TUBERCULOSIS RESEARCH CENTRE

CHETPUT MADRAS-600 031

REPORT ON RESEARCH ACTIVITIES DURING 1995

INDIAN COUNCIL OF MEDICAL RESEARCH
NEW DELHI

TUBERCULOSIS RESEARCH CENTRE
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PREFACE

During this year, the Centre continued to evolve methods to operationalise the regimens developed here to optimise the efficiency of the programme in achieving higher cure rates and better drug compliance. Accordingly, studies on the utilisation of sub-centres for drug delivery and its impact on case-holding and on the feasibility of involving Non-Governmental Organisations in tuberculosis control are in progress.

The results of clinical studies which were completed during this period have been encouraging and showed that split double drug combinations were effective and had the possibility of helping to increase patient compliance by reducing adverse reactions. The results also showed that in brain tuberculosis short course chemotherapy could be highly effective.

Clinical studies on further shortening the treatment using ofloxacin containing regimens, evaluation of treatment regimens for failure and relapse cases, quality of life measurement at the end of treatment, chemotherapy for pulmonary tuberculosis in children, lymphnode tuberculosis, abdominal tuberculosis, cutaneous tuberculosis and multibacillary as well as paucibacillary leprosy are in progress.

In conjunction with clinical studies, the laboratory studies have been augmenting our efforts in developing better regimens at a time when the problem of multidrug resistant tuberculosis and HIV associated tuberculosis are on the rise. The bactericidal action of the quinolone, ofloxacin, and the beta-lactam antibiotic / beta-lactamase inhibitor combination, sulbactam / ampicillin are being evaluated. Research is in progress to understand the mechanism of action of pyrazinamide and to develop quicker

methods for determining the early bactericidal activity of antituberculosis drugs, drug sensitivity testing using simpler method such as slide culture and advanced techniques such as luciferase reporter phage assay.

The importance of microsomal oxidases, cytokine profiles and HLA in tuberculosis are also being analysed. Neopterin level was evaluated as an indicator of cell mediated immune response in tuberculosis. Laboratory studies are being continued on the development of tools for early and specific diagnosis of tuberculosis through recombinant DNA technology. Studies are also being carried out on the immunopathology of tuberculosis and in the development of an experimental model for fibrosis.

Apart from a major ongoing study on the development of surveillance methodology for tuberculosis, a multicentric study involving major city hospitals to develop diagnostic criteria in childhood TB is in progress. The longitudinal follow up of HIV infected individuals and surveillance of HIV infection among tuberculosis patients is being continued.

The tubercle bacilli and environmental mycobacteria isolated from this region are being characterised using molecular biological tools. Laboratory and animal model studies on the environmental mycobacteria in this region have shown that plasmid profiles could be useful markers and the environmental mycobacteria could induce modulation of immune response to BCG.

The results of the study on the evaluation of the combination of diethylcarbamazine and ivermectin for lymphatic filariasis are also encouraging. The usefulness of DEC enriched salt in the prevention of adenolymphangitis (ADL) is in progress. Studies for estimating the typhoid fever in the community as a prelude to an

Indo-US collaborative research programme with a new antityphoic vaccine is ongoing.

Like previous years, the Centre conducted several training programmes, workshops and the scientists of this Centre participated in several national and international conferences and won prizes and awards.

The Centre is in the process of establishing a national data base on tuberculosis with the assistance of National Informatics Centre. The 'state of art' facility available at the Centre's library provides speedy literature search to the end users. Periodic compilation of 'TB alert services' and TRC News Bulletin help in highlighting and disseminating of diverse aspects of tuberculosis research undertaken by this Centre and elsewhere.

The research activities presented here were initiated and carried out under the guidance of Dr.R.Prabhakar, our Director till September 1995. During his tenure as Director, the calibre of work carried out at this Centre was uniformly high and compromises were not made at any level which resulted in the Centre gaining greater recognition. We would like to place on record our gratitude for the role he has played in guiding the research activities of this Centre for well over a decade.

In conclusion, I wish to express my deep sense of gratitude for the untiring efforts of my colleagues at this Centre in carrying out high quality research during this period. I also express my sincere thanks to the technical and administrative staff of this Centre for their able support.

Dr. C.N.Paramasivan
Officer-in-Charge

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Mr.P.R.Somasundaram	Statistics	Former Deputy Director, (Sr.Gr.), Tuberculosis Research Centre, Madras.

Prof. K.V.Thiruvengadam	Medicine	Former Professor of Medicine, Madras Medical College, Madras.
Dr.S.Thyagarajan	Ophthalmology	Former Professor of Ophthalmology, Government Rajaji Hospital, Madurai.
Dr. N.S.Venugopal	Ophthalmology	Former Superintendent, Government Ophthalmic Hospital, Madras.

OPERATIONAL RESEARCH STUDIES - IN PROGRESS

Utilisation of sub-centres for drug delivery and its impact on case-holding

(Ongoing study, 1993-96)

Patients' poor compliance for drug intake under programme conditions is attributed to many reasons and one important factor identified is the inability to attend PHC due to long distance of PHC from patients' residence and consequent loss of wages. In this study, drug delivery was organised through the sub-centres situated closer to the patient's residence as a measure to improve compliance of patients. Twelve PHCs in West Godawari district of Andhra Pradesh were randomly selected for the study and were further randomly allocated to the intervention(6) and non-intervention (6) areas. These centres were distributed in tribal, upland and delta areas. As a preliminary measure, training on all aspects of tuberculosis and the programme was given to the PHC staff including pharmacists and MPWs incharge of sub-centres.

In the study centres when a treatment card was opened, for all newly diagnosed cases, the option of collection of drugs was given to the patient; he was asked to collect either from the main PHCs or sub-centres. The MPW was asked to issue the drugs to the patients on a weekly basis and in case of default, MPW will do the defaulter chasing by sending a message or by personal visit. In control centres, the drug supply was through main PHC only.

The study population consists of 85 patients in study centres and 36 in control centres; 58% in study centre opted for treatment at PHC and 42% at sub-centres. All patients in control centre, collected drugs from the main PHCs. In the study area, only 47% had collected more than 80% of the prescribed treatment at the PHC as compared to 92% at the sub-centre. In

the control centre the treatment completion rate was 47%. Fifty percent of the patients were lost in the study centre who opted for treatment at PHC in contrast to 3% among sub-centre patients; 50% were lost in the control centre.

It was observed that it was feasible to supply drugs at sub-centres and the completion rate at the sub-centre was high (92%). The proportion of lost cases was also negligible (3%). The study is in progress.

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Feasibility of involving Non-Governmental Organisations (NGOs) in tuberculosis control

(Ongoing study, 1994-97)

The Tuberculosis Research Centre in collaboration with the Tamilnadu Slum Clearance Board has entered into a network of working with various NGOs to explore the feasibility of involving the latter in tuberculosis control activities.

The major thrust areas of this strategy will be,

1) training of grass-root level workers of the NGOs on tuberculosis control activities in order to
   a) communicate to the public through information and awareness campaigns on tuberculosis,
   b) equip them with skills necessary to identify chest symptomatics and
   c) organise health camps to screen for chest symptomatics.

The outcome will be the dissemination of proper information and training on tuberculosis to the grass-root level workers of the NGOs who in turn can take the initiative in spreading the

information to the communities in which they work.

2) active collaboration between TRC and the NGOs in tuberculosis control activities with reference to case finding and case holding.

Activities: The training programmes on tuberculosis for grass root level workers of various NGOs was inaugurated on 21.12.1994. Up to December 1995, 12 training programmes have been conducted. A total of 297 participants, comprising of programme development officers, community development organisers, health workers, multipurpose workers, AIDS educators, balwadi teachers and animators have been trained. Seven community awareness campaigns have also been organised in different areas of Madras city.

As a result of our training programmes, a total of 114 chest symptomatics have been referred to Tuberculosis Research Centre for investigations. Nine of these have been diagnosed as cases of tuberculosis and started on treatment.

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CLINICAL STUDIES - COMPLETED

Six-month regimen for pulmonary tuberculosis with 2 double-drug combinations on alternate days for the first two or three months

(Completed study, 1990-95)

Several highly effective short-course chemotherapy regimens of 6-8 months duration have been evolved for the treatment of pulmonary tuberculosis and in most of these regimens, four drugs, namely, rifampicin, isoniazid, pyrazinamide and streptomycin or ethambutol are given together in a single dose, either daily or intermittently. The number of tablets/capsules to be consumed in a single dose is therefore large and the incidence of adverse reactions such as arthralgia and jaundice is high with daily regimens. The Centre is investigating, both at Madras and its unit at Madurai, a regimen of rifampicin and ethambutol on one day and isoniazid and pyrazinamide on the next day, each combination given thrice a week for the first 2 or 3 months, followed by rifampicin and isoniazid twice a week for the next 4 and 3 months, respectively; so that, the toxicity is expected to be low, while the high level of efficacy is unlikely to be affected. These two regimens are to be compared with a control regimen of rifampicin, isoniazid, pyrazinamide and ethambutol given together in a single dose, thrice a week for the first 2 months, followed by rifampicin and isoniazid twice a week for the next 4 months. Intake to this study has been completed.

The percentage of culture negativity based on 3 sputum specimens per month for patients with initially drug sensitive organism showed that, the sputum conversion was similar in all the three regimens.

Favourable response at the end of treatment was similar in all the 3 regimens. Adverse reactions were not a serious problem and was similar in all the 3 regimens.

All patients are being followed up for a period of 5 years.

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Controlled clinical trial of fully oral short-course regimens in Madras and Madurai: follow-up phase

(Completed study, 1986-95)

Earlier studies at this Centre have shown that short-course regimens of 5 to 7 months' duration are highly effective in the treatment of sputum-positive pulmonary tuberculosis. All these regimens were fully supervised, included intramuscular streptomycin and were studied in patients who had not received significant previous chemotherapy. These conditions are difficult to apply in the field and hence, a controlled clinical trial has been undertaken to investigate fully oral regimens of varying duration, rhythm of drug-administration, frequency of attendance and supervision of drug administration at the Centre and its unit in Madurai. The regimens investigated include :

1 .$2EHRZ_7$(ow)/$6EH_7$(tm) : Fully unsupervised 8-month regimen.

2.$2EHRZ_2$/$4EHR_2$(tw/ow) : Fully/partially supervised 6-month regimen.

3. $2HRZ_2$/$4HR_2$(tw/ow) Fully/partially supervised 6-month regimen.

All patients have completed treatment and the results at the end of chemotherapy have been presented in 1991 annual report. Patients with bacteriologically quiescent disease are being followed up for relapse. Among patients completing 52/54 months of follow-up, 8%, 13% and 13% of patients with initially drug sensitive organisms and 11 %, 26% and 15% with initially drug resistant organisms in the three regimens, respectively, have had a bacteriological relapse requiring treatment. Two thirds of the relapses have occurred during the first 3-6 months after stopping treatment.

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Collaborative study of brain tuberculoma: follow-up phase

(Completed study, 1992-95)

As mentioned in previous annual reports (1990-94), the Centre is carrying out a collaborative study of brain tuberculoma with the Institute of Neurology, Government General Hospital (Prof. Ramachandran), Madras and Railway Hospital (Prof. Zaheer Sayeed), Perambur.

The objects of this study are:

1. to evaluate the efficacy of short course regimens for treating tuberculoma of the brain and

2. to study the CT scan appearance, before, during and at the end of chemotherapy and upto 60 months after the start of treatment.

A secondary objective was to study the role of surgery in the treatment of brain tuberculoma.

The patients admitted to the study were randomly allocated to one of the following 9-month regimens:

Regimen I : $3RHZ_7/6RH_2$(daily)

Regimen II : $3RHZ_3/6RH_2$ (intermittent)

All patients have completed treatment and were followed up for a period of 5 years and none of them had relapsed.

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A double blind study to evaluate the safety, tolerability and efficacy of different combination of diethyl-carbamazine (DEC) and ivermectin

(Completed study, 1993-95)

The objectives of this study were:

To investigate, in patients with asymptomatic **W. bancrofti** microfilaremia, the efficacy, tolerability, interaction laboratory and clinical safety of single administrations of ivermectin/DEC combinations at the following dosage levels, 20 µg/kg + 6mg/kg; 20 µg/kg + 12 mg/kg; 200 µg/kg + 6 mg/kg and 200 µg/kg + 12 mg/kg. In addition a concurrent open trial to be carried out on two groups of asymptomatic microfilaremics who will be treated with either a single dose of 400 µg ivermectin or a single dose of 6 mg/kg of DEC.

Eighty-eight asymptomatic male microfilaremics in the age group 18-65 were enrolled in this study. Of these, 68 have been enrolled in the ivermectin-DEC combination double blind study while the remaining 20 participated in an open trial, receiving single doses of ivermectin or DEC. Their microfilaria (mf) levels ranged from 100 to 4500 mf/ml. Seventy-six patients have

completed 1 year of follow-up while all the 88 have completed six months. In all patients in the double blind study microfilaria levels reached zero by the 5th day and at follow up at the first month the majority of the patients did not show any reappearance of microfilariae. At 6 months 44 of the 61 patients who were tested had no reappearance of microfilariae. At the end of the first year of follow up of the 61 patients in the double blind study who were tested 35 had no microfilariae in circulation. In contrast a majority of the patients in the open trial were positive for microfilariae even at 6 months of follow up.

Adverse reactions which were seen in previous studies were observed in the present study also. These included fever, headache, myalgia and cough. Scrotal reactions and postural hypotension were also seen in a few patients. None of the reactions were severe enough to warrant any special treatment and were generally managed using symptomatic therapy.

In all patients on combination drug therapy mf levels reached zero by the fifth day and at one month the majority of the patients did not show reappearance. At six months 72% continued to be mf negative. At one year, the mf levels were between 1 to 3% of pre-treatment levels while 59% had no mf in circulation. No significant differences were observed between the four combinations in terms of efficacy and safety. In the open study the mf levels ranged from 13% (Iver) to 15% (DEC) of pre-treatment levels at 12 months. Also, 90% of these patients were positive for mf. Adverse reactions which occurred were not severe enough to warrant any special treatment. It was concluded that a combination drug therapy with ivermectin and DEC is superior to the use of these drugs given singly.

Pharmacokinetics were carried out on 20 patients who were part of the ivermectin DEC double blind study.

CLINICAL STUDIES - IN PROGRESS

3-5 month regimens containing ofloxacin in the treatment of sputum positive pulmonary tuberculosis

(Ongoing study, 1995-98)

Several effective 6-month short course regimens given either daily or intermittently have been evolved in the treatment of sputum-positive pulmonary tuberculosis. One of the main problems encountered in implementing these regimens in the program has been poor treatment completion. With the 6-month regimens, treatment completion reported is around 50% as against 30% with 12-18 month regimens.

With the advent of another powerful bactericidal drug, ofloxacin, which is reported to be as powerful as rifampicin and isoniazid and superior to streptomycin in terms of bactericidal activity, the Centre is currently undertaking a study to find out whether the duration of treatment can be further shortened to, say 3 or 4 months. In an earlier study, a 3 month regimen of SHRZ, all given daily, was near 100% effective in patients with initially drug sensitive organisms and 18% of these patients had a bacteriological relapse during a 5-year follow-up. Patients with sputum-positive pulmonary tuberculosis with previous chemotherapy not exceeding 2 weeks, are randomly allocated to one of the following regimens:

1. 3OHRZ/-
2. 3OHRZ/1RH_2
3. 3OHRZ/2RH_2
4. 2OHRZ/2RH_2

All drugs are given under supervision in the clinic. The study is being undertaken at Madras and the Madurai unit. The study is in progress.

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Treatment regimens for patients who fail or relapse on short course chemotherapy

(Ongoing study, 1987)

Pulmonary tuberculosis patients who have been treated with short course regimens and who (i) show a serious clinical deterioration, (ii) have a persistent radiographic deterioration, (iii) have an unfavourable bacteriological response, or (iv) have a bacteriological relapse requiring retreatment are prescribed an appropriate regimen depending on the last available drug sensitivity test results.

The chemotherapeutic regimens are as follows:

1. $3EmbHRZ_2/6/9RH_2$ for patients with organisms sensitive to isoniazid and rifampicin.

2(a). $6SREmbZ_2/6REmbZ_2$ for patients with organisms resistant to isoniazid

(b). $6KREmbZ_2/6REmbZ_2$ for patients with organisms resistant to streptomycin and isoniazid

3(a). $3S_3EmbEthZ_2/9EmbEthZ_7$ for patients with organisms resistant to isoniazid and rifampicin

(b). $3K_3EmbEthZ_2/9EmbEthZ_2$ for patients with organisms resistant to streptomycin, isoniazid and rifampicin

So far 103 patients have completed treatment in Reg. 1, 43 in Reg.2(a), 46 in Reg. 2(b), 31 in Reg. 3(a) and 44 in Reg.3(b).

Among patients who had received more than 75% of chemotherapy, 92.5% in Reg.1, 74% in Reg.2(a) and (b), 43% and 41% in Reg.3(a) and (b) had a bacteriologically quiescent disease at the end of treatment. Thus, patients with organism resistant to rifampicin along with isoniazid alone or isoniazid and streptomycin pose a problem in management. The study is in progress.

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Quality of life measurements at the end of treatment for patients treated for pulmonary tuberculosis

(Ongoing study 1993-96)

Quality of life is a multidimensional concept concerned with the impact of physical symptoms and side effects of treatment on patients' functioning and psychosocial wellbeing. It is generally assumed that treatment of pulmonary tuberculosis with potent chemotherapeutic agents and making them non-infectious will be accompanied by improved health and well being. However, disturbances in physiological functions persist, even though the precipitating event (bacillus) has been eliminated. Activities that may be disturbed by disturbances in physiological functions are physical, social, emotional, intellectual, economic and spiritual. Impairment is an abnormality of physiologic functions and disability is the effect of Impairment on patients life. Quality of life measurements utilising general health questionnaires such as the Sickness Impact Profile and Quality of Wellbeing Scale (J Chronic dis 1984, 37: 85-95) are designed for application to a very wide range of diseases and hence there are limitations regarding their

precision and sensitivity. Hence, it has been suggested that disease - specific questionnaire will provide a more precise and sensitive measurement of quality of life than a general index. Two quality of life measures developed for chronic lung diseases are Chronic Respiratory Questionnaire and St.George's Respiratory Questionnaire (Thorax 1987; 42: 773-78).

The objectives of the study are:

1. to assess quality of life measurements using Disease - specific questionnaire (Chronic Respiratory Questionnaire) in patients who had undergone treatment for pulmonary tuberculosis.

2. to compare the Disease - specific questionnaire (Chronic Respiratory Questionnaire) with 6-minute walking test and pulmonary function tests in patients treated for pulmonary tuberculosis.

A group of 200 pulmonary tuberculosis patients treated with short-course chemotherapy will be included in the study if they had no previous history or any other illness and had not received any anti-tuberculosis treatment at the time of initiation of short course chemotherapy. Initial clinical and respiratory symptom assessment including chest x-rays are done using "Questionnaire of the European Community For Coal and Steel on Respiratory symptoms". Disease - specific quality of life measurement is assessed using chronic respiratory questionnaire.

The following objective measurements of impairment are also undertaken:

1. Pulmonary function tests: Flow-volume loops are recorded in each patient using Morgan Transfer Test Model C. At least 3 acceptable readings are obtained from each patient as per

American Thoracic Society recommendations (Am Rev Respir Dis 1987; 136: 1285-96).

2. Six-minute walking test: This test (JE Cotes, Lung Function, 5th Edition 1993) is carried out in a level corridor. Each patient is instructed to cover as much ground as he could on foot for 6-minutes and to keep going continuously if possible, but not to be concerned if he had to slow down or stop to rest. The patient's aim should be to feel at the end of the test that he could not have covered more ground in the time. An investigator accompanies the patient, acting as timekeeper and giving encouragement as and when necessary. The actual distance covered is measured.

So far 137 patients have been admitted. The study is in progress.

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Short course chemotherapy for pulmonary tuberculosis in children

(Ongoing study, 1992-96)

Evaluation of various therapeutic regimens for the treatment of pulmonary tuberculosis has been the major point of focus for more than 3 decades. The accent has been on Short Course Chemotherapy (SCC). Though there are many reports available on SCC in adults, information regarding the same for tuberculosis in children is limited. Hence this Centre has started an SCC study in pulmonary tuberculosis in children, in collaboration with the Institute of Child Health & Hospital for Children (ICH & HC), Egmore, Madras (Director: Dr. Merlyn Joseph). In brief, patients aged between 1 and 12 years who had not received more than 2 weeks of previous anti-tuberculosis treatment are admitted to the study. The diagnosis is based on chest radiography.

The patients are randomly allocated to one of the following 2 regimens:

Regimen I: 9HR: Isoniazid and rifampicin daily for 9 months.

Regimen II: $2H_3R_3Z_3/4H_2R_2$: Isoniazid, rifampicin and pyrazinamide thrice a week for the first 2 months followed by isoniazid and rifampicin twice a week for the next 4 months.

It is proposed to admit a total of 200 patients (100 in each regimen). So far 116 patients have been admitted to the study, 57 to the daily regimen and 59 to the intermittent regimen.

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Collaborative controlled clinical trial on treatment of lymphnode tuberculosis: follow-up phase

(Ongoing study 1988-98)

During the year under review, follow-up of patients admitted to the randomised controlled clinical trial on treatment of lymphnode tuberculosis was continued. This study is being conducted in Madurai, South India, in collaboration with the Paediatric and Adult Surgery Departments of the Government Rajaji Hospital (Dr.D.Anantha Raj, Dr.M. N.Kamaludeen and Dr.V.Anantha Lakshmi). Patients with biopsy confirmed superficial lymphnode tuberculosis were randomised to either of the two following 6 month regimens, viz., Regimen 1 : An unsupervised daily regimen of isoniazid and rifampicin, with the drugs being supplied twice a month for self-administration ($6RH_7$), or Regimen 2: A fully supervised twice a week regimen of isoniazid, rifampicin

and pyrazinamide for two months followed by isoniazid and rifampicin for four months ($2RHZ_2/4RH_2$).

Intake to the study was completed in September 1993. Two hundred and seventy seven patients were admitted to the study. The age and sex distribution, lymphnode culture results and the results at the end of treatment were presented in the earlier annual report (1993). In brief, after excluding 15 patients from analysis, 116 (87%) of 133 in Regimen 1, and 112 (87%) of 129 in Regimen 2 had a "Favourable" response at the end of treatment. Thirteen (10%) patients in Regimen 1 and 17 (13%) in Regimen 2 had "Doubtful" response. Four (3%) patients (all Regimen 1) had an "Unfavourable" response and had their treatment changed. Patients have now been followed up from 21 to 54 months after completing treatment. During this period, among patients who had a "Doubtful" response at the end of treatment, 11 of the 13 treated in Regimen 1 and 15 of the 17 in Regimen 2 were reclassified as "Favourable", as the nodes regressed subsequently. Two patients relapsed in Regimen 1, one each from the "Favourable" and "Doubtful" categories. Three patients relapsed in Regimen 2, two from the "Favourable" and one from the "Doubtful" category. Two patients died, one from each regimen, both due to non-tuberculous causes.

In summary, excluding 2 deaths (1 in each regimen), after 21 months of follow-up after completing treatment, 125 (95%) of 132 patients who were treated with Regimen 1, and 124 (97%) of 128 patients who were treated with Regimen 2 had a favourable outcome. Follow-up is continuing.

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Collaborative study of abdominal tuberculosis : follow-up phase

(Ongoing study, 1992-2001)

A collaborative controlled clinical study of abdominal tuberculosis was carried out at the Centre. The objectives of the study are as follows :

(a) to identify the clinical and laboratory profiles of peritoneal, intestinal and mesenteric tuberculosis in South Indian patients, and

(b) to compare the efficacy of a short-course regimen with that of a standard regimen in the treatment of abdominal tuberculosis.

Patients with bacteriological, histopathological or radiological confirmation, as well as those with a clinical condition highly suggestive of abdominal tuberculosis, were admitted to the study. Patients were randomly allocated to either of the following regimens.

2RHZ/4RH (R6 - rifampicin series): Rifampicin, isoniazid and pyrazinamide daily for 2 months, followed by rifampicin and isoniazid daily for the next 4 months.

SEH/EH (E12 - non-rifampicin series) : Streptomycin, ethambutol and isoniazid daily for 2 weeks, followed by ethambutol and isoniazid daily for the next 50 weeks.

Results upto 60 months after admission : Of the 157 (84 R6, 73 E12 series) patients who were symptom free or had clinically improved at the end of treatment, one (R6 series) died due to

tuberculosis in the 7th month after the start of treatment, following surgery for acute abdomen, 10 (7 R6, 3 E12 series) died due to causes other than tuberculosis and 6 (2 R6, 4 E12 series) required retreatment for other types of tuberculosis. Three patients (1 R6, 2 E12) were lost to follow-up in the 60th, 11 th and 18th month, respectively, and all were asymptomatic at that time. None of the remaining 136 (72 R6, 64 E12 series) patients had relapse of abdominal tuberculosis and are being followed up to 120 months after admission. The follow-up is in progress.

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Collaborative clinical study of cutaneous tuberculosis

(Ongoing study, 1992-96)

A collaborative clinical study of skin tuberculosis with an aim to evolve diagnostic criteria and to assess a SCC regimen of 9 months' duration is carried out at the Centre.

Patients diagnosed clinically as having cutaneous tuberculosis by the dermatologist are admitted to the study after a skin biopsy. All patients aged 12 years or more admitted to the study are treated with rifampicin (450 mg) and isoniazid (300 mg) daily for 9 months and those aged less than 12 years are treated with weight adjusted dosages. The patients are assessed at the Centre and also at the collaborating hospitals at monthly intervals during treatment and at 3 monthly intervals up to 24 months.

A total of 219 patients were admitted to the study and so far 194 have completed chemotherapy. After excluding 39 patients (non-Tb: 19, early default: 14, HIV positive:2, non-tb death:2, change of treatment due to leprosy:2) there remains 155 in the analysis. Fifty percent had lupus vulgaris, 37% verrucosa cutis,

8% scrofuloderma, 3% tuberculid and 2% multiple types. A total of one hundred and twenty seven patients (82%) had single lesion; 20 (13%) 2 lesions and 8 (5%) multiple lesions.

The diagnosis of cutaneous tuberculosis was confirmed by bacteriology or histopathology in 135 (87%) of 155 patients. At the end of 6 months the lesions resolved in 69 (88%) of 78 patients with lupus vulgaris, 44 (77%) of 57 with verrucosa cutis and the over all resolution was 131 (85%). However, at the end of 9 months lesions resolved in 144 (93%) of 155 patients; 1 (lupus vulgaris) did not resolve and treatment was changed; 1 (lupus vulgaris) was lost. In the remaining 9 patients (all verrucosa cutis), the induration subsided subsequently but verrucosity persisted which disappeared after applying keratolytic agent without specific antituberculosis retreatment. All patients are being followed up for a period of 3 years. The study is in progress.

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A **controlled clinical study of multi-drug therapy for multi-bacillary leprosy - a 5 year report**

(Ongoing study, 1988-97)

The study was undertaken to find out the feasibility of fixed duration chemotherapy. Treatment was stopped at the end of 24 months irrespective of BI value and the patients were clinically monitored up to 84 months. Chemotherapy was extended for one more year for patients who had reaction and required prolonged steroids and the case reviewed after one year.

Patients were followed up every month till 48 months, and every 3 months till 60 months and once a year up to 84 months. A total of 80 patients were admitted to the study of whom 64

patients have completed 60 months. Seventeen were excluded from analysis for different reasons (6 died not due to leprosy, 2 migrated, 1 toxic to dapsone, 4 non-cooperation, 1 taking treatment elsewhere, 3 absent for more than 6 months). Of the remaining 47 patients, one had reactivation requiring retreatment, 12 had chronic ENL reaction and as they required high doses of steroids, treatment was extended beyond 24 months. At 60 months all these 12 patients had positive BI though there was a gradual fall. Among the remaining 34 patients who did not have reaction, 13 had negative BI and in 21 there was gradual fall at 60 months. The study is in progress.

*****

A study to evolve objective criteria for diagnosis and assessing the progress in paucibacillary leprosy

(Ongoing study, 1993-96)

A pilot study was initiated to evolve an objective criteria for diagnosis and assessing the progress in paucibacillary leprosy. A patient was eligible for the study if he/she was aged 5 years or more, disease was classified as BT/TT clinically, skin smear for AFB was negative and has had no previous specific chemotherapy (DDS for more than one month or even a single dose of rifampicin) in the last 6 months. All the patients were prescribed NLEP regimen (rifampicin once a month plus DDS daily for 6 months) and were treated on ambulatory basis.

A total of 60 patients have been admitted and all have completed 12 months of treatment. On admission, 80% were confirmed histopathologically as having leprosy, 12% were reported as doubtful and 8% as not leprosy. In addition to histopathological examination, presence of antigen was looked for

and in 78% it was found to be positive.

Of the 60 patients who had completed 12 months, 7 were excluded (3 toxic to DDS, 4 not available at 6 months for assessment). Among the remaining 53 patients, at the end of 6 months 36 (68%) were clinically inactive, 15 (28%) were clinically active and 2 (4%) were positive for BI (0.33 and 0.67) though clinically inactive. Of the 15 patients who were clinically active at 6 months, 5 remained active at 12 months also and of the 36 patients who were clinically inactive at 6 months, 1 became active at 12 months. At 12 months one patient developed a fresh lesion (BI negative) and was retreated and one patient who was clinically inactive was positive for BI (1.00). The study is in progress.

*****

Controlled clinical trial of dapsone as continuation chemotherapy beyond 7 years

(Ongoing study, 1977-97)

As mentioned in the previous annual reports the centre undertook a controlled clinical trial of a rifampicin and non-rifampicin regimens in the treatment of leprosy at the Leprosy Unit of Tuberculosis Research Centre, at Government Royapettah Hospital, Madras.

Among 210 patients who were admitted to the study 59 were excluded at the end of 13 years (10 died-not due to leprosy, 17 migrated, 16 failed to attend for more than 1 year, 10 absconded/discharged against medical advice, 3 discharged, 2 treated for tuberculosis and 1 toxic to DDS) and the remaining 151 were analysed. One patient was retreated at 106 months for reactivation. In more than 95% of the cases at 120, 132, and

144 months the BI was less than 0.50 and the patients were clinically inactive. Hence, it was decided to stop anti-leprosy drugs for all the patients at 144 months and follow them up once a year till 240 months.

A total of 3 patients relapsed both clinically and bacteriologically (at 162, 177 and 210 months) and they were managed with multibacillary NLEP regimen. Fourteen patients showed occasional positive BI after attaining negativity but there were no clinical signs suggestive of relapse and their subsequent skin smears were negative for BI. They are being monitored clinically and bacteriologically. The study is in progress.

*****

A randomised double blind multicentric controlled clinical trial of 2 regimens in the treatment of paucibacillary leprosy

(Ongoing study, 1995-97)

A WHO sponsored multicentric study in the treatment of paucibacillary (PB) leprosy patients is being conducted by CJIL field unit, Avadi. The leprosy unit of Tuberculosis Research Centre is one of the participants in the study.

Paucibacillary leprosy patients having two or three lesions will be eligible for the study. Satellites will be counted as separate lesions. Patients with trunk enlargement or positive bacterial index will not be eligible.

The objective is to evaluate the efficacy of a combination of rifampicin plus minocycline plus ofloxacin administered as a single dose.

The sample size required is 500 per regimen of which CMD unit will admit 50 cases.

The total duration of the study will be 18 months (6 months of treatment phase and 12 months of follow-up phase).

Control Regimen: Rifampicin once a month with daily dapsone for 6 months.

Study Regimen : Rifampicin plus ofloxacin plus minocycline as a single dose.

The intake is continuing.

*****

A double blind study to compare the efficacy of penicillin and DEC in prevention of adenolymphangitis (ADL)

(Ongoing study, 1995-98)

The objective of this double-blind, placebo controlled study is to compare the efficacies of four treatment regimens, given over a period of one year, for patients with filariasis, in preventing adenolymphangitis.

Each patient will be initiated to a programme of cleaning of the affected limb. This would be standardized by the investigator and will include for the following:

1) Cleaning of the affected limb every night with soap and water.

2) Keeping the affected limb dry.

3) Clipping the nails.

4) Applying salicylic acid ointment to webs of the toes, nails and sides of the feet every night.

Patients will then be randomly allocated to one of the five following treatment regimens (30 in each group):

1. **Oral penicillin group:** Two capsules - 1 containing 800,000 units of penicillin G potassium and the other containing placebo, every day for 1 year.

2. **DEC group:** Two capsules - 1 containing DEC 1 mg/kg and the other containing placebo, every day for 1 year.

3. **DEC plus antibiotic group:** Two capsules - 1 containing DEC 1 mg/kg and the other containing 800,000 units of penicillin G potassium every day for 1 year.

4. **Local antibiotic ointment group:** Two capsules of placebo every day and will apply framycetin ointment locally to the affected limb whenever indicated for 1 year.

5. **Placebo group:** Two capsules of placebo every day for 1 year.

A total of 64 patients satisfying the criteria have been admitted. There were 28 males and 36 females. The duration of illness was less than 5 years in 13 patients, 5 to 10 years in 23 and greater than 10 years in the remaining 28. Sixty-two patients had lower limb edema while two had upper limb edema. Thirty-five of the patients had less than 5 ADL attacks in the past year while the remaining 19 had 5 or more attacks during the previous year. There were 12 patients with Grade I edema, 8 with Grade 2 edema, 22 with Grade 3 edema and 12 with Grade 4 edema; 42 were accustomed to using footwear. All patients are being monitored for the occurrence of ADL attacks by visits every 15 days. The study is in progress.

LABORATORY STUDIES - COMPLETED

Immune response and modulation of immune response induced by M .fortuitum complex isolates in guinea-pigs

(Completed study, 1994-95)

A total of 24 guinea-pigs were divided into 4 groups of 6 animals each. Group 1 was the control in which the animals were not immunized. At 6 weeks, guinea-pigs in group 2 were sensitized with a soil isolate of **M.fortuitum** followed by immunization with BCG. Guinea-pigs in group 3 were immunized with BCG alone while guinea-pigs in group 4 were immunized with the soil isolate of **M.fortuitum** alone. The delayed type hypersensitivity (DTH) response to PPD-RT23 and PPD-B was negligible in the control group (group 1) which had not been immunized. Compared to this group, higher responses to PPD-RT23 were observed in all the other groups ($p = 0.05$). On the other hand, the DTH response to PPD-B in the animals sensitized with **M.fortuitum** prior to immunization with BCG (group 2) was significantly higher than that in the control animals and in the animals immunized with **M.fortuitum** alone (group 4) ($p = 0.03$) but not significantly different from that in the animals immunized with BCG (group 3). At 2 weeks after challenge with a South Indian low virulent strain of **M.tuberculosis,** the $\log_{10}$ cfu in spleen was high (> 3.0) in the control animals. Compared to this group, the counts were lower in the animals immunized with BCG, or with M.fortuitum, and in the guinea-pigs sensitized with **M.fortuitum** prior to immunization with BCG though the differences were not significant. Considering the reduction in the $\log_{10}$ cfu in the animals immunized with BCG as 100% protection, 33.3% protection was seen in the animals immunized with **M.fortuitum** and 95.2% protection in the animals immunized with BCG after

prior sensitization with **M.fortuitum.** At 6 weeks after challenge, **M.tuberculosis** organisms could still be detected in the spleen of animals either immunized with **M.fortuitum** or sensitized with **M.fortuitum** prior to immunization with BCG, but could not be detected in the spleen of the animals immunized with BCG. Thus, in these experiments a modulation of delayed type hypersensitivity and protective response to BCG by **M.fortuitum** complex organisms from soil was observed.

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Characterization by plasmid profile of MAC isolates obtained from various sources in the South Indian BCG trial area

(Completed study, 1994-95)

Out of a total of 61 MAC isolates from the South Indian BCG trial area including 13 each from water and dust, 16 from soil, 18 from sputum and the standard strain **M.intracellulare,** TMC 1403, which were studied for their plasmid profile, 18 strains were found to be plasmid- carrying. The maximum number of plasmid-carrying strains were found among the non-pigmented strains isolated from water while a few MAC strains from sputum also yielded plasmids.

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Antimycobacterial effect of chloroquine alone or in combination with isoniazid, pyrazinamide or rifampicin in H37Rv infection in mice

(Completed study, 1994-95)

Chloroquine has been shown to inhibit the multiplication of **M.tuberculosis** under **in vitro** condition. Based on such reports,

the potential of chloroquine as a therapeutic agent in experimental murine tuberculosis was planned. It is shown that chloroquine does not have an antimycobacterial effect either alone or in combination with isoniazid, rifampicin or pyrazinamide. Besides, as chloroquine is known to increase the phagolysosomal pH, and pyrazinamide requires an acid environment for its antimycobacterial activity, it is logical to expect interference of antimycobacterial activity of pyrazinamide by chloroquine. However, no such effect was found.

*****

Neopterin as a marker for cell mediated immunity in patients with pulmonary tuberculosis

(Completed study, 1994-95)

Neopterin, a biochemical marker for CMI was estimated by HPLC in serum, pleural fluid, and culture supernatants of mononuclear cells after stimulation with PPD from pulmonary tuberculosis patients. These values were compared with the conventional method of assessing CMI - namely blastogenic response to PPD. The results suggested that neopterin is a reliable marker for CMI.

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HLA and immune response: Role of HLA class-ll genes/gene products on immunity to tuberculosis

(Completed study, 1990-95)

To elucidate the role of HLA class-ll genes and their gene products (HLA-DR and -DQ) on antibody and cell mediated

immune responses against **M.tuberculosis** antigens, the present study was undertaken.

The influence of HLA-DR and -DQ antigens on lymphocyte response, antibody titre and antigen recognition by the plasma samples to **M.tuberculosis** culture filtrate antigens and the presence of lymphocytotoxins in the plasma samples were studied in 50 active pulmonary tuberculosis, 50 inactive pulmonary tuberculosis patients and 50 control subjects. The results on these immune responses are under analysis.

*****

HLA studies - Investigation in quiescent and relapse cases of pulmonary tuberculosis

(Completed study, 1992-95)

An exploratory study was undertaken to find out whether there is any association between HLA-antigen and/or haplotype and the occurrence of relapse of tuberculosis in successfully treated pulmonary tuberculosis patients. It was planned to carry out HLA-A, -B, -DR and -DO serological determination in 100 quiescent patients and 100 relapse patients. However, it was possible to carry out HLA-determination only in 51 relapse and 51 quiescent patients, because of the availability of limited number of patients.

The results of the study reveal that an increased antigen frequency of HLA-A1 and B-17 was seen in the relapse patients than the quiescent control patients. Further, the frequency of A1 - DR7 haplotype was also seen higher.

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LABORATORY STUDIES - IN PROGRESS

Evaluation of bactericidal action of ofloxacin and sulbactam/ampicillin, in comparison with rifampicin and isoniazid, and metronidazole alone, and in combination with rifampicin and isoniazid, on M.tuberculosis in the murine model

(Ongoing study, 1993-6)

As reported earlier (annual report 1994), a study has been initiated to investigate the bactericidal and sterilizing action of different doses of ofloxacin (O) and sulbactam/ampicillin (S/A), and metronidazole (M) alone and in combination with rifampicin (R) and isoniazid (H), on a drug sensitive strain of **M.tuberculosis in vivo** using the murine model.

A total of 200 Balb/C female mice in the 1-2 months age group were infected with the **M.tuberculosis** strain by tail vein injection. Treatment was started on the 14th day after infection. Immediately after infection (0 day) and before starting treatment (14th day), 4 mice from each group were sacrificed and viable counts were set up from the spleen and lungs. The remaining mice were divided into 12 groups and were treated six days a week for 3 months as described earlier (annual report 1994).

At 4, 8 and 12 weeks after start of treatment and at 3 months after stopping treatment, 3 mice from each group were sacrificed and viable counts were set up on LJ slopes from spleen and lungs. The colony counts on the LJ slopes will be read at 4 and 8 weeks after incubation at 37ºC. Spleen and lung homogenates have also been inoculated into Kirchner's liquid (KL) medium. The KL medium will be sub-cultured onto LJ slopes after 6 weeks incubation to determine the organ positivity. Comparison of colony

forming units (cfu) in spleen and lungs and positivity of these organs for **M.tuberculosis** in the different groups of mice will be used to evaluate and compare the bactericidal and sterilizing action of rifampicin, isoniazid, ofloxacin, sulbactam/ampicillin and metronidazole.

*****

Action of pyrazinamide, alone and in combination with isoniazid and rifampicin, on M.tuberculosis in vitro under different growth conditions

(Ongoing study 1994-96)

As reported earlier (annual report 1994), a study is being carried out to determine the activity of pyrazinamide (Z) alone and in combination with isoniazid (H) and rifampicin (R), and metronidazole (M) alone on **M.tuberculosis in vitro** under different growth conditions. Two strains. of **M.tuberculosis,** H37Rv and a drug sensitive clinical isolate, are being used in these experiments. The growth curves and colony forming units (cfu)/ml of these 2 strains in normal 7H9 liquid medium incubated at 37°C and in acidic 7H9 liquid medium (pH 5.6) at 37°C have been determined in the presence of Z alone and in combination with H and R, and M alone. Similar experiments are in progress using normal 7H9 liquid medium incubated at 37°C under anaerobic conditions. Further experiments will be carried out using acidic 7H9 liquid medium (pH 5.2), nutrient deficient liquid medium as well as low temperature incubation.

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WHO-assisted multicentric study of early bactericidal activity

(Ongoing study, 1994-96)

A WHO-assisted multicentric study, of which the Centre is one of the participants, has been started (Annual Report 1994) to see whether the early bactericidal activity (EBA) of drugs in pulmonary tuberculosis patients as estimated by viable count and total counts will be comparable between the two methods as well as between different centres. About 40 patients have been admitted to the study so far. They have been randomly allocated to the following groups:

1. Isoniazid 300mg daily for 5 days
2. Isoniazid 18.75mg daily for 5 days
3. Rifampicin 600mg daily for 5 days
4. Ofloxacin 800mg daily for 5 days
5. No drugs

From each of these patients admitted to the study, overnight sputum samples are collected before the start of treatment, after 2 doses of drugs and after all the 5 doses. The EBAs of the drugs are being estimated by carrying out viable counts of **M.tuberculosis** and total counts of acid-fast bacilli (AFB)/ml in the sputum samples. At the end of the study, the estimates of EBAs obtained by viable count will be compared with those obtained by total counts. The study is in progress.

*****

Evaluation of slide culture sensitivity test against the indirect sensitivity test

(Ongoing study, 1994-96)

Slide culture sensitivity test is being standardised and evaluated against the indirect sensitivity test that is carried out routinely in the laboratory (see annual report 1994).

An interim analysis showed that, of the 102 smear positive specimens (smear positive by either of the two control direct smears) only 56 (54.9%) showed growth (growth is considered to have occurred when the slide culture smear grade is 2+ and more). Of the 44 high grade direct smears (grades 2 + and 3 +), 31 (70.5%) showed growth. Of the 58 low grade direct smears (grade 1 +), 25 (43.1 %) showed growth.

The comparison of smear grades in 97 pairs of control slide cultures revealed that 49 (51%), 32 (33%) and 16 (16.5%), showed no grade, 1 grade and 2 grades difference, respectively.

The criteria of resistance in the slide culture method for INH and rifampicin are being worked out using the results of indirect sensitivity tests as the standards. The study is in progress.

*****

Characterization of Mycobacterium Avium Complex (MAC) isolates obtained from various sources in the South Indian BCG trial area: Analysis of fatty acid composition of MAC by gas chromatography-mass spectrometry (GC-MS) and the DNA probes DT1, DT6 and LIPA

(Ongoing study, 1995-96)

A total of 62 MAC isolates from soil, water, dust and sputum in the South Indian BCG trial area were earlier characterized by their susceptibility to drugs and heavy metals (Annual Report 1994). When 29 of these strains were further characterized for their fatty acid composition by GC-MS, 23 were identified as MAC, 4 were identified as **M.xenopi** and 2 as **M.phlei.** The strains identified as MAC by standard biochemical methods and by GC-MS did not show any source-related significant differences in their drug and heavy metal susceptibility patterns.

A total of 42 MAC isolates with known drug and heavy metal susceptibility patterns were tested by 2 probes, DT1 and DT6, developed in the Institut Pasteur, Paris, for the specific identification of **M.intracellulare** and **M.avium,** respectively. Of these, 16 strains tested positive with DT1 **(M.intracellulare)** and no strain was identified as **M.avium** (DT6 negative). Using the LIPA DNA probe developed at the Prince Leopold Institute for Tropical Medicine, Belgium, a total of 14 strains were identified as MAC, 15 as different species, 2 as **M.malmoense** and 1 as **M.scrofulaceum.**

Currently, more number of strains from the South Indian BCG trial area are being analyzed by GC-MS and by using these DNA probes. The study is in progress.

*****

Drug sensitivity testing of M .tuberculosis cultures by luciferase reporter phage assay

(Ongoing study, 1994-96)

Luciferase reporter phage, genetically engineered to express luciferase gene, confers the ability to produce luciferase to the viable mycobacteria which it infects and they liberate photons in the presence of luciferin which is measured as relative light units (RLU) in luminometer.

Following preliminary experiments to standardise the technique (vide annual report, 1994), it has been planned to screen about 50 cultures of **M.tuberculosis** consisting of both drug sensitive and drug resistant strains, using a crude phage of a titre of 10^{-12} approximately.

A standard inoculum of 10^5 organisms/ml in 7H9 medium is being used for drug sensitivity testing by conventional method, bioluminescence assay and luciferase reporter phage assay.

This study is funded by DBT under Indo-US VAP for 3 years starting from 1995. The study is in progress.

*****

Studies on the mechanism of pyrazinamide action

(Ongoing study, 1994-96)

The role of pyrazinamide deamidase in the susceptibility and antimycobacterial activity of pyrazinamide and its principal metabolic product pyrazinoic acid, against **M.tuberculosis,** at neutral and acidic pH of liquid medium, is being investigated.

M.tuberculosis H37Rv, a pyrazinamide susceptible strain and M.bovis BCG, a pyrazinamide resistant strain are being used in this study. The study is in progress.

*****

Microsomal mixed function oxidases in experimental tuberculosis

(Ongoing study, 1994-97)

The study was initiated with the aim of finding out the role of cytochrome P-450 in relation to drug resistance in **M.tuberculosis.** Establishing the occurrence of cytochrome P-450 in sensitive and resistant strains of **M.tuberculosis** H37Rv (towards anti-TB drugs of current interest) and characterisation of cytochrome P-450 are being carried out. It is thus aimed at finding out the relative differences in the content of cytochrome P-450 in sensitive and resistant strains. The hemoprotein has to be further purified and quantitated. The methods in relation to quantitation by this hemoprotein in mycobacteria (both in sensitive and resistent organisms) are in progress.

*****

HLA studies - HLA genotyping : DNA typing in pulmonary tuberculosis patients and contacts

(Ongoing study, 1994-97)

The main objective of this project is to use a combination of serological and DNA probes to analyse the phenotype and the genotype of a number of individuals to find out whether there exists an association between any serological and/or DNA marker and the occurrence of pulmonary tuberculosis.

HLA phenotyping and genotyping will be carried out using HLA-anti sera and HLA gene probes, respectively.

Further, the role of HLA class-ll genedgene products on immunity to tuberculosis will also be studied in patients with active pulmonary tuberculosis and healthy volunteers.

HLA-DR and -DQ genotyping will be carried out in 100 pulmonary tuberculosis patients and 100 contacts.

In addition to serological determination of HLA-A, -B, -DR and -DQ antigens, DNA typing of HLA-DR genes will be carried out using Amplified Fragment Length Polymorphism (AFLP) technique. For HLA-DQ genotyping, Heteroduplex analysis of HLA-DQ alpha and -DO beta DNA typing will be carried out.

During the year 40 contacts and 40 tuberculosis patients were HLA typed by serological method. DNA was extracted and stored at -200C. The technique on AFLP for HLA-DR genotyping is being standardized. The study is in progress.

*****

Development of DNA probes of M.tuberculosis

(Ongoing study, 1988-96)

The main objective of this project is to develop and evaluate DNA probes for early diagnosis of tuberculosis. The cloning and sequencing of pTRC4 has been described in the previous Annual Reports. It has also been mentioned that one pair of PCR primers namely 750/751 was to be evaluated for its use in diagnosis. The evaluation of the primers 750/751 carried out in 1994 was not satisfactory hence one more set of primers namely 868-1013

targeting TRC4 fragment in the **M.tuberculosis** genome was chosen for further work. This set of primers gives an amplification product of 173 base pair. This is under evaluation.

*****

Characterisation and purification of antigenic components of M .tuberculosis

(Ongoing study, 1988-98)

It has been mentioned in the previous Annual Report (1994, page 39) that rabbits and mice were immunised for production of polyclonal and monoclonal antibodies, respectively.

The monoclonal antibodies (Mabs) produced were characterised for their antigen recognition pattern, sub class of isotype and cross reactivity with other mycobacteria. Slot immunoblotting was employed as one of the techniques for antigen detection. By this technique, 40 ng of antigen was detected by Mabs 27.1 and 41.10 and 8 ng of antigen, by Mabs 31.3 and 1 H12. Six Mabs containing tissue culture supernatant and 4 ascitic fluids were tested for detection of an antigen in formalin fixed skin sections and positive reaction was observed. Using polyclonal antibody both as primary and secondary capture antibody in ELISA, antigen concentration upto 10 pg/ml could be detected.

Additionally, **M.tuberculosis** H37Rv 30 KDa antigen also has been isolated in purity by a combination of methods i.e., Preparatory IEF and SDS-PAGE preparatory electrophoresis.

*****

RFLP analysis of M.tuberculosis isolates from various regions of India using IS6110 probe

(Ongoing study, 1995-97)

DNA fingerprinting of clinical isolates of **M.tuberculosis** from Madras using IS6110 and DR has been described in detail in the previous annual report. Fingerprinting of **M.tubercutosis** from various regions of India is being carried out.

*****

Cytokine profiles in pre and post BCG vaccinated adult population: Analysis by PCR detection of cytokine mRNA

(Ongoing study, 1993-96)

As reported in the annual report 1993, the methodology of RT-PCR (Reverse Transcriptase Polymerase Chain Reaction) was used for studying cytokine profiles in pre and post BCG vaccinated adult population.

During the year, 17 pairs of pre and post BCG vaccinated samples were collected. In addition, 17 more samples were collected from PPD positive adult individuals.

In-vitro cultures were set up as described in 1993 annual report. The culture supernatants were collected for 24,48 and 96 hours time points. The cells were lysed and stored at -20ºC for performing RT-PCR to see the expression of cytokines. The project is in progress.

*****

Immunopathology of cutaneous tuberculosis

(Ongoing study, 1992-97)

The aim of this study is to understand the immunopathology of skin tuberculosis as detailed in the previous annual reports. During the year, the scope of the project has been expanded to include biochemical parameters of the lesions such as zinc, collagen and elastin level before and after treatment. This is in addition to the features such as the delineation of T-lymphocytes and their subsets, B-lymphocytes, etc., in the lesion and in the biopsies from Mantoux tested site at days 3 and 21. The study is in progress.

*****

Development of an experimental model for fibrosis

(Ongoing study, 1993-96)

Since fibrosis is an important consequence of tuberculosis leading to disability, on animal model to study the fibrogenic mechanisms in experimental tuberculosis is being developed. As outlined in the 1994 annual report, levels of collagen, elastin, hexosamine and zinc have been measured in the spleen, liver and lungs of infected guinea pigs up to 48 weeks. The results are being analysed.

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EPIDEMIOLOGICAL STUDIES - IN PROGRESS

Development of surveillance methodology for tuberculosis

(Ongoing study, 1990-2000)

This is a long term epidemiological study undertaken in BCG Trial area with high non-specific sensitivity, with a view to identify a simple, inexpensive tool for the surveillance of tuberculosis in the community. The following are the parameters being studied:

1) Age specific prevalence of infection and its trend.

2) Age-sex specific rates of disease prevalence and trend.

3) The proportion of chronic excretors among prevalence cases and other drug sensitivity status.

The methodology has been described in detail in the annual reports of 1990 & 1991. The planned intake of about 100,000 could not be completed due to lack of X-ray units even during the year reported. So, also, the 30th month Selective Follow-Up (SFU) could not be taken up. The selective follow-up of 24 months was completed in the remaining villages of Thiruvalangadu panchayat union and 48 months follow up in 8 villages of Kadambathur panchayat union. To increase the sample size of Kadambathur panchayat union two more villages were added for intake during the period. The first resurvey was completed in 3 villages of Thiruvalangadu panchayat union.

The coverages obtained for the follow-up rounds and resurvey are found to be maintained at high levels for all examinations like X-ray, sputum and tuberculin testing.

In all, 63 sputum positive cases were diagnosed during the year 1995. Of these, 15 were from follow-up rounds and the remaining from resurvey. Thirty two cases were positive only on culture; 8 were positive on smear and negative by culture. Of the total culture positives, drug sensitivity results were available only for 38 cases; of these, 7 had a history of previous treatment; 36 (95%) cultures were sensitive.

Management of cases: Sputum positive cases were referred for anti-tuberculous treatment with Short Course Chemotherapy (SCC) at the nearest Primary Health Centre. Information on their symptomatic and drug regularity status was obtained along with two specimens of sputum.

Passive case finding: A total of 1728 symptomatics were registered in all PHCs and sputum collected. Of these, 170 (10%) became sputum positive and were put on treatment with SCC by the medical officer of the health facility. The study is in progress.

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Testing of children for comparison of 1TU-RT23 and 3IU of PPD-S

(Ongoing study, 1995-97)

In the BCG prophylaxis study 3IU of Freeze dried PPD-S received from Copenhagen was used. The same PPD-S was used even in 20 years retesting. In the TB surveillance the tuberculin, 1TU RT23 with Tween 80, is being used. As per the decision of the Sub-committee of Epidemiology, a study is initiated to compare these two antigens in Thiruvalangadu panchayat union were first resurvey is ongoing.

This study will be done only in the 9 groups of Thiruvalangadu panchayat union, in which 20 year retesting was also conducted. It is proposed to register approximately 3000 children in these groups at the time of intake.

Children aged (0-9) years and cases in these villages will be included for this study. Others will be retested as per the routine procedure.

The three coded (2 antigens, 1 placebo) tuberculins viz., S, T and U are supplied to field for testing. For the study population the combination of 2 codes i.e., ST, TU or SU were given randomly on right forearm or left forearm. The reactions were read after 3 days and the cross section indurations were recorded.

During the year under report,. 1222 children were tested and 1202 reactions were read. The study is in progress.

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Multicentric study for diagnostic criteria in childhood tuberculosis

(Ongoing study, 1995-98)

The diagnosis of childhood tuberculosis has remained one of the most controversial issues. Since bacteriologic confirmation is possible only in 20-30% of cases, the diagnosis is usually based on clinical, epidemiologic and radiologic features and the tuberculin test results. Although several diagnostic schemes have been suggested and tried out, reliable and objective criteria are yet to be developed. To be applicable on a wide scale, the criteria developed should be simple, reliable and valid and as specific for tuberculosis as possible. The task force convened by the ICMR examined the available information and made the following

recommendations for diagnostic criteria. They are as follows:

1. Persistent radiological lesion even after 4 weeks of adequate non specific antibiotic treatment.

2. X-ray lesion with a positive Mantoux test or with AFB on smear.

3. Histopathology proved in cases of glandular swelling.

It was therefore proposed to do a multicentric study to evaluate the task force criteria and the study was started in January 1995.

The centres involved in the study are the Institute of Child Health, the Pediatric departments of the Stanley Medical college, Sri Ramachandra Medical college and the Child Trust Hospital, Madras. Children aged 6 months to 12 years will report to these centres and those considered referable to TB clinic will form the study population.

So far, 769 children have been registered, all examinations were completed in 694 (90%) children. All symptomatic children are followed up at 2 weeks, 1, 2, 3 months and at 3-monthly intervals thereafter upto 1 year. All symptomatic children are examined clinically and chest X-ray, Mantoux test and gastric lavage for AFB smear and culture are done. In all, 2548 specimens were collected and among them 77 were found to be bacteriologicaily positive. Among 22 biopsies done, 15 were reported as positive on histopathology.

So far, 99 children have been started on antituberculous drugs on the guidelines of ICMR-among them 74 based on clinical features and 25 on bacteriological basis. A panel of doctors will

review once a month the case status and reasons for anti-TB treatment. The study is in progress.

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Typhoid fever in a rural community

(Ongoing study, 1995-96)

It is proposed to undertake a Typhoid Vaccine Trial in Tiruvallur taluk of Chingleput district. A survey has been planned to be undertaken to document the descriptive epidemiological information of typhoid fever like incidence, efficiency of active versus passive surveillance, risk factors for transmission of typhoid and burden of illness due to typhoid in the community.

Twenty villages comprising a base population of 33,285 have been selected from Poondi panchayat union covering the Govt. Hospital at Uthukottai and the two PHIs at Katchur and Poondi. A simple random sample of 8 villages selected from these 20 villages with a population of 9383 is followed for active surveillance while the remaining villages are kept under passive surveillance. Eight surveillance centres have been identified in the active surveillance villages. The Medical Officers at these health facilities have been informed of their involvement in the passive surveillance.

A Census has been completed and the data is transferred onto the computer. The morbidity form for screening the population, the clinical examination form for active and passive surveillance, blood investigation form, Daily Work Report and other forms were tested under field conditions.

The procedure for measuring the temperature using the thermoscan instant thermometer has been standardised. The incubator has been installed in the field for incubating the blood specimens collected and brought to the field laboratory under aseptic condition till it is transported to the laboratory at Madras. The laboratory procedures have been finalised for receipt of the specimens and processing the same using BACTEC NR-730 instrument for culture and sceptor lpette for identification and anti-biogram. The study is in progress.

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A double blind controlled trial of efficacy of DEC enriched salt in preventing adenolymphangitis of lymphatic filariasis

(Ongoing study, 1994-98)

The objective of the study is to evaluate the efficacy of DEC medicated salt given for 1 year in preventing the occurrence of acute episodes or chronic filarial disease in asymptomatic individuals living in highly endemic areas, and to study the duration of that effect.

The study area chosen comprises of two panchayat unions in Tiruvallur taluk with atleast 15% endemicity and an annual incidence of attacks of adenolymphangitis (ADL episodes) of at least 3%. The following are 3 treatment groups which are randomly allocated:

1. Continuous administration of DEC salt (0.2%) for one year followed by plain salt for one year.

2. Single dose of DEC 6 mg/kg and ivermectin 400 µg/kg once a year for 1 year along with plain salt for one year followed by plain salt for next year.

3. Continuous administration of plain salt for 2 years.

Initially, selected persons aged 5 years and above, will be administered DEC + ivermectin tablets or placebo tablets followed by DEC enriched salt or common salt for continuous usage will be supplied for one year. Each house-hold in the study hamlets will be visited by trained and standardised health visitor every fortnight. These health workers are already engaged in a similar activity in an ongoing study to evaluate the socioeconomic aspect of lymphatic filariasis. The prevalent attack will be identified by health visitors and confirmed by a physician within 3 days. The physician will also examine a 5% random sample of the ''normal'' to validate the examination of the health workers.

ADL attacks will be managed symptomatically. Specific treatment will not be given by the research team at this stage in order to avoid contamination. All attacks will be confirmed by a physician.

During the year census operations were completed and a baseline survey of chronic disease and the occurrence of ADL attacks in the population were estimated. Distribution of single doses of ivermectin and DEC combination and salt were initiated during the year. The study is in progress.

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Surveillance of individuals infected with the Human Immuno-deficiency Virus (HIV) for the development of tuberculosis

(Ongoing study, 1989-99)

A longitudinal cohort study was started in July 1989 with the objective of monitoring the occurrence of tuberculosis among patients with HIV infection.

Patients identified to be positive for HIV infection of ELISA testing from the various surveillance centres (Madras, Vellore and Pondicherry) are included. They are registered in the Centre and followed up at 6-monthly intervals with clinical examination, comprehensive sociological assessment and detailed investigations.

The family members including the spouse and other sexual partners are also registered and followed up to study the pattern of transmission of HIV infection.

The study cohort contains 239 HIV positive patients of whom 100 had tuberculosis (83 at registration and 17 during follow-up). They were treated with $2EHRZ_7$-$7RH_7$ or routine 8-month short course regimen at the nearest centre. Five of these had multi-drug resistance.

Forty-six patients had died over 60 months follow-up, of whom 30 had tuberculosis. The various causes of death were ascertained. The study is in progress.

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ANIMAL FACILITY

In view of the importance of animal model experiments to research, it is essential that proper care is taken for planning and running the laboratory animal facilities so that the validity of research data, welfare of the animals and safety of animal care staff are ensured. Good husbandry minimises variations that can modify an animal's response to experimentation.

In the new animal facility being established it is planned to raise part-barrier and also barrier maintained animals. In the present set up, non-barrier or "conventional" animals which are free from all evidence of infectious diseases communicable to those handling the animals are being raised and maintained. Prescribed breeding and maintenance programmes and general overall care of the animals and their environment, hygiene, health monitoring, disease checking and recording of conditions are being taken care of.

Rabbits, guinea pigs and mice are maintained and used for experimental purposes in the present set up. These animals are being used in various experimental models such as foot-pad inoculation of **M.leprae** for DDS susceptibility testing, ascitis generation in monoclonal antibody production, macrophage work, DTH and protective immunity studies, antibody generation, and H37Rv virulence maintenance.

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LIBRARY & INFORMATION SERVICES

The Library and Documentation Centre continued to serve the doctors, researchers and faculty of most of the medical colleges and medical research institutions in Madras. In addition, several other services such as Tuberculosis Alert, a fortnightly computerised Selective Dissemination of Information (SDI), MEDLINE searches on the CD-ROM Diskettes (1991 +), Online Search of Bibliographic databases at NIC, E-Mail & Bulletin Board and other network facilities through the SIRNET, CSIR and the RENNIC, NIC, New Delhi, Updating and maintenance of Bibliographic databases, viz., Library Book Catalogue (LIBCAT), the TUBERCULOSIS, TRC Publications (TRCPUB), journal holdings (SERHOLD), MAIL LIST etc., CC on Disc : Life Science Services, Resource sharing with Vector Control Research Centre, Pondicherry, Institutional membership facility at the British Council Library, Madras and publication of the quarterly TRC Bulletin were also carried out.

With TRC as the focal point, the National Database Project on Tuberculosis and Allied Diseases with support from the ICMR-NIC Centre for Biomedical Information, NIC, New Delhi, has started, covering literature drawn from Indian journals which are presently not covered by any of the noted international indexing systems; 45 journals have been identified for inclusion and the period of coverage will be for 10 years from 1986 and expected to be operational by 1998. Upon commissioning, the database shall be online accessible on NICNET, the computer network of NIC.

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APPENDICES

TRAINING PROGRAMMES

WHO Fellow

Dr.Shyam Sunder Mishra, Nepal, from 4.12.95 to 8.12.95.

Trainees

The following underwent training in different departments as follows:

Bacteriology

Mr.P.Nagarajan, Laboratory Technician, Thanjavur Medical College, Thanjavur, from 20.2.95 to 5.3.95.

Mr.Koshy Abraham, Microbiologist, Christian Fellowship Hospital, Oddanchathiram, from 17.4.95 to 28.4.95.

Ten students of Diploma Course in Medical Laboratory Technology from Voluntary Health Services, Adyar, Madras, from 2.5.95 to 8.5.95.

Forty-five students of Diploma Course in Medical Laboratory Technology from King Institute, Guindy, Madras (3 batches), from 7.7.95 to 4.8.95.

Dr.Vijayachari, Regional Medical Research Centre, .Port Blair, Andaman & Nicobar Islands, from 17.7.95 to 21.7.95.

Mr.I.Raaz Ahamed, Lab Technician, Ehrlich Institute of Technology, Madras, from 22.1 1.95 to 22.12.95.

Cardio-Pulmonary Medicine

Dr. Deepa Chockalingam, Devaki Hospital, Madras, from 6.2.95 to 8.2.95.

Dr.H.G. Sadhu, Senior Research Officer, National Institute of Occupational Health, Ahamedabad, from 6.3.95 to 8.3.95.

Immunology

Ms. R. Meera, Department of Biotechnology, Central Leather Research Institute, Madras, from September, 1994 till date.

Ms. Latha, Central Leather Research Institute, Madras, from 2.1.95 to 9.1.95.

Three staff members of Dr. Madhavan's Laboratory, Sankara Netralaya, Madras, from 6.1.95 to 13.3.95.

Fifteen MD students of Govt. General Hospital, Madras, from 6.2.95 to 8.2.95.

Dr. Thenmozhi, Kilpauk Medical College, Madras, from 21.8.95 till date.

Dr. Thomas, Department of Rheumatology, Government General Hospital, Madras, from 3.1 1.95 to 21.1 1.95.

Dr. Anuradha, Government General Hospital, Madras, from 27.11.95 till date.

Pathology

Mrs.Alamelu Chandrasekaran, Department of Experi-mental Medicine, Tamil Nadu Dr. MGR Medical University, Madras, from 01.04.95 to 30.04.95.

Mr.Sai Prasad, medical student, Kilpauk Medical. College, Madras, from 15.04.95 to 31.05.95.

General

Mr. S. Senthil Kumar and Mr. Deepak Jayakumar, M.Sc., (Micro-biology) students, Dr. A. L. Mudaliar Post-graduate Institute of Basic Medical Sciences, Tharamani under the Science Talent Promotion Scheme from University Students Advisory Bureau, University of Madras, Madras, from 15.5.95 to 15.6.95.

Dr. Vishnu Sharma, MD (TB & RD) student from JIPMER, Pondicherry, from 4.10.95 to 13.10.95.

Dr.R.Selvam, MD (TB & RD) student from JIPMER, Pondicherry, from 16.10.95 to 25.10.95.

Others

One- or two-day training programmes were arranged at the Centre for batches of medical students, post-graduates, nursing students and para-medical personnel, as given below:

Post-graduate students

Four M.Sc. (Microbiology) and 2 MD (Microbiology) students from Christian Medical College, Vellore.

Seven Post Graduate Diploma course students and a staff from K. J.College of Continuing Medical Education, KJ Hospital, Madras.

Post Graduate students from Sri Ramachandra Medical College and Research Institute, Madras - 1 batch.

Post Graduate students from Kuvempu University, B. R.Project 577 115.

Ten M.Sc. students from Bharathidasan University, Tiruchirapalli .

Thirteen M.Sc. (Microbiology) students from Gulbarga University, Gulbarga.

Medical students

Sri Ramachandra Medical College & Research Institute, Madras - 1 batch.

Compulsory Rotating Resident Internee posting students, Sri Ramachandra Medical College & Research Institute, Porur, Madras - 3 batches.

Nursing and para-medical students

B.Sc.(Nursing) students from Madras Medical College, Madras -2 batches.

B.Sc. (Nursing) students from Christian Medical College and Hospital, Vellore - 2 batches

Students of Sanitary Inspectors' course from Faculty of Rural Health and Sanitation, The Gandhigram Rural Institute, Ambathurai - 1 batch.

Students and staff members from Vivek Laboratories, Institute of Medical Laboratory Technology, Nagerkovil - 1 batch

B.Sc. (Nursing) students from CSI Jeyaraj Annapackiam College of Nursing, Christian Mission Hospital, Madurai - 1 batch.

Medical Laboratory Technology students from Durgabai Deshmukh Poly clinic, Madras - 1 batch.

B.Sc. (Nursing) students from FR. Muller's College of Nursing, Mangalore - 1 batch.

Nursing students and staff members from St.Mary's School of Nursing, Tenkasi - 1 batch.

B.Sc. (Nursing) students from M. A. Chidambaram College of Nursing, Adyar, Madras - 1 batch.

Students of Diploma Course in Nursing from School of Nursing, Lakshmi Paramedical & Nursing Institute, Madras - 1 batch.

Students of Diploma Course in Nursing from School of Nursing, CSI Kalyani General Hospital, Madras - 1 batch.

SYMPOSIUM ON "UPDATE ON IMAGING TECHNIQUES WITH SPECIAL EMPHASIS ON DIAGNOSIS OF TUBERCULOSIS"

In the diagnosis and management of pulmonary and extra pulmonary tuberculosis a great deal of emphasis is laid on imaging and important clinical decisions are made on the basis of radiological findings. A symposium was organised by TRC to critically evaluate the various techniques in imaging and formulate guidelines for the proper usage in clinical medicine in general and tuberculosis in particular.

The symposium was held on 23rd July, 1995 at Madras and was inaugurated by Thiru.R. Poornalingam, Health Secretary, Government of Tamil Nadu. Dr.R. Prabhakar, Director, welcomed the gathering, Dr.Baskar Rao, Consultant Obstetrician and Gynecologist, Madras, presided over the function. A souvenir was released by Dr. Major Raja. Dr. Rajeswari Ramachandran thanked the gathering.

There were 2 sessions addressing different aspects of the subject. Presentations were made by experts in the field followed by lively discussion. The details are as follows :

Session I

Subject	Speaker
Radiographic appearances of the chest and their clinical correlation	Dr. K.V.Thiruvengadam
Inter and intra observer variation in chest X-ray readings	Dr.T.Santha Devi
lohexol bronchography	Dr.Roy Santhosam
Radionuclide scanning of the lung : indications & technique	Dr. K.Thirumurthy
CT/MRI of brain tuberculoma - Impact & Management	Dr.A.Gajaraj
Role of imaging in modern neurosurgery	Dr.K.Ganapathy

Session II

Subject	Speaker
Barium studies in abdominal tuberculosis	Dr.RaniBalasubramianian
Role of ultrasound in the diagnosis of extrapulmonary tuberculosis	Dr.S.Suresh
Experience with CT scan in diseases of chest & abdomen	Dr.Vishnu Srinivas
lnterventional radiology of spinal lesions	Dr.J.R.Daniel

WORKSHOP ON "ROLE OF NGOs IN TUBERCULOSIS CONTROL"

A workshop was conducted on the 14th of September, 1995 on the "Role of Non-Governmental Organisations in Tuberculosis Control" in collaboration with the Slum Clearance Board of the Government of Tamilnadu. The purpose of this workshop was to find out from the NGOs how they could contribute to tuberculosis control activities.

The workshop was inaugurated by Mrs. Shanthini Kapoor, Collector of Madras, and was presided over by Mr. K. N. George, Former Director, Madras School of Social Work. Dr. R. Prabhakar, Director, welcomed the gathering. Thiru K. R. V. Ramani, Chairman, Tamil Nadu Slum Clearance Board, released the training manual. Mrs. Kannan Verma and Ms. Shameem Siddique representing the NGOs shared their experiences on the "NGOs Viewpoint". Dr. Geetha Shanmugam thanked the gathering.

There were 69 participants representing 30 NGOs. During the morning session the subject of 'Tuberculosis Control' was introduced. The afternoon session was interactive. The details are given below:

Session I

Subject	Speaker
Introduction and Familiarisation	Mrs. Sudha Ganapathy
Report of activities	Mr. S. Sivasubramanian
Tuberculosis - medical aspects	Dr. M. S. Jawahar
Role Play	Medical Social Workers
Discussion on role play highlighting sociological aspects of tuberculosis	Mrs. Niruparani Charles
Sharing	Mr. Gajendran & Mr.Bhasker of Guild Plan International, Madras

Session II

Subject	Speaker
Group Work	-
Presentation of work plans	-
Quiz Competition	Mrs. Mohanarani Suhadev
Role plays & Slogan competition	Medical Social Workers
Summing up	Dr. T.Santha Devi
Valedictory - Distribution of prizes & certificates	

INAUGURATION OF THE LABORATORY ANIMAL HOUSE FACILITY

The newly built laboratory animal house facility in the campus of the Tuberculosis Research Centre, Madras, was declared open on 20th September, 1995. Dr. C.N. Paramasivan welcomed the gathering. Dr. V.D. Padmanabhan, Registrar, Tamilnadu Veterinary and Animal Sciences University, Madras, presided. Thiru R. Gopalakrishnan, Chief Engineer, Central Public Works Department, Madras, delivered the felicitation address. Dr. R. Prabhakar, Director, explaining the importance of having such a facility to meet the increasing demand to validate any newer vaccines; to learn the pathogenesis in tuberculosis, to evaluate newer anti-TB drugs and drug-regimens and also to obtain several well delineated inbred colonies for scientists involved in tuberculosis research, dedicated the animal house facility. Dr. M. Naseema thanked the gathering.

SYMPOSIUM TO COMMEMORATE 40TH ANNIVERSARY OF THE TUBERCULOSIS RESEARCH CENTRE, MADRAS

A Symposium was organized to commemorate 40th Anniversary of the Tuberculosis Research Centre, Madras on 24th September, 1995. Dr.R. Prabhakar, Director, welcomed the gathering. Dr. K.V.Thiruvengadam, Former Professor of Medicine, Madras Medical College, Madras, presided. Scientific presentations were made by the experts in the field. This was followed by a lively discussion. The details are given below:

Speaker	Subject
Prof .V.Ramalingaswami, Former Director-General, ICMR, New Delhi	Re-emerging infectious diseases (Guest lecture)
Dr.C.V. Ramakrishnan, Former Deputy Director, TRC, Madras	Tuberculosis research down the years
Dr. R. Parthasarathy, Former Deputy Director, TRC, Madras	Unsupervised domiciliary chemo-therapy with triple oral drugs in the treatment of sputum positive pulmonary tuberculosis patients in a community - Madanapallee experience
Dr. R. Prabhakar, Director, TRC, Madras	Tuberculosis research - future challenges

85TH ANNIVERSARY CELEBRATIONS OF THE INDIAN COUNCIL OF MEDICAL RESEARCH

The Indian Council of Medical Research is celebrating its 85th Anniversary from November, 1995, to disseminate information and educating the general public and target groups on the various aspects of health, including the expertise and knowledge gained by the various ICMR institutions situated far and wide in India, over a period of one year from November, 1995, emphasising one aspect will be focussed each month.

As envisaged by the Council, this Centre co-ordinated by the two other ICMR Institutions, namely, the Institute for Research in Medical Statistics, Madras, and the CJlL Field Unit for Leprosy, Avadi, Madras, identified the core groups to plan for the celebrations of the coming months.

The awareness programme pertaining to nutrition and allied activities was launched on 28th November, 1995, at "World Vision of India", a NGO involved in the community development programmes. Similar programmes were conducted in Madras city, Tiruvallur (sub-urban) and lrulancheri village (rural). A brief write-up on the 85th anniversary celebrations of ICMR was highlighted in news dailies such as "The Hindu" (dated 7.12.95) and "Trinity Mirror" (dated 13.12.95). Programmes on various other aspects of health, identified for each month, are being conducted.

STAFF DEVELOPMENT PROGRAMMES

1. Dr. Soumya Swaminathan, Dr. Rema Mathew and Dr. R. Balambal attended a basic course in statistics for doctors at the Institute for Research in Medical Statistics (Madras Chapter), Madras, from 20.2.95 to 4.3.95.

2. Dr.N.Selvakumar underwent a 6-month training programme on molecular biological techniques at London School of Hygiene and Tropical Medicine, London, under the British Government Technical Co-operation Training Award, from April 1995.

3. Mr.D. Suryanarayanan underwent training in "PC-Based Statistical Software in Health Care - Advanced and Epidemiologic methods and analysis" at Christian Medical College, Vellore, from 12.6.95 to 30.6.95.

4. Dr. Rajeswari Ramachandran was awarded a 12-week WHO Fellowship for training in "Tuberculousis control" at Chicago TB Control Programme, Chicago, from 24.7.95 to 1.8.95 and at New York TB Control Programme, New York, from 5.8.95 to 13.10.95.

5. Dr. Manjula Datta was awarded a 4-month Fellowship under Canadian Common Wealth Programme for "Vaccine and immunization working for the development of new TB vaccines" at the McMaster University, Canada, from November, 1995.

6. Mr. T. Nataraj underwent training in "Biostatistical methods in inference and evaluation" organised by the Indian Society for Medical Statistics, Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, from 11.12.95 to 16.12.95.

7. Mr. P.Veeramani underwent training in "Biostatistical methods in inference and evaluation" organised by the Indian Society for Medical Statistics, Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, from 11.12.95 to 16.12.95.

PAPERS PRESENTED AT SCIENTIFIC CONFERENCES

Name of conference, venue and date	Title of paper	Name of staff member
The Golden Jubilee of the Association of Physicians of India, Madras, 17-22 January, 1995	Correlation of lung inflammation with pulmonary function changes in victims of Bhopal tragedy	Dr.V.K.Vijayan
- do -	Nitric oxide and the lung (update session)	Dr.V.K.Vijayan
First National Conference on Bronchoscopy, Indian Association of Bronchology, Calcutta, 11-12 March, 1995	Flexible fibreoptic bronchoscopy in sputum smear negative pulmonary tuberculosis (Guest lecture)	Dr.V. K.Vijayan
34th Annual Conference of the National Academy of Medical Sciences(India), Madras, 18-19 March, 1995	Course of lung function in patients treated with tropical eosinophilia	Dr.V. K.Vijayan
Conference on Global Lung Health and Annual Meeting of the International Union Against Tuberculosis and Lung Diseases,Paris,France 9-12 September, 1995		Dr. N. Selvakumar
XIX National Congress of Indian Association of Medical Microbiologists(IAMM), JIPMER, Pondicherry, 6-8 October, 1995.	Characterization of **M.avium** and **M.fortuitum** complex organisms isolated from the environment and clinical samples of South Indian BCG trial area	Dr.C.N.Paramasivan
- do -	Evaluation of bactericidal action of ofloxacin and sulbactam/ampicillin, alone and in combination with rifampicin and isoniazid, on **M.tuberculosis in vitro**	Dr. Daniel Herbert

Name of conference, venue and date	Title of paper	Name of staff member
XIII Annual Conference of Indian Society for Medical Statistics and Symposium on Measurement of Change in Maternal and Child Health, Madras, 22-24 November, 1995	Some practical problems in the application of statistical methodolog in controlled clinical trials	Dr.T.Santha Devi
- do -	Reduction of prediction error in logistic regression using ridge estimation	Dr.P. Venkatesan
- do -	Two-way analysis of variance with missing values	Dr.P. Venkatesan
- do -	Cluster analysis in diagnosis of tuberculosis infection	Mr.R. Selvaraj
- do -	Quality of symptomatic status in district tuberculosis programme	Mr. P.G.Gopi
- do -	Assessing BCG coverage from children attending out-patient departments of hospitals	Mrs.M.P.Radhamani
Golden Jubilee Conference on TB & Chest Diseases, Thiruvananthapuram, 6-8 December, 1995	Interstitial lung diseases -diagnosis and management (CME lecture)	Dr.V.K.Vijayan
- do -	Characteristics of bacteriological relapse after the short course chemotherapy and management of patients who relapse with drug sensitive organisms	Dr.T.Santha Devi

Name of conference, venue and date	Title of paper	Name of staff member
Golden Jubilee Conference on TB & Chest Diseases, Thiruvananthapuram, 6-8 December, 1995	Utilisation of subcentres for drug delivery and its impact on case holding	Dr. Rajeswari Ramachandran
- do -	-	Dr. Soumya Swaminathan (Panel member)
World Conference on Cardio-Pulmonary & CriticalCareMedicine organised by the American College of Chest Physicians (West India Chapter), Bombay, 7-10 December, 1995	Pulmonary eosinophilia (Symposium)	Dr.V.K.Vijayan
- do -	Occupational asthma (Symposium)	Dr.V. K.Vijayan
- do -	Sepsis & MODS in developing countries (Symposium)	Dr.V.K.Vijayan
19th Biennial Conference of Indian Association of Leprologists, B. J. Medical College, Pune, 15-17 December, 1995	The status of long absentees among multibacillary leprosy patients admitted to a controlled clinical study	Mrs.K.Jagga Rajamma
- do -	-	Dr.A.Thomas
National Seminar on BiotechnologyonRural and Industrial Development, Gulbarga, 22-23 December, 1895	Evaluation of PCR-SSCP against indirect sensitivity test in the classification of rifampicin resistance in M.tuberculosis	Dr.N.Selvakumar

Name of conference, venue and date	Title of paper	Name of staff member
XXll Annual Conference of the Association of Clinical Biochemists of India, Perundurai Medical College, Perundurai, 21-30 December, 1995	Impact of anti-tubercul-osis - drugs on clinical biochemistry values	Dr.M.Kannapiran
Third Asia-Pacific Aids Conference and Work-shop in TB Control in HIV era, Chiang Mai, Thailand, 20-22 September, 1995	HIV-TB situation in India	Dr.Manjula Datta (Working group member)

PARTICIPATION BY THE CENTRE'S SCIENTISTS IN SYMPOSIA, WORKSHOPS, MEETINGS AND TRAINING COURSES HELD AT OTHER INSTITUTIONS

Name of the event, venue and date	Title of paper	Name of staff member
CME Programme in respiratory pathogens,Indian Association of Medical Microbiologists, Tamilnadu and Pondicherry Chapter, Vellore, 7 January, 1995	Multidrug resistant **M.tuberculosis**	Dr.N.Selvakumar
Calicut Medical College Alumni Oration, Calicut, 15 January, 1995	Health effects of Bhopal gas disaster	Dr.V. K.Vijayan
National Workshop on Mycobacterial Infections in Livestock, Tamilnadu Veterinary Animal Sciences University, Madras, 22-23 February, 1995	Multi-drug resistant tuberculosis - laboratory aspects	Dr.N. Selvakumar
- do -	Recent advances in the laboratory diagnosis of mycobacterial infections	Dr. C.N.Paramasivan
Workshop on Antimicrobial Assessment, Indian Association of Medical Microbiology Tamilnadu Dr. M. G. R. Medical University, Madras, 24 February, 1995	Drug resistance in tuberculosis: prevalence, types and measurement	Dr. C.N.Paramasivan
Refresher Course in Environmental Science, Bharathiar University, Coimbatore, 24 February, 1995	a. Bacterial pathogens b. Bacterial diseases	Dr. N. Selvakumar

Name of the event, venue and date	Title of paper	Name of staff member
Symposium on the Role of Medical Laboratory Technologists in Human Health, Loyola College, Madras, 24-25 February, 1995	The pharmacologi-cat and biochemical aspects of adverse reactions to drugs with particular refer-ence to anti-tuber-culosis drugs	Dr.Prema Gurumurthy
Meeting of the Filariasis Field Trials Task Force, TDR/WHO, Geneva, 13-16 March, 1995	-	Dr. V. Kumaraswami
4th European Symposium, Berlin, Germany, 22-24 March, 1995	Application of saliva in clinical practice and research	Dr.Prema Gurumurthy (Chair person)
Joint ICMR/TDR/WHO IV Workshop on Socio-Econo-mic Impact of Lymphatic Filariasis, Madras, 25-31 March, 1995	-	Dr.Manjula Datta
- do -	-	Mrs.M. P. Radhamani
Workshop on Revised National TB Control Programme (NTCP), Directorate General of Health Sciences, New Delhi, 11-12 April, 1995	Development of training modules for revised National TB control programme	Dr.V. K.Vijayan (Expert member)
Annual meeting of State TB Programme Officers, Directorate General of Health Sciences, New Delhi, 4-5 May, 1995	-	Dr.V. K.Vijayan (Expert member)
National Workshop on Laboratory Diagnosis of Opportunistic infections in AIDS, Madurai Medical College, Madurai, 12-13 May, 1995	Laboratory diagno-sis of mycobacterial infections in AIDS	Dr. Daniel Herbert

Name of the event, venue and date	Title of paper	Name of staff member
Meeting of the Indo-Russian Collaboration in the Field of Tuberculosis, Central TB Research Institute, Moscow, 14-23 May, 1995	-	Dr. R. Prabhakar, Dr.P.R. Narayanan & Dr. C.N.Paramasivan (Delegates of ICMR)
Image Analysis Workshop, BIO-RAD, Indian Institute of Science, Bangalore, 5-6 June, 1995	-	Dr. D. Sulochana
Seminar on Information Technoloy and Resource Sharirg, Tamilnadu Dr.M.G.R. Medical University, Madras, 15 June, 1995	-	Mr. M.G. Sreekumar
Seminar on Tuberculosis Update, Academy of Medical Sciences, Annamalai University Anna malai Nagar, 23, June, - 1995	Laboratory diagnosis of tuberculosis	Dr. C.N.Paramasivan
Recent Advances in the Epidemiology and Diagnosis of Zoonotic Diseases, Education Summer Institute, Madras Veterinary College, Madras, 23 June, 1995	Recent advances in diagnosis and immunoprophylaxis of tuberculosis in human beings	Dr. C.N.Paramasivan
-do-	Current Status of tuberculosis in human beings-epidemiological features	Dr.M.S.Jawahar
Training Course for Medical Officers, Institute of Thoracic Medicine, Madras,26-30 June, 1 995	Managing tuberculosis at district level	Dr.V. K.Vijayan (Facilitator)

Name of the event, venue and date	Title of paper	Name of staff member
Workshop on Community Information Services, Development and Environmental Matters, Indian National Trust for Art and Cultural Heritage, Madras, 27 June, 1995	-	Mrs. Sudha Ganapathy
- do -	-	Dr. Geetha Ramani Shanmugam
- do -	-	Mrs.Beena Thomas
Refresher Course on Tuberculosis for Medical Officers (North Arcot Ambedkar district), Vellore, 30 June, 1995	Chemotherapy of tuberculosis and drug resistant tuberculosis	Dr.T.Santha Devi
Symposium on Genetics and Gene Expression, Acid Fast Club University of East Anglea, Norwich, England, 7 July, 1995	-	Dr. N. Selvakumar
Workshop on Internet For Information Professionals (IFIP), National Centre for Science Information, Indian Institute of Science, Bangalore, 18-20 July, 1995	-	Mr. M.G. Sreekumar
Respiratory Update, American College of Chest Physicians, (South India Chapter), Pondicherry, 29 July, 1995	Inhalation therapy in bronchial asthma (Guest lecture)	Dr.V.K.Vijayan
13th Annual CME Programme of Lakeside Educational Trust and IAP Respiratory Chapter,Bangalore, 30 July, 1995	Evaluation of Stridor in children (Guest lecture)	Dr.Soumya Swaminathan

Name of the event, venue and date	Title of paper	Name of staff member
Expert Committee Meeting on Drug Dosages in Revised Strategy of NTCP \Directorate General of Health Services, New Delhi, 3 August, 1995	Introduction of short course chemotherapy in the NTCP of India - TRC trial	Dr.V.K.Vijayan
IAL Workshop on "Issues during and after elimination of leprosy " Sakthi Nagar, 12-13 August, 1995	Issues for basic and laboratory research pertaining to elimination of leprosy	Dr.V.D.Ramanathan
Symposium, Apollo Hospitals, Madras, 24 August, 1995	Bronchial asthma	Dr.V. K.Vijayan
- do -	Pulmonary function testing in children (Guest lecture)	Dr.Soumya Swaminathan
Meeting of the Filariasis Field Trials Task Force, TDR/WHO, Geneva, 18-21 September, 1995	-	Dr. V. Kumaraswami
Refresher Course on Tuberculosis for Medical Officers, Joint Director of Health Services, Tiruvannamalai, 23 September, 1995	Revised strategy of managing tuberculosis at district level	Dr.V.K.Vijayan
- do -	Chemotherapy of tuberculosis	Dr.T.Santha Devi
Association of Physiologists and Pharmacologists of India, Tamil Nadu Chapter, Madras, 27-28 October, 1995	Cardio-pulmonary responses to exercise training (Guest lecture)	Dr.V. K.Vijayan
CME Programme of IMA, Salem Branch, Salem, 29 October, 1995	Childhood asthma	Dr. Soumya Swaminathan

Name of the event, venue and date	Title of paper	Name of staff member
Workshop on Information Technology for Libraries, Indian National Scientific Documentation Centre (CSIR), Madras, 1 November, 1995	–	Mr. M.G. Sreekumar
Andhra Pradesh Chest Hospital, Hyderabad, 25 November, 1995	Tropical eosinophilia (Guest lecture)	Dr.V. K.Vijayan
- do -	Pulmonary function tests	Dr.V.K.Vijayan (Resource person)
Global Congress on Cardiac Sciences, Institute of Cardiovascular Diseases, Madras, 13-1 6 December, 1995	-	Dr.V. K.Vijayan (Delegate)
CME Programme, IMA-Apollo Thousand Gate branch, Madras, 28 December, 1995	Chronic bronchitis and emphysema	Dr.V.K.Vijayan
Third Annual Convention of Pi-Beeta Mathematical Association, Madras, 29-30 December, 1995	Basic concepts of applied statistics (Presidential address)	Dr.P.Venkatesan
DPT sponsored VAP Meeting New Delhi, July, 1995	Epidemiology of ARI	Dr.Manjula Datta
- do -	Epidemiological factors in typhoid in the choice of vaccine	Dr.Manjula Datta
Meeting of Indo-US VAP Typhoid Project, Washington, USA, 6-15 September, 1995	-	Dr.Manjula Datta

Name of the event, venue and date	Title of paper	Name of staff member
Research Seminar, London School of Hygiene and Tropical Medicine, London, 26 April, 1995	Studies on simple procedures in diagnostic mycobacteriology	Dr. N. Selvakumar
Research Seminar, London School of Hygiene and Tropical Medicine, London, 18 May, 1995	Drug resistant pulmonary tuberculosis in India	Dr. N. Selvakumar
A Symposium on Tuberculosis Chest, Heart and Stroke. The Royal College of Physicians, Edinburgh, Scotland, 2 June, 1995	-	Dr. N. Selvakumar
Conference on Tuberculosis in 1990s. Royal College of Physicians of London, London, 12 June, 1995	-	Dr. N. Selvakumar
International Conference on New Applications of Emerging Molecular Diagostics for Infectious Diseases, London, 26-27 June, 1995	-	Dr. N. Selvakumar
64th Annual Meeting and Summer Conference of The Society of Applied Bacteriology, University of Southampton, England	-	Dr. N. Selvakumar

LIST OF PUBLICATIONS

Papers published

1. Rajeswari, R., Sivasubramanian, S., Balambal, R., Parthasarathy, R., Ranjani, R., Santha, T., Somasundaram, P.R., Ganapathy, S., Sudarsana, K., Zaheer Ahmed Sayeed, Kalyanaraman, S. and Prabhakar, R. A controlled clinical trial of short course chemotherapy for tuberculoma of the brain. **Tubercle and Lung disease,** 1995, **76,** 311-317.

2. Rajeswari Ramachandran, Diwakara, A.M., Sudha Ganapathy, Sudarsanam, N.M., Rajaram, K. and Prabhakar, R. Tuberculosis awareness among educated public in two cities in Tamil Nadu. **Lung India,** 1995, **13,** 108-113.

3. Somu, N., Swaminathan, S., Paramasivan, C.N., Vijayasekaran, D., Chandrabhooshanam, A., Vijayan, V.K. and Prabhakar, R. Value of bronchoalveolar lavage and gastric lavage in the diagnosis of pulmonary tuberculosis in children. **Tubercle and Lung Disease,** 1995, **76,** 295-299.

4. Soumya Swaminathan, Venkatesan, P., Sankaran, K., Prabhakar, R., Vijayan, V.K., Somu, N. and Vijayasekaran, D. Cellular profile of bronchoalveolar lavage fluid in pulmonary tuberculosis. **Archieves of Disease in Childhood,** 1995, **73,** 182.

5. Balasubramanian, R., Sadacharam, K., Selvaraj, R., Xavier, T., Gopalan, B.N., Shanmugam, M. and Prabhakar, R. Feasibility of involving literate tribal youths in tuberculosis case-finding in a tribal area in Tamil Nadu. **Tubercle and Lung Disease,** 1995, **76,** 355-359.

6. Vijayan, V.K., Sankaran, K., Sharma, S.K. and Misra, N.P. Chronic lung inflammation in victims of toxic gas leak at Bhopal. **Respiratory Medicine,** 1995, **89,** 105-111.

7. Vijayan, V.K. Nitric oxide and the lung. **In: Medicine update. Ed. P.S. Shankar. Association of Physicians of India,** Bombay. 1995, **4,** 396-399.

8. Vijayan, V.K., Subramaniam, P., Venkatesan, P., Sankaran, K. and Gnanaguruparan, K.S. Characterization of airway inflammation in stable bronchial asthma. **Lung India,** 1995, **13,** 132-135.

9. Vijayan, V.K. and Reetha, A.M. Rehabilitation for chronic obstructive pulmonary disease patients - Exercise training component. **Lung India,** 1995, **13,** 71-74.

10. Raghu, G., Sarma, G.R. and Venkatesan, P. Effect of anti-tuberculosis drugs on the iron-sequestion mechanism. **Indian Journal of Pathology and Microbiology,** 1995, **38,** 287-292.

11. Prabhakar, R. Needs in tuberculosis research. **IndianJournal of Tuberculosis,** 1995, **42,** 179-1 81.

12. Prabhakar, R. Drug resistant tuberculosis - Overview. Integral Physician's Digest, TB Issue, 1995, **1,** 4-15.

13. Mohanarani Suhadev, Sudha Ganapathy, Sivasubramanian, S. and Santha Devi, T. A retrospective study of 'Non-compliant' patients in controlled clinical trials of short course chemotherapy. **Indian Journal of Tuberculosis.** 1995, **42,** 221-224.

14. Sara Mathew, Paramasivan, C.N., Manjula Datta and Prabhakar, R. Vancomycin for controlling contamination of selective Kirchner's liquid medium in the culture of gastric lavage for tubercle bacilli. **Indian Journal of Medical Research,** 1995, **102,** 152-155.

15. Selvakumar, N., Vanajakumar, Gopi, P.G., Venkataramu, K.V., Manjula Datta, Paramasivan, C.N. and Prabhakar, R. Isolation of tubercle bacilli from sputum samples of patients in the field studies by the cetylpyridinium chloride-sodium chloride and sodium hydroxide methods. **Indian Journal of Medical Research,** 1995, **102,** 149-151.

16. Alamelu Raja, Narayanan, P.R., Rema Mathew and Prabhakar, R. Characterization of mycobacterial antigens and anti-bodies in circulating immune complexes from pulmonary tuberculosis. **Journal of Laboratory and clinical medicine,** 1995, **125,** 581-587.

17. Subramanian, V.S., Selvaraj, P., Narayanan, P.R., Prabhakar, R. and Damodaran, C. Distribution of HLA (class I and class II) antigens in the native Dravidian Hindus of Tamil Nadu, South India. **Gene Geography,** 1995, **9,** 15-24.

18. Das, S., Paramasivan, C.N., Lowrie, D.B., Prabhakar, R. and Narayanan, P.R. IS6110 restriction fragment length polymorphism typing of clinical isolates of **Mycobacterium tuberculosis** from patients with pulmonary tuberculosis in Madras, South India. **Tubercle and Lung Disease,** 1995, **76,** 550-554.

19. Paramasivan, C.N., Daniel Herbert and Prabhakar, R. BCG: Do we have an alternative? **ICMR Bulletin,** 1995, **25,** 33-40.

20. Daniel Herbert, Paramasivan, C.N., Manjula Datta, Vallishayee, R.S. and Prabhakar, R. IgG antibodies against antigens of various mycobacterial species in children and in pre- & post-BCG young adults. **Indian Journal of Tuberculosis,** 1995, **42,** 15-21.

21. Sara Mathew, Paramasivan, C.N., Fathima Rehman, Balambal, R., Rajaram, K. and Prabhakar, R. A direct rifampicin sensitivity test for tubercle bacilli. **Indian Journal of Medical Research,** 1995, **102,** 99-103.

22. Reetha, A.M., Krishnamurthy, P.V., Santha Devi, T. and Prabhakar, R. Interim findings on the evaluation of split drug regimens for pulmonary tuberculosis - A randomised controlled clinical trial. **Indian Journal of Tuberculosis,** 1995, **42,** 201-206.

23. Kolappan, C., Selvaraj, R., Abdul Khudoos, Appe Gowda, B.N., Manjula Datta and Prabhakar, R. Repeatability of nerve thickness assessment in the clinical examination for leprosy. **Leprosy Review,** 1995, **66,** 224-228.

24. Shenoy, R.K., Sandhya, K., Suma, T.K. and Kumaraswami, V. A preliminary study of filariasis related to acute adenolymph-angitis with special reference to precipitating factors and treatment modalities. **South East Asian Journal of Tropical Medicine and Public Health,** 1995, **26,** 301 - 305.

25. Sahadevan, R., Sujatha Narayanan, Paramasivan, C.N., Prabhakar, R. and Narayanan, P.R. Restrictidn fragment length polymorphism typing of clinical isolates of **mycobacterium tuberculosis** from patients with pulmonary tuberculosis in Madras, India, by use of direct-repeat probe. **Journal of Clinical Microbiology,** 1995, **33,** 3037-3039.

Papers accepted for publication

1. Vijayan, V.K. Transbronchial lung biopsy. **In: Medicine Update. Ed. Manoria PC. Association of Physicians of India,** Bombay.
2. Vijayan, V.K., Paramasivan C.N. and Sankaran, K. Comparison of bronchoalveolar lavage fluid and sputum culture examinations in the diagnosis of sputum smear negative pulmonary tuberculosis. **Indian Journal of Tuberculosis.**
3. Vijayan, V.K. Methyl isocyanate toxicity: A review of animal experimental studies. 1 . Short-term effects. **Lung India.**
4. Vijayan, V.K. Methyl isocyanate toxicity: A review of animal experimental studies. 2. Long-term effects. **Lung India.**
5. Vijayan, V.K. Tropical eosinophilia: a review. **Indian Journal of Chest Diseases and Allied Sciences.**
6. Vijayan, V.K. and Sankaran, K. Relationship of lung inflammation with changes in lung function and severity of exposure in victims of Bhopal Tragedy. **European Respiratory Journal.**
7. Vijayan, V.K. Chronic obstructive pulmonary disease - complications. **In: Monogram on COPD. Ed: P.S. Shankar. Indian College of Physicians, Bombay.**
8. Vijayan, V.K. Tropical eosinophilia. In: Recent Advances in Respiratory Medicine. **Ed: S.K. Sharma (AIIMS) and D. Behera (PGI).**

9. Moses, A.K., Vijayan V.K., Kuppu Rao, K.V. and Radha, S. Effect of different pedalling speeds on anaerobic threshold and acid-base balance. **Indian Journal of Physiology and Pharmacology.**

10. Paramasivan, C.N., Kamala, T., Daniel Herbert, Venkatesan, P., Alugu Palli, S., Larsson, L. and Prabhakar, R. Heterogeneity within myco bacteria belonging to **M. avium** complex and **M.fortuitum** complex isolated from environmental and clinical samples of South Indian BCG trial area. **Microbiology.**

11. Kamala, T., Paramasivan, C.N., Daniel Herbert, Venkatesan, P. and Prqbhakar, R. Immune response and modulation of immune response induced in the guinea pigs by Mycobacterium Avium Complex (MAC) isolates from soil and sputum samples from the South Indian BCG trial area. **Indian Journal of Medical Research.**

12. Selvakumar, N., Vanajakumar, Thilothammal, N. and Paramasivan, C.N. Isolation of **M.tuberculosis** from CSF specimens by the centrifugation and filtration methods. **Indian Journal of Medical Research**

13. Brahma Jothi, V., Pichappan, R.M., Paramasivan, C.N., Rajaram, K., Sankar Kumar and Prabhakar, R. Immune status and chemotherapy in pulmonary tuberculosis in South India. **Tubercle and lung diseases.**

14. Suresh, S., Kumaraswami, V., Suresh, I., Rajesh, K., Suguna, G., Vijayasekaran, D., Ruckmani, A. and Rajamanickam, M.G. The ultrasound diagnosis of subclinical filariasis. **Journal of ultrasound in medicine.**

15. Jagga Rajamma, K., Vijaya Baskar, D., Narayana, A.S.L., Rajeswari Ramachandran and Prabhakar, R. Health seeking behaviour, acceptability of available health facilities and awareness on tuberculosis in a tribal area **Indian Journal of Tuberculosis.**

JOURNAL CLUB

Journal Club meetings were held each week, at which published scientific articles covering different areas of research were reviewed by staff members of various departments in turn. A synopsis of the paper(s) to be presented and the reference details were circulated in advance, to facilitate better participation by the audience in the discussion that followed the presentation. In all, 43 such meetings were conducted during the year.

In addition, a quiz programme on tuberculosis and related diseases was conducted.

LECTURES BY VISITING SCIENTISTS

Subject	Speaker
Surfing the information super-highway	Dr. Nithya Raghavan, Department of Molecular Micro-biology & Immunology, School of Hygiene & Public Health, John Hopkins University, Baltimore, USA.
Health social science research	Ms. Shubha Kumar, INCLEN Social Scientist, Madras Medical College, Madras.
Recent advances in the diagnosis and management of osteopenia osteoporosis	Dr.S. Krishnan, Director, Medical Physics, Toronto General Hospital & Osteoporosis Research Lab., Toronto, Canada.

GUEST LECTURE

Dr.C.V. Ramakrishnan, Former Deputy Director, Tuberculosis Research Centre, Madras, delivered a lecture on "The Creator's bequest to human body".

DISTINGUISHED VISITORS

1. Dr.S.Lakshminarayanan, Chief, Pulmonary Medicine, University of Washington, USA.
2. Dr.T.B. Nutman, National Institutes of Health, USA.
3. Dr. Peter Davies, Director, Tuberculosis Research Unit, Cardio-thoracic Centre, University of Liverpool, UK.
4.. Ms.Gretchen Roedde, Ms. Karin Revuelta & Ms.Verner Kristiansen DANIDA team.
5. Dr.Sergid Spinaci, Consultant, WHO Tuberculosis Programme, Geneva.
6. Dr.W.J. Terpstra and Mr.H.Korver, The Royal Tropical Institute, Amsterdam.
7. Dr.C.O.R.Everard, The Medical Research Council, U.K.
8. Dr. James Paton, Paediatric Pulmonologist, University of Glasgow, Glasgow, U.K.
9. Dr.S.L. Chan, Wanchai Chest Clinic, Chest Service, Hong Kong.
10. Dr. Lee B Reichman, National Tuberculosis Centre, Newark N.J., U.S.A.
11. Mr.S. Bhargava, Senior Deputy Director General, ICMR, New Delhi.

STAFF MEMBERS ON ADVISORY COMMITTEES OF OTHER INSTITUTIONS

Staff member	Name of committee
Dr. C.N. Paramasivan	Editorial Board, Indian Journal of Tuberculosis, New Delhi.
- do -	Editorial Board, Indian Journal of Medical Microbiology, JIPMER, Pondicherry.
- do -	Board of Studies in Microbiology, University of Madras, Madras.
- do -	Member, Standing Technical Committee, Tuberculosis Association of India, New Delhi.
Dr. T. Santha Devi	Steering Committee of Therapy for Mycobacterial Diseases and Joint Steering Committee for Mycobacterial Diseases and Immunology of Mycobacterial Diseases, WHO Geneva.
Dr. V.K. Vijayan	Expert member, Central Crisis Group (CCG) for Chemical - Disasters, Ministry of Environment and Forests, Govt. of India, New Delhi.
- do -	Respiratory Medicine Panel, Institute of Integral Health Studies, Madras.
- do -	Expert member, Crisis Management Group for Chemical Road Transportation Emergency, Tamilnadu Pollution Control Board, Government of Tamilnadu.

Staff member	Name of committee
Dr. V.K. Vijayan	Editorial Board, Indian Journal of Chest Diseases & Allied Sciences, V.P. Chest Institute, Delhi.
- do -	Assistant Editor, Lung India, Madras.
- do -	Governor, International Academy of Chest Physicians & Surgeons, USA.
- do -	Nominating Committee member, American College of Chest Physicians, Northbrook, USA.
- do -	National Advisory Committee, World Conference on Cardio-Pulmonary Diseases and Critical Care Medicine, (1995), Bombay.
Dr. Manjula Dutta	Curriculum Development Committee for Clinical Epidemiology. The Tamilnadu Dr.M.G.R University of Medical Sciences, Madras.
- do -	Scientific Advisory Committee, Regional Medical Research Centre for Tribals, Jabalpur.
Dr.V. Kumaraswami	Filariasis Field Trial Task Force, UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), Geneva.
- do -	Expert, WHO Panel on Parasitic Diseases (Filariasis), WHO, Geneva.
Dr. Soumya Swaminathan	Editorial Committee, IAP Journal of Practical Pediatrics, Madras.

Staff Member	Name of committee
Dr.V. D. Ramanathan	Consultant for histopathology Central Leprosy Training Research Institute, Chingleput, and CJIL Field Unit, Avadi, Madras.
Dr.K.V. Kuppurao	Executive Council Member, Indian Association of Biomedical Scientists, Madras.
Dr. P. Selvaraj	Board of studies in lmmunolog / Immunogenetics (Zoology), Lady Doak College, Madurai.
Dr. P. Venkatesan	Editorial Board, Biomedicine, Madras.

PRIZES AND AWARDS RECEIVED By THE STAFF MEMBERS

1. Dr.V.K.Vijayan was awarded the " Prof.K.C.Mohanty Award" by the Tuberculosis Association of India, New Delhi, for the year 1995.

2. Dr.V.K.Vijayan was awarded the Fellowship of the Indian College of Cardiology.

3. Mrs. Sara Mathew was awarded the "Dr.R.Krishna memorial cash prize" for the best paper entitled "A direct rifampicin susceptibility test for tubercle bacilli", presented at the 49th National Conference on Tuberculosis and Chest Diseases held at JIPMER, Pondicherry, during 1994.

ACKNOWLEDGEMENT

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