connection with UN International Women's Day, Chennai, 24 February, 2005

    Talk on "AIDS Control" - **Ms. Mohanarani Suhadev.**

84. Workshop on "Child line" for the college students sponsored by National Initiative for child protection. Chennai, 25 February, 2005

Paper presented: "Child Rights and Child Welfare Committees" - **Dr. Geetharamani Shanmugam.**

85. FORUM 2005 –organized by Sundaram Medical Foundation, Chennai, 26-27 February, 2005
    Guest lecture: 'Do we have diagnostic markers for tuberculosis?' – **Dr.M.S. Jawahar.**
86. Workshop on Medical paper writing for publication organised by Lancet and ICMR - CMC, Vellore, February, 2005 – **Dr. C.Padmapriyadarsini.**
87. Indo-Australian conference at Manipal, 1-3 March, 2005.
    Paper presented: "Biotechnology in infectious diseases" – **Dr. Sujatha Narayanan.**
88. "Advocacy to control TB internationally", New Delhi, 2 March, 2005 – **Dr.N. Selvakumar.**
89. 4th Annual Regional Meeting. Building Communities of Practice for Achieving Millenium Development Goals. One World South Asia. New Delhi, 3-4 March, 2005 – **Dr.N. Selvakumar.**
90. Kerala State task force for medical colleges involvement in RNTCP - The Residency Hotel, Trivandrum, 9 March, 2005
    Paper presented: "Scientific basis of DOTS, Extra-pulmonary TB and Paediatric TB"– **Dr. Rani Balasubramanian.**
91. Workshop organised by Department of Social Defence, sponsored by National Institute of Social Defense, Chennai, 10-12 March, 2005
    Paper presented: "Juvenile Justice Act" – **Dr. Geetharamani Shanmugam.**
92. National seminar on Gender Mainstreaming in Budget organized by Dept of Applied Economics Sri Padmavati Mahila Visvavidyalayam, Women's University, Tirupathi, 11-12 March, 2005
    Paper presented: "Gender budget initiative with special reference to women development in India" – **Mr.M. Muniyandi.**
93. National seminar on Epidemiology of communicable diseases, organized by Madras Diabetes Research Foundation & University of Alabama at Birmingham, at Chennai, 11-13 March, 2005
    Lecture: 'Risk factors for chronic obstructive pulmonary disease' - **Dr.M.S. Jawahar.**
94. Live programme on All India Radio, Chennai as a part of World TB day celebrations 2005 - 20 March, 2005 - **Dr. Rani Balasubramanian, Ms. Sudha Ganapathy.**
95. "Extra-pulmonary TB" - "TIPS 2005- Tuberculosis in Practice- Scientific approach" as a part of World TB day celebrations 2005, Hotel Savera, Chennai, 20 March, 2005 - **Dr. Rani Balasubramanian.**
96. "Experience Sharing on MDR TB' - Central TB Division, Ministry of Health & Family Welfare, Govt. of India, New Delhi, 21 March, 2005 - **Dr. Rajeswari Ramachandran.**
97. Attended Mw vaccine meeting at Ministry of Science & Technology, Department of Biotechnology, New Delhi, 22 March, 2005 **- Dr. Rajeswari Ramachandran.**
98. Seminar on Recent trends in research in statistics at Manonmaniam Sundaranar University, Tirunelveli, 23-24 March, 2005
    Paper presented: "Recent trends in research in medical statistics" - **Dr. P. Venkatesan.**
99. National workshop on Empirical research in social sciences, Chennai, 24-25 March, 2005
    Paper presented: "Multivariate statistical methods for social sciences" – **Dr. P. Venkatesan.**

Special Assignments

Dr.C.N. Paramasivan

Temporary Advisor, WHO: WHO/SEARO, Workshop on drug resistance surveillance in tuberculosis for the TB Laboratory Directors of the SEARO, held at National Tuberculosis Institute, Bangalore 21-26 June, 2004

Temporary Advisor, WHO : WHO/SEARO, Regional Training course on TB Control, 16-20 August, 2004. National Tuberculosis Institute, Bangalore.

Consultant IUATLD Paris : Served as IUATLD consultant for the Union of Myanmar, 1-10 September, 2004

Temporary Advisor, WHO : Served as a member of the Subgroup on Laboratory strengthening (SGLS), including supra National Reference Laboratory Networking held at Paris 1-2 November, 2004.

Temporary Advisor, WHO : Reviewed the performance of laboratory services of Indonesia 29 November – 7 December, 2004.

Temporary Advisor, WHO : WHO/SEARO Technical Working Group Meeting on Tuberculosis 8-9 February 2004.

IUATLD, Paris : Chair Person: Session on MDR TB-35th IUATLD World Conference on Lung Health, held at Paris, 29th October-1st November 2004.

Elected to the Chair of the Bacteriology section of the International Union Against Tuberculosis and Lung Diseases (IUATLD), Paris for a period of four years at the 35th Global meeting on Lung Health held at Paris in October, 2004.

Dr.V.D. Ramanathan

- Consultant for the ILEP Nerve Function Impairment and Reaction in leprosy project.

Dr. Ranjani Ramachandran

- Temporary Advisor, WHO/SEARO workshop on drug resistance in tuberculosis for TB laboratory directors of the SEARO held in NTI, Bangalore 21-26 June, 2004.
- Member of organizing committee of the Symposium on HIV TB funded by the National Academy of Medical Sciences, New Delhi.

Dr. N. Selvakumar

- IUATLD - National Consultant for EQA of sputum AFB microscopy in India. August, 2004-November, 2005.
- SAC member to CLTRI, Chengleput, Chennai.
- Temporary Advisor to Regional Director, SEARO, New Delhi. 21-24 September, 2004. Inter-country work-shop on TB surveillance, monitoring and evaluation in SEA countries.
- Training of WHO-RNTCP Consultants on new initiatives in RNTCP. 28-30 March, 2005. Suraj Kund, New Delhi. (Facilitator)

Dr. P. Selvaraj

- Executive Council Member, Indian Society for Histocompatibility and Immunogenetics, New Delhi.
- External Examiner for M.Sc., Human Genetics and M.Sc., Biotechnology.

  Sri Ramachandra Medical College & Research Institute,Chennai.
- Reviewer for International and National journals (Reviewed one paper for each journal)–
  i. Indian Journal of Experimental Biology (National Journal)
  ii. Am. Rev. Resp. Crit Care & Med (International Journal)
  iii. Journal of Leucocyte Biology (International Journal)

Dr. Sujatha Narayanan

- Doctoral committee member for two Ph. D. students from the Department of Biotechnology, Anna University
- Member of Advisory committee for syllabus (Biochemistry) of Meenakshi College, Chennai

Dr. P.Venkatesan

- Chairman – Board of Studies - M.Sc., (Bioinformatics) - Sri Ramachandra Medical College & Research Institute (Deemed University), Chennai
- Member - Board of Studies - M.Sc., (Human Genetics) & B.Sc., (Biomedical Sciences)- Sri Ramachandra Medical College & Research Institute (Deemed University), Chennai
- External Examiner - University of Madras.
- External Examiner - M.Sc., (Human Genetics), M.Sc., (Bioinformatics), M.Sc., (Biotechnology). Sri Ramachandra Medical College & Research Institute (Deemed University), Chennai
- Member- Editorial Board: Journal of Pure and Applied Spectrophysics.
- Coordinator-Pre-Conference workshop on "Recent Advances in Survival Analysis" in the 22nd ISMS conference at JIPMER, Pondicherry.
- Served as Judge for selecting "Best Poster Presentation" at the 22nd ISMS conference at JIPMER, Pondicherry and 8th IEA/SEA International Conference at Jhansi.
- External Examiner - Ph.D Public viva-voce examination, Karnataka University, Dharwar.
- General Secretary - Indian Society for Medical Statistics (ISMS).
- Member - Executive Committee: International Biometric Society (IR).

Ph.D Scholars - Students

Students who have registered (full-time) for their Ph.D. programme at the University of Madras

Name	Source of Funding	Title	Supervisor-Guide
Ms.R. Priya	ICMR	Apoptosis of human monocytes and macrophages by *M. tuberculosis* and its implications on cell mediated immune response	Dr. Sulochana Das
Ms.C. Prabha	ICMR	Immune response in tuberculosis: TH1/TH2 paradigm	Dr. Sulochana Das
Ms. Nisha Rajeswari	ICMR	Influence of HLA-DR antigens on macrophage phagocytosis, perforin positive cells and cytokine response in pulmonary tuberculosis	Dr. P. Selvaraj
Ms.M. Vidyarani	ICMR	Regulatory role of variant genotypes of vitamin D receptor gene on vitamin D_3 modulated cytokine response in pulmonary tuberculosis	Dr. P. Selvaraj
Ms.G. Senbagavalli	ICMR	Serum and tissue complement profile in tuberculosis	Dr. V.D. Ramanathan
Mr.K. Alagarasu	ICMR (Project)	Polymorphism studies on cytokine, chemokine, vitamin D receptor and mannose binding lectin genes in HIV and HIV-TB patients	Dr. P. Selvaraj
Mr.S. Raghavan	ICMR (Project)	Human Leucocyte Antigen (HLA) polymorphism studies in HIV and HIV-TB patients	Dr. P. Selvaraj
Ms.G. Radha	CSIR	Cloning, expression and characterization of a serine threonine protein kinase, *Pkn*I of *M. tuberculosis* H37Rv	Dr. Sujatha Narayanan
Mr.V. Aravindhan	CSIR	Construction of recombinant BCG based HIV-1 PND eiptope delivery system	Dr. P.R. Narayanan
Mr. Deepak Jayakumar	CSIR	Cloning, expression and characterization of a serine threonine protein kinase, *Pkn*E of *M. tuberculosis* H37Rv	Dr. Sujatha Narayanan
Dr.P.L. Natarajan	CSIR	Cellular immunology of TB and HIV/TB	Dr. Sujatha Narayanan
Mr.D. Anbarasu	CSIR	Identification and characterization of immuno-reactive T-cell antigens of *M. tuberculosis*	Dr. Alamelu Raja
Mr.S. Manivannan	CSIR	The role of complement activation and antibody in the early interaction of *M. tuberculosis* and macrophages	Dr.V.D. Ramanathan

Name	Source of Funding	Title	Supervisor-Guide
Mr.V. Narayana Rao	CSIR	Complement activation by strains of mycobacteria wild type and gene disrupted *M. tuberculosis* and recombinant BCG	Dr. V.D. Ramanathan
Mr.S. Prabhu Anand	CSIR	Regulatory effects of vitamin D_3 and vitamin D receptor genotypes on macrophage and lymphocyte functions in pulmonary tuberculosis	Dr. P. Selvaraj
Ms.G. Chandra	UGC	Studies on the influence of vitamin D_3, and the polymorphic variants of vitamin D receptor gene on the immune functions to *M. tuberculosis* antigens in pulmonary tuberculosis	Dr. P. Selvaraj

Standing: (L-R) - I row — Mr. S. Dhinakaran, Dr. T. Lakshmi Prashanth, Mr. D. Anbarasu, Mr. S. Manivannan, Mr. V. Narayana Rao, Mr. S. Raghavan

Standing: (L-R) - II row — Ms. Harini Laxminarayan, Mr. S. Basirudeen, Mr. K. Alagarasu Mr. S. Prabhu Anand, Mr. V. Aravindhan, Mr. Deepak Jayakumar, Mr. P.V. Ramana Rao, Dr. P.L. Natarajan, Ms. R. Priya

Sitting: (L-R) — Ms. A. Nusrath Unissa, Ms. G. Senbagavalli, Ms. Aparna Josephine Christy, Ms. Lakshmi Rajesh, Ms. C. Prabha, Ms. P. Rajashree, Ms. M. Vidyarani, Ms. P. Supriya, Ms. D. Nisha Rajeswari

Ph.D. Scholars – Staff

Staff who have registered (part-time) for their Ph.D. programme

Name	Title	Supervisor-Guide
Ms. Beena E. Thomas	Psychosocial and sexual impact of HIV/AIDS- Gender differentials	Dr. K. Shanmugavelayutham Loyola College, Chennai.
Mr. M. Muniyandi	The economic and health status of of tuberculosis patients covered under DOTS and non-DOTS programme in south India	Prof. G Rama Rao International Institute for Population Sciences, Mumbai
Ms. Mohanarani Suhadev	Family Burden of HIV/AIDS	Dr. Udaya Mahadevan Loyola College, Chennai..
Ms. Sulochana Somasundaram	*In vitro* studies of quinolones against *M. tuberculosis*	Dr. C.N. Paramasivan
Dr. Ranjani Ramachandran	Opportunistic infections in HIV/TB patients	Dr. C.N. Paramasivan
Mr.L. Prabhakaran	Isolation, characterization and construction of luciferase reporter phage for diagnosis of *M. tuberculosis*	Dr. P.R. Narayanan
Ms. Gomathy Sekar	Optimizing sputum microscopy to detect AFB	Dr. N. Selvakumar
Ms.N.S. Gomathy	Development of rapid methods for Diagnosis and drug susceptibility testing of *M. tuberculosis*	Dr. Vanaja Kumar
Ms. Nalini Sundar Mohan	Measurement of drug resistance in tuberculosis	Dr.C.N. Paramasivan
Ms. Silambu Chelvi	Antimycobacterial bioactive compounds from marine actinomycetes	Dr. Vanaja Kumar
Mr.C. Ponnuraja	Frailty models	Dr.P. Venkatesan
Mr.N. Arunkumar	Causal inference	Dr.P. Venkatesan

Our thanks to

- Prof. N. K. Ganguly, Director-General, ICMR for continued encouragement and unstinted support.

- DGHS & NACO (MOH, GOI), WHO, USAID, NIAID (USA), UCLA, IAVI, Sir Ratan Tata Trust, World Food Programme and TNSACS that supported research projects relevant to the health needs of our country by their timely funding.

- Ministry of Health, Government of India in general and the CTD in particular for according us the status of the "most favoured partners" in all aspects of TB control and research.

- Corporation of Chennai, staff of collaborating hospitals and the Government of Tamil Nadu for their continued support.