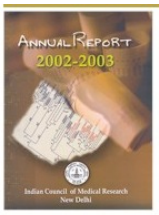

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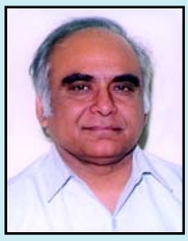


From the Desk of the Director-General

I am pleased to report the activities, progress and achievements of the Indian Council of Medical Research (ICMR) for the year 2002-2003. This year has been as much interesting as it was exciting. Besides addressing the existing health problems confronting the country, scientists of the Council could successfully confront new challenges such as SARS. As in the last year, our researchers tackled these health problems with the conventional means as also with help of tools of modern biology. Not surprisingly, the ICMR's contributions during this year found a new thrust and focus, purpose of which is betterment of the health of Indian people.

During 2003, two of the Council's Institutes-the Malaria Research Centre, Delhi and the Institute of Research in Medical Statistics, New Delhi completed 25 years of their inception. This is an opportune time for these Institutes to take stock of their significant contributions, identify strengths and weaknesses and chart out new action plans to meet the new and emerging health problems, and rededicate themselves for national development. I am also pleased that during this year, in view of its pioneering contributions, the Enterovirus Research Centre, Mumbai was recognized as WHO's Global Specialized Laboratory for Polio and the Tuberculosis Research Centre, Chennai recognized as International Centre of Excellence in Research by the National Institutes of Health, Bethesda, USA.

There have been major achievements in the areas of diagnostics and vaccines for several disease conditions. The incidence of HIV infection has reached alarmingly high levels worldwide and India is not an exception. We are making an attempt to develop an HIV/AIDS vaccine using modified Ankara vaccinia as vector in collaboration with the Therion Biologics, USA with support of the International AIDS Vaccine Initiative, New York. Vaccines are also being developed for hepatitis A, cholera, Japanese encephalitis, typhoid and leishmaniasis. In another significant development, the ICMR scientists have established a single cell PCR for prenatal diagnosis of thalassemia. Some technologies like production of HepA-IgM kit, antigen detection kit for rotavirus and hepatitis B and PCR based tests for hepatitis B/C have been developed and are being transferred to the industry.

In the area of drug development, phase III clinical trials have been successfully completed for miltefosine, an oral drug for kala azar. Over 93% efficacy was noticed in new as well as unresponsive cases. Praneem, a neem based microbicide, developed in partnership with Panacea Biotech has entered into phase II clinical trial. Picroliv, an indigenous preparation for liver diseases has gone into Phase IV clinical trial in collaboration with the CSIR. Anti-malarial combination therapy using artesunate and sulphapyridoxamine has shown very promising results.

Several new disease outbreaks were investigated by the ICMR. Some of these infections were found to be caused by new agents like the multi drug resistant *Shigella dysenteriae* type 1 strain; Gp B adult rotaviruses like *Vibrio parahaemolyticus* 03:kp. A new simian retrovirus-SRV 6 was also isolated. This is the first report of SRV in langur.

To cope with the challenges in biomedical research some new Units have been established in the areas of Biomedical Ethics, Intellectual Property Rights, Bioinformatics, Modern Biology, Medicinal Plants and Social Sciences. Guidelines have been published for regulating research in stem cells, use of genetically modified foods, animal experimentation and assisted reproductive technology for use in infertility clinics in India.

Other major initiatives include the starting of MD-Ph.D programme in collaboration with the Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow. During the financial year 2002-2003, 629 research schemes and 181 fellowships were funded. As many as 1800 scientific personnel, 2700 technical staff and 800 supporting staff were trained during the period. The scientists of the ICMR's institutes published over 330 scientific papers in national and international journals during the year 2002. The impact factor per paper of ICMR was 2.092 for the year. Twenty patents were filed, out of which 2 were filed abroad in USA.

In the year 2002-03 only Rs 116 crore was sanctioned by the Government to ICMR leaving unmet need of 27 crore. Despite the sub-optimal funding, the scarce resources were very judiciously utilized. In the coming years also, the Council shall strive hard to serve the nation even better.

Nirmal Kumar Ganguly
Director-General

OVERVIEW

The Indian Council of Medical Research is an autonomous body funded by the Ministry of Health & Family Welfare. It undertakes and supports basic, epidemiological, applied and operational research in the areas of national public health importance. Its research activities are carried out not only through its network of 26 institutes and large number of field stations, but also through extramural research programmes, wherein grant-in-aid is provided to investigators in non-ICMR institutions.

During the year, two Institutes celebrated 25 years of their existence *viz.*, Malaria Research Centre, Delhi and the Institute for Research in Medical Statistics, New Delhi. In recognition of their excellence the Enterovirus Research Centre, Mumbai has been designated as WHO's Global Specialized Laboratory for Polio and the Tuberculosis Research Centre, Chennai has been recognized for the establishment of International Centre of Excellence in Research by National Institutes of Health, Bethesda, USA.

The year 2002-03 was the first year of the 10th five-year plan. Against the Council's need of Rs 2500 crores for the Plan period, the Planning Commission has made an allocation of Rs 970 crores (Rs 870 crores for Health and Rs 100 crores for Family Welfare) as compared to Rs 5368 crores for ICAR; Rs 1450 crores for DBT; Rs 2575 crores for CSIR. During the year (2002-03) Rs 116 crores were sanctioned under Plan (Health) leaving an unmet need of Rs 27 crores.

Judicious use of the limited resources was made. In addition to funding the traditional areas of research (like communicable diseases, non-communicable diseases, reproductive health and nutrition), new Cells/Units were established in the areas of Ethics, Modern Biology, Bio-informatics, Medicinal Plants, Social Sciences and Intellectual Property Rights to give a thrust to these disciplines. Special thrust to research in North Eastern states has been given with 11 new schemes initiated. For the year, the average impact factor (IF) per paper of ICMR is 2.092 as compared to 1.661 for 2001 and 1.456 for year 2000. During the period 2000-03, 20 patent applications including two US patents were filed.

VACCINES

Appreciable progress has been made towards development of an HIV/AIDS vaccine using Indian strain of HIV-1 sub-type C. In partnership with the International AIDS Vaccine Initiative (IAVI), New York, USA a

HIV vaccine using a modified Ankara vaccinia as a vector is being developed. Pre-clinical toxicity studies are in progress. Two additional approaches are in the research mode, one using recombinant BCG as a vector, and the other multiple epitope vaccine. Phase I of an oral recombinant cholera vaccine (developed in partnership with CSIR) has been completed. A vaccine for hepatitis -A has been developed and the technology has been transferred to Bharat Biotech, Hyderabad for commercialization. Research on chimeric peptide vaccine and DNA based Japanese encephalitis vaccine has been stepped up. Preparations are ongoing for undertaking trial of cholera, typhoid, GABH Streptococci vaccine against rheumatic fever/ rheumatic heart disease, HPV for cervical cancer and malaria vaccine(s). Discovery of a new gene regulating the growth of *Leishmania donovani* has potential for developing an attenuated vaccine candidate.

DRUGS

Phase III clinical trials with miltefosine (an oral drug for kala-azar) have been successfully completed. Over 93% efficacy has been reported in new as well as unresponsive cases. *Praneem* (a neem based microbicide, developed in partnership with Panacea Biotech) has entered into Phase II for clinical trial. Picroliv (an indigenous preparation for liver diseases) has gone into Phase IV in collaboration with CSIR. Anti-malaria combination therapy using artesunate and sulfapyridoxamine or chloroquine has shown very promising results.

DIAGNOSTICS

Technology for production of HepA- lgM kit has been transferred to industry. Antigen detection kit for rotavirus and hepatitis B and PCR based tests for hepatitis B\C and E have been developed. A diagnostic test for leptospirosis is being developed. An ELISA test for amastigote antigen of *L.donovani* compared well with PCR test thereby becoming a simpler and cost effective choice for diagnosis of kala-azar. A single cell PCR has been established for the prenatal diagnosis of β thalassaemia.

MICROBIAL REPOSITORIES

Repositories are being nurtured as national resource centres by providing research institutes and others biological material for testing of new drugs, understanding host-parasite interaction *etc.* Presently, ICMR has repositories of malaria parasites, *L. donovani*, mycobacteria, cholera, HIV and other viruses.

NEW AND EMERGING INFECTIONS

During the year the Council investigated several outbreaks. Some of them were found to be caused by new agents like the multi-drug resistant *Shigella dysenteriae* type 1 strain; Gp B adult diarrhoea rotaviruses and *V. parahaemolyticus* 03: kp in Jalpaiguri and Sunderban areas of West Bengal. A new simian retrovirus- SRV-6 was also isolated. This is the first report of Indian SRV in *langur*.

REPRODUCTIVE AND MATERNAL HEALTH

Clinical evaluation of newer contraceptive technology is being done. Studies were conducted for prevention of postpartum haemorrhage by administration of misoprostol by paramedical workers in rural areas.

ICMR INSTITUTIONAL NETWORK

NUTRITION

Technology is being developed for double fortification of salt, sugar and wheat flour. Molecular analysis and genetic typing of obese rats was continued during the year.

LIFE STYLE RELATED DISEASES

Surveillance of cancer and risk factors for non-communicable diseases *i.e.* tobacco and alcohol use, physical activity, intake of fruits and vegetables and blood pressure level have been taken up. National consensus on guidelines for prevention and management of diabetes mellitus were evolved. Information on mental morbidity and health service needs for urban population and disaster affected people in Gujarat is being collected.

HUMAN RESOURCES DEVELOPMENT

In addition to regular and short-term training courses offered by its Institutes, a Junior Research Fellowship programme has been introduced in which 200 candidates are selected, of them half are offered fellowship for pursuing a Ph.D programme. A MD-Ph.D programme has been launched in collaboration with Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow. A scheme for providing support for M.D. thesis in priority areas has also been initiated. As part of extramural research programme, during 2002-2003 over 2700 technical staff, 1800 scientific personnel and 800 supporting staff were trained.

EXTRAMURAL RESEARCH PROGRAMME

Of over 900 projects funded during the year about 60% were bagged by research institutes and 18% by medical colleges. Universities, hospitals and the like contributed the remaining 22%. About half of these projects were in modern biology and laboratory based studies and 30% were clinical studies. Operational research, epidemiological studies *etc.* formed the remaining 20%.

RESEARCH CAPACITY STRENGTHENING

The Council has initiated a programme for strengthening research capacity in medical colleges. In first phase of the programme, colleges in Kerala, Karnataka, Maharashtra, West Bengal and Orissa have been targeted.

GUIDELINES

The ICMR has prepared ethical guidelines to regulate stem cell research in India, and for use of genetically modified foods. Guidelines for the use of animals and animal facilities for experimentation/teaching in medical colleges have also been formulated. In May 2002, a document on Intellectual Property Rights Policy was released to provide appropriate technological, professional and legal expertise and services to file patents in India and abroad. Guidelines have also been promulgated for accreditation, supervision and regulation of assisted reproductive technology for use in infertility clinics in India.

INTERNATIONAL COLLABORATIONS

The year 2002-03 saw further strengthening of research activities between ICMR and USA, Japan, Italy, France, Armenia, Russia and Germany.

CENTRAL SCHEMES TRANSFERRED

During the year several of central sector schemes were transferred to ICMR. These included Diabetes Control Programme; Diseases to which SC and ST are Generally Prone; Environmental Health and Risk Assessment; National Programme for Control and Treatment of Occupational Diseases; Medical Care for Remote and Marginalized Tribal and Nomadic Communities; Tribal Sub- Plan and Special Component for SC/ST; and Programme for North-Eastern States. However, no additional budget was sanctioned for these schemes.

COMMUNICABLE DISEASES

Communicable diseases are a major public health problem of developing countries like India. The Government of India is operating various National programmes for their control and the ICMR supports research for control of these diseases by carrying out various intramural and extramural research projects. Most of the ICMR Institutes/Centres conduct research on various aspects of communicable diseases. Extramural research projects are funded at medical colleges, universities and research institutes throughout the country.

The ICMR has given top priority to research in bacterial (TB, leprosy, diarrhoeal diseases), parasitic (malaria, filariasis and leishmaniasis) and viral (Japanese encephalitis, poliomyelitis, hepatitis and HIV/AIDS) diseases. AIDS is the most dreaded scourge in India and the Council is striving to meet the new challenges of its control and prevention.

BACTERIAL DISEASES

TUBERCULOSIS

Tuberculosis remains by far the biggest public health problem of the country. The Tuberculosis Research Centre (TRC) of the Council at Chennai continues to serve its mandate of research in the clinical, laboratory and epidemiological aspects of tuberculosis. In recent times there has been a deliberate realignment of the focus of the Centre's research to address issues directly relevant to the needs of the National Tuberculosis Control Programme.

Clinical Studies

Ofloxacin-containing Short Course Treatment Regimens

The findings of a randomized clinical trial showed that a four-month regimen of ofloxacin, isoniazid, rifampicin and pyrazinamide daily for three months followed by isoniazid and rifampicin for one month was successful in 99% of drug-susceptible patients at the end of treatment and relapse occurred in only 4 % of patients followed up for 24 months but the Revised National Tuberculosis Control Programme (RNTCP) which is being implemented in a phased manner, is geared for thrice-weekly administration of directly observed treatment. Therefore, if the full benefit of a shorter duration treatment is to be realized then the ofloxacin containing regimen should be effective when administered three times a week. The regimen can then be dovetailed into the existing RNTCP. With this in view the TRC in collaboration with the state government hospital and the Chennai Corporation initiated a randomized control trial to test the efficacy of intermittent ofloxain-containing regimens for the treatment of patients with smear

positive pulmonary tuberculosis. The test regimens being studied are ofloxacin (O), isoniazid (H) and rifampicin (R) three times a week for four months with either pyrazinamide(Z) or ethambutol(E) for the first two months; *i.e.* a) 2 OHRZ thrice weekly/ 2 OHR thrice weekly, and b) 2 OHRE thrice weekly / 2 OHR thrice weekly. These regimens are compared with a control regimen of isoniazid and rifampicin three times a week for six months with ethambutol and pyrazinamide for the first two months (2 EHRZ thrice weekly/ 4 HR thrice weekly). The results in 265 patients enrolled in the study are being analysed.

Oral 8 -month Regimen for Treatment of Sputum Positive Pulmonary Tuberculosis

An oral 8 –month regimen with a non-rifampicin continuation phase for treatment of sputum positive pulmonary tuberculosis was evaluated at TRC.

The follow up of patients enrolled in this study, in which newly diagnosed smear-positive pulmonary tuberculosis patients were treated with an 8-month regimen of isoniazid, rifampicin, ethambutol and pyrazinamide three times a week for 2 months followed by isoniazid and ethambutol daily for 6 months, is continuing. Of the 467 patients enrolled, the relapse rates in those who completed treatment successfully were 3%, 9% and 4% in the groups with second month sputum culture negative, positive without extension of intensive phase and positive with extension of the intensive phase, respectively. The differences were not statistically significant.

Role of Inhaled Steroids in TB Patients with Impairment of Residual Lung Function

An earlier study at TRC revealed that about 50% of patients treated for pulmonary tuberculosis with standard short course regimens had pulmonary function abnormalities. Physiological and functional changes/ abnormalities in lung function in patients treated for pulmonary tuberculosis and the effect of inhaled steroids in reducing or reversing the residual defect were studied. Till date 158 patients have been recruited in the study and have been randomly allocated to receive either inhaled steroids or placebo. Fifty per cent of patients were found to have abnormal pulmonary function at 3 months. The patients will be followed up with PFT every 3 months.

Epidemiological Studies

Community Survey of Tuberculosis Infection and Disease

As part of the Model DOTS Project, the TRC is carrying out surveys to estimate the prevalence of tuberculosis infection and disease in Thiruvallur district, covering a population of 5,80,000. The aim of these surveys is to study the trends over time for both infection and disease and thereby to measure the impact of DOTS implementation in this region. The baseline surveys have been completed and the first resurvey is in progress since June 2001. Of the 65983 subjects targeted for the disease survey, 92% were covered for symptom screening, 91% for X-ray screening, 96% for sputum collection and 97% for tuberculin survey.

Data from the baseline survey indicated that the prevalence of tuberculosis is 605 per 1,00,000 population which increases with age and is higher in males (Fig 1). The male: female ratio is 5.5 for culture positive tuberculosis. The annual risk of TB infection in children aged less than 10 yr. was found to be 1.6%.

Study of Risk Factors for Default, Failure and Death in RNTCP in the Model DOTS Area

A detailed study of the risk factors associated with default, failure, and death,

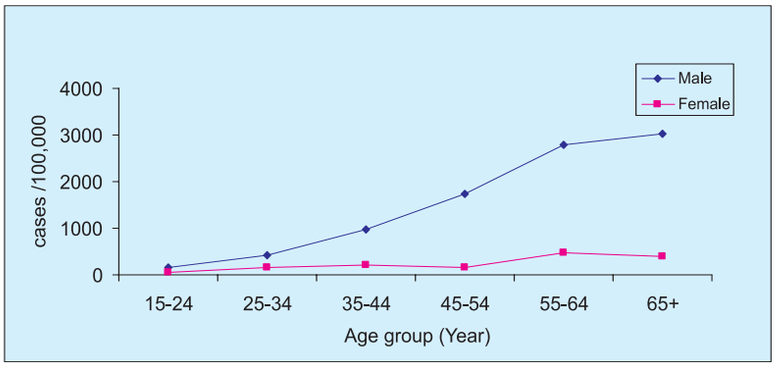


Fig. 1. Prevalence of culture positive pulmonary tuberculosis in Model DOTS area

among tuberculosis patients treated in the DOTS programme in Thiruvallur district in South India showed that higher default rates were associated with irregular treatment, being male, history of previous treatment for tuberculosis, alcoholism, diagnosis by community survey and age > 45 years. Multi-drug resistant tuberculosis patients were more likely to fail treatment. Higher death rates were independently associated with body weight < 35 kg and history of previous treatment for tuberculosis.

Treatment of Tuberculosis Patients from a Field Area by DOTS

The CJIL,Agra is carrying out a survey on incidence of tuberculosis in the Mw vaccine trial area of Ghatampur (Kanpur). In a population of 29420, pulmonary tuberculosis was detected in 69 patients, 63 of them completed DOTS therapy. Of these, 35 were previously untreated, 10 had taken treatment for 1 to 2 months and 18 had taken 4 to 12 months of irregular treatment. All the previously untreated cases as well as patients who had taken treatment for 1 to 2 months earlier also responded very well to DOTS therapy of 6 months. (Fig. 2)

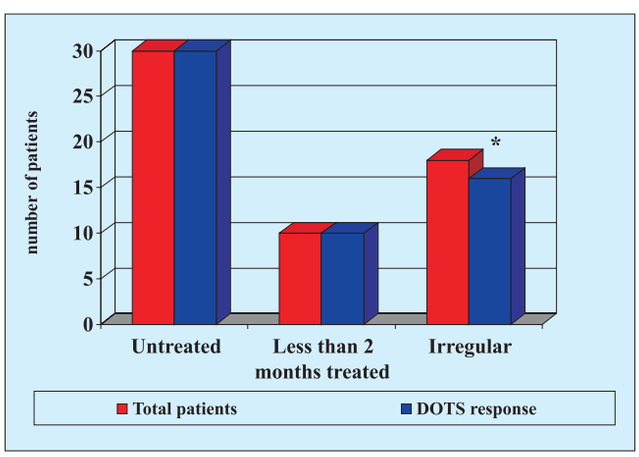


Fig. 2. Response of TB patients to DOTS at Ghatampur field area

This response was assessed clinically, radiologically and bacteriologically (acid fast bacilli, culture and polymerase chain reaction). Of the 18 earlier irregularly treated patients (4 to 12 months),88% responded well to 9 months of DOTS therapy. Only 18% required addition of ofloxacin and clofazimine daily for two months during 9 months of DOTS. This experience is very encouraging and shows the potential usefulness of DOTS in the field in this area.

Prevalence of Multidrug Resistant Tuberculosis (MDRTB) in the Community

The DOTS Demonstration and Training Centre in Thiruvallur has 17 peripheral health institutions where tuberculosis patients are diagnosed and started on treatment. Two sputum samples were collected from patients started on treatment in these centres and tested for culture and drug susceptibility to anti-TB drugs. The results in 1376 newly diagnosed patients and in 327 patients with a history of previous anti-TB treatment are illustrated in Fig. 3. It is heartening to note that prevalence of MDRTB was less than 2% in newly diagnosed patients.

Laboratory Studies

Role of Tumor Necrosis Factor - alpha (TNF-α) in Tuberculous Pleuritis

The role of TNF-α at the site of disease in tuberculous pleuritis patients is being studied at TRC. Concentrations of TNF-α were

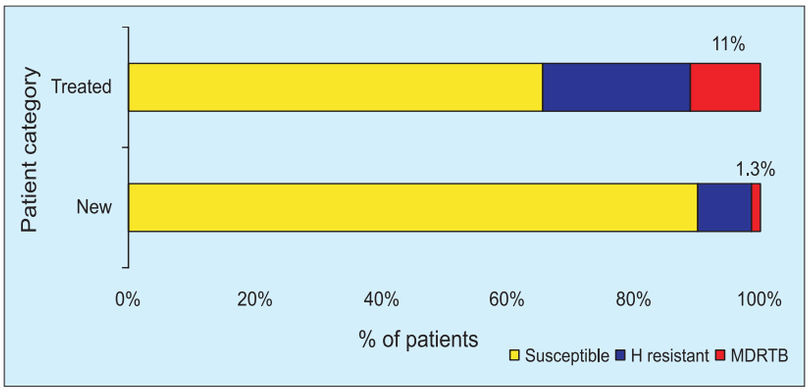


Fig. 3. Anti-TB drug susceptibility pattern in Model DOTS area

measured directly in blood plasma (BL) and pleural fluid (PF) samples. *In vitro* levels of TNF-α were also compared by stimulating the peripheral blood mononuclear cells (PBMC) and pleural fluid mononuclear cells (PFMC) with various mycobacterial antigens like PPD, culture filtrate (CF) and heat killed MTB (MTB). The increased *in vivo* TNF-α in pleuritis subjects suggests the compartmentalization of TNF-α secreting cells at the site of disease, supported by the PPD and MTB specific increase in *in vitro* TNF-α. This may contribute to the containment of infection by synergising with IFN-γ to activate infected macrophages or by regulation of T-cell apoptosis (Fig 4).

Re-staining of Sputum Smears for AFB for Precise Evaluation of False-positive Errors.

Precise evaluation of performance of laboratory technicians is an important component of sputum AFB microscopy in RNTCP. Storage of slides in ambient conditions result in increased false-positive errors for laboratory technicians in microscopy centres. In order to reduce the errors, re-staining was attempted. Four hundred twenty two slides (positive - 103; negative - 319) not stored properly in the last quarter of 1999, were read in the first quarter of 2000 without and with re-staining. Re-staining of slides reduced the false positive errors from 27% to 7%(Fig. 5). The study suggests that re-staining of slides will be very useful to assess precisely the performance of laboratory technicians in microscopy centres.

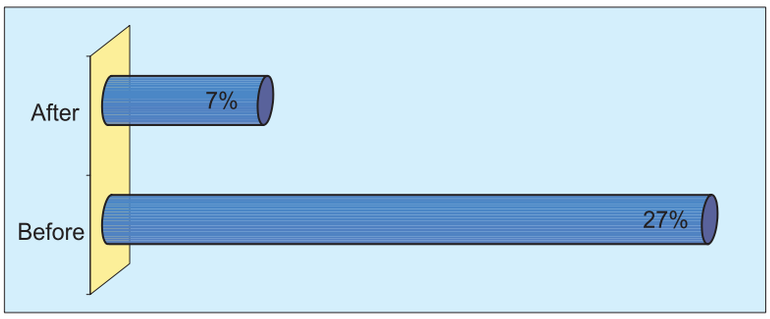


Fig. 5. Percent false-positive errors before and after re-staining

Molecular Biology of Mycobacteria

Molecular and Immunological Characterization of M. tuberculosis Strains with Single Copy of IS 6110

The insertion sequence IS6110 is widely used as a DNA fingerprinting probe for the classification of *M.tuberculosis* strains based on its copy numbers and its insertion sites on the genomes. The TRC has

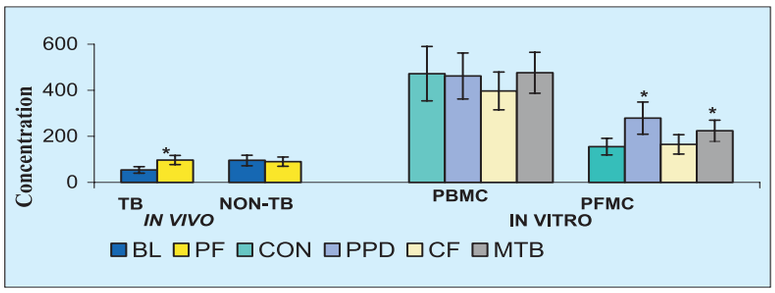


Fig.4. *In vivo* concentrations of TNF-α in plasma (BL) and pleural fluid (PF) of TB and non-TB patients and *in vitro* production by PBMC and PFMC of TB patients in control (con) and PPD, Culture Filtrate (CF) and heat killed *Mycobacterium tuberculosis* (MTB) stimulated conditions (*p<0.05).

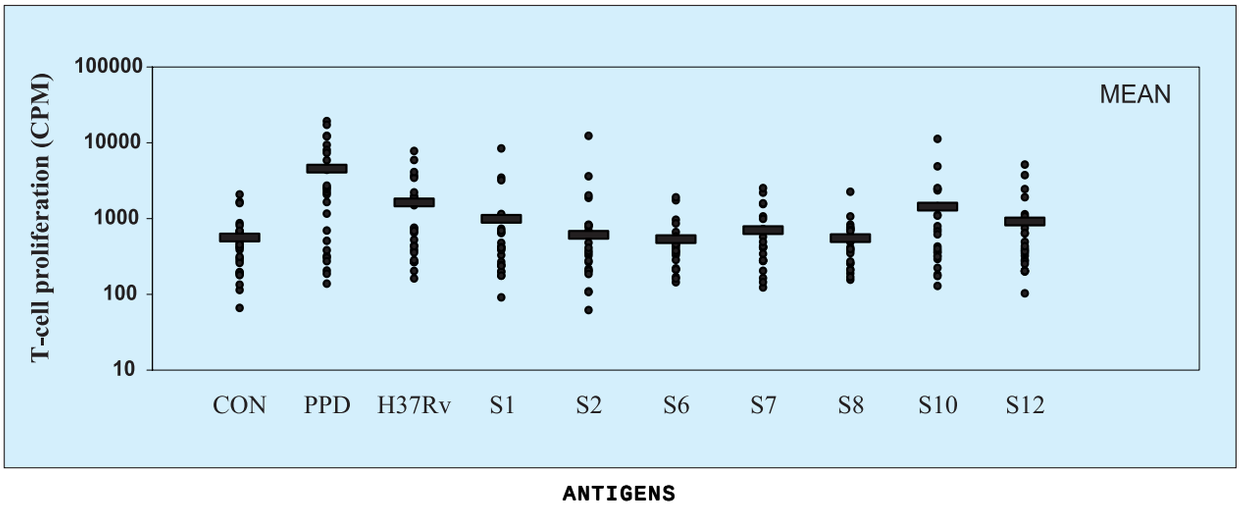


Fig. 6. Lympho-proliferative response of 25 normal subjects to sonicate antigens from clinical isolates.

reported *M.tuberculosis* strains with single IS6110 copy in south India and was found to be the most prevalent strain in the area. Hence, protein profiles of these strains were carried out.

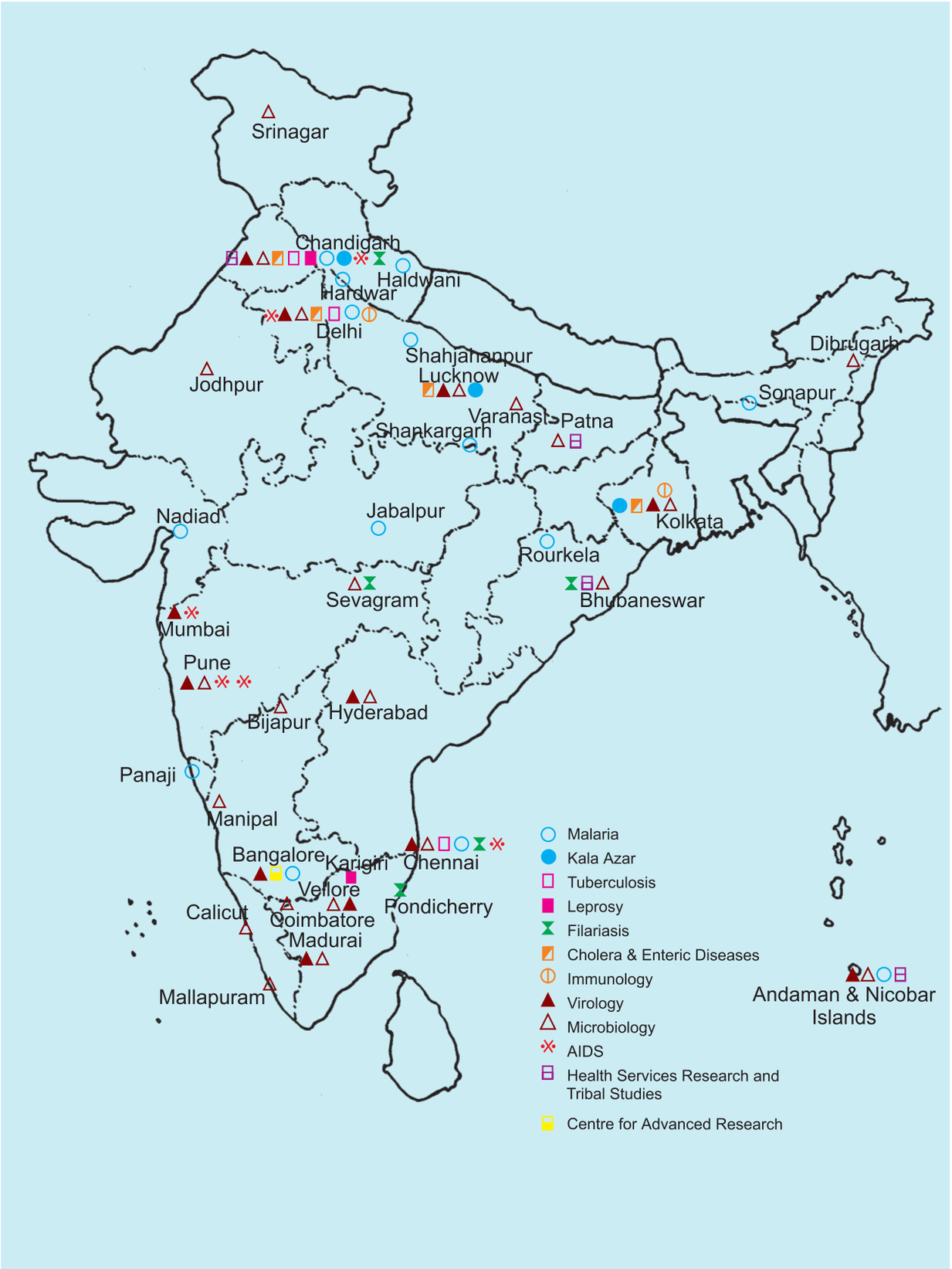
The immunological characterization of seven sonicate antigens that showed differential protein expression was done by studying their ability to induce T cell proliferation and interferon (IFN)-γ and interleukin(IL)12 secretion and compared with standard purified protein derivative (PPD) and heat killed H37Rv antigens. (Fig. 6). The results suggest that sonicate antigens from most prevalent and recent strains of *M. tuberculosis* from clinical isolates have potential to induce T-cell activation and may have newer and specific antigens to be further characterized for diagnostic and vaccine development.

Non-HLA Gene Polymorphisms in Pulmonary-TB: Vitamin D Receptor Gene Polymorphism

Earlier studies at TRC have shown an association of vitamin D receptor (VDR) genotypes of *BsmI, ApaI* and *TaqI* polymorphism with the differential susceptibility or resistance to pulmonary TB in male and female patients. Another VDR gene *FokI* polymorphism was studied and the frequency of FF genotype (wild homozygotes) was more in male pulmonary tuberculosis patients compared to male contacts. In contrast, increased frequency of ff genotype (mutant homozygotes) was observed in male contacts compared to male patients. No such difference in the genotype frequencies was observed among female patients and contacts suggesting that FF may be associated with susceptibility and ff with resistance to pulmonary tuberculosis in male subjects.

Role of HLA-DR2, Mannose Binding Lectin and Vitamin D Receptor Gene Variants on Immune Function in Pulmonary Tuberculosis

Earlier studies have shown association of HLA-DR2, functional mutant homozygotes of mannose binding lectin (MBL) and vitamin D receptor gene variants with the susceptibility to pulmonary tuberculosis. To understand the immunoregulatory role of these polymorphic gene variants on the immune mechanism of tuberculosis susceptibility, macrophage phagocytosis with live *M. tuberculosis* and lymphoproliferation to *M. tuberculosis* culture filtrate antigen (CFA) was carried out with and without vitamin D3. A decreased lymphocyte



MAJOR ICMR RESEARCH PROJECTS IN COMMUNICABLE DISEASES

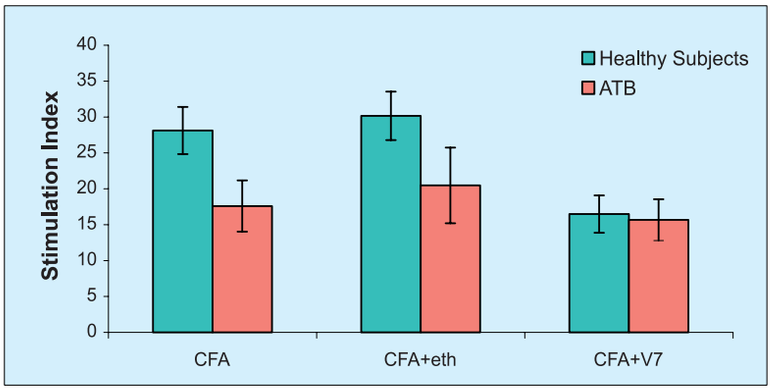


Fig.7. Lymphocyte response to *M.tuberculosis* CFA in active pulmonary tuberculosis (ATB) patients and healthy subjects. CFA - Culture filtrate antigen of *M tuberculosis*;Eth - Ethanol; V7 - 10^{-7} concentration of Vit D3

response to *M. tuberculosis* CFA was observed in the presence of vitamin D3 compared to that without vitamin D3 in normal healthy subjects. Such a decrease was not observed in active pulmonary tuberculosis patients (ATB) (Fig. 7).

Identification of Target Genes dev R-devS Two Component System of M.tuberculosis

M. tuberculosis is an intracellular pathogen that is remarkably well adapted to survival in the human host. Tubercle bacilli can remain dormant within tissues for decades and then cause reactivation disease when the immune system of the host is suppressed. Attemps are on to identify target genes of the dev R -devS two-component system of *M.tuberculosis* and development of rapid assays to measure its activity. A hypoxia-responsive DevR-DevS two-component signal transduction system of *M. tuberculosis* was identified and it was demonstrated that this genetic system is crucial for survival of mycobacteria during hypoxia and is upregulated under conditions of oxygen limitation. Therefore, it is vital to understand the role of DevR-DevS in virulence and adaptation to hypoxia. Several target genes like *devR-devS* locus itself, *sigF* and *icl* encoding Sigma factor F and isocitrate lyase, respectively have been identified. A GFP-based Hyg^R reporter plasmid vector pFPV27-Hyg (derived from pFPV27 received from USA) was constructed. The activity of several *M. tuberculosis* target promoters in the surrogate host *M. smegmatis* was assessed under aerobic and hypoxic conditions by flow cytometry using intact cells. The development of reporter assays based on these promoters will enable to understand the expression pattern of *M. tuberculosis* during its adaptation to hypoxia. Furthermore, the whole cell reporter assays provide a rapid means to identify compounds that interfere with the functioning of the DevR-DevS regulon and thereby provide novel target for drug discovery.

Gene Regulation in Mycobacteria

Regulation of gene expression can be studied by analyzing the promoter region of the gene. One such promoter taken for analysis was a 400bp upstream region of *guaA* gene of *M. tuberculosis* H37Rv encoding the purine biosynthetic enzyme, guanosine mono phosphate synthetase. To learn if the *Gua A* gene of *M. tuberculosis* is needed for this and whether it gets induced in the intracellular environment of macrophages, the 400bp putative promoter region of the *guaA* gene was PCR amplified and cloned upstream to green fluorescent protein gene in an *E.coli*-mycobacterial shuttle vector and was named pKK TRC. The promoter of *Gua A* gene of *M. tuberculosis* was found induced in the intracellular environment of the macrophages (Fig. 8) indicating that the *Gua* gene expression is necessary for the intracellular survival of *M. tuberculosis*.

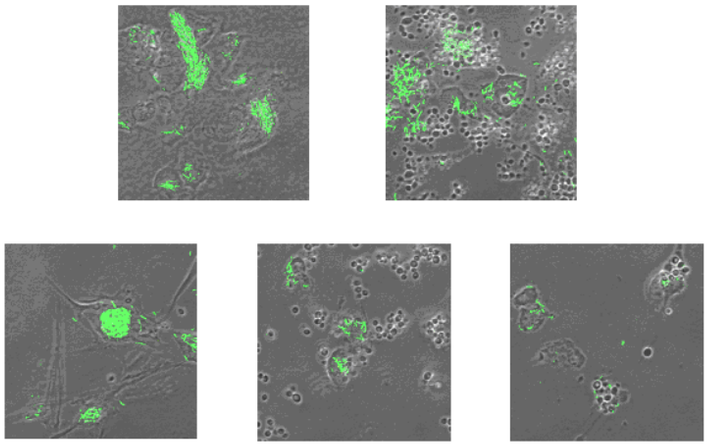


Fig.8. Human macrophages isolated from PBMCs infected with *M. tuberculosis* H37Rv harbouring pKKTRC

Designing Probes for Rifampicin Resistance

In a multicentric study (carried out at New Delhi, Agra and Hyderabad) novel mutations in the rpoB gene locus of rifampicin resistant isolates of *M. tuberculosis* were reported. Based on this information, probes have been designed and their application studies are continuing. It has been observed that these probes accurately detect the mutations (observed by the absence of hybridization to a particular probe) (Fig. 9)

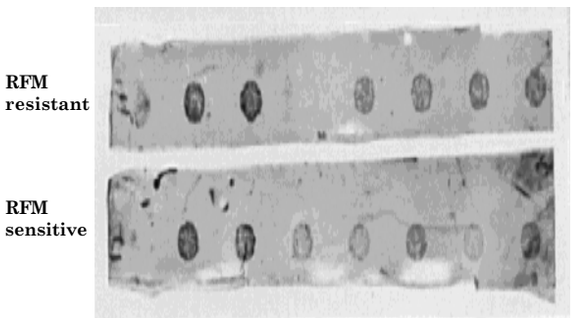


Fig. 9. Detection of mutations in rpoB gene region of *M.tuberculosis* with indigenously designed probes

The technique has been tested on isolates as well as clinical specimens and overall concordance of 87 % with microbiological results in three sets of samples has been observed (Fig.10). The results are available within 48-72 hours of getting the specimens/ isolates.

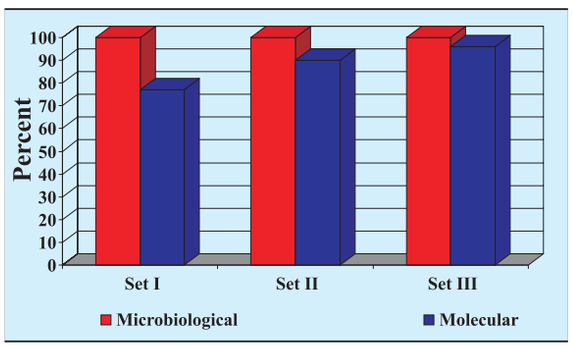


Fig. 10. Correlation of microbiological and molecular probes for rifampicin testing

LEPROSY

The Council's Central JALMA Institute for Leprosy continues research on leprosy, some areas of tuberculosis and HIV infection. The focus of research is on pathology, immunopathology and nerve electrophysiology using immunological, molecular and electron microscopy tools for better understanding of disease process in leprosy. Studies include developing technologies for diagnosis, molecular detection of drug resistance, molecular epidemiology, drug permeability and metabolism for mycobacterial diseases and medical as well as surgical management of leprosy.

Histopathological Studies

Application of New in situ Methods for Improving the Diagnosis

During 2002-03, studies on the newly developed in situ methods based on gene probes and gene amplification were continued. These methods were applied to histology specimens from early cases as well as cases having suspicious lesions. It was observed that in case of early lesions, histopathology could clinch the diagnosis in 32% whereas

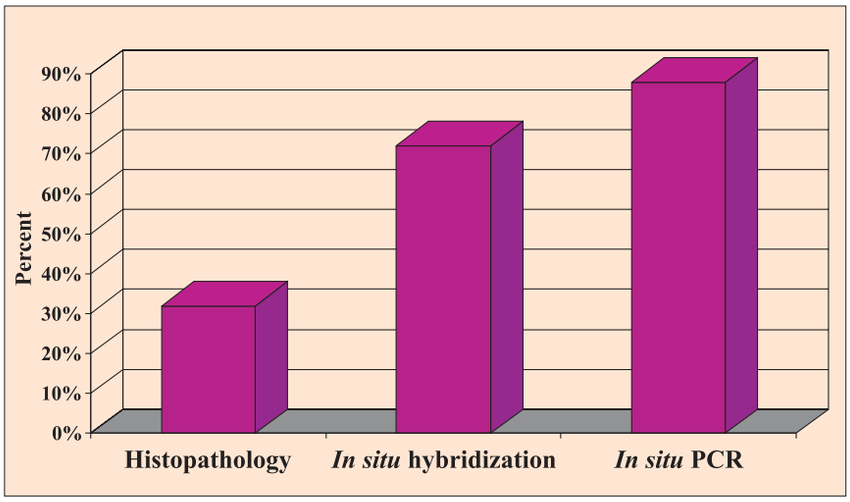


Fig. 1. Comparative sensitivity of different techniques for diagnosis of early cases of leprosy

combining the same with *in situ* probe hybridization and *in situ* PCR enhanced the diagnosis to 72% and 88% respectively. (Fig. 1)

In case of the lesions from suspicious cases, histopathology was useful in 20%, *in situ* hybridization in 64% and *in situ* PCR in 76% of the specimens in confirming the diagnosis (Fig. 2).

Immunological Studies

Auto-antibody Positivity in Children with Leprosy

Earlier studies in experimental animals showed that mycobacterial injections can induce auto-antibodies to ds DNA and myosin.

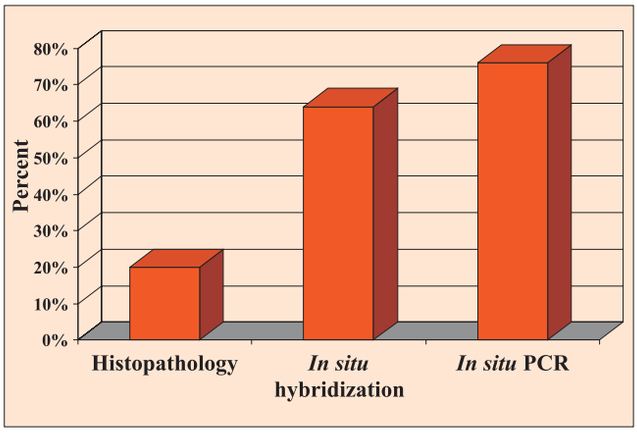


Fig. 2. Comparative sensitivity of different techniques for diagnosis of suspicious cases of leprosy

These antibodies could be induced both in mice as well as rabbits. The studies now have been extended to leprosy cases in children. It was observed that antimyosin antibodies were present in 27% of the paucibacillary and 76% of the multibacillary cases of childhood leprosy. Similarly, anticardiolipin and anti-dsDNA antibodies were present in 18% of the paucibacillary cases whereas these were present in 35-40% of multibacillary leprosy cases. (Fig. 3)

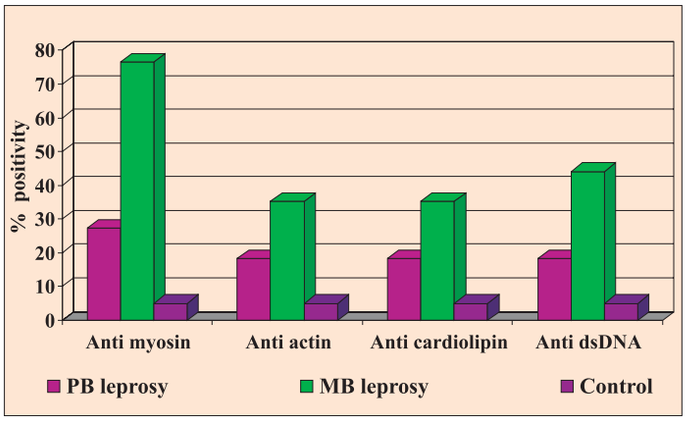


Fig. 3. Auto antibody positivity (%) in children with and without leprosy

Only 5% of the controls (cases of pyrexia) had these antibodies. It is thus apparent that in leprosy, these auto-antibodies are generated in humans at an early stage. Their significance is being investigated.

Lactoferrin in Tears of Leprosy Patients

A study has recently been completed on lactoferrin and antibodies to lactoferrin in tears of leprosy patients. Lactoferrin, a bacteriostatic protein released during inflammatory episodses chelates iron and interrupts normal metabolic pathway of the microorganisms. It plays a major role in non-specific immune mechanism of the eye and is

a major protein secreted in the tears. Hence levels of lactoferrin in tears as well as serum were quantitated in order to identify its role as an inflammatory protein. Mycobacterial 65kDa antigen has been reported to cross-react with lactoferrin hence any cross-reactive antibodies in the tears of leprosy patients with or without eye complications was looked for. Competitive ELISA was done to quantitate serum and tear lactoferrin. Anti-lactoferrin in tears was detected by dot immunoblotting. The mean tear lactoferrin levels of patients were 5.6587mg/ml (control - 2.5541 mg/ml) while that for serum were 0.4940 µg/ml (control - 0.27741 µg/ml). Antibodies to lactoferrin were detected in 7 patients and 6 controls. Immuno blotting data showed that a chance for cross reactivity of antibodies to 65kDa mycobacterial protein to lactoferrin is minimal confirmed by BLAST analysis on the amino acid sequence homology.

Surgical Studies

Study on Early Diagnosis of Nerve Damage

In earlier studies, electrophysiological investigations on peripheral nerves were carried out which showed that latency period is increased in early stages of nerve involvement whereas the conduction velocity and amplitude are decreased in established disease at a later stage. These studies have been extended to early cases having no neurological problems and /or defined nerve damage. So far 170 such cases have been investigated for these electrophysiological changes. Among these, 32 patients showed these early changes of which 40% developed neurological deficit in the follow up. (Fig. 4). The results thus confirm the utility of such investigations in assessing the prognosis of the cases.

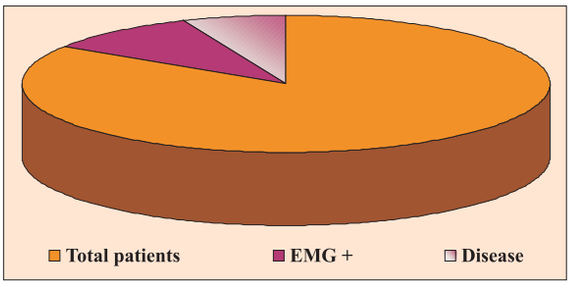


Fig. 4. Early diagnosis of nerve damage using EMG

Therapeutic Studies

Combined Chemotherapy and Immuno-therapy in Borderline Leprosy

Long term follow up studies of combined immunotherapy + MDT in highly bacillated borderline lepromatous (BL)/ lepromatous (LL) cases showed that immunotherapy with Mw/ BCG had additive effect to chemotherapy by enhancing the killing, clearance of the organisms as well as granuloma. As the patients in the borderline spectrum have problems of persisting residual activity and late reactions, the addition of immunotherapy with Mw is being studied. These cases have been treated with MDT for 6 months and 2 doses of Mw vaccine (one initially and one at six months). This regimen has been well tolerated and no complications like late reactions and nerve damage have been observed. In the borderline tuberculoid cases, complete subsidence of erythema and clearance of infiltration was observed in all cases as compared to about 15% persistence of these activities in cases treated with only MDT. Further, there was significant reduction of the granuloma fraction in 6 months (Fig. 5).

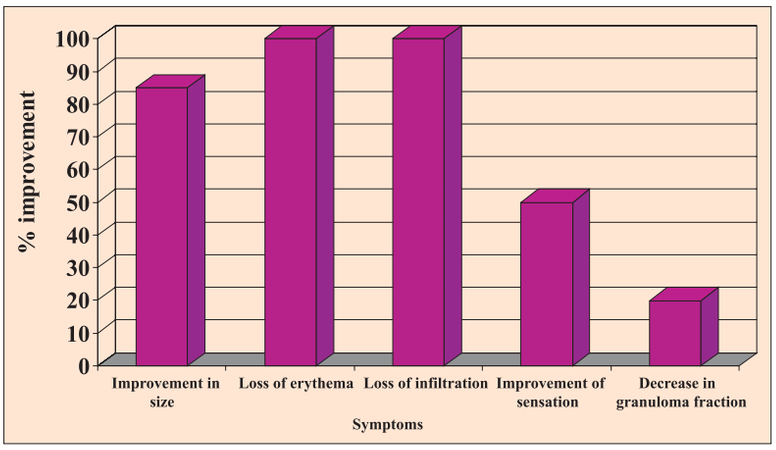


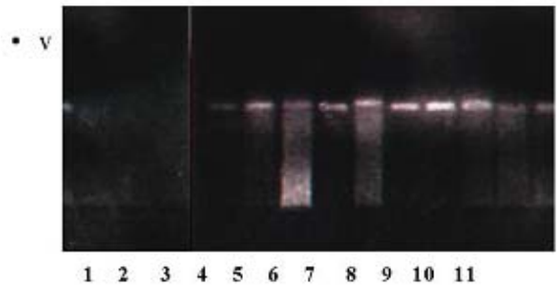
Fig. 5. Clinical and histological improvement in BT cases on MDT + Mw

These results are promising and indicate the potential usefulness of addition of immunotherapy in borderline cases also.

Studies on Molecular Biology

DNA Fingerprinting of Mycobacteria

Studies are being continued at CJIL to develop and apply different DNA fingerprinting methods for various species of mycobacteria. During the year, a ttc repeat based method for *M. leprae* has been established at this Institute. This technique could amplify the desired fragment in 38% of the specimens from multibacillary cases. While the sensitivity needs to be improved, variation in the size of the bands generated was observed (Fig. 6)



Lane no.1,2,3,4,6,9,10,11 at 201 bp : Lane no. 5,7 and 8 at 200bp

Fig. 6. Mobility variation In PCR amplified products

The sequencing showed that the number of ttc repeats varied from 18-54 in these amplicons. Thus the technique appears to be promising for understanding the strain variation but it needs to be further improved and assessed alone or in combination with other methods for understanding the molecular epidemiology of leprosy in field settings.

Studies on Viability

A project carried out at CJIL to study the viability of *M. leprae* in lepromatous patients after completion of 12 and 24 months of multidrug therapy has been completed. Skin and nerve biopsies were done in three groups of patients. One group had biopsies before taking treatment, second group after 12 doses of MDT and the third after 24 doses of MDT. Undiluted bacillary inoculum was injected into 4-5 T900r mice and harvesting was done at 6th, 9th and 12th month. Rees technique was used and a count of 10^5 bacilli was considered as significant growth in 12th and 24th dose biopsies. Less than that were considered as equivocal growth. To find the viability of bacilli in the skin of lepromatous patients, 60 patients (after taking 12 doses of MDT) were recruited, of these only 2 skin biopsies showed significant growth (viable bacteria) in the mouse foot pad (MFP). Both these cases had an initial high bacillary index (BI) of 4+ and above. Resolving granulomatous inflammation was seen only in 28.5% of patients' tissues. However, after 12 doses of MDT treatment no nerve biopsies showed significant growth. None of the skin and nerve biopsies from patients who had taken 24 doses of MDT showed any growth. Ninety six percent of skin and 88% of nerve biopsies from untreated patients showed significant growth in the MFP. It is, therefore concluded that drug schedule of 24 doses is adequate to treat leprosy patients irrespective of the bacterial index. Biopsies taken from 3.3% of patients on 12 dose MDT regimen showed viable bacteria in the MFP experiments.

Epidemiological Studies

Epidemiological Studies on Leprosy in Agra District

Studies on understanding the prevalence, incidence and profile of the disease in Agra district are continuing. So far, a total of 239044 persons have been screened during 1999-2002 and overall prevalence of leprosy has been found to be 27.19 per 10000 and new case detection rate (NCDR) of 22.80/ 10000. The data have been further analyzed according to disease classification and it has

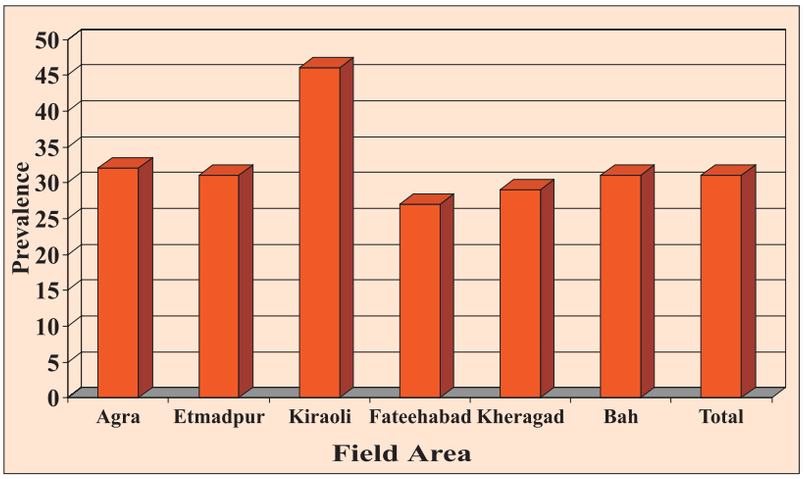


Fig. 7. Proportion of MB cases in Agra field area

been seen that of all the cases detected, 30-35% are of multibacillary (MB) type (Fig. 7).

The prevalence has been found to be consistently high all over the district. These trends suggest a very high pool of cases with possible bacterial load which suggests the need for regular survey for coming years to understand the effect of interventions in this population.

DIARRHOEAL DISEASES

Diarrhoeal diseases are the second leading cause of mortality and morbidity worldwide. Although underreported in the tropics, these diseases are the most common and prevalent in our country. Most diarrhoeas are mild and self-limiting. Infectious diarrhoeas are by far the commonest and are caused by pathogens like - enterohaemorrhagic *Escherichia coli* (EHEC), *Salmonella*, *Shigella*, *Cyclospora*, *Cryptosporidium*, *Giardia*, *Campylobacter jejuni*, *Clostridium difficile*, Caliciviruses, other enteric viruses, and rotavirus. The Council's NICED, Kolkata and Regional Medical Research Centres at Bhubaneswar and Port Blair continued their research on common pathogens besides assisting various State Governments in conducting investigations on diarrhoeal diseases outbreak including cholera.

Epidemiological Studies

Hospital based Surveillance System for Diarrhoeal Diseases

A project is being carried out by NICED, Kolkata to establish a diarrhoeal disease monitoring and research support activity to identify common causative organisms of diarrhoeal illness seen at Infectious Diseases Hospital (IDH), Kolkata, in relation to clinical, epidemiological and socio-economic characteristics. During the study period, a systematic sample (*i.e.* every 5th patient on two randomly selected days per week) of a total of 938 patients with diarrhoea or dysentery (with or without other complaints) attending the casualty of the hospital were enrolled in the surveillance system. The faecal specimens were collected and screened for detection of enteropathogens using microbiological techniques. The results of antimicrobial susceptibility test revealed that most of the *Vibrio cholerae* O1, non O1 and non O139 strains were highly resistant to ampicillin, co-trimoxazole, furazolidone and nalidixic acid, with a few strains (18%) showing reduced susceptibility to ciprofloxacin. On the other hand, all the isolated strains of *Shigella dysenteriae* type 1 showed multiple drug resistance and were uniformly resistant to ampicillin, co-trimoxazole, tetracycline, nalidixic acid and norfloxacin. These strains also had reduced susceptibility to ciprofloxacin and were sensitive to ofloxacin only. Majority of *S. flexneri* strains were found resistant against ampicillin, tetracycline and co-trimoxazole and 40% strains exhibited resistance to nalidixic acid. All the *S. sonnei* isolates were uniformly resistant to ampicillin, cotrimoxazole and nalidixic acid while *V. parahaemolyticus* strains were resistant to ampicillin and furazolidone.

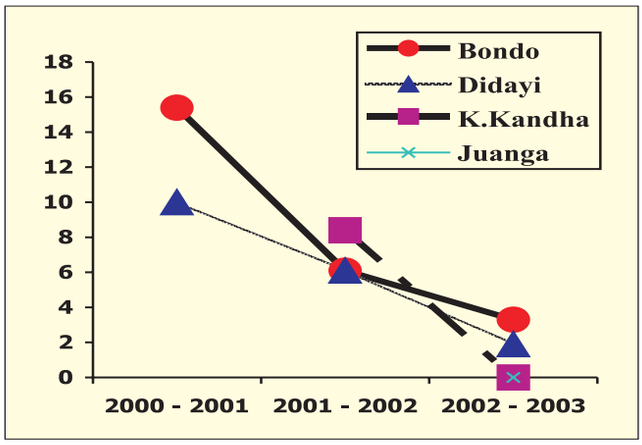


Fig.1 Year wise occurrence of cholera in different studied tribes (Study in *K.Kandha* was initiated in 2001 - 2002 and *Juanga* in 2002 - 2003)

Intervention Programme for Diarrhoeal Diseases in Tribals of Orissa

The diarrhoeal diseases including cholera are a perennial health problem in tribal communities in Orissa attaining a peak from July to October. Studies were undertaken by RMRC, Bhubaneshwar for collecting baseline data in tribals (*Bondo, Didayi, K. Kondha* and *Juanga*). It was found that cholera accounted for 3.2% of the culture positive cases (*V.cholerae* O1: 3.1% and O139 : 0.09%) followed by *Shigella* spp: 2.2% and *Salmonella* spp: 0.3% on bacteriological analysis of rectal swabs. Yearwise occurrence of cholera in different tribal communities during 2002-2003 is depicted in Fig. 1. Majority of organisms isolated were *E.coli* (37.3%). Molecular analysis of selected *V.cholerae* strains from these tribal areas revealed the presence of *ctx* A and *rfb* genes by multiplex PCR (Fig. 2). Intervention and IEC activities for health awareness have decreased the occurrence of the cholera cases.

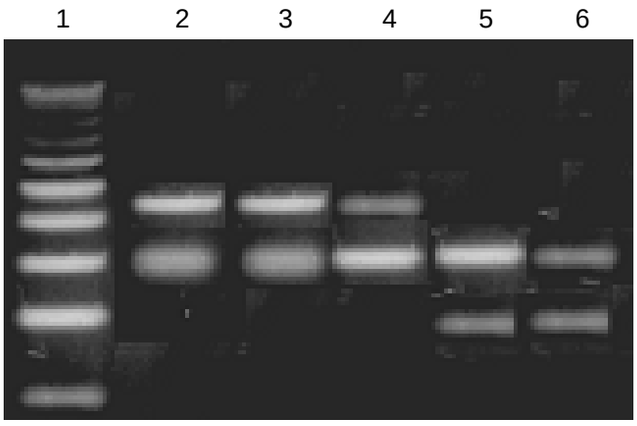


Fig. 2. Ethidium bromide stained PCR amplicons of ctx A and rfb O1 and O139 genes. Lane 1 100 bp ladder, Lane 2, positive control for ctx A & rfb of O139, Lane 6 positive control for ctx A & rfb of O1 VC 20, Lane 3 - 5, O1 and O139 test samples.

Outbreak of Cholera in Andaman & Nicobar Islands

An outbreak of diarrhoea occurred in Nancowry group of islands during October - November 2002. Epidemiological and microbiological investigations were carried out by RMRC, Port Blair during the outbreak. A temporary field station was set up at Kamorta CHC and a total of 468 cases were admitted during October/November. Attack rates in different villages ranged from 0.9% to 82%. The epidemic curve showed multiple peaks indicating secondary spread. Age specific attack rates (Fig. 3) showed two peaks, one at 0-1 yr age group and the other at 20-25 yr age group. There were a total of 6 deaths.

Fig. 3. Age-specific attack rates

Twnty-two isolates of *V. cholerae* were obtained from 66 stool samples processed. The predominant serotype was *V. cholerae* O1 Ogawa El Tor biotype. Genetic characterization using different tools showed

that the strain was similar to the strains isolated in Kolkata during the recent years. Clinical presentation was characterized by severe watery diarrhoea, vomiting and occasional abdominal pain. The patients developed hypovolemic shock and anuria if not treated with parenteral fluids early.

The movement of tribes from one village to another played a role in the spread of the epidemic. More than 50% of the drinking water sources were found to be contaminated with *E. coli*. Some of the sea water samples from shore areas were also contaminated. The possible source of infection are effluents from passenger ships, non-tribal carriers staying in the tribal village or poachers from neighbouring countries. Control measures such as super-chlorination of water sources, IEC activities etc. were carried out by the Health Department and other Government organizations.

Vibrio cholerae

Preferential Association of the Heat Stable Enterotoxin Gene (stn) with Environmental Strains of V. cholerae belonging to the O14 serogroup

The heat-stable enterotoxin, 17-amino-acid peptide, encoded by the *stn* gene which exhibits remarkable similarity, especially in the carboxyl-terminal toxic domain, to the heat-stable enterotoxins (STs) produced by enterotoxigenic *Escherichia coli* (ETEC), is a well studied virulence factor of *V. cholerae* non-O1. This gene was found to occur is a small proportion of both environmental and clinical *V. cholerae* non-01 isolates from Kolkata, Thailand, Mexico and the U.S.

Under a human volunteer study in Kolkata, 559 strains of *V. cholerae* were collected during different time periods from environmental samples. Of the total, only 9 harboured the *stn* gene as detected in the PCR assay. Three strains (X67, X119, VCE101) were positive for the El Tor tcpA and one (X67) of them was also positive for *ctx*A. Of the 9 *stn* positive strains, 6 belonged to the O14 serogroup and 2 to serogroups O43 (VCE89) and O6 (X67). One strain (X140) was identified as a rough strain. However, all the strains produced a biologically active toxin. In the RFLP analyses of the *stn* gene with HindIII and EcoRI, 8 strains showed a single copy of the *stn* gene, whereas X119 had two copies of this gene against the presence of a single copy in GP156. RFLP of ctxA using restriction enzymes PstI, BglI and BglII revealed two bands for the strain X67. For GP156, there was a single band for PstI and BglII digests and two bands seen for the BglI digest. With the exception of the strains X4 (O14) and X142 (O14), the NotI PFGE profiles of the *V. cholerae* strains revealed dissimilar patterns indicating that the *stn* gene harbouring *V. cholerae* strains are clonally unrelated (Fig. 4). The level of similarity between the strains X4 and X142 was 73% thus indicating that in spite of the diverse genetic background and *stn* polymorphism, preferential association of *stn* gene with O14 serogroup was detected among *V. cholerae* isolated from the environment.

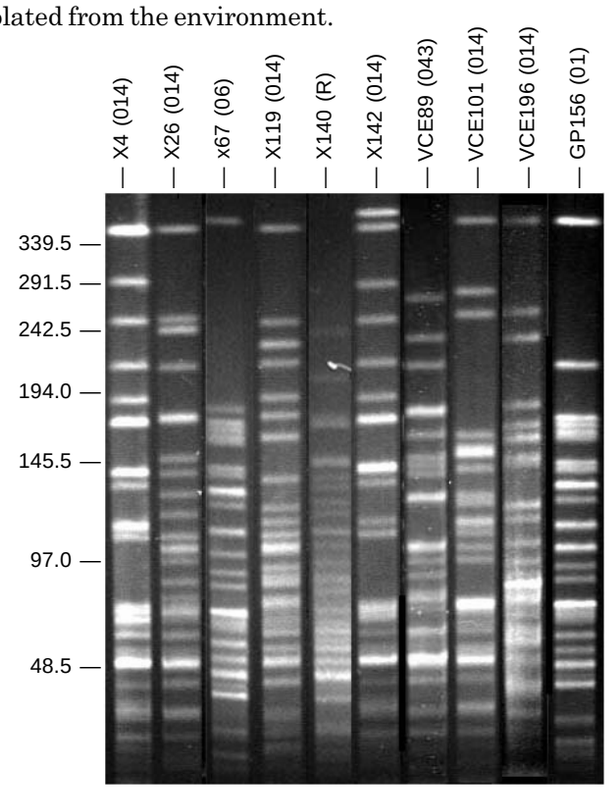


Fig. 4. PFGE of *stn* positive *V. cholerae* O14 strains after NotI restriction digestion.

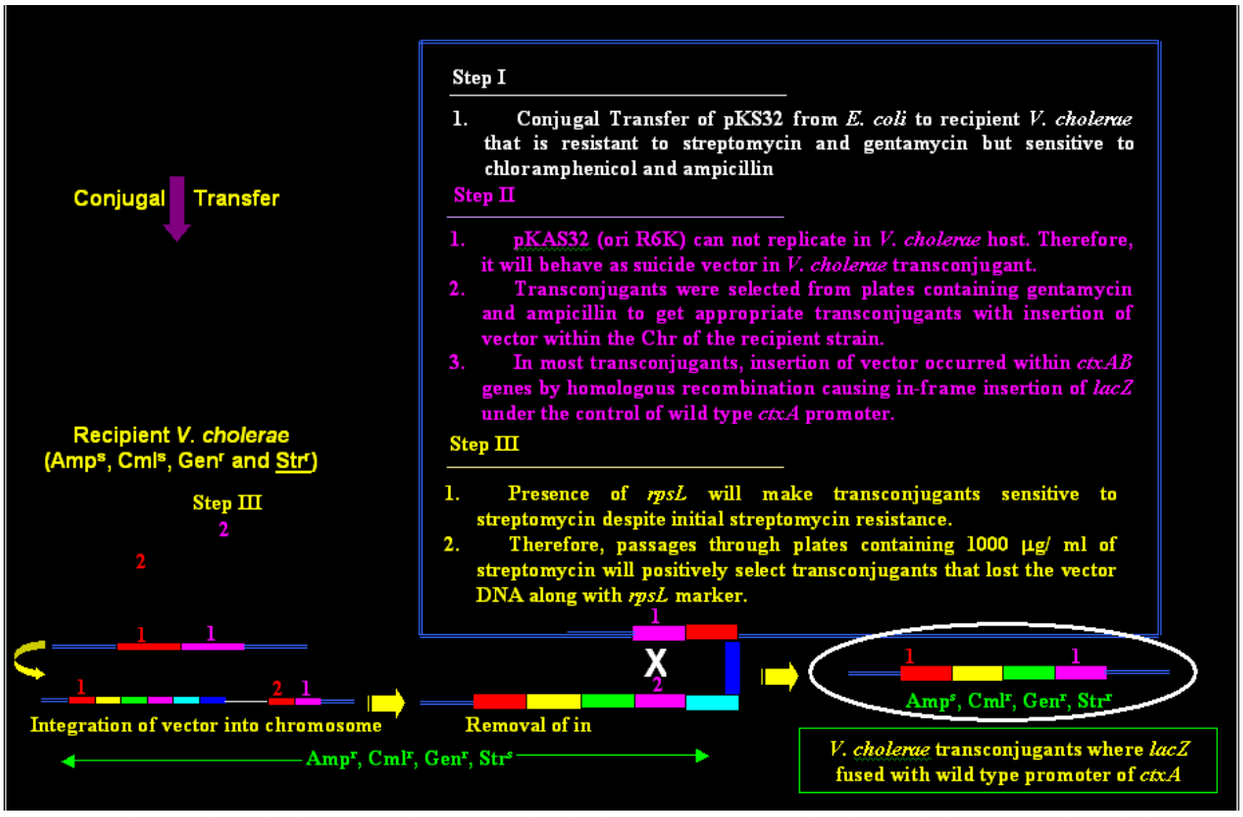


Fig. 5. Schematic diagram showing the steps involved to generate promoter-fused isogenic *lacZ* mutants in *V. cholerae*

Molecular Characterization of Rough Strains of V. cholerae isolated from Diarrhoea Patients

Study was initiated at NICED, Kolkata to understand the potential of rough *V. cholerae* strains to cause diarrhoea and the role of `O' antigen biosynthesis genes in regulating virulence factors isolated over a period of time from different parts of India. This was further confirmed by generating promoter ctx-LacZ fused genetically tailored strains (Fig. 5) as well as by the determination of the competitive colonization efficiencies of smooth and corresponding rough strains in suckling mice model. Measurement of β -galactosidase activity of the genetically tailored strains (KD05 and KD06) showed that β -galactosidase production by the KD06 (O395R, ctx-lacZ) was higher compared to KD05 (O395S ctx-lacZ) under comparable conditions. Similarly, toxT-lacZ fusion mutants of the rough strains of both classical and El Tor background showed higher expression of ToxT compared to their isogenic smooth counterpart. The study revealed that the rough strain of classical background colonizes about 35 times more efficiently compared to its smooth counterpart and that the colonization of the El Tor rough strains is 7 to 10 folds more efficient as compared to the corresponding smooth strain. The study thus elucidated that *V. cholerae* strains in rough phenotype are potentially more virulent as compared to their smooth counterpart, although this is not reflected in the epidemiological observation, where isolation rate of rough strains remains very low. Further study on role of 'O1' antigen biosynthesis genes to regulate virulence factors in *V. cholerae* is under way.

Escherichia coli

Binding of E. coli Heat-Stable Enterotoxin to Intestinal Epithelial Cells and Brush Border Membranes in Animals

The enterotoxigenic *E. coli* that produce heat stable toxins (Sta) are responsible for

50% to 80% of reported cases of diarrhoea. STa are also a major cause of diarrhoea in laboratory and domestic animals. The heat stable toxins bind to cell surface receptors in intestine which leads to activation of guanylate cyclase.

Since there are controversies on whether guanylate cyclase and heat stable enterotoxin (STa) receptors are same protein or two different proteins, a study was initiated at NICED, Kolkata to determine the presence and density of the STa receptor in intestinal epithelial cell and brush border membranes of different animals. Attempts were made to purify and characterize the receptor for *E. coli* STa from a high density receptor system and to evaluate mechanism of action of STa. A single class of receptors was present in all the tested animals and the number of receptors remained lower in hamster in comparison to rat, rabbit and guineapig. Autoradiographic demonstration of SDS-PAGE of intestinal brush border membranes showed STa binding proteins of apparent molecular weight of 160 KDa in rat, 118 KDa in guineapig, 140 and 38 KDa in rabbit and 65 KDa in hamsters. The study also reported that STa binds to a single class of receptors in human colonic carcinoma cells (COLO-205). Besides stimulating cGMP, STa also involves two potential intracellular signals. It increases rapidly inositol triphosphate and cytosolic free calcium in COLO-205 cells prelabelled with myo[2-^{3}H] inositol. Using fluorescent indicator, Fura 2AM, intracellular free Ca^2+ was found to increase 5.12 fold compared to control. This study thus demonstrated for the first time a change in cytosolic calcium in cultured human colonic cells by STa, which was accompanied by inositol tri-phosphate activation.

Antibiotic Resistance, Virulence Genes and Molecular Profiles of Shiga Toxin producing E. coli isolated from Diverse Sources in Kolkata

Shiga toxin producing *E. coli* (STEC) is a serologically diverse group of food borne, zoonotic pathogen of which the serotype O157:H7 has been epidemiologically significant worldwide because it causes life threatening disease. To determine whether its transmission occurs between human and bovine sources, a study was carried out at NICED, Kolkata to determine the relatedness of STEC strains isolated from different sources. Of the 63 strains isolated during the study period, 40 were from cow stool and 19 from human stool samples while the remaining 4 strains were isolated from beef samples obtained from a city abattoir. The STEC strains were tested for resistance against 15 antimicrobial agents. Resistance was observed most commonly to ampicillin, tetracycline and streptomycin and less frequently to cephalothin , co-trimoxazole, nalidixic acid and neomycin. Multidrug resistance was seen in 14 strains and there was no common resistance pattern among the strains.

The virulence gene profiles of STEC strains are depicted in Table 1. STEC strains possessing both *stx*1 and *stx*2 was the most prevalent (245) toxin genotype followed by strains carrying *stx*1, *stx*2a and *Ehly*A (19%). The study thus suggested that the STEC in

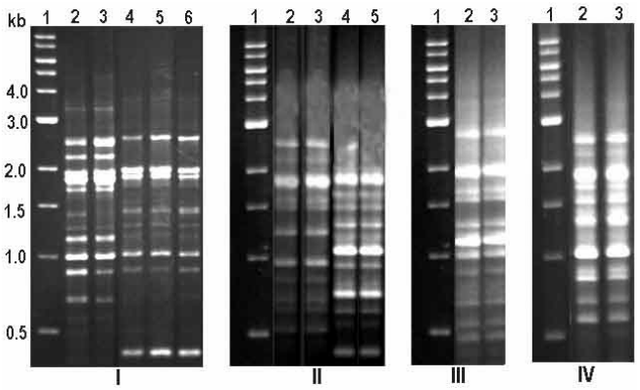


Fig. 6. RAPD-PCR results of STEC strains that exhibited identical DNA banding patterns, Panel 1, lane 2 and 3 are strains SD2 and SD5; lanes 4-6 are strains SD8, SD10 and SD12 respectively. Panel II, lane 2 and 3 are SD4 and SD7, lane 4 and 5 are SD1 and SD3 respectively. Panel III, lane 2 and 3 are AK33 and AK36 respectively. Panel IV, lane 2 and 3 are AK48 and AK54 respectively. Lane 1 in each panel is 1 Kb DNA ladder marker.

Table 1 Virulence gene profile of STEC strains.

Virulence genes	Number of strains with virulence genes			Total/percentage (%) of strains
	Human	Cow	Beef	
*Stx*1	6	5	0	11 (17.5)
*Stx*2	3	4	0	7 (11.0)
*stx*1 and *stx*2	4	9	2	15 (23.8)
*stx*1 and *E-hly*A	0	1	0	1 (1.6)
*stx*2 and *E-hly*A	0	3	0	3 (4.8)
*stx*1, *stx*2 and *E-hlyA*	3	9	0	12 (19.0)
*stx*1 and *eae*	1	2	1	4 (6.4)
*stx*1 and *katP*	1	1	0	2 (3.2)
*stx*1, *katP* and *eae*	0	1	0	1 (1.6)
*stx*2, *katP* and *E-hlyA*	0	2	0	2 (3.2)
*stx*1, stx2, katP and *E-hlyA*	0	0	1	1 (1.6)
*stx*1, *eae*, *katP* and *E-hlyA*	1	0	0	1 (1.6)
*stx*1, *eae* and *etpD*	0	1	0	1 (1.6)
*stx*1, *eae, katP, etpD* and *E-hlyA*	0	2	0	2 (3.2)

eastern India lacks some factors that are essential for it to become a frequent cause of diarrhoea.

The STEC strains were further characterized by RAPD-PCR to analyze the genetic diversity among the strains, the results of which are shown in Fig. 6. The PFGE profiles of 25 STEC strains that gave identical or nearly similar DNA fingerprints in RAPD-PCR and had similar virulence genotype are shown in Fig. 7. The study indicates that clones present in bovine sources are not transmitted to humans in Kolkata setting.

Development of a Diagnostic Probe for Escherichia coli

Molecular cloning, sequencing and expression of adhesin-gene of enteroaggregative *E.coli* (EAggEC) for development of a specific probe was carried out. EAggEC is an emerging cause of persistent diarrhoea and is associated with persistent enteric symptoms as well as acute diarrhoea. The pathogenicity of the organism has been attributed to its aggregative adherence property. Sequencing analysis did not show homology with any known adhesin

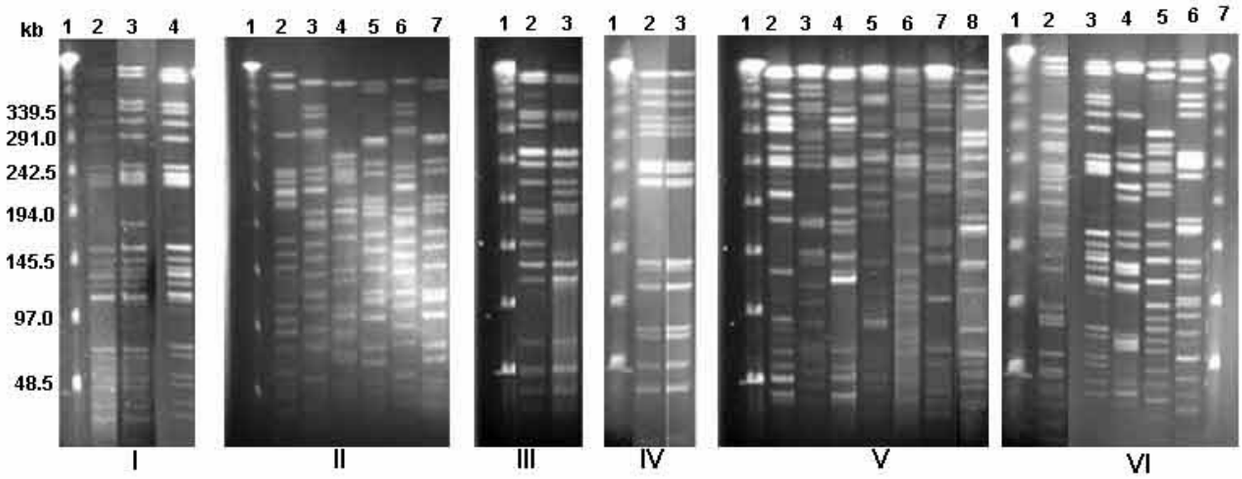


Fig. 7. PFGE profiles of XbaI digest of STEC strains. PFGE of STEC strains that exhibited identical profile in the RAPD-PCR and different virulence gene analysis are shown from panels I to IV and V and VI respectively. Lane 1 in all the panels and 7 in panel V are the ladder molecular size markers.

suggesting a new adhesin in Indian strain. One such recombinant plasmid was isolated and used for the identification of various clinical isolates. In dot blot hybridization, this radiolabelled recombinant plasmid could detect 90% of the clinical isolate.

Antiadhesin sera was also able to detect the different forms of the adhesin in the crude fimbrial preparation from 8 out of the 10 representative clinical EAggEC isolates. However, it could not identify any protein from the crude preparation of *Salmonella typhimurium* (fim +ve or fim - ve strains), *Vibrio cholerae, E. coli* DH5 or the plasmid cured strains of EAggEC. These findings have clearly indicated that the antiadhesin sera is highly specific for EAggEC strains. Hence, the probe may be useful for the detection of EAggEC strains as well as for their differentiation from other diarrhoeagenic organisms.

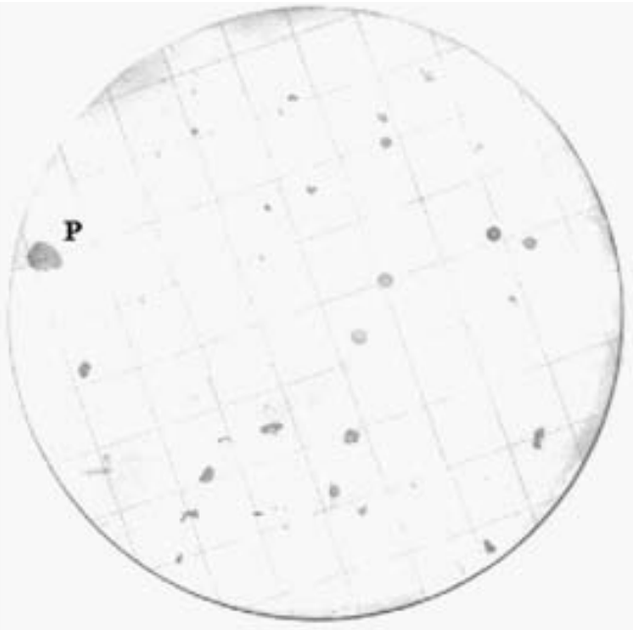


Fig.8. Colony hybridization test for the detection of *cag*A positive environmental isolates. P: positive control strain *H. pylori* 26695

Helicobacter pylori

Environmental Isolates of Aeromonas spp. harbouring the cagA Gene of H. pylori

The *cag* pathogenicity island (*cag* PAI) is a well-known virulence marker of *H. pylori* which is believed to be acquired initially by horizontal gene transfer from an unrelated species and over its evolution has adopted various intermediate types by chromosomal re-arrangement mediated by direct repeats and IS605. The *cag*PAI is a 40 kb DNA segment with 31 predicted open reading frames, of which the gene *cag*A, localized to the 3' end of the island, encodes an immunodominat antigen *cag*A. At present, however, nothing is known about the evolution of *cag* PAI or how it was acquired by *H. pylori*. A study was conducted at NICED, Kolkata for determining the prevalence of *cag*A in the aquatic microflora.

A total of 41 environmental strains from 100 ml of water samples collected from four fresh water ponds and a fresh water lake of Kolkata were found to possess *cag*A-like gene by colony hybridization test (Fig. 8). Of these, 14 strains yielded the desired 208 bp amplicon with Cf2 (5'GAATCAGTATTTTTCAGAC) and Cr2 (5' GGGTTGTATGATATTTTCC) indicating the presence of *cag*A-like gene. Twelve of these strains were also positive by PCR using another set of *cag*A-specific primers- *cag*A5 (5'-GGCAATGGTGGTCCTGGAGCT AGGC) and *cag*A2 (5'- GGA AAT CTT TAA TCT CAG TTC GG) that gave the appropriate amplicon of 324 bp. Since, Western blot analysis with *cag*A specific antibody used to detect the presence of surface-exposed *cag*A in the whole-cell protein of 6 PCR positive stable strains did not yield positive results, therefore, the *cag*A specific PCR products of 5 out of the above 6 strains were sequenced directly and were found to be 99-100% similar to each other and 97-98% identical to the corresponding portion of *cag*A of control

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                 *        20         *        40         *        60         *        80
CE3   : ..................................................................................: 88
26695 : ................A.................................................................: 88
C-15  : ..................................................................................: 88
C-8   : ..................................................................................: 88
C-45  : ..................................................................................: 88
I-18  : ...............G..................................................................: 88
I-30  : ...............G..................................................................: 88
I-47  : ...............G..................................................................: 88
I-77  : ...............G..................................................................: 88
C-92  : ..................................................................................: 88
        TTTAATCAACAAAGAC cTCTCATTGATGTAGAATCTTCCACAAAGAGCTTTCAGAAATTTGGGGATCAGCGTTACC AATTTTCACA

         *       100         *       120         *       140         *       160         *
CE3   : ...............................................CG.................................- : 169
26695 : ..................................................................................- : 169
C-15  : ..................................................................................- : 169
C-8   : ..................................................................................- : 169
C-45  : ..................................................................................- : 169
I-18  : ..................................................................................- : 169
I-30  : ..................................................................................- : 169
I-47  : ..................................................................................- : 169
I-77  : ..................................................................................- : 169
C-92  : ...................G..............................................................- : 169
        AGTTGGGTGTCCCATCAAAa GATCCGTCTAAAATCAACACCCGAtcGATCCGAAATTTTATGGAAAATATCATACAACCC
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Fig. 9. Alignment of 169 bp sequence within *cag*A gene of five environmental isolates of *A. hydrophila* (C-8, C-15, C-45, C-92 and CE3) and four clinical *H. pylori* strains (I-18, I-30, I-47 and I-77) determined in this study and *H. pylori* reference strain 26695 (accession number AE000511). The alignments of all the sequences were carried out using the CLUSTAL-X software program.

(26695) and Calcutta *H. pylori* strains (Fig. 9).

Since both *H. pylori* and *Aeromonas* spp. are known to survive in raw water and since both are human enteric pathogens, the study indicated that gene transfer between *H. pylori* and *Aeromonas* is directly responsible for the presence of *cagA*-like gene in *Aeromonas* spp.

H.pylori Infection in Early Childhood: Characterization of Isolates

A study is being carried out at AIIMS, New Delhi to characterize the paediatric *H. pylori* isolates to better understand the genotypic distribution of the *H.pylori* related virulence genes. Of the 142 patients screened for *H. pylori* in the biopsy tissue with rapid urease test, smear imprint examination, histopathological staining and isolation on culture, almost half were found to have *H. pylori* infection in the antrum or corpus. The results revealed that 43 paediatric isolates were positive for urea locus, whereas 38 had the *cagA* locus and 1.5 kb *vac*A gene was present in 41 of these isolates. Also, a large number (86%) of strains, which are *cagA* positive, are also cytotoxin producers. Unlike studies from south-east Asia, these isolates have not yielded the s1c allele till now. The study further showed that among the characterized strains, the m2 subtype appears to be more common (33%) than the m1 allele (5%) and that a large number of strains are non-typeable (62%) and do not belong to either m1 or m2 type. Active chronic gastritis is more commonly seen in those with *H. pylori* infection (33%) as compared to those without infection (15%). Further study on examination of any association between iron or B12 deficiency and *H. pylori* infection is underway.

Natural History of H. pylori Infection in a Birth Cohort in an Urban Slum Setting

A pilot study was conducted at AIIMS, New Delhi in infants recruited from the paediatric outpatient clinic. The results showed that there is a very high prevalence (71%) of *H. pylori* infection among infants as young as 6-14 weeks of age. Past or present evidence of infection was present in three quarters of mothers. Most infants were anti-*H. pylori* IgG negative 4 weeks after showing a positive 13 C urea breath test. The IgG antibodies detected in a small proportion of infants seemed to be of maternal origin as indicated by maternal IgG positivity in all such infants, decreasing prevalence of positivity over time (maternal antibodies decline with a half life of 4-6 weeks) and a complete lack of IgA sero-positivity among infants.

Development of Helicobacter pylori Model

A project is ongoing for development of an animal model for Indian strains of *H. pylori*. A total of 9 *H. pylori* (DU, 5; NUD, 3; PHT, 1) and a control strain (ATCC 26695) was used. They were positive for 16*sr* RNA and *ureA* genes, Six strains were positive both for *vacA* and *cagA* gene. Gerbils and Balb/c mice were inoculated with genotypically different strains. The results show that both gerbil as well as Balb/c mice can be infected with Indian strains of *H.pylori* as per the histological, microbiological, molecular and immune responses.

Entamoeba histolytica

Studies on Electron Dense Granules of E. histolytica containing Collagenase Activity

During the course of invasive intestinal amaebiasis, *E. histolytica* actively penetrates the mucosa of host intestine. But the exact mechanism and factors by which parasite destroys the human tissue are still unclear. In view of this, a study was initiated to characterize electron dense granules (EDG) of *E. histolytica* and clone the genes coding for these proteins at NICED, Kolkata. The electron dense granules produced during incubation of pathogenic *E. histolytica* with human collagen type I (purified from human placenta) and Ca2+ showed that EDG have 8 fold more collagenase activity than whole trophozoites. Antibodies raised against EDG were used in immuno-screening of pathogenic *E. histolytica* cDNA library. Sequencing and BLAST search analysis of plasmid DNA of 10 clones revealed homology with four genes in GenBank *viz.* actinin like protein grainin 1, serine rich protein and gEh29 gene for alkyl-hydroxyperoxidase reductase. Attempts were also made to amplify genes encoding for collagenase of *E. histolytica* by PCR. All the four fragments which were amplified *viz.* TE51 (585 bp), TE52 (485bp), TE35 (240 bp) and TE31 (190 bp) were sequenced and showed resemblances with *E. histolytica* gene (Ehvmal) encoding catalytic peptide of a putative vacuolar proton-transporting ATPase (V-ATPase), *E. histolytica* chaperonin-containing TCP-1 gene, zeta subunit gene and two new genes. In dot blot and Southern hybridization, all fragments showed hybridization with only *E. histolytica* genomic DNA, thereby suggesting authenticity of its being part of *E. histolytica*.

Studies on Multiple Genes in E. histolytica during Human Collagen type I and Ca^{2}+ Interaction

Since collagen is a major component of extracellular matrix and basal lamina of human intestine, it is thought that collagenase which was detected in pathogenic

E. histolytica is one of the important factors of tissue lysis during invasive amoebiasis. In view of this, attempt was made by NICED, Kolkata to clone and sequence some of the genes that are differentially expressed during activation with human collagen type I and Ca2+ and campare homology analysis with sequence in Gene bank.

The global expression of genes in *E. histolytica* during collagen activation was analyzed for the first time by genomic DNA microarray. This was developed using 6144 clones from a random fragment genomic DNA library of *E. histolytica.* Out of at least 14 genes which showed reproducible overexpression in collagen-activated trophozoites after hybridization with the microarray (Fig.10), five genes were sequenced. They showed homology with *E. histolytica* gene encoding pore forming peptide (amoebapore), EhCP1, EhCP2 cysteine proteinases, 40S ribosomal protein S19 and mRNA for protein containing SH3 domain. Most of these genes are important for pathogenesis of *E. histolytica.*

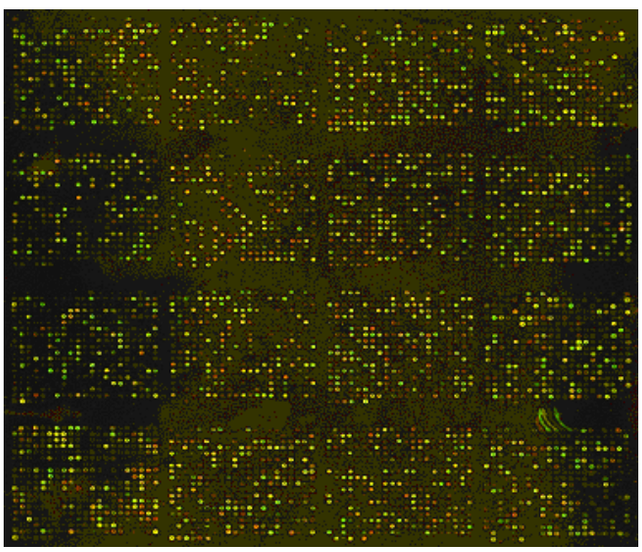


Fig. 10. *E. histolytica* genomic DNA microarray construction from 6144 clones. cDNA from normal *E. histolytica* was labelled with Cy3 dye (green) and cDNA from collagen-activated *E. histolytica* was labeled with Cy5 dye (red). Yellow shades were derived from the combination of red and green, indicating relatively equivalent expression levels.

Interaction of Galactose-binding Lectin of E. histolytica with Immune-competent Cells

Killing of host cells by *E. histolytica* trophozoites *in vitro* is mediated by an amoebic lectin that recognizes N or O linked oligosaccharides. A study was carried out at PGIMER, Chandigarh to understand the interactions of this lectin with the host immunocompetent cells. The results of the study revealed that the purified lectin induced death of approximately 10-20% of lymphocytes and monocytes from both intestinal and hepatic amoebiasis cases as compared to controls. Further, NK cells and CD25+ cells significantly increased in intestinal amoebiasis, while in amoebic liver abscess (ALA), CD19+, CD8+, NK and CD25+ positive cells significantly increased. There was, however, no significant difference in the total number and percentage of T cells in ALA patients who had significantly reduced CD4+ and increased CD8+ cell counts.

Further, the results showed that the lectin induced high degree of proliferation in lymphocytes in both ALA and intestinal amoebiasis patients. The CD8+ cells proliferated, *in vitro*, in response to stimulation with the lectin and these proliferating cells also produced cytokines of both Th1 and Th2 types. Since both lymphocytes and monocytes from infected persons bound lectin with increased intensity as compared to the controls, the study suggested an increased expression of receptors for the same.

Human Astrovirus

Detection and Molecular Characterization of Human Astrovirus

Astrovirus is recognised as an important viral pathogen causing gastroenteritis among children and other young ones of animal species. Astrovirus associated

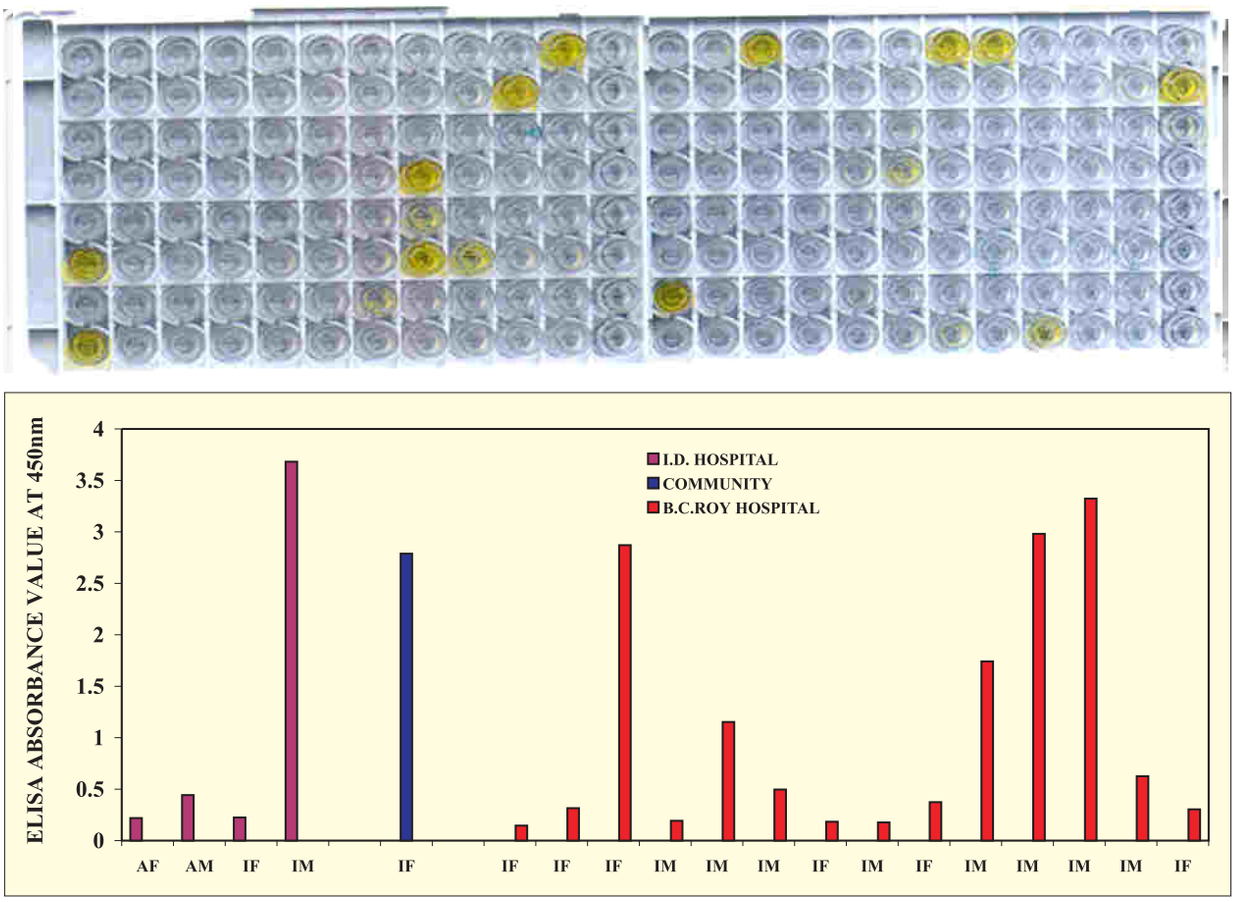


Fig. 11. Detection of astrovirus infection among adults and children in Kolkata
[af/m = female /male adult; if/m = female /male child]

gastroenteritis among 17 children and 2 adults was detected for the first time in Kolkata by NICED in 187 specimens. By monoclonal antibody based enzyme immunoassay using the astrovirus detection kit (Fig. 11), 7 cases were found to be astrovirus and rotavirus positive (mixed infections). RT-PCR of astrovirus RNA extracted from semi-purified faecal specimens confirmed astrovirus infection through 289bp amplicons. The 289 bp PCR product of Sapporo strain of astrovirus from the Sapporo Infant Home was sequenced and data was analysed to detemine the sequence homology with other serotypes of astroviruses. The sequence has been submitted to DNA data bank of Japan against 1984 outbreak strain of astrovirus which was confirmed as serotype I.

OTHER MICROBIAL INFECTIONS

Leptospirosis

Leptospirosis is caused by microorganisms of genus Leptospira which usually occur in rodents. The infections are transmitted from rodents, dogs and swine to man by contact with contaminated pond water. *L. grippotyphosa* is the etiological agent of leptospirosis in Andaman & Nicobar islands.

Assessment of Disease Burden

A task force study on disease burden due to leptospirosis was conducted with the objective of assessing the role of leptospirosis in causing acute febrile illness in different

parts of the country and to generate data on the clinical spectrum, infecting serogroups and the risk factors of leptospirosis. Thirteen Centres participated in the study and RMRC, Port Blair was the Coordinating Centre.

Of the 3609 patients screened, 14.7% were diagnosed to have leptospirosis based on dipstick results. Microscopic agglutination test (MAT) was done on 951 patients. Out of these, paired samples were available for 670 patients. Based on seroconversion, four-fold rise in titre or a minimum titre of 1:160 in either of the samples, 264 patients were diagnosed to have leptospirosis. Diagnosis in 200 patients was based on paired MAT and in the remaining 64 it was based on a minimum titre of 1:160 in a single sample. Based on MAT titres, the commonest serogroup was found to be *autumnalis* followed by *icterohaemorrhagiae*, *grippotyphosa* and *australis*. The largest distribution was for serogroup *icterohaemorrhagiae* followed by *autumnalis*. Dipstick positivity rates among samples with different MAT titres showed a logarithmic trend (Fig. 1).

The sensitivity of dipstick test done at the participating centres in comparison with paired MAT was found to be 97.7% and specificity was 71%. The overall concordance between dipstick and MAT was 71%. The study also identified important symptoms / signs, haematological and biochemical changes predicting leptospirosis and major risk factors.

Prevalence of symptoms/signs among MAT positive and negative patients was compared and the rate ratios were calculated. Multiple logistic regression (MLR) done with MAT result as the dependant variable and various symptoms/signs as independent variables showed that headache, diarrhoea, hematuria and oliguria are independent predictors of leptospirosis.

A univariate analysis showed that several socio-economic, environmental, behavioural and occupational factors had significant association with leptospirosis. The presence of rivers near the house, use of well water for drinking purpose, bathing in ponds and working in farms were found to be independent risk factors of leptospirosis.

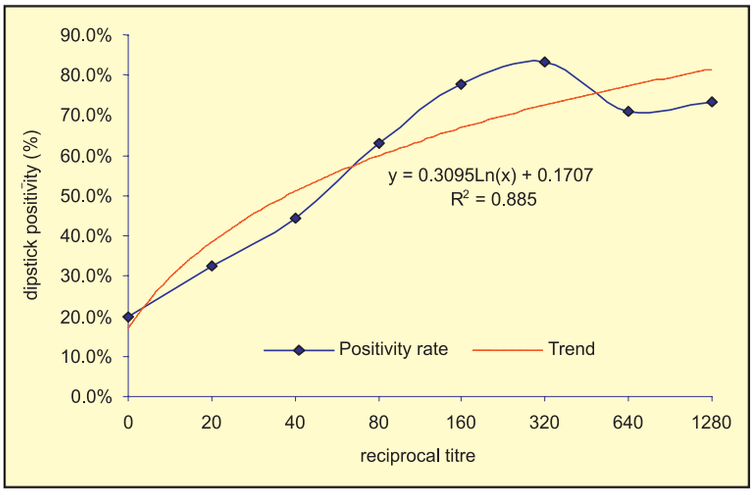


Fig. 1. Dipstick positivity rate among samples with different MAT titres

Genetic and antigenic relatedness of L. grippotyphosa in 1929 and 2001

The first authentic report of successful isolation of leptospires from India dates back to 1929, when 28 strains of leptospires were isolated from 78 suspected cases of Weil's disease among the penal settlement in Andaman islands. These isolates (CH31) belonged to serogroup *grippotyphosa*. No further information was available till 1988 when outbreak of a febrile illness occurred showing haemorrhagic tendencies and very high mortality rate. In 1994, the etiology of this illness was established as leptospirosis. An attempt was made to compare the recently isolated strains of leptospires with the earliest available one by employing molecular tools like random

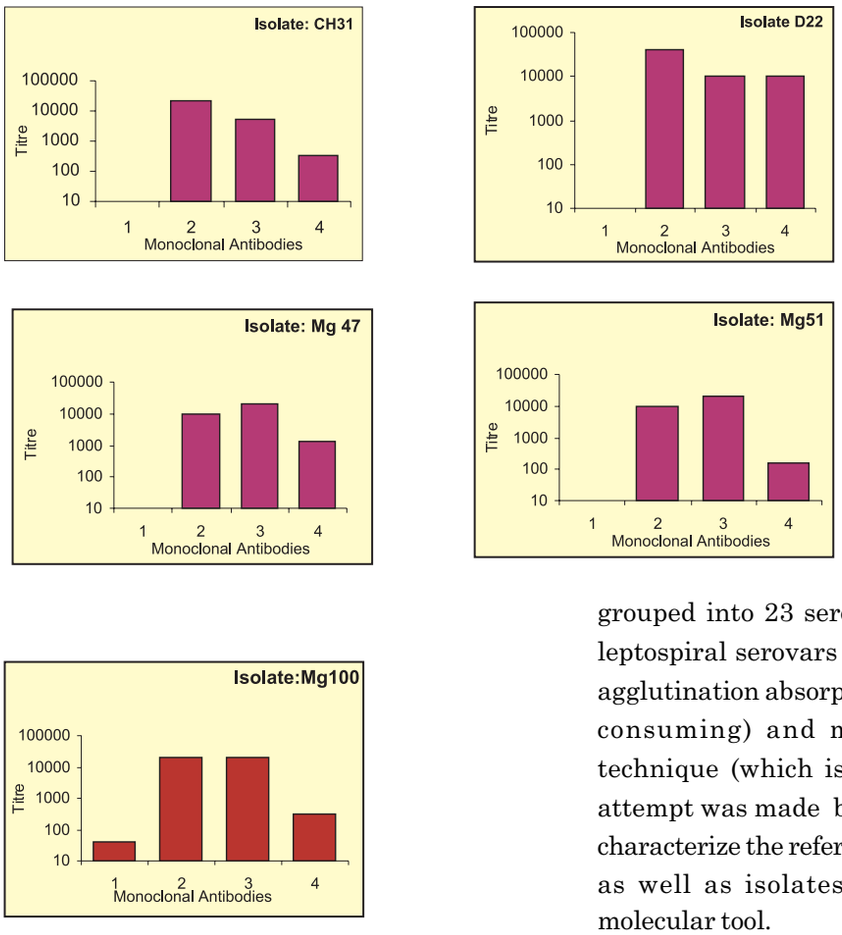


Fig.2. Antigenic properties of the different strains with monoclonal antibodies (1:F71C3, 2:F71C9, 3:165C3, 4:165C8).

amplified polymorphic DNA (RAPD) and restriction fragment length polymorphism (RFLP) in conjunction with customary serological techniques at RMRC, Port Blair.

Employment of monoclonal antibody technique revealed that 4 recent isolates of leptospires (D22, Mg47, Mg51, Mg100) showed antigenic patterns similar to the 1929 isolate CH31 (Fig.2), and all were found to belong to the serogroup *grippotyphosa* like CH31. Genetic characterization by RAPD (Fig.3) and PCR-restriction enzyme analysis (REA) (Fig.4 & 5) also revealed a close similarity between the 1929 isolate and the recent isolates. The results suggest that the strain CH31 has remained in these islands for over 70 years without undergoing any apparent changes in its antigenic and genetic nature and continues to cause leptospirosis in humans.

Molecular Characterization of Leptospiral Isolates

Over 212 serovars of leptospires are known to exist till date, which are grouped into 23 serogroups. Serologically, leptospiral serovars are identified by cross agglutination absorption test (which is time consuming) and monoclonal antibody technique (which is not serospecific). An attempt was made by RMRC, Port Blair to characterize the reference leptospiral strains as well as isolates using RAPD as the molecular tool.

RAPD produced characteristic banding patterns for different reference strains. It was able to differentiate between strains of

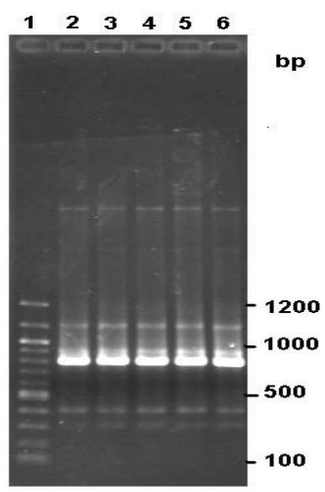


Fig.3. RAPD banding patterns of the isolates amplified with PB1 primer in PCR. (Lane 1: Marker 100bp ladder (NEB) Lane 2: CH 31, Lane 3: D 22, Lane 4: Mg 47, Lane 5: Mg 51, Lane 6: Mg 100)

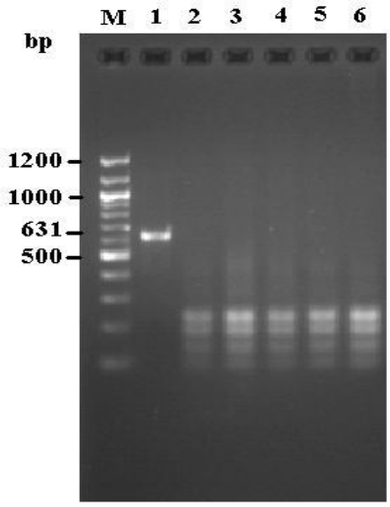


Fig.4. PCR-REA of Hin f1 digested 16 s variable region of *Leptospira* isolates. Lane 1: Marker 100bp ladder (NEB); Lane 1: Undigested PCR product; Lane 2: CH 31; Lane 3: D 22; Lane 4: Mg 47; Lane 5: Mg 51; Lane 6: Mg 100.

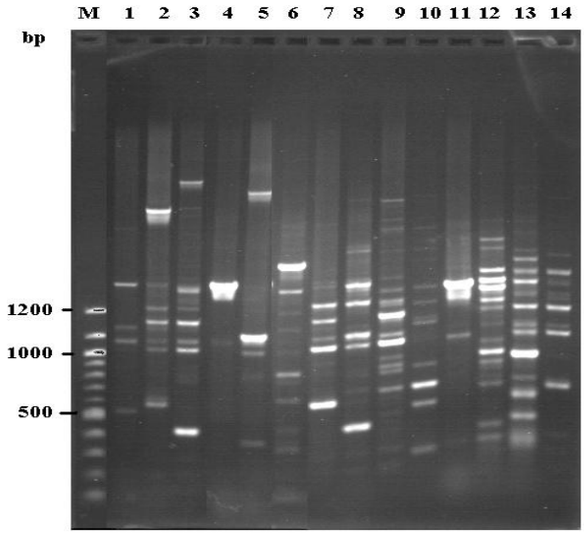


Fig.6. RAPD banding patterns of reference strains representing different serogroups. Lane
1: *Andamana*; 2: *Australis*; 3: *Autumnalis*; 4: *Ballum*
5: *Canicola* 6: *Cynopteri* 7: *Grippotyphosa*
8: *Hebdomadis* 9: *Icterohaemorrhagiae* 10: *Panama*
11: *Pomona* 12: *Shermani* 13: *Sejroe* 14: *Semaranga*.

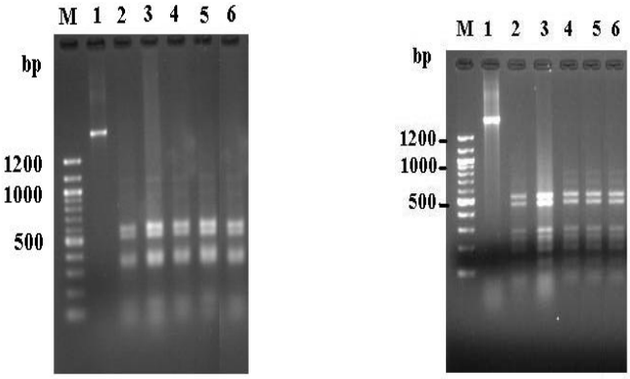


Fig.5. PCR-REA of 23 s variable region of *Leptospira* isolates. Lane 1: Marker 100bp ladder (NEB); Lane 1: Undigested PCR product; Lane 2: CH 31; Lane 3: D 22; Lane 4: Mg 47; Lane 5: Mg 51; Lane 6: Mg 100.
(a) HaeIII Digest (b) Hin f1 Digest.

different serogroups (Fig. 6 & 7), serovars (Fig. 8, 9) and even within the same serovar (Fig. 10). Twenty two of the 24 isolates could be typed by this method and the results were similar with those obtained serologically by MAT. The study shows that RAPD can be used as a tool to understand genetic relatedness/difference of leptospiral isolates. However, RAPD results do not always correlate with serological classification.

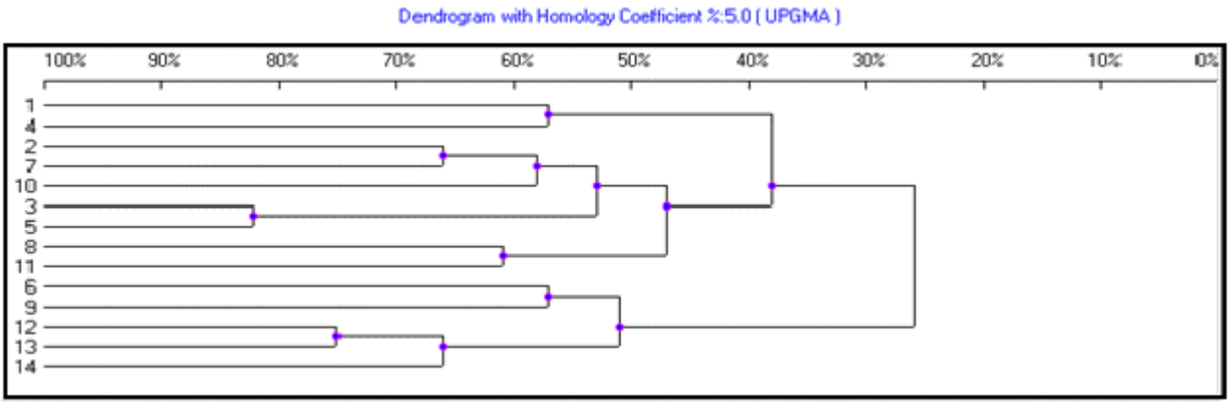


Fig 7. Dendrogram of the RAPD profiles of the reference strains representing different serogroups.

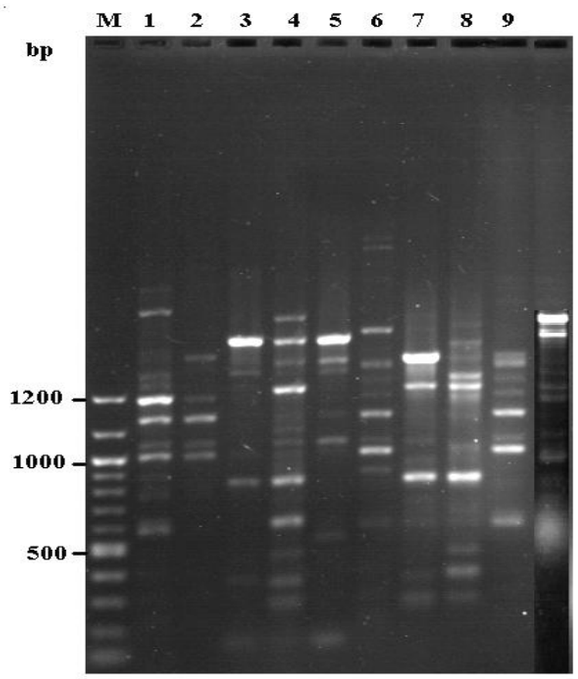


Fig.8. RAPD banding patterns of reference strains representing different serovars of the same serogroup *grippotyphosa*. Lane 1: Valbuzzi, 2: Vanderhoedeni, 3: Bananal, 4: Dadas, 5: Liangg, 6: Huanuco, 7: Canalzonae, 8: Mulleri, 9: Ratnapura.

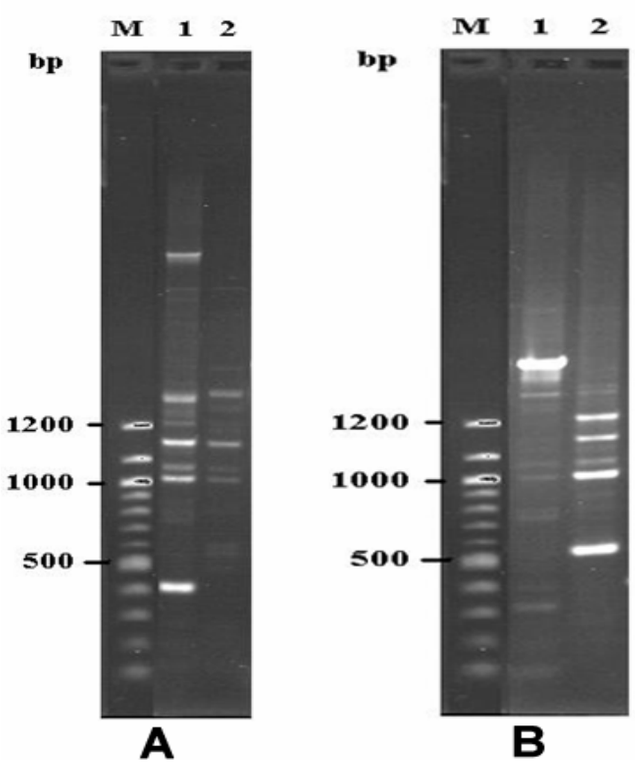


Fig.10. RAPD banding patterns of (A) reference strains representing 1 Rachmati, and 2 Autumnalis serovars of the serogroup *Autumnalis*. (B) different strains 1 Moskva V, and 2 CH31 representing the same serovar *grippotyphosa* of the serogroup *grippotyphosa*.

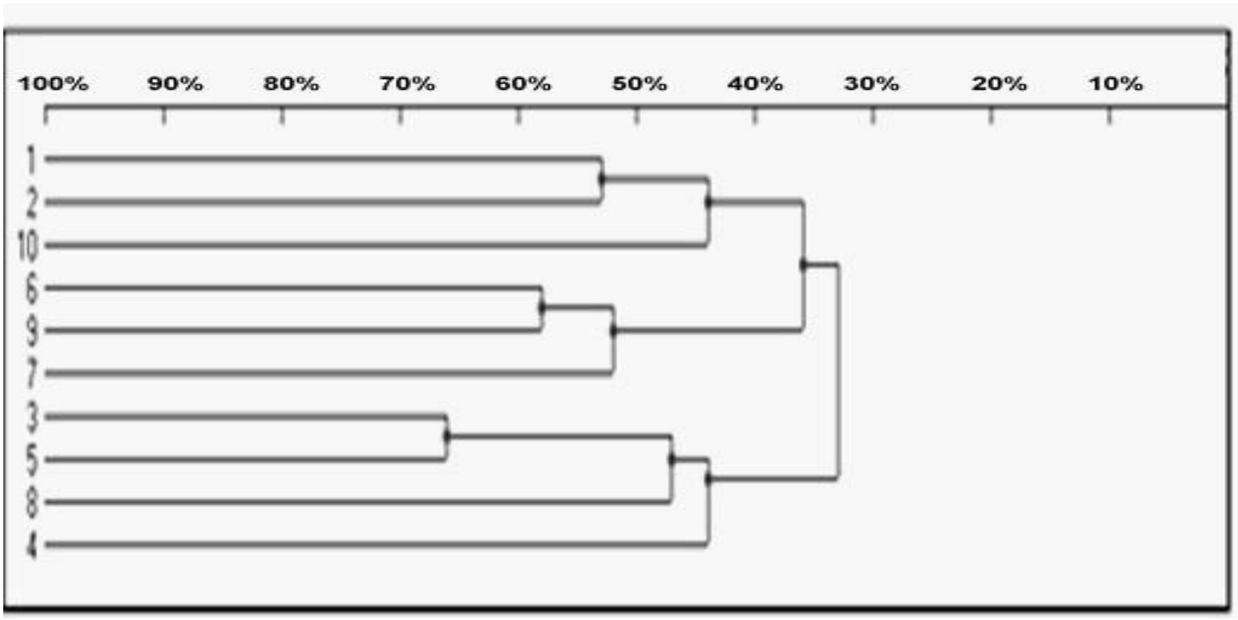


Fig.9. Dendrogram of RAPD profiles of reference strains representing different serovars of the same serogroup *grippotyphosa*

Campylobacter Infection

Preceding *Campylobacter jejuni* infection has emerged as the most important triggering agent of Guillain-Barre syndrome (GBS). In a project initiated at Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow, 43 patients with GBS and 25 healthy controls have been admitted. Stool culture and PCR was done to confirm *Campylobacter* enteritis in them. Sera were also tested for the presence of herpes simplex virus (HSV) and cytomegalovirus (CMV) antibodies using commercial kits. Based on clinical and electro-physiological studies, 36 patients were found to suffer from acute motor axonal neuropathy and 7 from acute inflammatory demyelinating polyradiculoneuropathy. Muscle power weakness in GBS patients varied from grade 1 to 5 in both fore and hind limbs. *C.jejuni* was isolated from two of the 43 patients both of whom had history of diarrhoea 8 and 11 days before the onset of disease. Eight GBS patients including 2 culture positive cases were found to have *C.jejuni* DNA in their stool by PCR while none of the healthy controls was positive for *Campylobacter* either by PCR or culture. The interim results suggest that only a small proportion (7%) of cases had seroevidence for HSV and CMV infection. The results of HLA typing will be correlated with various preceding infections, especially *Campylobacter*, after the typing is complete in the total study population.

Penicillium marneffei Infection

Penicilliosis marneffei is a very important opportunistic infection in certain countries in Southeast Asia. In India the disease has been recognized very recently in some AIDS patients in Manipur State. The mode of acquisition of the fungus by rodents and man is not known. A project has been initiated at V.P. Chest Institute, Delhi to understand the natural history and pathogenesis of *Penicillium marneffei* infection in humans and to develop a simplified serological procedure for early diagnosis of the infection.

Of the 97 bamboo rats (*Cannomys badius badius*) trapped from bamboo plantations in Weiphy and Irung in Manipur state, 9 were found to be carriers of *P. marneffei*, demonstrating for the first time the natural host of the fungus in India. The isolates exhibited typical morphological and microscopical features. None of the 197 soil samples from burrows of bamboo rats and other sites in bamboo plantations yielded *P. marneffei*.

In vitro interaction studies demonstrated overgrowth of *P. marneffei* by *Aspergillus flavus*, *A. fumigatus* and *Fusarium solani*. *P. purpurogenum* exhibited type IV interaction *i.e* mutual slight inhibition with both fungi almost coming in contact, leaving a narrow demarcation zone of 2 mm. Type III interaction (intermingling growth) was exhibited with *Acremonium strictum*.

Molecular Characterization of Group A *Streptococcus*

In developing countries like India pharyngitis and rheumatic fever/rheumatic heart disease (RF/RHD) are the leading cause of morbidity and mortality (especially in children of 5-15 years). To control and prevent such disorders, the understanding of epidemiology of their etiological agent *i.e. Streptococcus pyogenes* becomes a prerequisite. Serotyping, based on M-antigen is the gold standard for characterization of group A *Streptococci* (GAS) isolates but due to its limitations DNA based molecular typing methods are widely used. Till date no information is available regarding the M antigen encoding *emm* gene containing the Vir (virulent region) regulon in case of these isolates. In this study for the first time molecular heterogeneity among North Indian GAS by Vir and *emm* typing has been reported.

Forty GAS isolates from pharyngitis and RF/RHD patients were differentiated into 16 Vir types, which further discriminated into 24 different *emm* types. However, for some *emm* types: *emm* 1-2C, *emm* 69, *emm* 75-1, ST854, different Vir types were observed within same Vir type reflecting the independent power of discrimination of both the typing methods. Out of 24 *emm* types: *emm* 49 (12.5%), *emm* 71 (7.5%), *emm* 69 (7.5%), and *emm* 75-1 (7.5%) were most prevalent as well as heterogeneous indicating high diversity of strains circulating throughout India. This is the first ever report from Northern India regarding the genotyping of GAS isolates. Although no clear demarcation was observed between type specificity of GAS and particular disease, specific association of VT4 and VT5 with RF/RHD strains was noticed.

Characterisation of *Pseudomonas aeruginosa* Isolates

P.aeruginosa has been found to be the most common etiological agent responsible for respiratory tract infections in cystic fibrosis patients leading to increased morbidity and mortality. Characterisation of *P.aeruginosa* isolates from 85 cystic fibrosis (CF) patients showed respiratory infection in 56.5%, 75% of which had infection due to *P.aeruginosa*. Out of 344 *P.aeruginosa* isolates collected from 36 patients, 93 were sensitive to all the antibiotics tested which included amikacin, gentamicin, ciprofloxacin, pipracilin and ceftazadime. The extended spectrum *B.lactamase* (ESBL) isolates were isolated from 3 patients of whom 2 were chronically infected with *P.aeruginosa*. These isolates were also multidrug resistant but remained sensitive to pipracilin.

With progression of infection, the organism adapts by showing different phenotypic and genotypic changes. Production of alginate, which is also termed as mucoidy, is an example of adaptation of this organism by showing different phenotypic and genotypic changes with the progression of infection. It was observed that patients harbouring mucoid colonies in their respiratory tract possessed higher level of alginate in their sputum samples as compared to patients having nonmucoid colonies.

Molecular typing of the isolates was done using two techniques - enterobacterial repetitive intergenic consensus (ERIC) sequences-PCR and PCR-ribotyping. *P. aeruginosa* was found to be the major cause of respiratory infection in patients suffering from cystic fibrosis and was responsible for respiratory exacerbations. With chronicity of the disease, the organism was found to become multidrug resistant, acquired a mucoid phenotype and became auxotrophic for various amino acids.

PARASITIC DISEASES

MALARIA

The ICMR's Malaria Research Centre (MRC) at Delhi and the RMRCs at Bhubaneswar and Jabalpur are actively engaged in multi-disciplinary research for better understanding of the complex epidemiology of malaria and to find solutions to the emerging challenges in malaria control. Over the years, new technologies have resulted that found application in the National Malaria Control Programme.

Integrated Disease Vector Control Project

Bio-environmental Control of Mosquitoes in Mormugao Port Trust (Goa)

A project on bio-environmental control of mosquitoes is being continued in Mormugao

Port Trust in Goa and this year the technology is being transferred to the Port. Simultaneously mosquitogenic surveys, anti-mosquito interventions and impact assessment are going on.

Operational Feasibility of Using Larvivorous Fish for Malaria Control

This study is being carried out in four *talukas* belonging to four districts of Karnataka. Geographical reconnaissance (GR) was first carried out in all the problematic PHCs and fish were released after carrying out the GR. Around 80% of breeding sources are wells while irrigation tanks, ponds and streams constitute the rest of the breeding sources. In 903 villages, fish were released in vector breeding sources with the active participation of the State Health Department and Panchayat Raj Institutions. Panchayat Raj institutions are involved in monitoring the survival of fish in the breeding habitats with the help of local PHC medical officers. The *Zila Panchayat* is providing funding for fish release work in one of the PHCs in Tiptur *taluka*.

Rainwater Harvesting and its Implications on Mosquito Breeding

In order to study the possible implications of rain water harvesting on mosquito breeding, a survey was undertaken in Chennai city. The possible breeding sources within the rain water harvesting system identified for observations were open recharge wells, percolation pits, percolation trenches, trenches and junction pits. Fortnightly observations on mosquito breeding in these sites clearly showed that the water collection in these structures was used by mosquitoes for breeding specially *Culex*.

Molecular Studies

Molecular Diagnostic Assays for Identification of Members of An.culicifacies Complex

The MRC, Delhi analyzed two regions, inter-transcribed sequence 2 (ITS2) of rDNA and cytochrome oxidase II (COII) of mitochondrial DNA to find species-specific variation in the five sibling species of *An. culicifacies* complex. The ITS2 amplicon (~ 500 bp) digested with *Rsa* I could differentiate the five sibling species into two groups - A/D and B/C/E. DNA sequencing of these two amplicons (ITS2 and COII) and their sequence alignment showed species-specific differences. The sequence alignment of COII was utilized to design primers that could differentiate all the five species in two PCR assays on the pre-grouped A/D and B/C/E species by D3/D2-PCR assay.

Diagnosis of Malaria by Detection of HRP-2 Antigen

An indigenous reagent for rapid and sensitive immunodiagnosis of malarial antigen, histidine-rich protein (HRP-2), of *Plasmodium falciparum* in the blood film is being developed. HRP-2 is a water-soluble antigen expressed by trophozoites of *P. falciparum*. The antigen was synthesized and purified and after physicochemical characterization, all peptides were found to be above 90% pure. Microsphere technology was used to generate anti-peptide antibodies in two species. Both the species generated high antibody levels which were maintained up to 90 days post immunization and the peak titres were observed up to 25,000 till the 5th bleed using microspheres as the delivery vehicle. After generation of antibodies, purification was done by affinity chromatography. The specificity of the antibodies was confirmed by cross reacting the antisera generated with the peptides from the blood stage antigens and also from the core protein of HIV to show the cross species reactivity. The antibodies were found to be highly specific for the antigen.

Study on P.vivax Refractory Strain

The MRC, Delhi initiated a study on *P.vivax* refractory strain in collaboration with

International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi. A 2.4kb composite sequence of prophenoloxidase cDNA encoding for 87 amino acid protein was isolated. Expression studies with pET32a expression vector and BL21DE3 *E.coli* host revealed that the phenoloxidase mRNA increases to great extent after blood feeding in the refractory female whereas it is low in the susceptible male. The Northern blot analysis and quantitiative RT -PCR transcripts have revealed that serine protease is produced only in the refractory strain of *An.culicifacies* and is absent in the susceptible strains and that serine protease has a role in immune responses of refractory female.

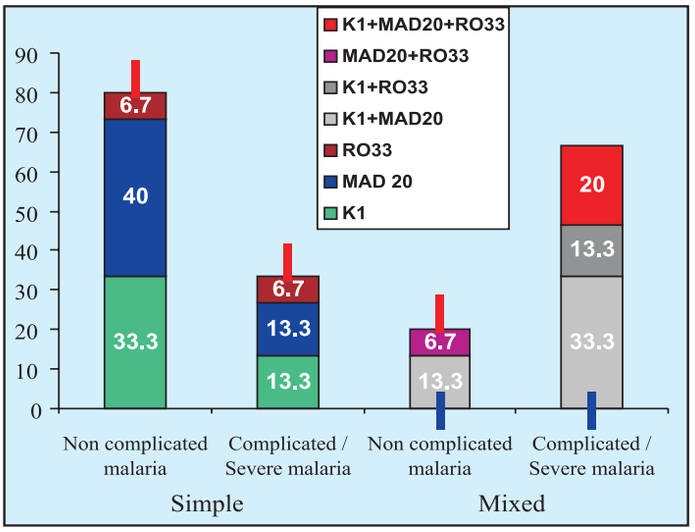


Fig. 1. Prevalence of sequence specific msp1 gene of *P.falciparum* in non complicated and complicated malaria cases

Population Structure of P.falciparum in Clinical Isolates of Orissa

In Orissa the malaria situation is of considerable concern. There is predominance of *P. falciparum* species which is responsible for severe cerebral malaria and high mortality. To analyse the genotypes of *P. falciparum* in severe/complicated and non complicated cases, a study was undertaken by RMRC, Bhubaneswar. Molecular analysis of merozoite surface protein (MSP1) and MSP2 genes was undertaken in 72 isolates (19 from severe and 53 from non-complicated cases of *P.falciparum* malaria). The results revealed that multiplicity of strains was more common in complicated cases in comparison to non-complicated cases (Fig.1 and 2).

Immunological Studies

Natural Human IgG Subclass Responses to P. falciparum Antigens

A study was undertaken by MRC, Delhi to measure host immune responses developed in the natural course of infection by determining antibody levels to three candidate *P.falciparum* antigens (MSP119, EBA175 and TRAP). $MSP1_{19}$ is a membrane bound (C terminal 19kD) fragment of the MSP1, highly conserved in different plasmodia species and has been shown to be a major vaccine candidate. Erythrocyte binding antigen-175 (EBA175) is an erythrocyte binding protein located in the micronemes of *P.falciparum*.

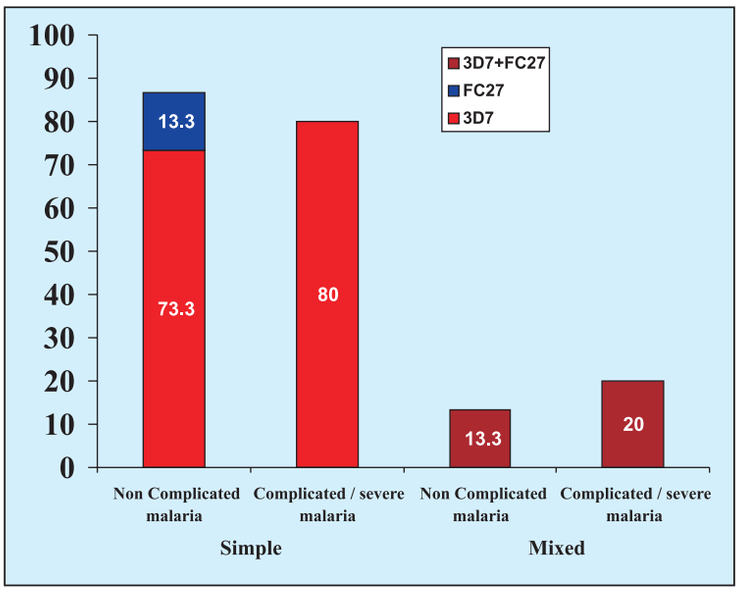


Fig. 2. Prevalence of sequence specific msp2 gene of *P.falciparum* in non complicated and complicated malaria cases

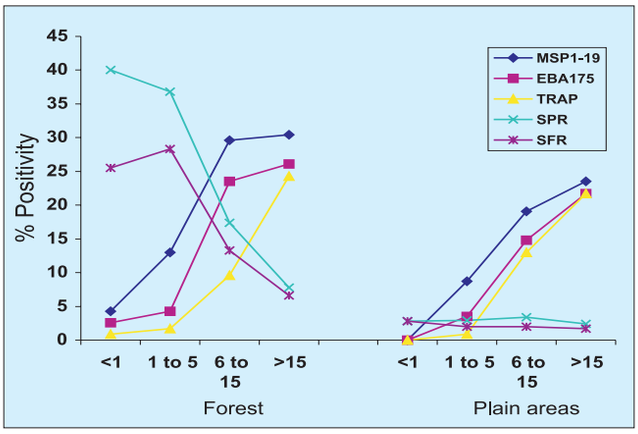


Fig. 3. Seropositivity and parasite positivity in people living in forest and plain areas in different age groups

Thrombospondin-related anonymous protein (TRAP) of *P.falciparum* was shown to be present on sporozoite surfaces and in the micronemes. Like circumsporozoite protein, TRAP binds to the basolateral domain of hepatocytes. Antibodies generated against recombinant TRAP inhibit sporozoite invasion.

The results of the study revealed that overall IgG antibody profile with three antigens was higher in individuals living in forest areas than plains. There was an age-wise increase in IgG level in both areas. Antigen specific IgM profile in study group was low and almost similar in two areas. Anti-TRAP antibody level was found moderately high in adults of both forest and plain areas. IgG1 and IgG2 were the predominant subclass responses to all three antigens. Proportion of high responders to $MSP1_{19}$ and EBA175 was comparable in children and adults. A group of sera from older age group showed elevated level of IgG3 to $MSP1_{19}$ and EBA175. An association between high IgG/IgG1 antibody to $MSP1_{19}$ and EBA175 responses and lower prevalence of *P.falciparum* parasitaemia (Fig. 3) was seen.

Parasite Biology

Characterization of P.falciparum Isolates available in Parasite Bank

Thirty five *P.falciparum* isolates available in the parasite bank were analysed for polymorphism of MSP-1, MSP-2 and GLURP using nested PCR with family specific primers. In MSP- 1 system, all the three families namely K-I, MAD20 and RO33 were observed with the predominance of first two (KI & MAD20). In MSP-2 system, both the families namely FC27 and 3D7 were observed with approximately similar prevalence. Most of the isolates were observed to be multiclonal and almost each isolate had a different genotype.

Genetic Diversity of Human Malaria Parasites

Analysis of blood spots of *P. falciparum* positive blood from patients for RFLP in MSP-1 and MSP-2 revealed presence of all the 3 families of MSP-1 (KI, MAD20 & RO33) and both of MSP-2 (FC27 & 307) (Fig. 4). Among Andaman & Nicobar isolates higher prevalence of RO33 of MSP-1 was observed while in mainland samples from Assam, Orissa, Delhi, Rajasthan and UP, RO33 is comparatively in low proportion. Analysis of paired samples collected from *P. falciparum* positive patients for MSP-1 and MSP-2

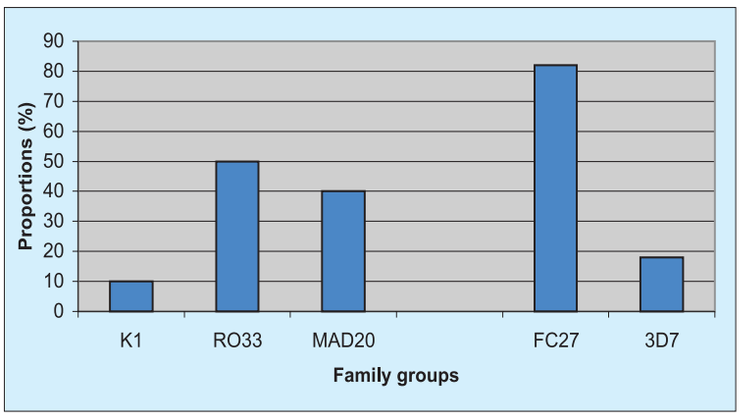


Fig. 4. Distribution of family group of MSP1 and MSP2 in *P. falciparum* isolates from *Jarawa* tribe of Andaman & Nicobar islands

variations on day zero and day of recrudescence revealed reinfection by different genotypes in six out of nine paired samples tested.

Diagnostics: PCR based Identification of Malaria Parasites

For diagnosis of malaria parasite infection, simple PCR assay using small subunit ribosomal DNA primers was employed at MRC. In a total of 79 *P. falciparum* positive blood spots tested, 98.7% gave amplification in PCR assay, however, in 11 *P. falciparum* negative blood spots, none of the samples showed amplification in PCR assay.

A multiplex PCR was standardized using a mixture of specific primers for each of the two species. The two species could be identified on the basis of size corresponding to 183 bp and 206 bp respectively for *P. falciparum* and *P. vivax*.

Malaria Parasite Bank

Malaria Parasite Bank, a well established national resource, is extending full support to many research organizations and universities by supplying human and non-human malaria parasites and imparting training to students and researchers. Besides the supply of non-human plasmodia, a total of 105 *P. falciparum* isolates was supplied for molecular analysis. Twenty isolates characterized for CQ sensitivity status were revived from cryopreserved condition and were cultivated *in vitro* to recheck their CQ sensitivity status. Negligible changes were observed in their CQ sensitivity status. Six *P. faIciparum* isolates characterized for their CQ sensitivity status, cytoadherence and erythrocytic invasion properties were cultivated *in vitro* to increase their stock for future studies. Cloning of few *P. falciparum* isolates is underway.

Remote Sensing and GIS Studies in Malaria

Studies were undertaken by MRC for mapping of vector distribution and spatiotemporal dynamics of malaria. Satellite remote sensing was found useful in delineation of major breeding habitats *i.e.* tanks, streams, ponds, marshy areas and landscape features suitable for malaria endemicity at village level in Tumkur district of Karnataka. Presence of water bodies, permanent vegetation cover, less barren area and scrub and less barren rocks were the landscape features associated with high malarious area. This tool was found to be a rapid method for ecological change detection.

Mapping of malaria receptivity and spatio-temporal dynamics of malaria was studied in Mewat region of Gurgaon (Haryana) using geographical information system (GIS). Five malaria paradigms namely irrigation command area, catchment area, mining area, urban area and flood prone areas were identified (Fig. 5). During inter- epidemic period of 1993, flood prone paradigm and non-catchment areas retained active pockets of malaria transmission. Maximum amplification of malaria occurred in urban/ semi-urban paradigms during 1996 epidemic.

To validate the GIS prediction of *An.minimus*, surveys were carried out in Banbasa (Uttaranchal). Larvae collected were identified as *An.minimus* both at larval and adult stages, thus confirming the presence of *An.minimus* as predicted by GIS.

Therapeutic Efficacy of Antimalarials

A study was initiated at MRC to evaluate the therapeutic efficacy of antimalarials being used in the country. The data generated so far reveal that there is no resistance to chloroquine in *P. vivax* [as evaluated at Chennai, Navi Mumbai and Gautam Budh Nagar (U.P.)]. As regards *P. falciparum*,

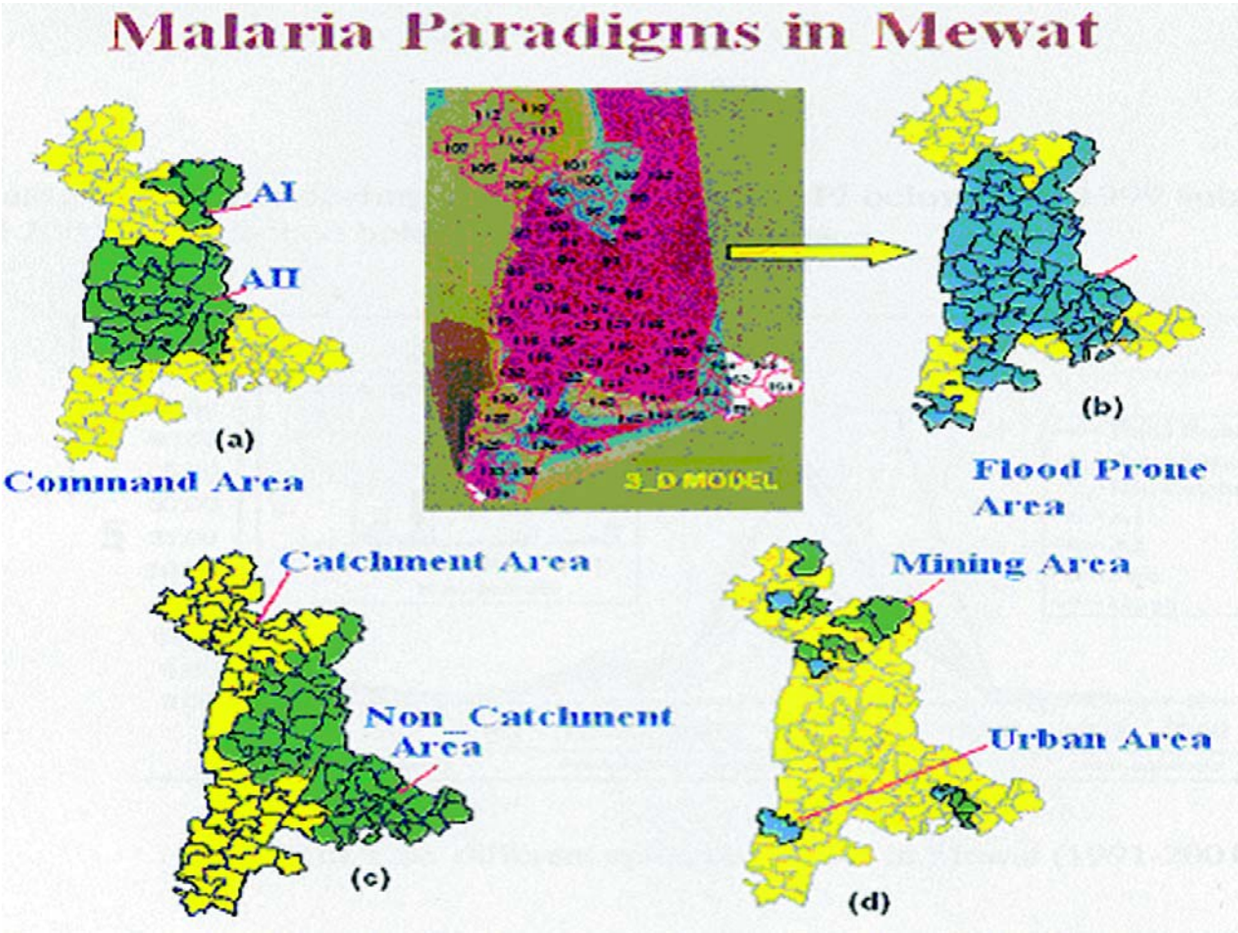


Fig. 5. a. Two command areas AI and AII in Mewat; b. Flood prone areas; c. Catchment and non-catchment areas; d. Urban and mining areas

there is evidence of treatment failure in Nowgaon and Kamrup districts of Assam while adequate response (in 95% cases) was observed in Keonjhar (Orissa). No resistance was detected for sulpha-pyrimethamine in these study areas.

Another study was carried out by MRC in district Mandla (MP) to evaluate the safety and efficacy of artesunate in combination with chloroquine or sulpha-pyrimethamine. Results have indicated that the therapy is safe, effective and well tolerated. Based on these data, long term studies are being planned to evaluate the impact of this strategy in delaying drug resistance.

Malaria in Tribals

Malaria Control in Tribals of Madhya Pradesh

A study was undertaken by RMRC, Jabalpur in 40 villages of 3 PHCs of district Betul. Inhabitants of these villages are mainly ethnic *Gond* tribe. The study revealed the presence of two efficient vector species *i.e. An.culicifacies* and *An.fluviatilis*. Both *P. falciparum* and *P.vivax* were present with predominance of *P.falciparum*.

State Government carried out mosquito control measures and follow up has revealed 28% reduction in mean indoor resting density

of anophelines, 64% reduction in slide positivity rate and 65% reduction in enlarged spleen cases.

Prevalence of Malaria among Tribals of Andamans

Jarawas, the primitive tribe of Andaman & Nicobar Islands, inhabiting the jungles of South and Middle Andaman in 3 groups were tested for Duffy blood group antigens by MRC, Delhi. One group inhabits the Lakra Lungta Island of Kadamtala area in the Middle Andaman, the second group in RK Nallah and Jirkatang area of South Andaman and the third group in the Tirur area of South Andaman. Fresh blood cells from the *Jarawas* were tested with Duffy antisera, anti -Fya and anti-Fyb. All the *Jarawas* of Kadamtala and RK Nallah were tested and found to be Duffy negative, while 18 out of 45 tested from Tirur area were Duffy positive. The findings are consistent with the view that Duffy negative phenotype, Fy/Fy constitutes the basis of innate resistance to infections with *P. vivax* but not towards infections with other *Plasmodium* species.

Malaria in Pregnancy

In a study carried out at RMRC, Jabalpur, a total of 208 pregnant women with or without fever were enrolled. Blood smears were made immediately after delivery from placenta in parallel with peripheral blood smear. Smears were also made from umbilical cord blood to determine the frequency of transplacental transmission of malaria. Of the 55 placenta found positive for malaria parasite, 51 were infected with *P.falciparum*. Only one was infected with *P.vivax* while 3 mixed infections of *P. vivax* and *P.falciparum* were found. One woman died in hospital before the onset of labour due to *P.vivax* infection. Besides, two post-natal cases infected with very high parasitaemia of *P.falciparum* (100000 parasites/µl of blood) died within 7 days after delivery. A clear correlation between parity and placental malaria was not found. Infants born to infected mothers were of low birth weight as compared to those born to non-infected mothers. Follow up revealed that these infants remained underweight till 6 months of age. *P. vivax* was detected from placenta for the first time in the Indian subcontinent.

FILARIASIS

The Council's Vector Control Research Centre (VCRC) at Pondicherry and Regional Medical Research Centre at Bhubaneswar continued to focus on applied and operational research for control/elimination of vector borne diseases especially filariasis. The areas covered included molecular epidemiology, molecular diagnostics for filarial parasites, immunity against filarial parasite, development of macrofilaricidal drugs, and safety and efficacy of drugs for case management.

Molecular Studies in Filariasis

Molecular Epidemiology and Genomics of Filariasis

The VCRC, Pondicherry continued studies on molecular epidemiology and genomics of filariasis. Genetic variation of populations and polymorphism of genes involved in key functions such as pathogenesis (allergen), drug sensitivity (ß-tubulin) and transmission of infection (Zn-metalloproteinase) of *W. bancrofti* were studied in isolates collected from wide geographic areas in India *viz.* Calicut, Rajahmundry, Jagadalpur, Varanasi and Pondicherry using molecular markers developed.

Differential immuno-reactivity of microfilariae(mf) of *W. bancrofti* collected from different geographic regions of India was studied using sera from patients with microfilaraemia and lymphoedema and

endemic normals. The results showed that the surface immunoreactivity of mf from different areas against lymphoedema sera varied significantly. The intensity of reactivity of mf from different regions also varied considerably. RAPD profiles were generated for isolates of *W. bancrofti* collected from Pondicherry (20), Calicut (7), Jagadalpur (7), Varanasi (6), Rajahmundry (2), Thirukovilur (9) and Chinnanergunam (7) and phylogenetic analysis was carried out. It showed that parasite populations from all urban and 1 rural area were genetically heterogeneous, exhibiting 2-5 different genotypes while those from 2 rural areas were homogenous revealing only 2 genotypes. A set of primers has been identified to generate AFLP profile of *W. bancrofti* that differentiate individual populations of the parasite.The allergen gene (ABA), known to be involved in pathogenesis of *W. bancrofti* isolates collected from different areas was amplified, cloned into a sequencing vector (pGEM-T) and sequenced. The Pondicherry isolate (P8) showed a variation. Further ß-tubulin gene, target for benzimidazole (BZ) based drug, albendazole is being actively used in combination with diethylcarbamazine (DEC) for elimination of lymphatic filariasis. BZ resistance in nematodes is closely associated with cytoskeleton protein, tubulin. The central region of the gene coding for this protein from 12 isolates of *W. bancrofti* collected from different locations was sequenced and information was used for the development of an allele specific polymerase chain reaction (AS-PCR) for the detection of mutation in the β-tubulin gene in the parasite populations. The study revealed that the nucleotide sequence of central region of β-tubulin gene has negligible divergence among local populations (Fig. 1) while those of distant geographic areas are highly divergent.

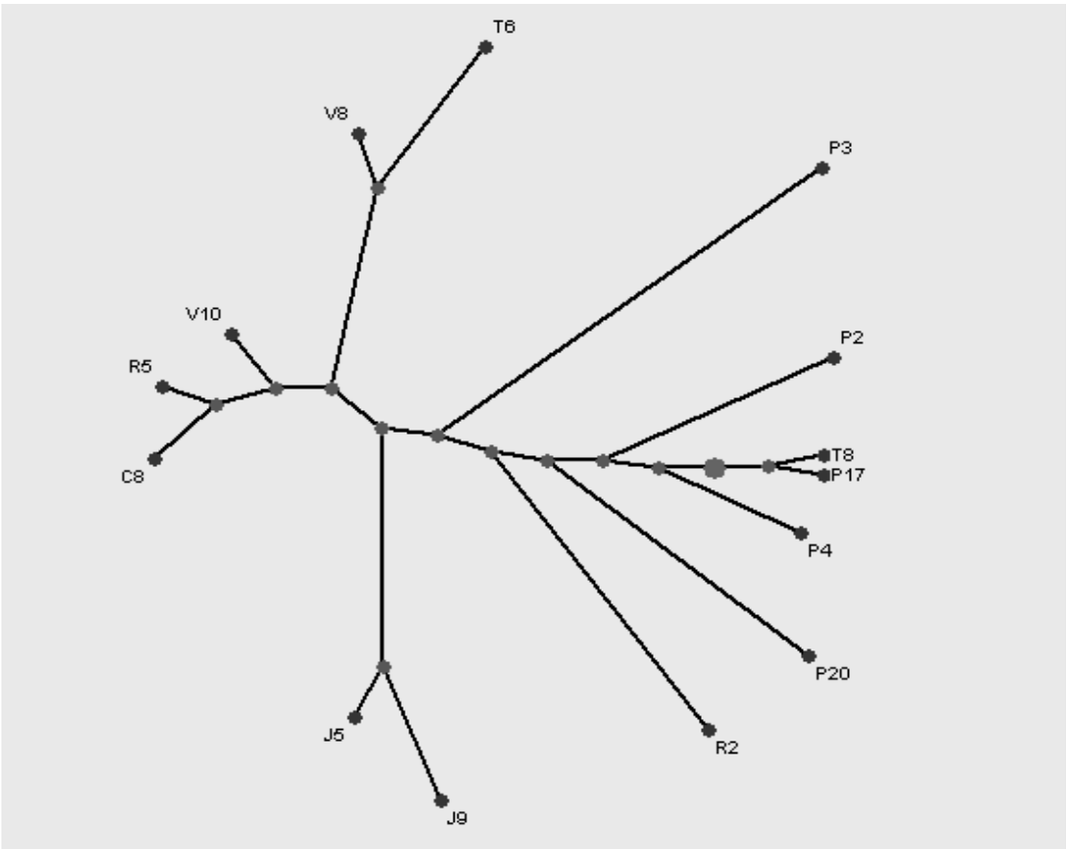


Fig. 1. Phylogram showing nucleotide divergence in the exon 5, intron 5 and exon 6 region of β-tubulin gene of *W. bancrofti* isolates from different geographic regions.

Molecular Studies in Mosquito Vector with reference to Development of B. malayi and W. bancrofti

As protein in thoracic tissues may significantly determine the parasite carrying capacity of the mosquito species, a study was initiated at Institute of Life Sciences, Bhubaneswar to address this problem by assessing the polypeptide synthesis in thoracic tissue in susceptible and refractory strains of *Aedes aegypti* and to understand gene product responsible for susceptibility or refractoriness to *W. bancrofti*. PAGE of radiolabeled polypeptides synthesized *in vivo* was compared in susceptible and refractory strains. Two polypeptide differences recognized by SDS-PAGE and one by two-dimensional electrophoresis were observed only with refractory strains, when they were given microfilaraemic blood meal. Further, inter-dietary differences within the group were seen in refractory strains. A 42 kDa polypeptide showed its appearance at 9 and 12 hr after infective blood feeding which then disappeared and reappeared at 24 hr and 48 hr respectively. The banding pattern of a 29 kDa polypeptide was found different in refractory strains from that of the susceptible ones. The presence of parasite in the blood meal stimulated the synthesis of these polypeptides. Presence of these polypeptides might be mediating the condition for refractoriness in mosquitoes.

Immunological Studies

Immunological Characterization of Filarial Antigens with Potential Protective Response in Endemic Population

Age-dependent prevalence of filarial infection and disease has been studied in many endemic regions. However, reports of similar studies for asymptomatic amicrofilaraemics (uninfected individuals / endemic normals) are limited. Study was undertaken at RMRC, Bhubaneswar in 1973 endemic normals to determine the age prevalence of this group in a filarial endemic region of Orissa.

In 1-5 yr age group, 96% of the population are found to be amicrofilaraemic as they would not be sufficiently exposed to the infection. However, as age advances there is rapid decline in amicrofilaraemic state so that by 15 yr of age, 65% of the population is asymptomatic amicrofilaraemic. Thereafter slow decline in this rate occurs (till age 30 yr), when prevalence of endemic normal population increases to 50%. Between 41 -60+ yr, the rate goes down to 35% and stabilizes and no further change in prevalence of endemic normals is observed (Fig.2). The onset of stabilized normal (uninfected) population indicates the acquisition of resistance as also indicated from circulating filarial antigen assay. To determine antigen negativity in asymptomatic amicrofilaraemic individuals at older age, individuals in 31-60+ years age group were analyzed for Og4C3 assay and an antigen positivity of 31.5% was noted. Since the individuals in the older age-group would be sufficiently exposed to infection, antigen negativity suggests the presence of infection free normal individuals.

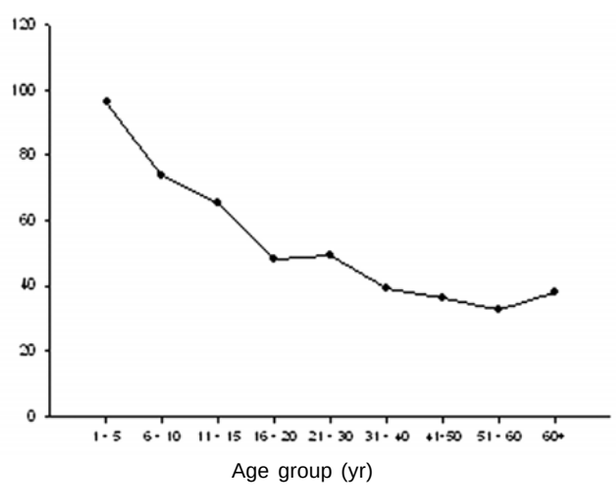


Fig. 2. Age - distribution of asymptomatic amicrofilaraemic (endemic normals, n=1973) individuals in an filarial endemic region of Orissa (Khurda district). The study was carried out involving 3654 individuals in three adjoining villages.

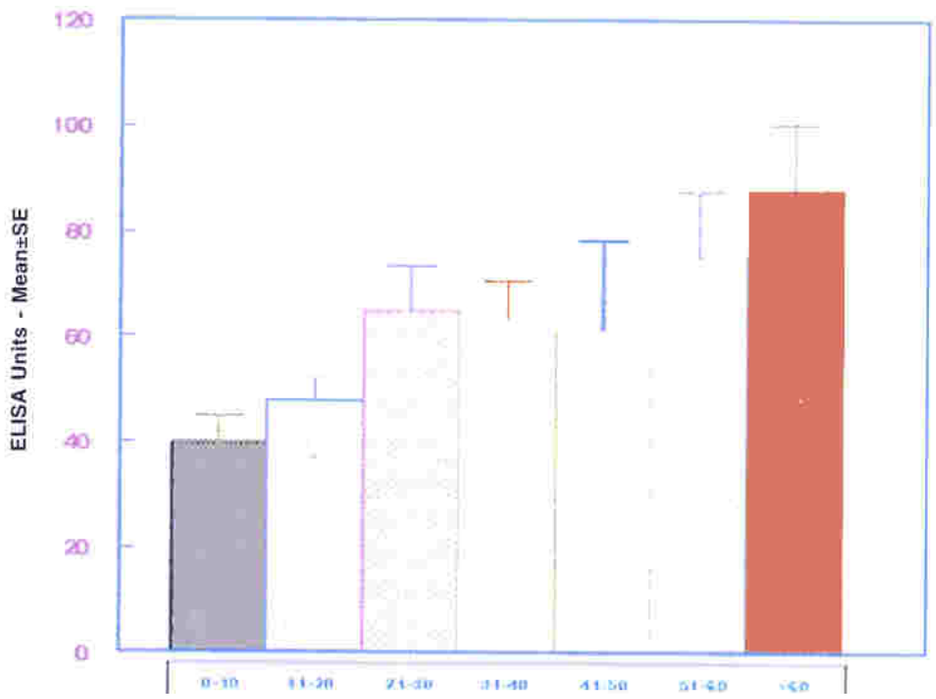


Fig. 3. Antibodies (IgG) to ALT-1 in age-stratified endemic population

Diagnosis of Infection and Morbidity in Lymphatic Filariasis: Development of Field Applicable Tools

Study was initiated at RMRC, Bhubaneswar to identify molecular markers for assessing morbidity, protective immunity as well as immunodiagnostics in human lymphatic filariasis. Since these issues are diverse, three different approaches are being attempted. For identifying morbidity markers to monitor progression of chronic disease, a large panel of pro as well as anti-inflammatory molecules in circulation were monitored. For identifying protective immunity, five different stage specific recombinant proteins of filarial parasites were used to study antibody responses. The following molecules were quantified in different clinical categories: IL-6, IL-8, IL-10, TNF-α, TNF-α receptor-55, TNF-α receptor 75, LPS binding protein (LBP), and ICAM-1. Significantly elevated levels of IL-8 were observed in patients with acute filariasis in comparison with endemic normals (EN), asymptomatic microfilariaemia carriers (AS), subjects with cryptic infection (CR) and chronic filariasis (CH). Similarly, IL-6 levels were found to be high in acute and elephantiasis cases in comparison to other categories.

The study revealed the role of IgG antibodies to ALT-1 proteins in restricting the infection load in human bancroftian filariasis. The results in age-stratified population indicate a progressive increase of anti-ALT-1 IgG with increasing exposure to infective larvae in the endemic population (Fig. 3).

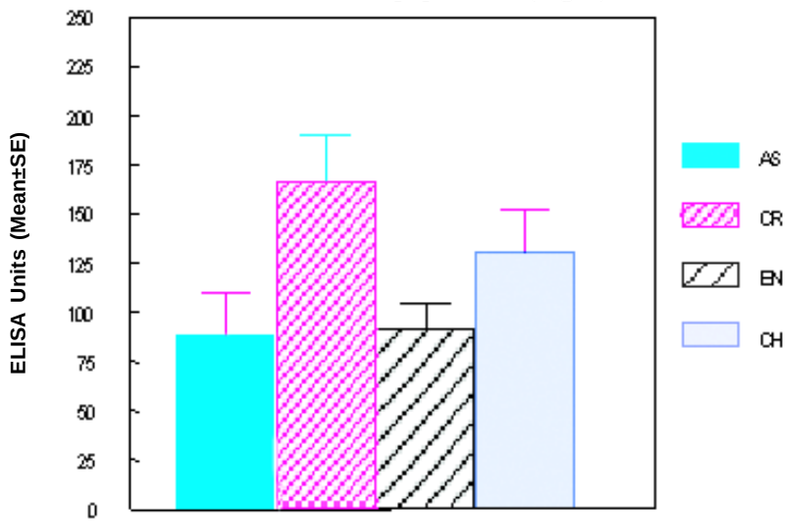


Fig. 4. Antibodies (IgG) to CPI-2 in different clinical categories of human filariasis

IgG levels to cystein proteinase inhibitor (CPI-2), present on the surface of adult worms were significantly more in CR in comparison to mf carriers (Fig.4). This indicates a clear role for this antibody in anti-microfilarial immunity since CR are free of circulating mf but harbour adult filarial worms. Further, IgG levels to serpin (SPN-2), an antigen present in microfilarial stages were significantly more in EN, CH and CR cases. This indicated a role for antibodies to SPN-2 in anti-microfilarial as well as anti-adult immunity. Higher levels observed in CH cases as compared to EN indicate that very high antibody response to SPN-2 could be associated with pathology.

Role of IgA in Protective Immunity in Human and Experimental Filariasis

IgA is generally considered to be an antibody isotype with a role in mucosal immunity. However, the importance of serum IgA in systemic helminthic infections is being increasingly realized since two high affinity receptors for IgA (Fc α) are found on the cell membranes of eosinophils which is considered an important effector cell in helminth immunity. Earlier using crude filarial antigens, RMRC, Bhubaneswar had demonstrated significantly elevated filarial IgA levels only in putatively immune endemic normals in comparison to infected subjects and patients with chronic disease. Studies were further extended by studying IgA levels to the recombinant filarial proteins, *viz.* abundant larval transcript- (ALT-1), ALT-2, VAL, SPN-2 and CPI-2. IgA antibodies to ALT-1 revealed an interesting feature that differentiated microfilaraemic subjects from those with CR. Subjects with microfilaraemia were found to contain significantly low levels of anti ALT-1 IgA in comparison with other groups (including those with CR) indicating that the presence of mf in circulation significantly downregulates IgA response to ALT-1 (Fig.5). No significant difference in IgA levels to CPI-2 and SPN-2 were observed in different clinical categories of human bancroftian filariasis.

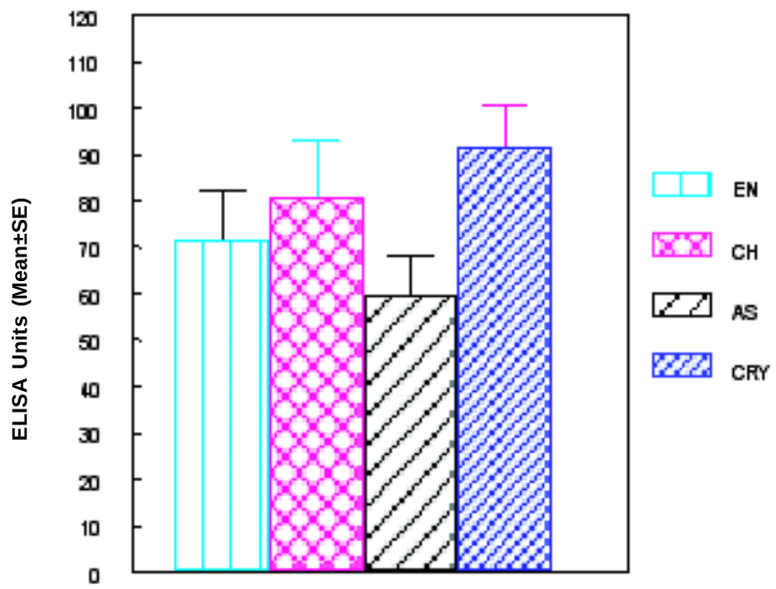


Fig. 5. IgA to Bm- ALT-1 in human bancroftian filariasis

Study on Different Immunological Factors across the Clinical Spectrum of Filariasis in an Endemic Area

A study was carried out at Sevagram, Wardha on the humoral immunity, T-cell proliferative response and cytokine levels against *Brugia malayi* microfilarial antigens. The circulating filarial antigen levels were determined in individuals representing all the groups across the clinical spectrum of filariasis in an endemic area. Circulating filarial antigen was detected in 95% of microfilaraemics, 60% of acute cases, 75% of different grades of chronic filarial cases, 100% of occult cases and none of the endemic normals. The results indicated presence of active filarial infection in majority of clinical

filarial cases with chronic and occult manifestations, where mf are usually not detected in peripheral circulation.

Against *B.malayi* microfilarial excretory-secretory antigen, microfilaraemics showed significantly elevated levels of IgG_4 and IgG_3 antibodies. While acute filarial cases had pronounced IgG_1 antibodies, grade I chronic and occult filarial cases showed higher levels of IgG_1 antibodies. IgE antibodies were found to be elevated in all chronic filarial cases. Against a 200 kDa *B. malayi* mf soluble antigen, SF-1, microfilaraemic individuals had significantly higher IgG_4 antibody levels than those from clinical filarial or endemic normal group. IgG_3 antibody levels were high in clinical filarial group compared to endemic normal group. Both microfilaraemics and clinical filarial cases showed cellular immunological hyporesponsiveness compared to endemic normal group against SF-1 antigen. A predominant Th-1 type immune response possibly involved in immune protection was noted in individuals from asymptomatic and amicrofilaraemic endemic normal group. Immunomonitoring of filarial cases showed significant decrease in filarial specific IgG_4 antibodies in all the three groups, *viz.*, microfilaraemic, chronic and occult filarial cases after treatment with DEC. While there was no significant decrease in filarial IgG_1 and IgG_2 subtypes, filarial IgG_3 antibodies increased significantly in chronic filarial cases followed by DEC treatment.

Immunological Responses in W. bancrofti and B. malayi infections in Endemic Areas in India

A study was carried out to analyse kinetics of *W. bancrofti* antigenemia by ELISA kit in serum samples collected at VCRC, Pondicherry from mf carriers at sequential intervals following treatment till 365 days, lymphoedema patients and endemic normals. The IgG antibody response to *B. malayi* L3 stage (infective stage) antigen was analysed by in-house ELISA technique in serum samples collected at T.D. Medical College, Alleppy at different time periods following treatment till 365 days from *B. malayi* mf carriers, acute lymphangitis and chronic filarial oedema patients and endemic normal subjects. Serum cytokine responses were also determined in above mentioned patients and controls using the ELISA kits (obtained from DIACLONE Research, France). Serum samples at PGIMER, Chandigarh from normal healthy subjects (amicrofilaraemic) who have not travelled to filariasis endemic areas during the past 5 years were included as non-endemic controls.

None of the *W. bancrofti* mf carriers became antigen negative till 365 post treatment day although no mf were detected in 42% and 13% carriers on 180 and 365 post treatment days. Significant antigenemia was detected in 13/24 endemic normals as compared to nil in non-endemic subjects. No significant difference was observed in IgG antibody response to *B. malayi* L3 stage antigen in pre and post treatment *B. malayi* mf carriers, although IgG response in carriers, acute lymphangitis, chronic lymphoedema and endemic normals was significantly higher than non-endemic controls. Cytokine response analysis revealed no significant difference in pre and post treatment samples of mf carriers, however, IL-2 and INF-γ responses in them were significantly low as compared to non-endemic controls.

Studies on Mass Chemotherapy

Co-administration of Albendazole and DEC for Controlling Lymphatic Filariasis

To compare the operational feasibility and impact of co-administration of DEC and

albendazole with that of DEC alone at district level, a study is being carried out by VCRC, Pondicherry in four districts, two each from Tamil Nadu (DEC: Thiruvannamalai; DEC+albendazole: Thanjavur) and Kerala (DEC: Kozhikode; DEC+albendazole: Alappuzha), covering a total population of 8.5 million. Filaria Prevention Assistants (FPA) were involved for 50 households each for training and social mobilization through improved advocacy using newer COMBI (communication for behavioural impact) plan.In Kerala, an attempt was made to strengthen the training and IEC.

The study revealed that the reported coverage of distribution was above 90% in two districts of TN. The assessed coverage of drug distribution was marginally reduced in 2003 compared to 2001. In Kerala the assessed coverage of distribution was about 80% in Alappuzha and below 50% in Kozhikode. The assessed consumption rates also decreased marginally in both these districts compared to previous year. Almost 20-25% individuals receiving the drug did not consume the same. The same figures for the two districts in Kerala were much lower (40 and 30% approximately). The coverage of distribution/consumption was independent of the drug in TN. No serious adverse reaction experience (SARE) was reported from any of the study districts, indicating the safety of the drugs in the given dosage. Fear of adverse reaction and lack of knowledge about the programme were the most important reasons for non-consumption of drug. Deworming was reported among 2% of those who consumed the drug. Overall, a significant decline in mf intensity and prevalence of mf was observed after two rounds of drug administration in TN (Fig 6). In Kerala, increase in prevalence and mf intensity was observed in Kozhikode but in Alappuzha there was decline in mf prevalence, but no appreciable decline in mf intensity compared to previous year (Fig.7). A significant reduction in the prevalence (over 50%) and intensity of geo-helminths was recorded in Alappuzha after the first round but the levels remained stable after second round.

The results of the study suggest that co-administration of DEC and albendazole is

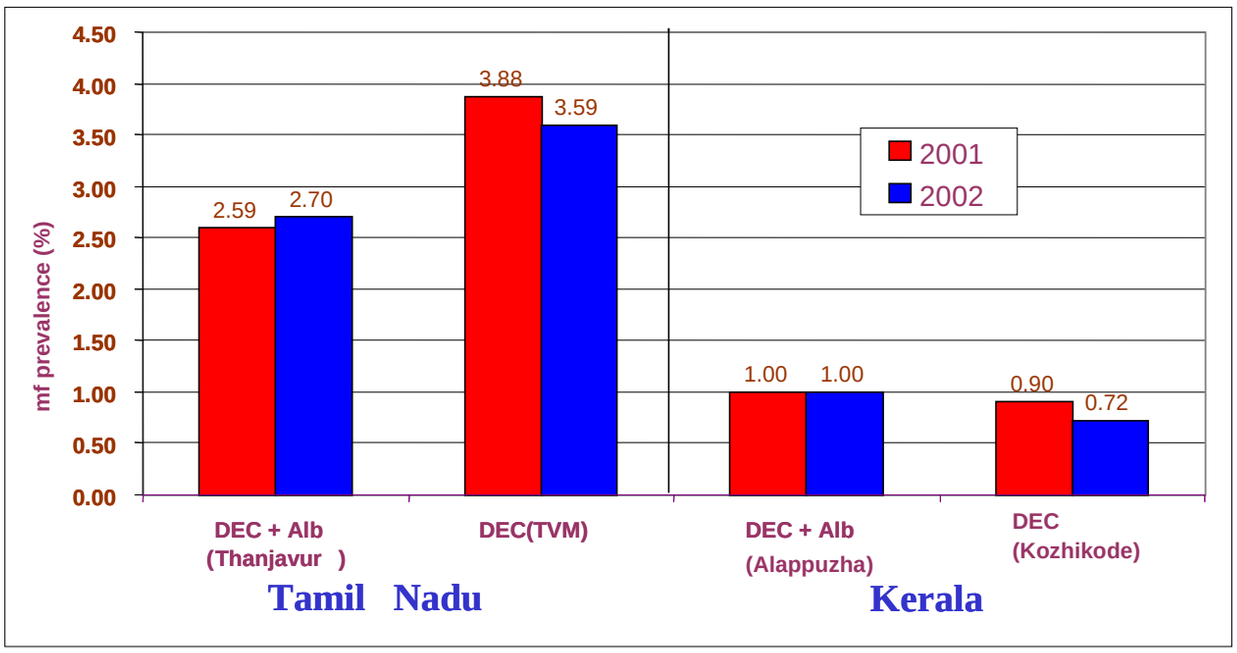


Fig. 6. Comparison of microfilaria prevalence between the first and second rounds of drug administration in Tamil Nadu and Kerala

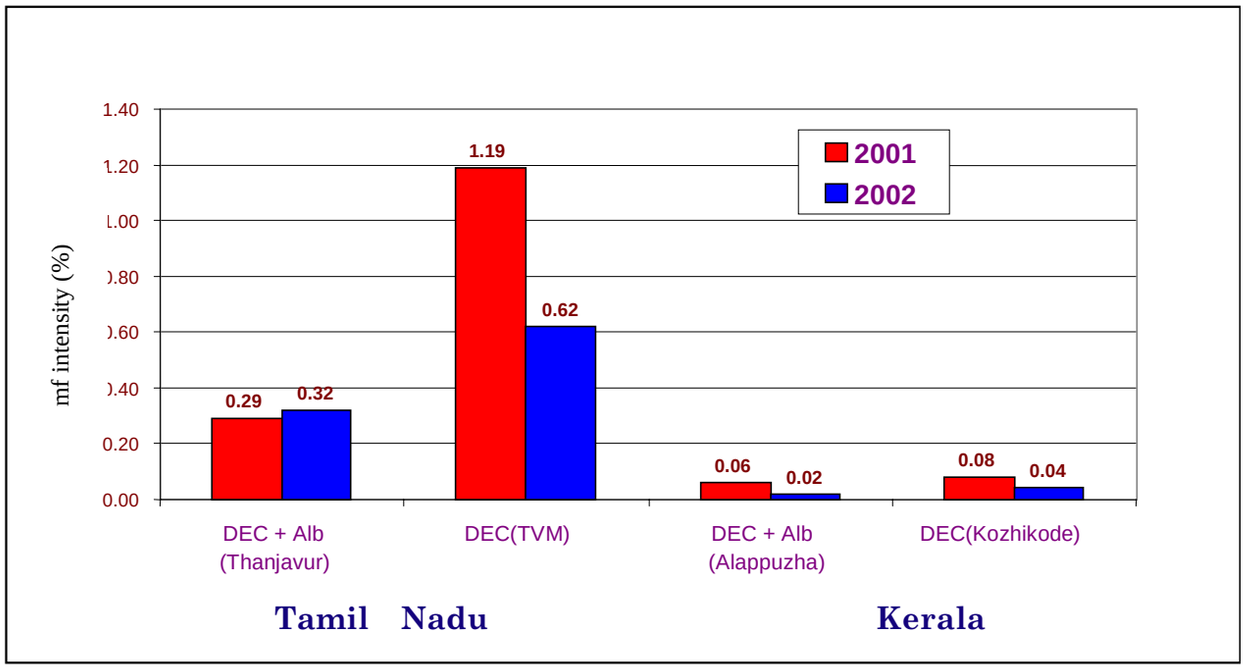


Fig. 7. Comparison of microfilaria intensity between the first and second rounds of drug administration in Tamil Nadu and Kerala

operationally as feasible as administration of DEC alone. It does not suggest that co-administration of albendazole with DEC improves the community compliance but is highly beneficial for the control of geo-helminths. There is no evidence to suggest that co-administration of DEC and albendazole has better impact than DEC administration alone with reference to filariasis control. Adverse reactions due to co-administration of DEC and albendazole are similar to administration of DEC alone.

Impact of Mass Treatment with DEC or Ivermectin or both on Transmission of Bancroftian Filariasis

A long-term study to evaluate the potential of annual mass administration of DEC or ivermectin to eliminate filariasis is being carried out at VCRC, Pondicherry. The study consist of four arms (i) DEC alone (ii) ivermectin alone (iii) DEC+ivermectin and (iv) DEC+albendazole. Each arm consists of five villages.

The effect of mass drug administration on microfilaraemia prevalence was assessed by night blood survey of all members prior to each round of mass drug administration. The impact on transmission was measured through changes in infection and infectivity rates of vector mosquitoes collected in each village while entomological surveys were carried out after each round of drug administration. The effect of mass drug administration on chronic disease was evaluated by comparing the prevalence of chronic disease between pre-intervention and post-last intervention period. The cumulative effect of seven rounds of annual mass drug administration with DEC or ivermectin, five rounds with DEC+ivermectin and first round with DEC+albendazole was evaluated. The compliance with mass drug administration was 60% in DEC arm, 64% in ivermectin arm, 61% in DEC+ivermectin arm and 69% in DEC+albendazole arm.

After seven rounds of treatment, the mf rate declined by 82% in DEC arm and 75% in ivermectin arm. The geometric mean intensity (GMI) of mf fell from the pre-treatment level of 0.66 to 0.07 in DEC arm

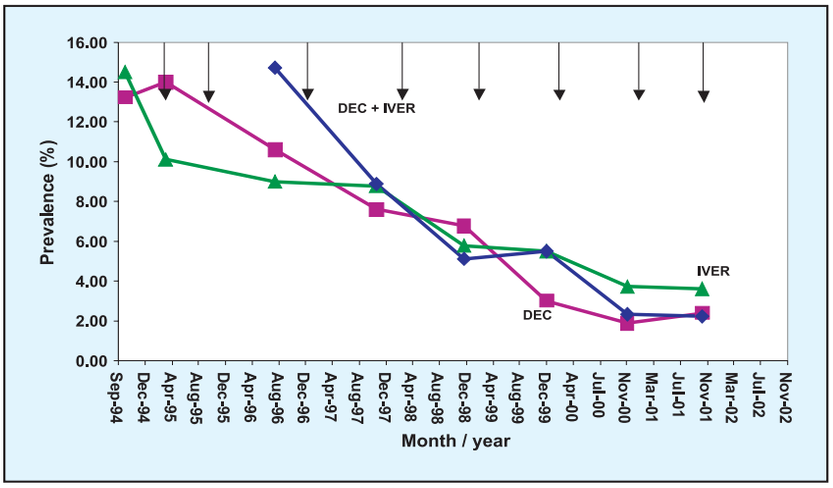


Fig. 8. Changes in prevalence of mf rate following seven rounds of mass treatment with DEC or ivermectin or DEC+ivermectin

and from 0.62 to 0.10 in ivermectin arm. The vector infection rate was reduced from pre-intervention level of around 18.0% in both the arms to 2.4% in DEC arm and 3.6% in ivermectin arm. The infectivity rate declined from pre-intervention level of 1.0% to 0.30% and 1.70% to 0.53% in DEC and ivermectin arms respectively. After seven rounds of treatment, the transmission intensity index declined from pre-control level of 0.73 to 0.14 in DEC arm and 0.85 to 0.37 in ivermectin arm. This is equivalent to 81% reduction in the former arm and 56% reduction in the latter arm. However, after five rounds of administration of DEC+ivermectin, the mf rate declined from pre-intervention level of 14.7% to 2.2% (Fig. 8), GMI of mf from 0.62 to 0.05 (=92%), vector infection rate from 13.4% to 4.3% and vector infectivity rate from 1.40% to 0.42% (70%). The transmission intensity index declined from 0.42 to 0.14 (67%). Mass administration of one dose of DEC+albendazole resulted in only marginal changes in mf prevalence and vector infection rate.

Remote Sensing (RS) and Geographical Information System (GIS)

A study was initiated at VCRC, Pondicherry to develop tools for decision-making for the control of filariasis using GIS. The RS image files have been calibrated to produce normalized differences vegetation index (NDVI). These composite NDVI values ranging between 145 and 158 were the areas found to be endemic for filariasis. However, there was no significant association between the NDVI and filariasis endemicity at the micro level. Using these variables, a geo-environmental filariasis risk model has been developed for predicting filariasis risk areas during the current year.

A GIS based model predicts the filarial endemicity based on seven geo-environmental factors viz. altitude, temperature, rainfall, relative humidity, soil type, saturation deficit and land use/land cover level-II categories. Since, these factors differentially persuade the endemicity, a standard protocol was used to give score to various environmental factors based on their influence over the transmission.

A filariasis risk map (Fig. 9) was created using a series of GIS techniques, and further it was stratified into four spatial entities, which are hypothesized as potentially high, moderate, low and no risk areas. The results showed 67% spatial agreements. Since the filarial endemicity is mainly due to man made features and geo-environmental factors are acting as confounders the level of agreement is good enough. Even though this GEFR model does not include manmade factors, the geo-environmental risk factors clearly give geographical boundaries to identify where the filarial transmission will not be taken or the areas free from filariasis.

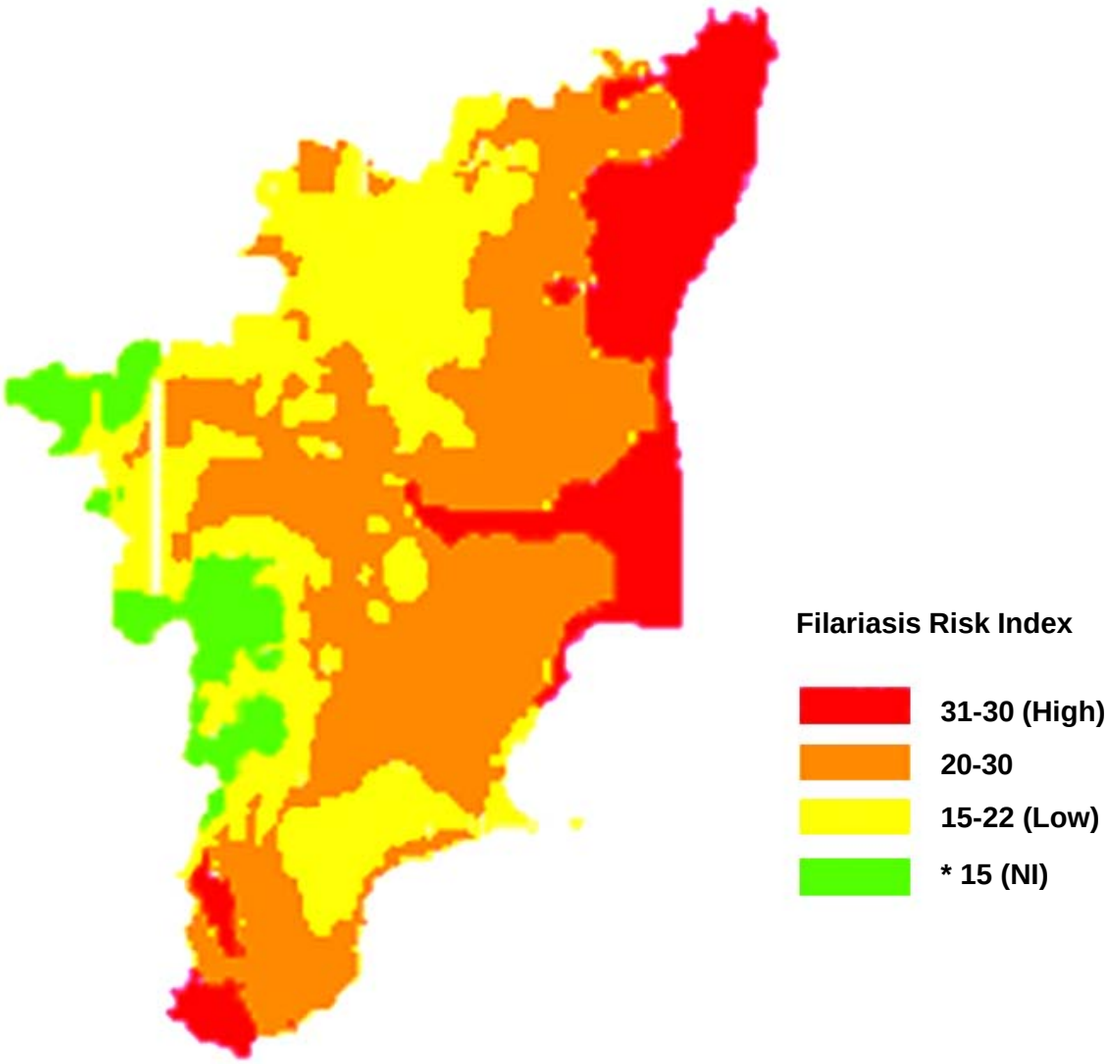


Fig. 9. Geo-environmental filariasis risk map (Tamil Nadu)

LEISHMANIASIS

Visceral leishmaniasis (VL), transmitted by the bite of a sand fly, is a deadly insect-borne disease and a major public health problem in the states of Bihar, West Bengal and Uttar Pradesh (with largest burden of the disease in the world). Currently there are indications that it is spreading in other states of the country. Research on various aspects of kala-azar (KA) is being conducted mainly through the Council's Rajendra Memorial Research Institute of Medical Sciences (RMRI) at Patna.

Epidemiological Studies

Hospital based Surveillance for Kala-azar

Hospital based surveillance was carried out at RMRI for monitoring the trend of the disease, creating a database on KA, developing early warning system for forecasting an epidemic, improving patient care and introducing better preventive measures. Out of a total of 427 clinically and parasitologically positive KA patients, 55% were in the age-group 5-15 yr and 40% in 20-50 yr age group in both sexes (66% males, 34% females). Eighty nine percent cases in <12 yr age group

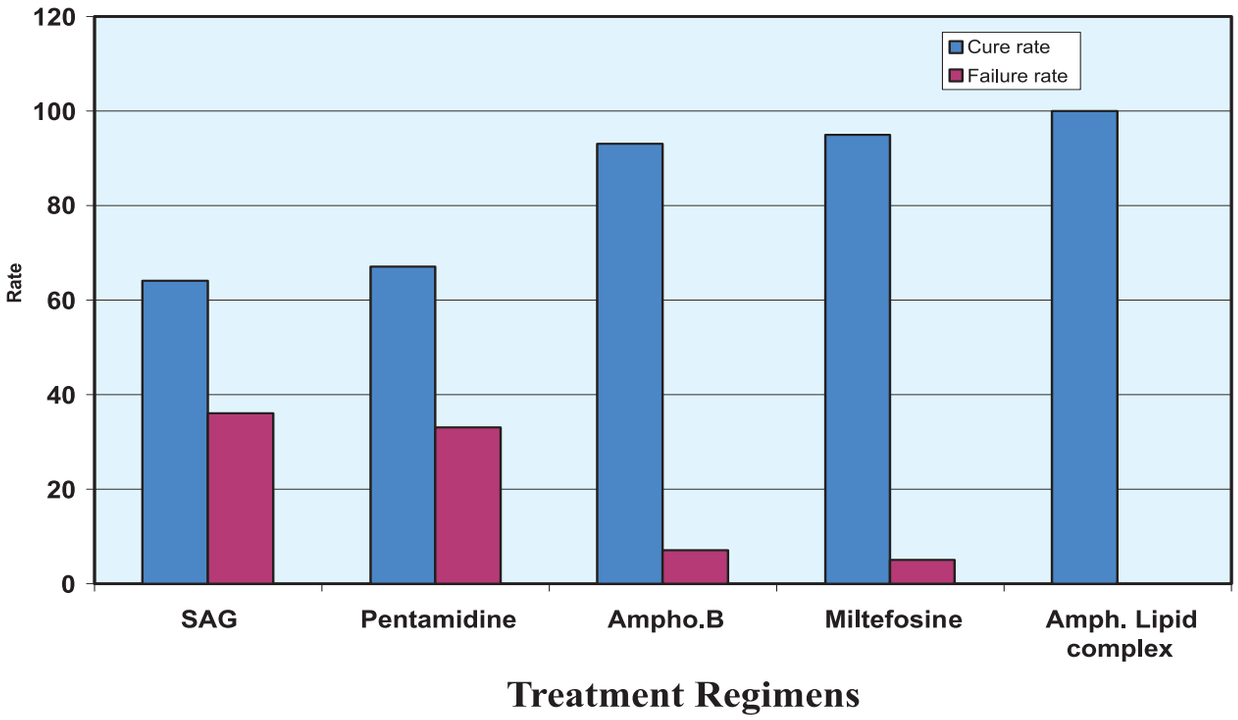


Fig. 1. Cure rate of different treatment regimens under hospital based surveillance of kala-azar

and 83% in >12 yr age-group had splenomegaly while 82% patients (<12) yr and 73% (>12 yr) had hepatomegaly. Ninety three percent of the cases treated with amphotericin B responded to it at the end of treatment. SAG unresponsiveness was observed in nearly 64% of the cases treated. The cure rate according to the treatment regimen is depicted in Fig.1.

Kala-azar and HIV Infection

Leishmaniasis has emerged as an opportunistic infection in HIV positive individuals. In an ongoing study at RMRI, Patna, it is expected to generate data in evolving timely intervention strategy to control *Leishmania*-HIV co-infection and to provide tools for assortment of specific intervention programme in this region. The prevalence of HIV infection among VL cases on the basis of the samples screened at RMRI during 1996-2003 has been found to be 13.8 per 1000.

Kala-azar in Family Contacts

In a follow up study on asymptomatic contacts of KA patients that were followed up for 3-9 months, VL could be predicted six months in advance, using rk 39 antigen. The results show that out of a total of 49 asymptomatic contacts from Muzaffarpur, 32 were confirmed KA cases. In the contacts subjected to clinical examination, 3 were antibody positive (for rk 39 ELISA) and became symptomatic in due course of time suggesting that rk39 ELISA could be used as a predictive marker for KA disease development and also as a screening tool for latent infection of *Leishmania*.

Clinical Studies

Clinical Trial with Miltefosine

In view of the increasing resistance/ unresponsiveness to antimony (and pentimidine being highly toxic), amphotericin B is expected to play a greater role. However, the cost of the drug is prohibitive. There is an urgent need to develop newer drugs, particularly for oral administration for kala-azar. With the results obtained so far, miltefosine appears to be highly promising with efficacy of more

than 95%. Recently, a WHO-sponsored phase IV, open-level, single armed clinical trial of this drug has been started in 13 clinical centres (including RMRI, Patna) spread over 6 endemic districts of kala-azar in Bihar, to test the efficacy, toxicity and feasibility in mild to moderately ill VL patients, without hospitalization. This would help to evaluate the patient compliance of miltefosine treatment in field conditions.

Out of a total 1153 KA confirmed patients enrolled in the trial, follow up at 4, 8 and 24 weeks was carried out in 1105, 984 and 116 cases respectively. Relapse was reported in 42 cases and serious adverse effects in 11 (Fig.2).

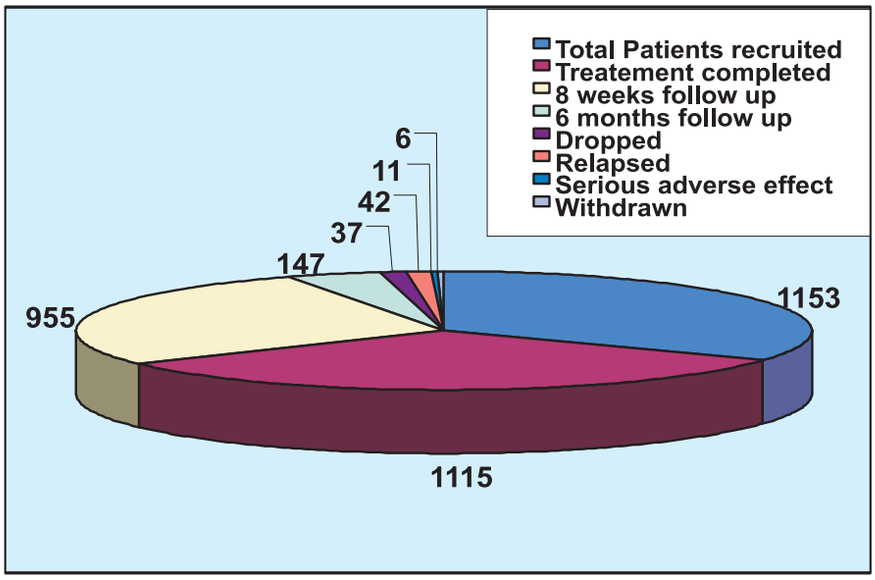


Fig. 2. Progress of miltefosine phase IV trial till Sept. 2003

Immunological Studies

Dendritic Cell based Therapy against Murine Leishmaniasis

Dendritic cells (DC), highly efficient at inducing primary T cell responses, are being investigated for their potential to prevent and /or treat many diseases. Studies to evaluate therapeutic efficacy of combined therapy (unfractionated soluble *L. donovani* antigen (SLDA)-pulsed dendritic cells + SAG) in murine VL induced by an antimony resistant strain (GE1F8R) showed that DC-based therapy is effective in reducing parasite burden when mice were infected with antimony resistant strain of *L. donovani* and that DC-based therapy synergises with antimony with respect to anti-leishmanial activity even in the case of antimony resistant strain. Antigen-specific T-cell proliferation was also observed in mice infected with this strain of *Leishmania* after receiving these therapies.

Development of DNA based Vaccine against Experimental Leishmainasis

Another study was undertaken to develop DNA vaccine against experimental visceral leishmaniasis in hamsters and mice. Analysis of expression of KMP-11 gene, a candidate surface membrane antigen, showed that the virulent *L. donovani* parasite, AG83, and *L. major* (as compared to the avirulent strains) elaborate significantly reduced expression of KMP11 by semi-quantitative RT PCR, taking the beta-tabulin gene as the house-keeping control gene. This result was further corroborated at the protein (RNA) level through confocal analysis using anti KMP-11 antibody. Through ligation independent cloning strategy, the KMP-11 was cloned in the mammalian expression vector and its sequence was checked by AMI prism sequence analyzer. Data analysis/ interpretation is underway.

Role of Free Radicals and Defensive Enzymes in the Pathogenesis of L. donovani Infection

The results of the study on role of free radicals and defensive enzymes in the pathogenesis of *L. donovani* infection highlighted that upon activation of death response by H_20_2, a dose and time dependent loss of mitochondrial membrane potential ($\Delta\Psi m$) occurs. Mitochondrial changes did not involve opening of the mitochondrial transition pore as cyclosporin A is unable to prevent $\Delta\Psi m$ loss. Antioxidant like N-accetylcysteine is able to inhibit the fall in $\Delta\Psi m$ and prevent apoptosis-like death. Together, these findings show the importance of non-selective cation channels in regulating the response of *L. donovani* promastigotes to oxidative stress that trigger downstream signaling cascades leading to apoptosis-like death.

Basic Studies

Antigen Characterization for Diagnosis of Visceral Leishmaniasis

A study is being continued at RMRI, Patna to characterize different polypeptides of *L. donovani* circulating in different areas of kala-azar prevalence and to develop a sensitive Western blot for diagnosis of the disease. SDS-PAGE pattern showed that 17kDa antigen was present in all isolates tested. It elicited a strong antibody response with sera of KA patients and a faint band with sera from PKDL patients. The study suggested the possible use of low molecular weight antigen for diagnosis of early and established cases of kala-azar. Further study is ongoing.

Leishmanicidal and Immunoprophylactic Activities of Plant Extracts

Another study to assess the efficacy of crude soluble antigen (CSA) preparations from different plant extracts showed that CSA of *Allium sativum* and *Curcuma longa* elaborated leishmanicidal effect with 64% and 65% leishmania inhibition after 24 hours, and that *Eclipta alba*, kidney bean-PHA, and *Fusarium* sp. exerted a greater leishmanicidal effect after 48 hours post initiation of cultures.

Entomological Studies

Identification and Characterization of Sibling Species of Phlebotomus argentipes

Morphological differences among *P. argentipes* have been reported from different geographical and ecological regions of India and abroad. However, to support the microscopic identification of vector by molecular means, a preliminary study has been carried out at RMRI, Patna, where one out of 20 samples of individual *P. argentipes* was found to be positive by PCR using the primer from NTS region of the rRNA gene with the reference strain of *L. donovani* (DD-8).

Identification / Characterisation of L. donovani Antigen of Infected P. argentipes

Attempts to identify and characterize *L. donovani* (promastigote) antigen in *P. argentipes* showed that of a total of 894 sandflies collected from different endemic areas, the SDS- PAGE protein profile showed several major proteins with molecular weight values ranging from 29.53 to 41.13kD.

Remote Sensing for predicting Kala-azar Epidemic

Studies on remote sensing being carried out at RMRI, Patna, to evaluate the feasibility of use of satellite data for

monitoring the macro-ecosystem, specific vegetation cover and human settlements and to relate them with the changing sandfly-genic conditions to evaluate its applicability as an epidemic predictor, ground survey map of almost all the selected villages under Patepur PHC of Vaishali district (as endemic foci) and Lohardagga Block of Lohardagga district (as non-endemic foci) has been completed. The collected land use data and flat colour composition (FCC), prepared by Indian Space Research Organisation's (ISRO) Regional Remote Sensing Service Centre (RRSSC), Khargapur, were compared to find out the correlation of geographical distribution of vector and disease distribution in periodic fashion. Detailed data analysis is being done.

Evaluation of Efficacy of DDT and Malathion

Under the multicentric study on evaluation of DDT and malathion for the control of kala-azar in selected villages of Bihar, first round spray was done in all the experimental villages except in village Bhorahan. Post spray evaluation of first round was carried out at different intervals after 4-5 months of the spray. From the data on vector prevalence and parity rate during post- spray evaluation, it was observed that densities ranged from 0.5 to 17.66 MHD, while the parity rates ranged from 11 to 34%. During the evaluation period, *P. argentipes* was prevalent in both the districts. Insecticide susceptibility tests in Vaishali district registered 18-53% mortality, while another endemic district of Bihar revealed variable susceptibility levels (56-100%) to DDT indicating presence of DDT resistance foci. Further evaluation and regular assessment of susceptibility of vector species to DDT is, however, required.

Other Studies

Socio-cultural and Demographic Studies

A study was taken up in Bihar with the aim to gather information on socio-cultural and demographic data on kala-azar. A cluster of 10 villages comprising 3493 households, covering 21312 population with sex ratio 877 females per 1000 males, having the history of kala-azar were selected for the study. The villages were interviewed for their awareness about kala-azar. The data revealed that majority (97%) of respondents were aware about the disease. Symptomatologically, 92% of respondents found fever as the most common factor, followed by chilled rigor (66.7%), splenomegaly (14.2%), hepatomegaly (13%) and blackening of skin (9%). Around one fourth (23.7%) had a false notion that kala-azar is a contagious disease while 19% had no idea about it. Kala-azar was, however, considered as a curable disease by 82.4% of the respondents. Regarding the causative factors, 65.6% respondents felt that mosquito bite is a major factor followed by polluted air (6.7%) and contaminated food/water (5.0%). However, the exact causative factor (sandfly) was indicated only by 5.8%, while 33.6% had no knowledge of vector involved. Regarding the facilities available at PHC for management and treatment of kala-azar, only 6.6% respondents gave a positive response, 22.5% said that some facilities are available while 52.4% think that PHC facilities are not sufficient to take care of the disease.

Risk Factors for Kala-azar in Endemic Areas of Bihar

In a pilot study taken up to investigate socio-economic variables as risk factors for KA, 25 factors were studied. Of these, seven factors were found to be significantly associated with disease, the most important being socially backward groups followed by educational status (illiteracy), type of house (thatched/

mud), marital status, presence of cattle shed and livestock and presence of granary.

Study of Grass root Level Functionaries of Kala-azar in Bihar

Kala-azar is a specific problem of Bihar and not much work has been done in respect to PHC's functionaries. A study was, therefore, initiated to examine and identify shortfalls, if any, in the existing pattern of functioning of health care services for kala-azar with regard to organizational and implementation aspects in Bihar.

Three known PHCs in highly epidemic districts have been selected and around 225 health workers have been interviewed so far. Out of the total health workers, 81% were females and 19 % males, with different rural backgrounds. The educational status revealed that 60 % had studied upto matric, 30% upto I.Sc., and 10% were graduates. Regarding disease symptoms, 99% complained of fever associated with cold of long duration, weakness (63%) loss of appetite (63%), enlargement of spleen (45%) and blackening of skin (7%). The major activities of PHC workers as reported by them were DDT spray (90%), case identification (82%), report for treatment at PHC (62%), investigation (52%) and awareness activities (66%). Lack of diagnostic facilities (99%), non-availability of medicines (99%) and lack of co-operation by PHC staff (51%) were the major problems encountered by the workers. More fieldwork for data collection is ongoing.

VIRAL DISEASES

JAPANESE ENCEPHALITIS

Epidemiological Studies

Studies in Karnataka, Andhra Pradesh and Tamil Nadu

During 2002-03, 116 specimens of suspected encephalitis (JE) cases were received from different districts of Karnataka (96 cases), Andhra Pradesh (18 cases) and Tamil Nadu (1 case). Diagnosis of JE was confirmed in 30 cases, West Nile (WN) virus in one and 85 were negative by MAC-ELISA. Maximum JE cases occurred in November (10) followed by October (9) and minimum cases occurred in May - June 2002. About 81% JE positive cases were children below 10 yr, 16% were children between 11-15 yr. and 3% were adults. There were 63 males with 20 positives and 53 females with 11 positives (1-WN positive).

Surveillance for JE in South India

JE virus infections in humans and animals and in vector population in JE prone areas are being studied longitudinally by the CRME, Madurai in order to select suitable parameters useful in prediction of JE outbreak.

In general, vector infection was high in Cuddalore district (endemic) compared to Thanjavur district (non-endemic). During previous 4 years, the overall mosquito infectivity rate (MIR) in Cuddalore district was fluctuating between 1.250 and 2.857 and has declined to 0.135 (12 times lesser) during the peak transmission period of this year (September-November 2002). In Thanjavur district, the vector infection was recorded "nil" during the corresponding period. The decline in the JE virus activity at greater level in Thanjavur district and to a minimum level in Cuddalore district is an indication of very low / or nil activity of JE virus in these districts. During the reporting year, due to acute shortage of water, rice fields were frequently dried up which resulted in the decline of mosquito breeding in rice-land agro-ecosystem.

Seroprevalence of flaviviruses was observed in all the survey periods in humans. The positivity ranged between 22% - 66 %. High seroprevalence was noticed in

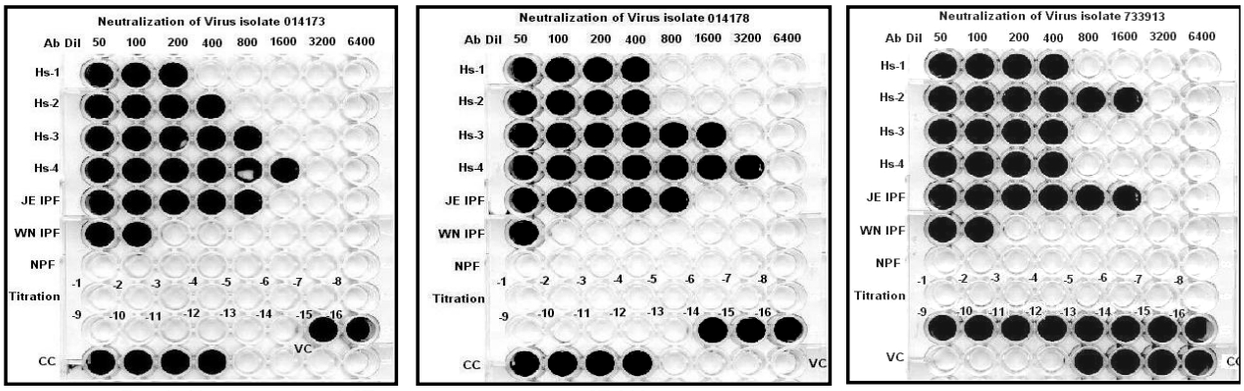


Fig. 1. Neutralization of JE virus isolates by anti JE MAbs and polyclonal sera

September when the MIR was also high (10.4) in the study villages.

Under JE surveillance network encompassing all the 8 endemic districts of Tamil Nadu, 327 pools of JE vectors obtained from the Zonal Entomological Teams of Tamil Nadu state were screened. One pool from Tirunelveli district was found to be positive for JE virus in the month of November 2002, and the concerned public health personnel were informed accordingly for follow up action.

Characterization of JE Virus Isolates from Uttar Pradesh

Two isolates of JE virus (014173 & 014178) from Lakhimpur(U.P.) were characterized using Mabs against JE virus and compared with 1973 Bankura (WB) isolate(733913). Differences in the virus titres were obtained in porcine (PS) cells and infant and adult mice indicating that the virus strains isolated are drastically different from the existing virus isolates. It was also observed that the virus titres obtained with new isolates were extremely high, the virus was found to be nonpathogenic by ip route in adult mice (even when inoculated with 9.0 $Log10LD_{50}$ in infant mice), and the pathogenic potential of Lakhimpur JE virus was very low although the virus titres of the new isolates were very high in PS cells and infant mice.

Both isolates were subjected to virus neutralization test using polyclonal and monoclonal anti JE virus antibodies. These isolates as well as Bankura strain could be neutralized by these antibodies (Fig.1).

Endophilism in Cx. tritaeniorhynchus

An unusually high occurrence of *Cx.tritaeniorhynchus* in indoors during day time was noticed in Bellary district. Of the 44264 mosquitoes belonging to four genera and 16 species collected in 327 man-hours from indoor resting places of human and domestic animal habitations, *Cx.tritaeniorhynchus* constituted 81.5% of the collection. Per man hour collection of *Cx. tritaeniorhynchus* in indoor situation was 446.1 in October compared to 76.6 in outdoor habitats in the same month. Increased endophilic resting behaviour may indicate that indoor residual insecticides may provide an effective control method for JE in this area.

Forecasting of JE Epidemic

The need for tools to forecast JE epidemics is evident as they occur suddenly and terminate within a few months in JE epidemic regions and hence sufficient lead-time is not available for adequate response. A project has been initiated to predict the outbreak of the disease in Andhra Pradesh by application of heuristic engine which is a

novel forecasting software tool. Of the 69 PHCs of Kurnool district, six areas (5 villages and 1 urban area) with highest number of JE case occurrence since 1996 were selected. Vector surveillance, dusk and light trap collections were carried out in the index areas. Preliminary survey indicated that *Cx. gelidus, Cx. tritaeniorhynchus, Cx. quinquefasciatus* and *An. subpictus* are the common mosquito species found in these areas. *Cx. gelidus*, an important vector of JE, was found in high numbers in the urban area. JE virus infection was found positive in *Cx. tritaeniorhynchus* and *Cx. gelidus*. (*Cx. tritaeniorhynchus* from Kurnool urban area and two villages). One pool of *Cx. gelidus* collected in Kurnool urban in February 2003 was found positive. This indicates that the active transmission of JE virus is going on in the study area. Serological and meteorological parameters and information on agriculture pattern, animal and human census and other physical parameters is being collected regularly from the study areas.

Immunological Studies

Development of ELISA for Detection of JE Virus Antigen

Antigen capture ELISA was standardized using JE virus specific MAbs Hs-2 and Hs-3 for capturing JE virus. Captured JE virus was probed with biotinylated flavivirus cross-reactive MAb Hx-2. The sensitivity of the ELISA was such that in 50 non-infected mosquitoes one infected mosquito could be detected. Using antigen capture ELISA, mosquito pools from suspected JE virus epidemic in Bhandara were tested. Samples giving the P/N ratio ≥ 2 were considered positive. Out of 54 mosquito pools, 19 were found to contain JE virus antigen. This was confirmed by inoculating suspensions in mice. Sickness leading to detection of JE virus antigen could be observed in 14 pools.

Identification of Individual Proteins of JE Virus

A project to identify the individual proteins of JE virus that are immunodominant in a naturally exposed human cohort showed the presence of serum antibodies as well as T cells recognizing the viral proteins in exposed volunteers. Proteins which serve as targets for human immune responses will also be identefied.

Five JEV genes proposed to be studied for their ability to elicit human immune response have been cloned from viral RNA and inserted into expression vectors. The NS1 and NS5 proteins were obtained in pure form while the capsid, membrane and NS2b proteins did not given expression in *E.coli* vectors. The B and T cell immune response to the NS1, NS5 and envelop proteins of JEV have been studied in 9 convalescent JE patients and 8 healthy exposed control individuals. The envelop protein alone was found to stimulate strong antibody responses. The T lymphoproliferative response to the NS1 and envelop proteins was stronger than that to NS5 while all three proteins stimulated comparable levels of interferon production from responding T cells. FACS analysis showed that the NS1 protein elicited IFN from both CD+ as well as CD 8+ T cells.

DENGUE

Community based Dengue Vector Control

A community based dengue vector control study supported by WHO/TDR was initiated by CRME, Madurai in Chennai city. Very poor awareness on dengue was recorded among people. Only 6.7% of them were found having knowledge about cause of this fever in this 90% literate community. Cement cisterns/tanks were found potential breeding sources of *Ae. aegypti* with high pupal

production rate. Larval density of vector was found to be a good indicator for the occurrence of dengue cases. Dengue epidemic (736 cases) was recorded in Chennai city with high larval density when average maximum Breteau index (BI) was >60 in the year 2001 whereas only 127 cases were reported when BI value remained below 25 in the year 2002. Dengue virus serotypes, DEN1 & DEN4 were isolated from the ELISA positive *Ae. aegypti* pools by Toxo-IFA system.

Studies in South India

During the year, a total of 1285 specimens (Karnataka-1232, Andhra Pradesh-22, Tamil Nadu-16 and others-15) were received from suspected dengue cases. This comprised 964 dengue fever cases, 133 DHF/DSS cases and in 188 the aetiology was not confirmed. Diagnosis of dengue was made by MAC-ELISA in 434 cases and of flavivirus in 16 cases by haemagglutination inhibition (HI) test. Maximum dengue positive cases were in Bangalore urban district (232) followed by Kolar (48). Positive cases were seen in all months with peak activity from June to November. Cases and positives were seen in all age groups in both sexes - 54% were adults. Of the 133 DHF/DSS cases - 113 were found positive for dengue.

Transovarial Transmission of Dengue Virus in Ae.aegypti Mosquitoes

Ae. aegypti larvae collected from Pune city and some areas of Saurashtra and Kachchh district, Gujarat were processed for detection of transovarian transmission by antigen capture ELISA using HX-2 and fluorescent antibody test. A number of larvae were found positive for flavivirus antigen suggesting natural occurrence of this phenomenon.

Detection of DEN by RT-PCR

The multiplex-RT-PCR was used successfully for identifying the serotypes of dengue in mosquitoes and clinical samples collected during an outbreak in Pune. Of the 21 samples, 15 were identified as DEN2 and one as DEN3. One isolate was sequenced partially and confirmed as DEN2. An additional isolate from mosquitoes was partially sequenced and confirmed to be DEN 3.

CHIKUNGUNYA

Genotyping of Chikungunya Virus Isolated in India

During the past four decades, several strains of Chikungunya virus have been isolated from India. A study was conducted at NIV to determine genotypes of these strains. 257bp sequence of E1 gene showed that there were three clades. All the Indian strains belonged to the Asian genotypes while the strain from Vishakhapatnam (AY253740) isolated in 1965 showed ~ 100% homology with Central African strains. However, based on these sequences another strain from Vishakhapatnam (AY253739), which was also isolated from same area in the year 1965 showed more homology with other Asian isolates from Thailand. The data reveal that during the span of last 37 years several strains were introduced in this country and many of them were re-circulating in different geographical areas (Fig. 2).

Role of Ascogregarina culicis in the Maintenance of Chikungunya Virus in Mosquitoes

Studies were carried out with a view to determine the possible role of gregarine parasites A.culicis in the vertical transmission of dengue and Chikungunya viruses from larval to adult stage and in the maintenance of viruses in the oocysts of mosquitous in nature. Experiments showed that CHIK virus survives inside the oocysts of parasites indicating that As. culicis may have an important role in the maintenance of CHIK virus during the inter-epidemic period.

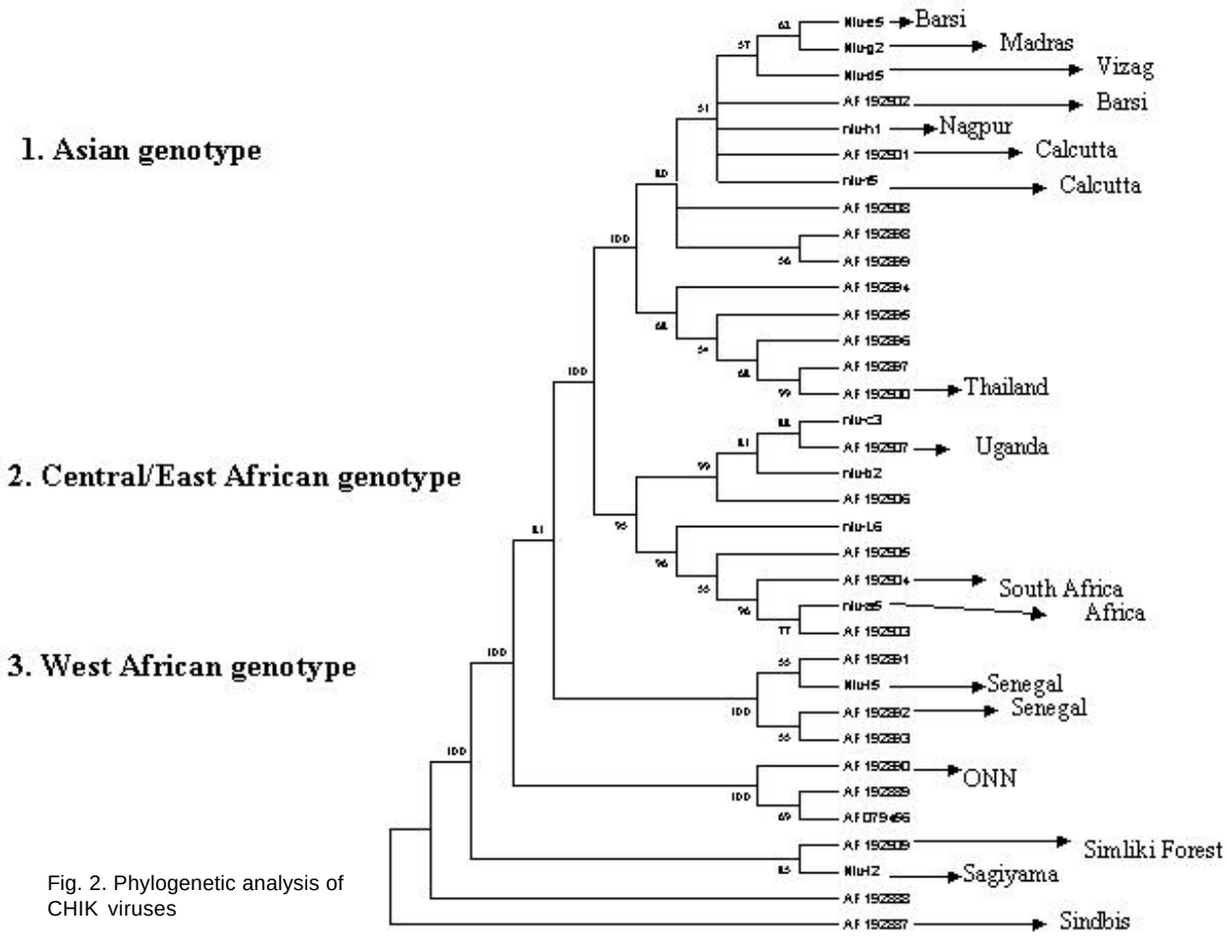


Fig. 2. Phylogenetic analysis of CHIK viruses

HEPATITIS

Hepatitis A

Phylogenetic analysis of genotypes of HAV based on the partial sequences of RNA polymerase and VP1/2A regions of HAV genome from clinical specimen demonstrated co-circulation of genotypes IB and III A among hepatitis A patients from Pune. Two PCR positive specimens characterized as genotypes IB and III A respectively were inoculated in tissue culture system to initiate the propagation of virus strains. Detection of anti-HAV positivity in only one out of 84 rat sera tested showed infrequent exposure of this species to HAV. Efforts made for improvement of diagnostic tests developed earlier for hepatitis A resulted in reducing the number of steps of the assay from 4 to 3 and total assay time from 5 hrs to 45 min.

Hepatitis B

At NIV 29 hepatitis B vaccine recipients were followed up for 13 years post vaccination. Of these, 19 tested anti-HBs positive and 10 tested negative. Of the ten negatives, 8 received a booster dose of vaccine and 4 seroconverted to anti-HBs. The non-seroconverters were either non or poor responders after primary vaccination. Of the additional 10 vaccinees 5-10 years post vaccination, 8 were anti-HBs positive. Twenty-five of these 39 vaccinated individuals were further studied for cellular response; 12 of the 14 anti-HBs positive and 3 of the 11 anti-HBs negative vaccinees showed T-cell response against recombinant HBsAg. All anti-HBs positive vaccinated individuals had significant levels of Th1 cytokines when compared with controls. The cellular response to HBsAg could be elicited after boosting the

anti HBs negatives and the Th1 cytokine profiles became comparable with the anti-HBs positives. The anamnestic response among anti-HBs negatives confirms the presence of B and T memory cells.

Hepatitis C

In order to investigate the significance of variability, the hyper-variable region (HVR1) of HCV genome in relation to clinical manifestations and response to interferon therapy, was investigated in asymptomatic carriers, chronic hepatitis C patients and patients undergoing antiviral therapy. Genotypes 3 and 1 were predominant among 8 asymptomatic carriers and 27 chronic hepatitis C patients tested so far. HVR1 region was amplified for 30 HCV isolates. Of these, for 8 PCR products 10-20 clones were sequenced for quasispecies analysis. The presence of one master species and 2-6 minor species was observed.

In order to characterize the mechanisms responsible for viral persistence in HCV infection, the proliferation of peripheral blood mononuclear cells (PBMCs) in response to recombinant core antigen and the cytokine production profile *i.e.* both Th1 and Th2 types were investigated in different categories. The results indicate that CD4+ T cell activation is stronger in patients with more severe liver disease as compared to the controls. HCV carriers with persistently normal and abnormal alanine transferase levels behave differently in their CD4+ Th cell responses.

Another study examining intrafamilial spread of HCV was conduced at NIV. Of the 127 ELISA positive blood donors investigated, only 13 were confirmed as true positives. 14 family contacts were examined of which one (brother of donor) was found positive for anti HCV and HCV RNA.

Hepatitis E

At NIV, attempts to develop hepatitis E vaccine were continued. For the development of DNA vaccine, HEV ORF2 gene was cloned into mammalian expression vector pcDNA 3.1. Though the HEV structural protein (ORF2) expressed in baculovirus system was found to react in ELISA with serum samples from epidemic (1976-2003) as well as sporadic (1978-2003) cases of hepatitis E, this membrane bound protein was unstable and therefore truncated form of this protein (with N-terminal 111 amino acid deletion) was expressed as a soluble protein. Swine HEV ORF2 protein was expressed in baculovirus expression system. This protein reacted well with both swine (genotype-IV) and human (genotype-I) sera. Truncated form of this protein (N-terminal 111 amino acid deletion) is also expressed to facilitate the purification. During the year, 22 outbreaks of hepatitis were investigated from different parts of Maharashtra of which 21 were attributed to hepatitis E and one to both hepatitis A and E viruses.

RESPIRATORY INFECTIONS

Influenza

During continuous surveillance on influenza in Pune in year 2002, specimens of throat/nasal swabs and nasopharyngeal aspirates were collected from 428 cases of influenza and other respiratory tract infections. There was an increase in the number of influenza cases in February and during rainy season from July to September, 2002. Respiratory specimens(250) were processed in MDCK cell culture. Out of the 17 virus isolates obtained, 5 were type A (H3N2), 8 type B and 4 could not be identified due to low haemagglutination antibody (HA) titre. All these 17 virus isolates were typed by ELISA; 9 were type A and 8 type B. The results of evaluation tests for respiratory syncytial virus (RSV), flu A, flu B and parainfluenza 3 antigens demonstrated that indigenous immunofluorescence (IF) and ELISA employing RSV MAbs developed at

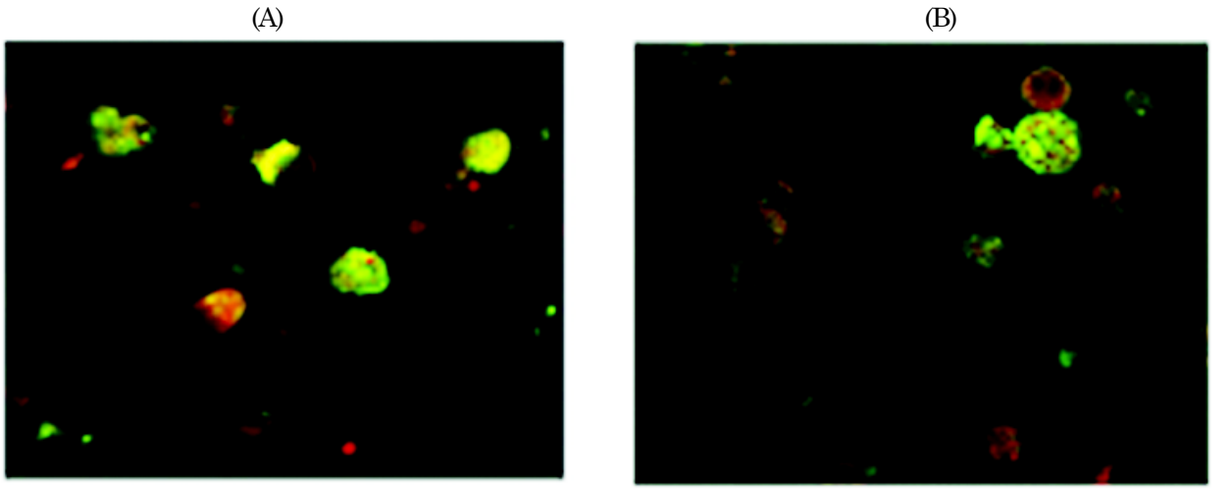


Fig. 3. Cells from nasopharyngeal isolate in IF test probed with anti RSV MAbs from (A) Chemicon kit (B) NIV showing bright punctate green fluorescence.

NIV are comparable with the Chemicon kit and hence will be very useful for RSV diagnosis. Immunofluorescence studies of nasopharyngeal specimens positive for RSV showed fluorescence in cytoplasm and small inclusions (Fig. 3).

MEASLES

Measles Outbreak in Chennai region

Outbreak of fever with rashes suspected to be measles was reported from Sri Kaligapuram village in Vanganoor PHC of Thiruvellore district of Tamil Nadu from December, 2001 to February 2002. A total of 59 cases with predominant involvement of preschool children below five yr (74%) was observed. Definite contact history could be elicited from 81% cases. It was found that 44% cases had documented measles vaccination. The case fatality was 1.7%. Virus isolation was attempted on throat swabs of serologically confirmed measles cases. One isolate was obtained using B95a cell culture.

OTHER STUDIES

Investigation of Saharanpur Outbreak of Encephalopathy

An outbreak of encephalopathy was reported from Saharanpur district of Uttar Pradesh during October to January 2003. Common clinical symptoms included mild to moderate grade fever for short duration, vomiting, irritability, altered sensorium followed by coma and death within 24 hours after hospitalization. Abnormal movements, inability to suckle and teeth grinding were observed in a few patients. Marked irritability was also observed which remained even after heavy sedation in few patients, however, no neck rigidity was observed. The age range was 1-10 yr with no significant difference in male to female ratio. On admission, general condition of majority of the patients was poor. Patients appeared malnourished and were from poor socio-economic background with poor hygiene.

Fifty-nine specimens [cerebrospinal fluid (CSF), serum, throat swab, urine] were collected from patients. Serological tests for JE, dengue, West Nile and measles viruses were found to be negative. Virus isolation and identification experiments are in progress.

Investigation of Aetiology of Neurological Illnesses in Vellore

A study aimed to investigate the enteroviral aetiology of acute and chronic neurological illnesses, to identify the prevalent enteroviral serotypes involved and to obtain information

on enteroviruses with increased neurovirulence has been completed. A total of 46 children and 41 adults (with acute neurological illness) and 50 adults with chronic neurological illnesses were enrolled in the study. Enteroviral etiology was evident by two-step RT-PCR in 45% of the children with clinical diagnosis of aseptic meningitis. Enteroviruses isolated from cases of aseptic meningitis were CA9, E2, E4, E 6, E 9, E 14, E 17 types. Echoviruses were isolated from 2 cases of enteroviral "sepsis" like illness in newborn infants. PCR-RFLP was not useful for typing of enteroviruses, but restriction enzyme (RE) digestion pattern may be useful in studying epidemics. Twenty-seven of the 28 enterovirus isolates could be assigned a serotype by partial sequencing of VPI in contrast to 26 by Lim Benyest-Melnick (LBM) pool obtained from WHO. This is the first report of testing strains from a given geographical area. The results revealed that non-polio enteroviruses play an important role in the etiology of acute neurological illnesses, RT-PCR is superior to conventional virus isolation from CSF by culture, VPI partial sequencing could replace LBM pool based neutralization test for identification of enteroviruses and molecular detection does not reveal enterovirus etiology in majority of cases of chronic neurological illnesses. Serological testing was found to be inadequate for this purpose in the region.

POLIOMYELITIS

The Council's Enterovirus Research Centre (ERC) at Mumbai has devoted its major resources to the National Polio Eradication Program. The Polio Network has laboratories at three levels of expertise *viz.*, Global Specialized Laboratories, Regional Reference Laboratories and the National Polio Laboratories. In India, the nine laboratories located in different parts of the country support the National Polio Eradication Program. The ERC has been designated as a fully accredited WHO Global Specialized Polio Laboratory (Fig. 4a).

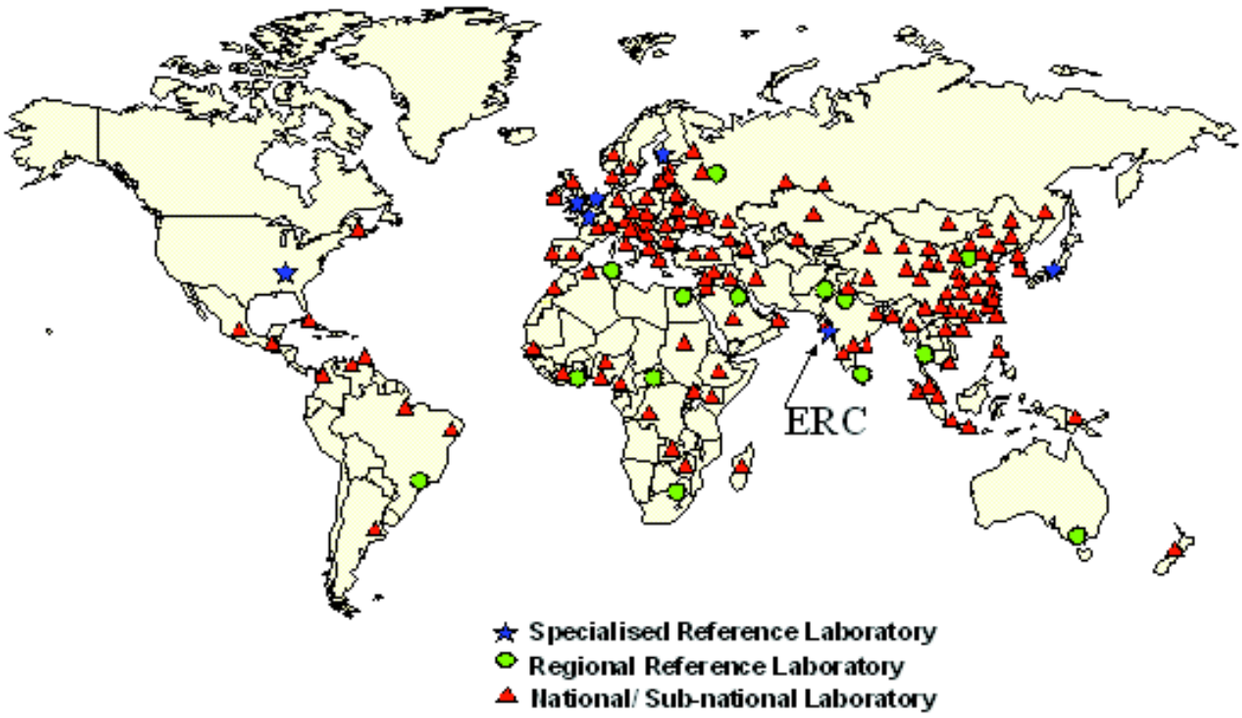


Fig. 4a. Global Laboratory Network for Polio Eradication, 2002

Fig. 4b. Geographical area covered by ERC for virological diagnosis of AFP cases

Surveillance for Acute Flaccid Paralysis (AFP)

AFP surveillance in India reached certification standards in 1999. Since then the programme has been using virological case classification of AFP cases. During the year, faecal samples (6351) were collected from 3214 cases of AFP from various states (Fig. 4b) and 2186 cases of AFP from all the Indian Network Laboratories.

A total of 1453 cases of paralytic poliomyelitis due to wild poliovirus type 1 and 112 cases due to wild poliovirus type 3 were reported. In the year 2002 highest number of cases were recorded in UP (1224 cases) followed by Bihar (119 cases).

Fig. 5 shows that incidence of polio started rising in the month of May 2002 and an epidemic situation was predicted in June 2002. The epidemic started in U. P. and rapidly spread to all adjacent states, especially to Bihar. The low-polio season was reduced to only 3 months as against 5-6 months in previous years.

Molecular Epidemiology of Wild Polioviruses

It was found that all the 3 lineages identified in 2001 continued to circulate in UP in 2002. Lineage B spread to wider geographic areas in UP during 2002. Sequence analysis provided evidence of transmission of wild poliovirus type 1 from UP to other states. Molecular data showed that the virus of lineage A was introduced from western UP into Gujarat and established transmission in the area. From Bhavnagar the virus transmission could be traced to other districts

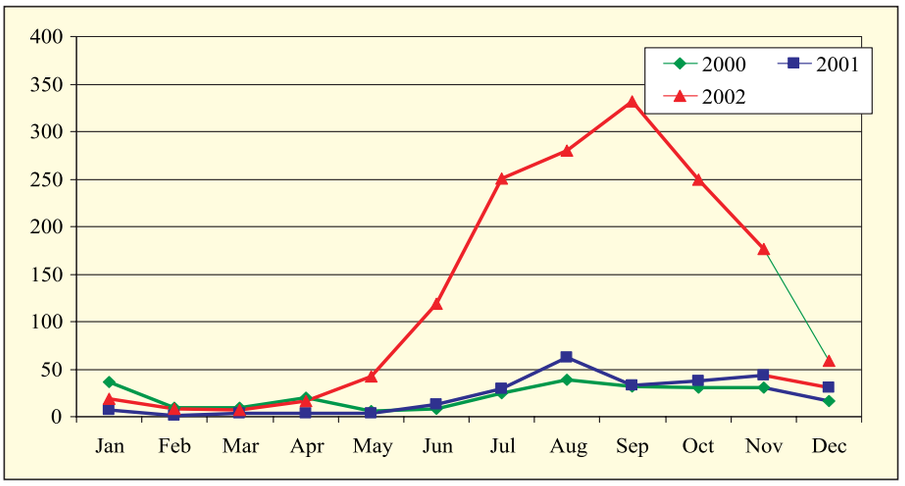


Fig. 5. Distribution of virologically confirmed cases of paralytic poliomyelitis by month

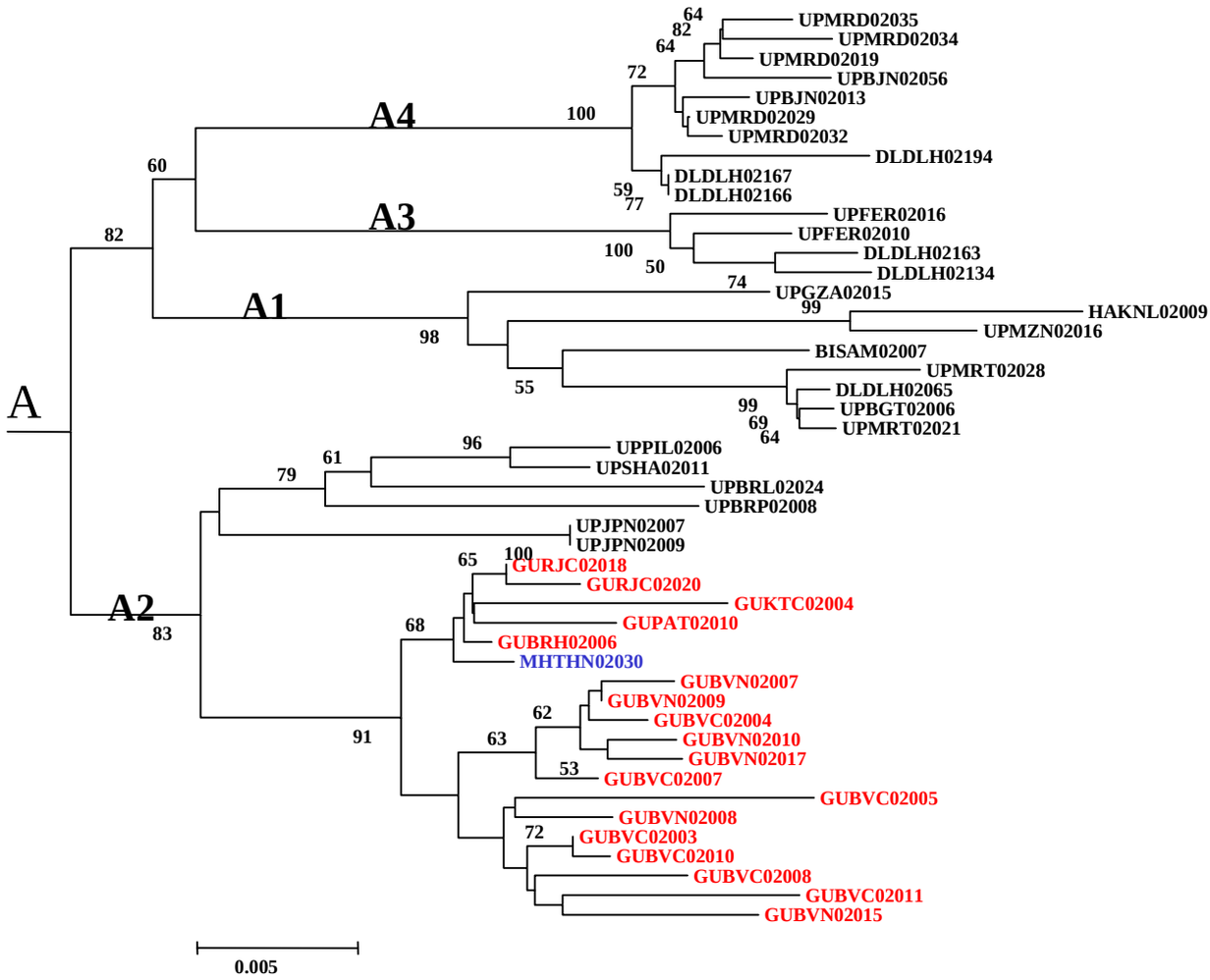


Fig. 6. Wild poliovirus type 1 transmission in Gujarat

(Fig. 6). Polio 1 was introduced from Bihar into Murshidabad district in West Bengal. After establishing transmission in the district the virus was found to have travelled to Jharkhand and then into Orissa. Polio 1 from more than one lineage and multiple transmission chains was introduced in Maharashtra. There was no evidence of virus establishing indigenous transmission in this state.

Poliovirus type 3 remained confined to western UP (Fig. 7). However, re-emergence of one lineage around Gonda district was documented. The results showed a period of more than 14 months of undetected transmission of polio 3 in this area. Three other lineages continued to circulate despite the several mopping-up rounds carried out in western UP in 2001.

Environmental Surveillance for Wild Polioviruses in Mumbai

A total of 153 sewage samples were collected from F, G and M wards of Mumbai for poliovirus isolation. Wild viruses were isolated from sewage from all the three wards. Sequence information revealed multiple introductions of wild poliovirus from UP into Mumbai. Wild poliovirus type 1 was detected in sewage in Mumbai throughout the year. Wild poliovirus type 3 was isolated from 2 samples (one each from G and M ward). The isolation from Mumbai sewage of wild re-emerging poliovirus type 3 lineage within

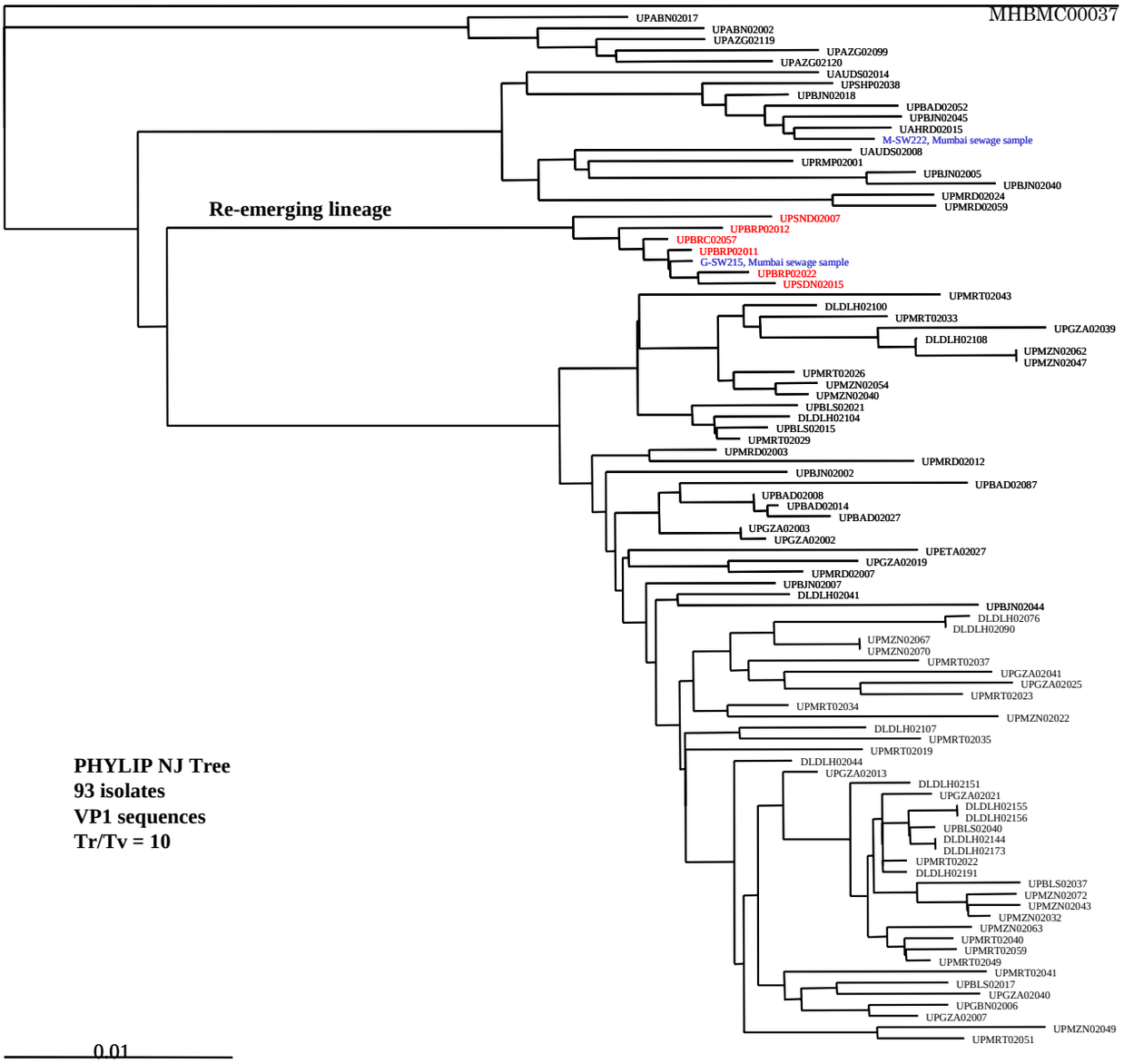


Fig 7. Wild poliovirus type 3 lineages in Western UP

weeks of its detection in U.P was noted. The second wild type 3 isolate from Mumbai sewage belonged to a lineage circulating in Bareilly district in UP. It was observed that environmental surveillance was highly sensitive in monitoring presence of wild poliovirus in the community.

During the year, a total of 714 stool specimens from 352 AFP cases were processed for virus isolation at NIV. Of these 325 cases were from Karnataka, 12 from Tamil Nadu, 8 from Andhra Pradesh, 4 from Kerala, 2 from Maharashtra and one from Goa. No wild poliovirus was isolated from any of the 680 samples from 335 AFP cases for which results are complete. During the same period 21 stool specimens from healthy contacts (children below 5 yr.) from Karnataka (Gulbarga, Kolar, Davangere and Raichur) were tested and no wild poliovirus was isolated. Last wild poliovirus case was found in December 2000 from Raichur district. In addition 84 stool specimens from healthy contacts (children below 5 year) were tested in Moradabad district in U.P. and no wild poliovirus was isolated.

HUMAN IMMUNODEFICIENCY VIRUS (HIV)/ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

The number of HIV infected persons in India in the year 2002 has been estimated to be over 4.5 millions, over half a million more than last year. There is need for renewed efforts for preventing new infections and for providing care and support to those already infected. This has been reflected in the research agenda of ICMR for HIV/AIDS. ICMR's National AIDS Research Institue (NARI) and NIV at Pune, NICED, Kolkata and TRC, Chennai have been carrying out research on various aspects of HIV/AIDS. One of the most significant achievements has been development of modified vaccinia Ankara based HIV vaccine. The high costs of anti-retroviral drugs and assays for monitoring the anti-retroviral treatment (ART) have always been the main obstacle for universal application of ART. Although the cost of ART drugs has declined markedly in the last one year, there is no alternative to assays used in monitoring the viral load and CD4 phenotyping. An effort is being made to study the correlation between CD4 counts and absolute leukocyte count and total leukocyte count so as to devise a cost effective assay for use in monitoring. The extra burden of new tuberculosis cases (15% annually) attributable to HIV is staggering. Sentinal surveillance for HIV-TB is being carried out by screening sera for anti-HIV antibodies in TB and chest disease patients since 1995. A significant increase in HIV-TB coinfections has been witnessed in the last seven years. The overall dysfunction of secretion of both Th1 and Th2 type of cytokines was observed in HIV-TB co-infected individuals. Immunological studies on the expression of HLA A, B and C alleles in HIV infected persons have revealed association of Cw allele with HIV infection for the first time in Indian patients. Epidemiologic study to find out the frequency of mutations in CCR5 genes and other co-receptors which have been identified for HIV disease progression in long term nonprogressors has also been undertaken.

Epidemiological Studies

Seroprevalence of HIV Infection in Population

A total of 14486 blood samples obtained from patients who attended any of the nine clinics of the NARI, Pune were tested for HIV antibodies. A very high rate of reactivity for HIV antibodies was seen in all samples from patients belonging to different risk groups. (Fig.1). The observation that is of prime concern here is the high rate of seropositivity among patients receiving blood and blood products.

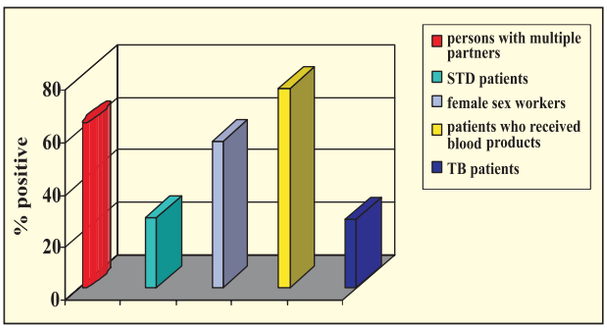


Fig. 1. HIV seropositivity in various risk groups of patients

Sexual Risk Behaviour of Young Men Attending Sexually Transmitted Disease Clinics

Sexual risk behaviour was studied among STD patients reporting to NARI clinics. As a part of a prospective study of HIV infection, 1872 men were evaluated and screened for HIV. It was found that nearly 70% of them were living with families and were educated up to primary level. Baseline HIV seroprevalance in this population was 22%. Bisexuality was significantly more common among those who had initiated sex at age below 18 years. Younger men also reported higher frequency of premarital sex. The choice of the first partner was sex workers for both men in older as well as younger age group.

Prevalence of Sexually Transmitted Infections in Rural and Urban Communities

A study has been initiated at Safdarjung Hospital, New Delhi to determine the prevalence of sexually transmitted infections in rural and urban communities in Delhi. During one year period approximately 500 specimens were collected from four designated zones of Delhi. The specimens were collected from symptomatic, asymptomatic and pregnant women and controls. The laboratory results showed that candidiasis was most prominent followed by bacterial vaginosis, chlamydial infection, trichomoniasis, HSV-2, syphilis and gonorrhoea in different groups. The study highlights the importance of carrying out laboratory based community surveillance for STI/RTI for control of HIV infection especially in inapparent cases which are not targetted under syndromic approach.

Burden of Disease (BOD) Estimation for HIV/AIDS for Pune

A study has been initiated on preliminary estimation of the disease burden for HIV/AIDS in Pune. Baseline work completed so far includes review of existing literature and collection of data on prevalence and incidence from studies conducted in different at risk groups. The available data were reviewed for usefulness in BOD estimation and collated. Attempts to establish networking with private hospitals are ongoing in order to estimate burden outside of government set up.

Clinical Studies

Mother to Child Transmission

The reference laboratory at NARI is a partner of National AIDS Control Organisation's (NACO) national feasibility study on azidothymidine (AZT) treatment for reduction of mother to child transmission of HIV infection. HIV-1 seropositive pregnant women enrolled under the study were given AZT from 36th week of gestation. The blood samples were collected for DNA PCR at 48 hr, 2 months and 6 months from the babies. Out of a total 1102 blood samples, approximately 1.2% were positive on the 2nd day and of the 373 and 20 samples received during the 2nd and 6th month, approximately 7% and 20% tested positive.

Another study on mother-to-child transmission of HIV-1 was initiated by NARI, Pune in collaboration with Kamla Nehru Hospital, Sonawane Hospital and Dalvi Maternity Hospital of Pune Municipal Corporation. HIV infected pregnant women were offered the Bangkok regimen of zidovudine to reduce mother-to-child transmission of HIV-1 infection. About 100 women delivered after receiving zidovudine during antenatal and intrapartum period. The transmission rate as deciphered from PCR at day 2 and 2 months was found to be 1.5% and 3.0% respectively. Cytokine (IL-2, IFN-γ, IL-4, IL-6, TNF-α) levels were estimated in the culture supernatants of placentae of HIV seropositive women and healthy controls. No placental cultures showed detectable levels of IL-2 and IL-4 while IFN-γ levels were same in HIV infected and healthy women. The IL-6 levels in HIV seropositives were higher than in healthy women and TNF $-\alpha$ levels were in detectable amount. A subset of HIV infected pregnant women was subjected to chemokine receptor studies. No woman was found to have delta 32 CCR5 mutation. Of the women showing SDF-1 mutation, 11 showed homozygous and 7 heterozygous mutation and two had wild type alleles; one woman had CCR2b mutation in heterozygous form.

HIV Surveillance in TB patients

Sentinel surveillance was carried out by screening sera for anti HIV antibodies in 400 new patients attending tuberculosis and chest diseases OPD at Sassoon General Hospital, Pune. This activity has been ongoing since 1995. Sentinel surveillance

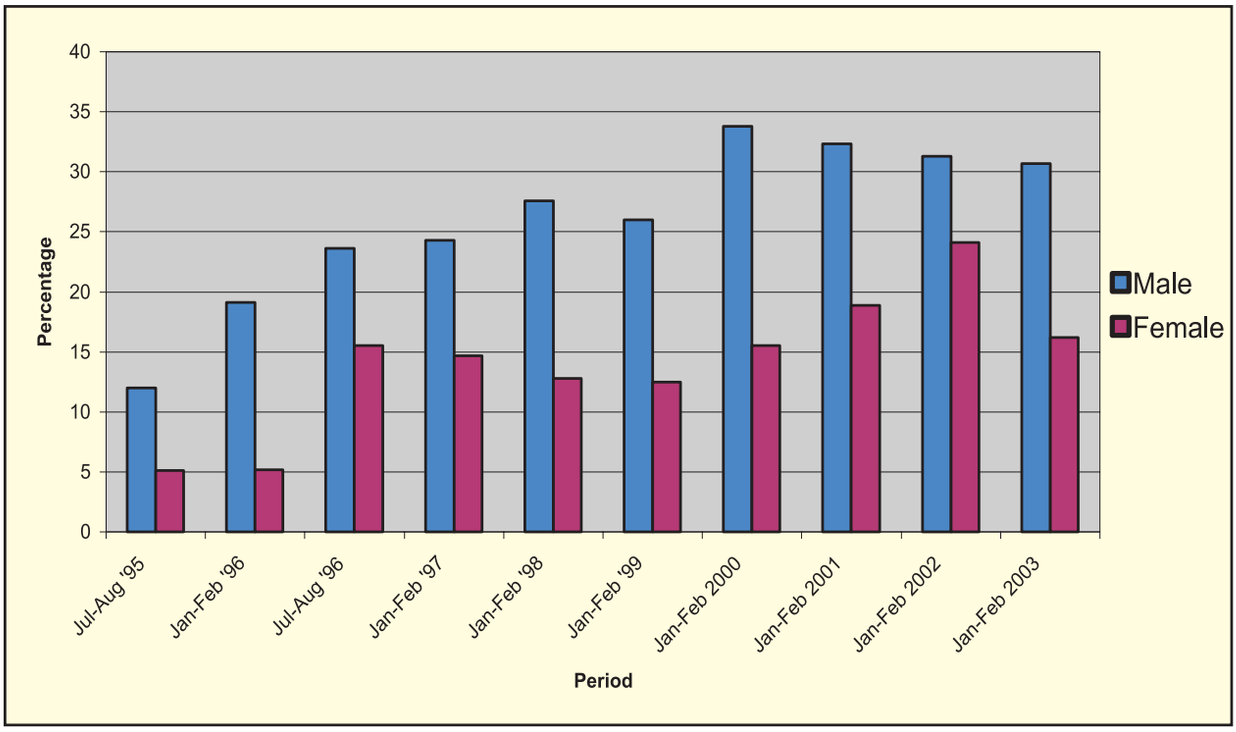


Fig. 2. HIV surveillance in TB patients in Pune : 1995 - 2002

indicated that HIV prevalence was 29.25%. HIV seropositivity was 30.3% in male and 19.6% in female TB patients for the year 2002 (Fig. 2).

Immunopathogenesis of Acute Primary HIV Infection

There is intense viral multiplication and also initiation and build up of HIV-specific immune responses during acute primary HIV infection. A study was carried out to identify individuals with acute primary HIV infection, study them immediately after seroconversion and to follow up them to study the virologic and immunologic factors and their association with the disease progression. The lymphocyte subset analysis of the individuals enrolled in the study showed immune activation in acute phase of HIV infection as evidenced by increase in the number of CD8+ and activated T lymphocytes (DR+), while CD4 lymphocytes were found to be considerably decreased. Negative correlation was observed between CD4 counts and viral load in these patients.

In another study on the clinical efficacy of pentoxiphylline (TNF α inhibitor) on the progression of disease in HIV infected individuals, 40 HIV infected patients were given pentoxiphylline in a dose of 400 mg thrice daily and followed up for 24 weeks. A mean increase in the CD4 counts was seen. No significant adverse effects were seen in these patients.

Clinical Progression of HIV

The study was initiated with the aim to develop the necessary clinical and laboratory infrastructure to offer clinical care and support to HIV infected individuals, to study the clinical presentation of specific opportunistic infections in them and to study the correlation between clinical and laboratory parameters. Of the 298 enrolled patients (191 men, mean age-33.9 yr.; 107 women, mean age-29.5 yr.). Nearly 30% men and 42% women were educated up to 10th/ 12th level. More than 58% women were housewives and 16.3% were unskilled

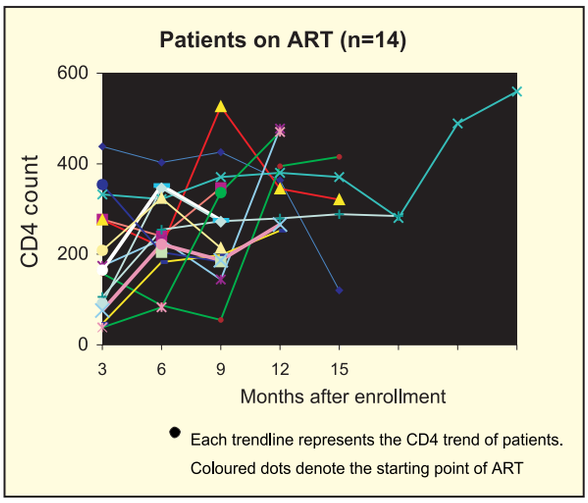


Fig. 3. CD4 count in patients on ART attending the clinic for 3 follow up visits

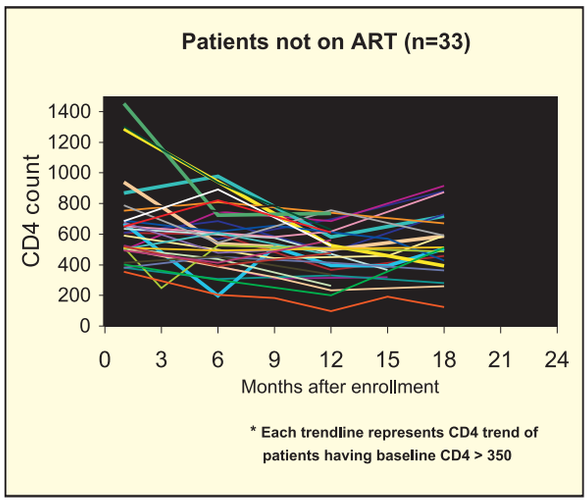


Fig. 4. CD4 count in patients not on ART attending the clinic for 3 follow up visits

workers whereas 18.2% men were unskilled workers. Majority of the persons were staying with their families except 8.9% men and 1.9% women who were staying alone. Of the enrolled patients, 3.7% women and 56% men reported practice of premarital sex. Nearly 93% women had spouses as their sexual partners while 61.3% men reported having sex with female sex workers, 29.8% with friends, 15.7% with casual contacts and 5.2% with male sex workers. Although 87.9% women never had sex besides their spouse, nearly 81% men reported more than one sexual partner. As many as 93.6% had heterosexual relationships. Of all enrolled patients, 58.7% reported condom usage. The presenting complaints of majority of the patients in the study were fever, weakness, cough with sputum, weight loss, loose motions and loss of appetite. *Cryptosporidia* and *Isospora belli* were commonly seen in patients with diarrhoea. The significant past illnesses reported by these patients were tuberculosis, herpes zoster, and oral candidiasis. Fig. 3 and 4 show the CD4 ranges of the subjects enrolled in the study and during follow up. There was inverse relationship between viral load and CD4 counts (Fig. 5).

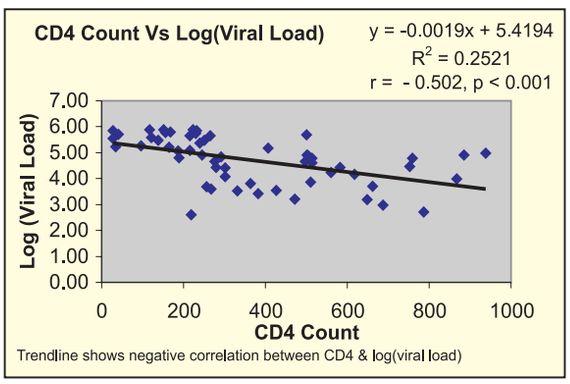


Fig. 5. CD4 counts in HIV patients (2002) (n=56)

Basic Studies

Anti-Retroviral Testing

The NARI is the only centre in India for carrying out anti-HIV testing of compounds. Of the sixteen herbal and three synthetic preparations tested for anti-HIV1 activity during the year, none showed anti-HIV activity. Two glycoproteins isolated and purified from first trimester placental tissue of HIV negative women were tested for anti-HIV1 activity. Both glycoproteins have shown inhibition of HIV-1 replication *in vitro* against cell associated HIV-1 IIIB strain.

Construction of MVA based HIV-1 Subtype C Vaccine

The ICMR and NACO have signed an agreement with International AIDS Vaccine

Initiative for development of a prophylactic modified vaccinia Ankara based vaccine with multiple gene inserts from HIV-1 subtype C strains from India. env and gag genes from six seroconverters were amplified, cloned and sequenced. A consensus sequence was developed using these sequences and earlier reported subtype C sequences from India. Sequences closest to the consensus sequence were selected for insertion in the vector. A recombinant MVA construct with four inserts, *env, gag, nef-pol* and *rev-tat* was engineered at Therion Biologics, Boston, USA by an ICMR scientist.

HIV Vaccine env, gag and nef Constructs

A collaborative study between NARI, NICED and NIV has been initiated to construct HIV vaccine employing *env, gag* and *nef* constructs. Of the 75 individuals with high-risk behaviour for HIV infection screened for p24 antigenemia 5 showed this antigen. Primers were designed for *env* (gp120), *gag* (p55) and *nef*. The gp120, p55 and *nef* genes were amplified from the p24 antigenemic individuals (C3 genotype). The gp120, p55 and full length *nef* genes were cloned into pGEM T Easy vector and the sequencing of the clones was carried out. From three p24 antigenic individuals, 4 clones were obtained. Sequencing of three *env* gp120 clones, the three gag and the three nef clones from the seroconvertors has been completed. The gp120 sequences confirmed the presence of C3 subtype sequences in the gp120 from all three seroconvertors with the GPGQ amino acid sequence at the tip of the V3 loop and absence of the N linked glycosylation site at the beginning of the V3 loop.

Genetic Resistance Study

Epidemiologic and geneologic study to find out the frequency of mutations in CCR5 genes

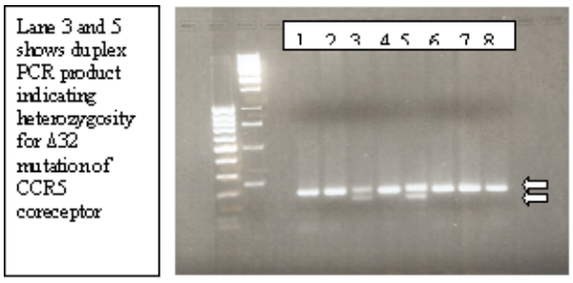


Fig. 6. Mutation in CCR5 gene

and other co-receptors which have been identified for HIV disease progression in long term nonprogressors(LTNP) was initiated at NARI, Pune. Of the 79 samples studied for CCR5 among long term non-progressors, two were found to have heterozygous delta 32 deletion giving a prevalence rate of 2.5% (Fig. 6). The CCR5 delta 32 mutation gene frequency among LTNPs is 0.013. One of the persons with delta 32 mutation is from Maharashtra state and the other is from Gujarat state. No homozygous mutation in CCR5 gene was detected among the 'exposed but uninfected' category. SDF1 mutation was found in 70 and heterozygous mutation in 29 samples. About 73.5% of exposed but uninfected persons harboured homozygous mutation for SDF-1 compared to 59.2% among long term non-progressors. Interestingly only one long-term non-progressor was found to have homozygous CCR2b mutation. About 28.5% subjects were found to be heterozygous for CCR2b mutation among LTNPs as against 32.5% among exposed but uninfected.

Immunological Studies

Cytokine Estimation in HIV-TB Co-infection

A pilot study was carried to analyze the pattern of cytokine secretion in peripheral blood mononuclear cells (PBMCs) in HIV seropositive patients with and without TB. The levels of proinflammatory cytokines, Th1(IFN-γ and TNF-α) and Th2 prototype cytokine (IL-10 and IL-4) were significantly

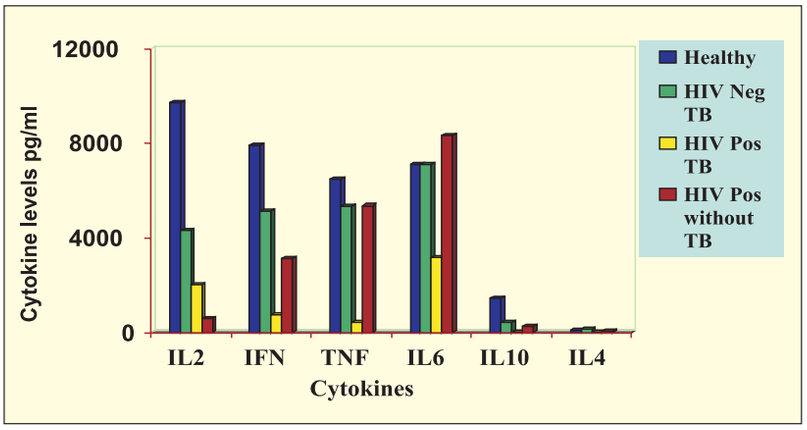


Fig. 7. Levels of cytokine secreted by mitogen stimulated PBMCs in different study groups

decreased only in HIV infected TB patients. The levels of IL-10 were found to be significantly low in HIV infected individuals irrespective of their tuberculosis status (Fig. 7). The Il-2 levels were found to be significantly decreased in HIV infection. The overall dysfunction of secretion of both Th1 and Th2 type of cytokines was observed in co-infected individual while Il-2 levels were altered in case of HIV infection only.

Association of Different HLA Alleles with HIV-1 Infection

The expression of HLA A, B and C alleles in 38 HIV infected individuals and 120 age and sex matched unrelated healthy controls from the same geographic region was performed at Institute of Immunoheamatology (IIH), Mumbai. HLA Cw*1507, B*3520 and B*1801 were significantly higher among the HIV infected individuals when compared to the healthy controls. Frequencies of HLA A*68011, A*7401, B*4001, B*1301, and Cw*12021 were higher while those of A*0203, A*2407, B*0702, Cw*0702 and Cw*04011 alleles were lower in the HIV infected individuals when compared with the controls. Association of Cw allele with HIV infection was observed for the first time in Indian patients.

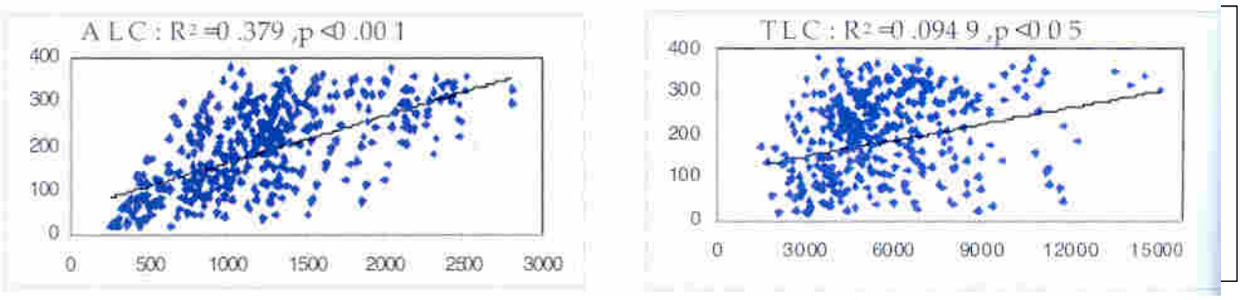
Evaluation of Total Leukocyte Counts (TLC) and Absolute Lymphocyte Counts (ALC) as a marker of Disease Progression in HIV-1 Infected Persons

The high costs of anti-retroviral drugs and assays for monitoring the anti-retroviral treatment have always been the main obstacle for universal application of ART. Although the costs of AR drugs have declined markedly in the last one year, there is no alternative to the expensive viral load and CD4 phenotyping assays used in monitoring. An effort is being made to study the relative utility of TLC and ALC as surrogate markers for disease progression as reflected by CD4 counts. In a retrospective analysis, TLC and ALC in 383 HIV positive individuals were assessed for the ability to predict CD4 counts, a most commonly used marker for starting chemoprophylaxis for opportunistic infections. When correlated with CD4, significant correlation was observed only between ALC and CD4 counts (Fig. 8). Thus ALC may be a useful and practical surrogate marker for predicting CD counts. The study is ongoing and the data available on a larger sample size are being evaluated.

Epitope Mapping in HIV-1 Subtype C gag Antigen

HIV-specific cytotoxic T lymphocytes (CTL) play a major role in controlling virus replication. Development of an effective vaccine requires the fundamental knowledge of the CTL epitopes that are targeted by infected persons. Data is not available on HIV-specific CTL epitopes that are presented by HLA class I molecules prevalent in the Indian population. Hence, NARI, Pune has initiated a study to identify immunodominant

a. Patients with CD4 counts<350/mm³ (n=203)



b. Patients with CD4 counts<200/mm³ (n : 108)

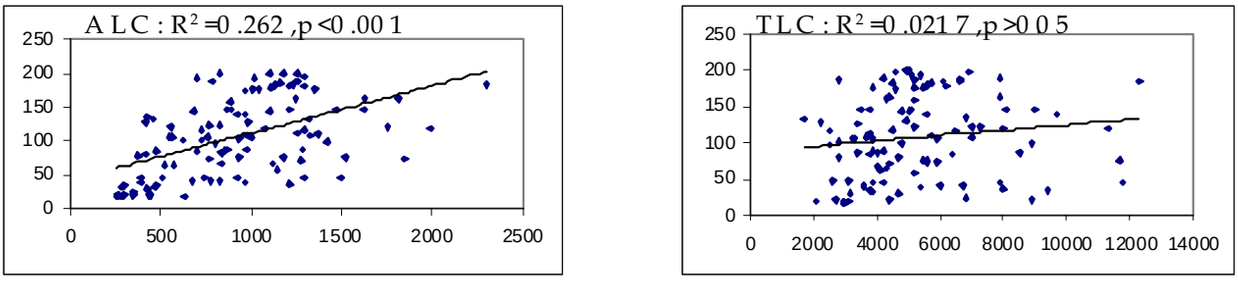


Fig. 8. Correlation of ALC and TLC with CD4 counts

CTL epitopes in HIV-1 subtype C infected individuals in Pune. Till date 19 epitopes have been identified in HIV-1 *gag* antigen, out of which 9 were in p17 region and 11 in p24 region. The peptides will be confirmed for the induction of CTL activity in the laboratory by intracellular cytokine assay and a conventional ^{51}Cr release assay.

Socio-Behavioural Studies

Community Awareness on HIV Vaccine Trials

HIV Vaccine Trial Network (HVTN) initiated a multicentric study in China, Thailand, India and USA to assess the willingness of the the high-risk individuals to participate in phase III prophylactic HIV vaccine trials. The preliminary findings show that concept of adult vaccine is not prevalent in India hence educating masses about this adult vaccine is the task ahead. More than half of all STD clinic attendees perceived HIV vaccine as useful. Nearly 70% clinic attendees showed willingness to participate in future vaccine trial if they know the safety results. While addressing to the incentive/compensation factor maximum number gave insurance as a preferred option. Many participants also preferred free medication as an important incentive.

Participants did mention that vaccine induced HIV reactive report could lead to social ostracisation. The study highlighted the need to probe the community through focused qualitative research that could give links to information gaps and community specific ethnocentric needs for success of future vaccine trials.

A phase I controlled clinical trial of the HIV-1 subtype C MVA vaccine will be conducted in normal healthy adults with low/no risk of HIV infection after obtaining all necessary clearances. Since this is the first HIV vaccine trial in the country, there is a need to educate the community. Community awareness on HIV/ AIDS and its prevention through small group meetings and talks with women in various identified communities are being done by NARI social workers in collaboration with respective NGOs in Pune.

Impact of Counselling on Behaviour Change

A study was initiated to gauge the impact of ongoing counselling on HIV infected individuals and to document the needs of HIV infected individuals attending the NARI clinic. Both the seropositive and negative individuals are provided psychosocial support at the counselling unit. The study found that unmarried men faced social, psychological, emotional and sexual problems. All reported social pressure for marriage. Married couples who were counselled for consistent condom use reported about regular condom use. The widows faced financial, emotional and psychological problems and are often not supported by the family members and reported uncertainty for their children's future.

Psychosocial Stressors among HIV Infected Individuals

Care for HIV infected people needs to be emphasized in the context of prevention of secondary transmission of HIV, reduction in stress and improvement in quality of life. This study aimed at identifying the mental health needs of HIV infected people and to understand various internally experienced stressors among people recently informed of their sero status was initiated at NARI, Pune. Patients are first screened for pre-existing psychiatric morbidity using hospital anxiety and depression scale (HADS) and are investigated for post-traumatic stress disorders and suitably intervened by the attending psychiatrist/psychologist or referred for specialized care as and when necessary. The study instruments namely screening instrument, needs instrument, distress instrument and post disclosure instruments have been developed / adopted and pre tested.The normal range in the HADS instrument is 8-10. Cumulative frequency of above normal range of anxiety is 44.4% while that of depression is 34.6%. Data is indicative of development of stressors in patients coming for HIV testing and counselling.

Community Involvement Activities

A three phase community education plan was initiated under HIV Prevention Trial Network project to create HIV/AIDS awareness in the community that could result in improved referral for voluntary counselling and testing. An 11 day Training of Trainers (TOT) Workshop was conducted at NARI for pre-identified NGOs in Pune as part of Phase-1 Community Involvement Plan (CIP). The goal of this Workshop was to train TOT level trainers from partner NGOs. The participants were given exhaustive information regarding the present research programmes at NARI. This effort is expected to be a step forward towards bridging the gap between community and the researchers. In addition, this Workshop provided opportunity for expanding field activities of NARI from clinics to the community.

REPRODUCTIVE HEALTH

Reproductive health is a reflection of health during conception, childhood, adolescence, and adulthood and sets the stage for health beyond the reproductive years for both women and men. It is estimated that reproductive ill health accounts for 36.0 % of the total diseases burden in women. The research and development activities of the Council are aimed to strengthen the RCH initiative of Government of India in reducing the disease burden associated with reproductive health and achieving population stabilization. Expanding contraceptive choices by conducting clinical evaluation of newer contraceptive technology and developing new molecules for contraception, management of obstetric complications at peripheral level, developing strategies and modules for domiciliary care to newborn and young infants, prevention and management of reproductive tract infections including research on microbicides and infertility (including genomics of male infertility) are the major research highlights during the year. These researches have been undertaken through the Council's National Institute for Research in Reproductive Health (NIRRH), Mumbai, Genetic Research Centre, Mumbai and network of Human Reproduction Research Centres (HRRCs) and several other non-ICMR institutes.

FERTILITY REGULATION

BASIC RESEARCH

Development of Improved and New Technologies for Fertility Regulation

Various events during mammalian reproduction such as gametogenesis, fertilization, implantation and embryogenesis are regulated by hormones and factors which are secreted by reproductive and accessory organs. Identification and characterization of these regulatory factors provide a better understanding of the reproductive processes and may lead to the development of newer approaches for fertility regulation. Studies carried out in this direction have led to the identification of several potential molecules for fertility regulation.

Identification and Characterization of Epididymal Antigens using Neonatal Tolerization

Development of a contraceptive vaccine using sperm as an antigen has been pursued over a number of years. Sperm antigens could either originate from the testis or the epididymis. Identification of epididymis specific proteins by conventional methods has not been very successful probably because the

testicular proteins are more immunogenic. Therefore, an alternate method of "neonatal tolerization" has been used which has resulted in production of number of monoclonal antibodies. These antibodies react specifically to epididymal proteins which appear to be synthesized in the supranuclear region of principal cells of distal caput and corpus epididymis. Immunofluorescent studies using serum from the mouse used for fusion shows localization all over the sperm. Different monoclonal antibodies identify proteins on different domains of spermatozoa namely, acrosome, post acrosome, equator and midpiece (Fig.1). The pattern of agglutination was either radial type (head to head) or comet shaped (midpiece to midpiece) (Fig. 2). Further studies are planned to purify and sequence the protein and study its mode of anchorage to spermatozoa. Identification and characterization of such epididymis specific proteins will help in understanding sperm maturation essential for fertility.

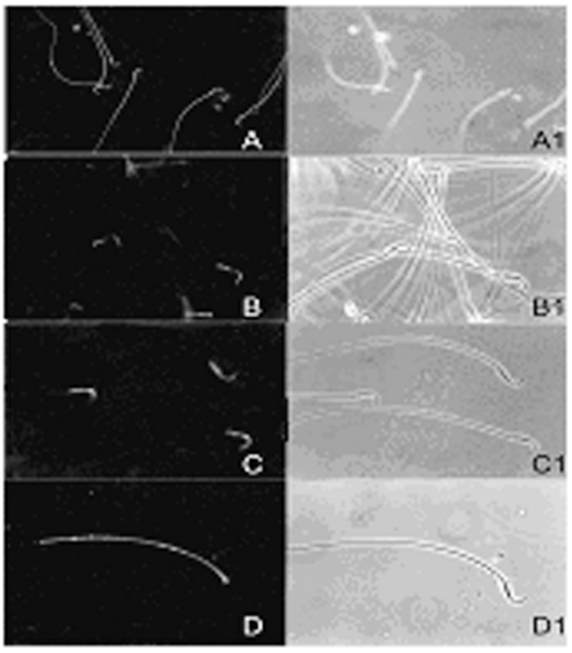


Fig. 1. Indirect immunofluorescence localization using monoclonal antibodies. A: Localization on rat sperm with serum of immunized mouse, B-D: Domain specific localization using different monoclonal antibodies, A_1-D_1: Phase contrast image.

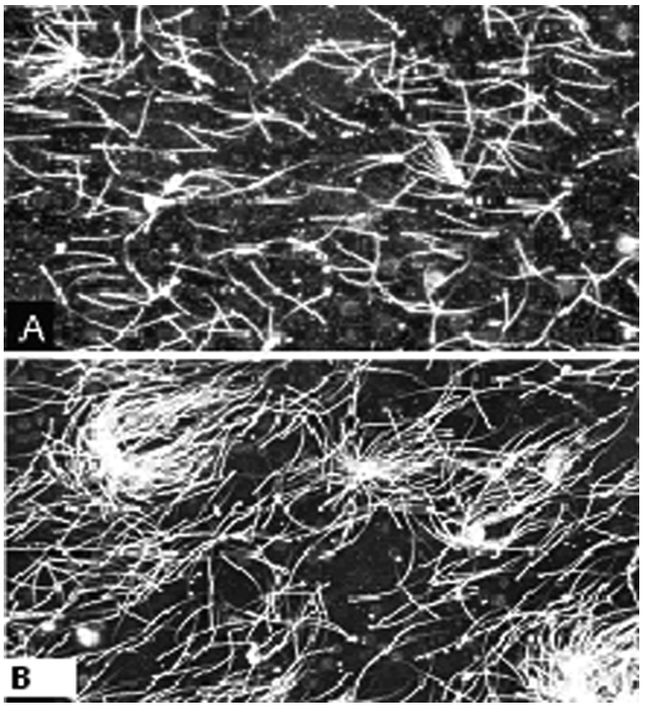


Fig. 2. Agglutination pattern using different monoclonal antibodies. A: Radial (head to head), B: Comet shaped (mid piece to mid piece).

Role of a Novel Androgen Regulated Hoxb2-containing Gene Expressed in Epididymis

Study was undertaken to elucidate the functional role of the androgen dependent Hoxb2 containing gene expressed in the epididymis in sperm maturation. To elucidate its role attempts to obtain a full length sequence of this gene were made. A human, monkey and rat epididymal library was constructed and screened using a DIG labelled oligonucleotide probe, the 591 base pair corresponding to the conserved Hoxb2 region. Seven positive clones from the rat epididymal cDNA library were identified with insert sizes ranging between 1-1.5 kb. The presence of the Hoxb2 region was confirmed by Southern hybridization. Further characterization of these clones is underway.

Studies with 80kDa Human Sperm Antigen and its Synthetic Peptides

An 80kDa human sperm antigen (80kDa HSA) responsible for inducing immunological

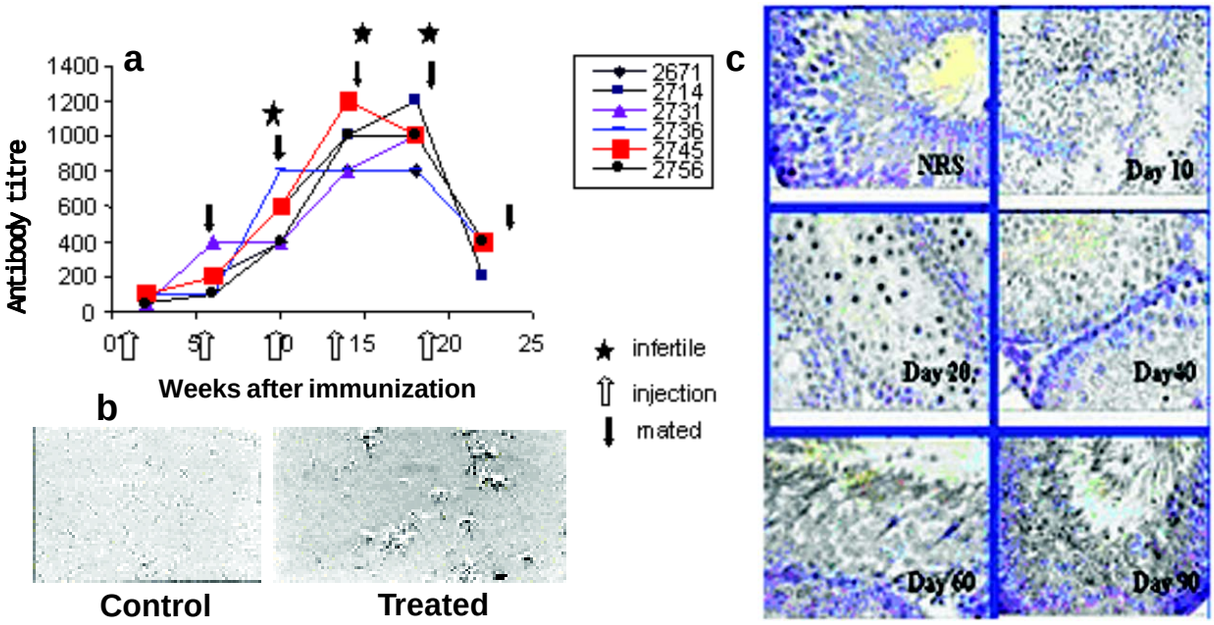


Fig.3. Generation of antibodies and mating studies with KLH-conjugated peptide-1 of 80-kDa HSA (a). Agglutination observed in semen of treated rabbits (b). Immunohistochemical localization of 80-kDA HSA in testes of rats from day-10 to day-90 (c).

infertility has been identified, purified and characterized. Active immunization of male and female rats with this antigen resulted in infertility. The peptides NT, 1, 2 and 4 were synthesized and conjugated to keyhole lymphocyte hemocyanin (KLH) and polyclonal antibodies generated in rabbits (Fig. 3a). Administration of these antibodies to male and female rats resulted in infertility. In rabbits, active immunization with peptide-1, conjugated to KLH, resulted in agglutination of ejaculated spermatozoa with complete loss of motility (Fig. 3b). Studies are in progress to evaluate the antifertility effects following active immunization with KLH conjugated peptide NT.

In an attempt to identify and characterize cDNA encoding 80kDa HSA, the testicular cDNA was PCR amplified using specific primers, designed on the basis of the amino acid sequence of the peptide-NT as a forward primer and sequence of peptide-6 as a reverse primer. The resulting amplified product of 540 base pair showed partial homology with the hypothetical testicular protein in the gene database. Immunohistochemical studies demonstrated that 80kDa HSA is predominantly present in the testicular sections of adult rats and not in immature rats suggesting that 80kDa HSA is expressed during development (Fig. 3c). The results of the study will help elucidate the role of 80kDa HSA in sperm function and lead to the possible development of a contraceptive agent, using either the peptides or a cocktail of peptides identified.

Molecular Cloning and Overexpression of Mouse Oviduct Specific Glycoprotein (OGP) using Yeast Expression System

Full length murine OGP cDNA was cloned into pPICZ A expression vector and recombinant plasmids were transformed into yeast cells, *Pichia pastoris*, and expressed. The protein secreted into the medium was purified followed by simple gel permeation chromatography and the > 250 kDa recombinant mouse OGP was identified by immunobloting and its glycosylated nature confirmed by lectin blotting studies (Fig. 4).

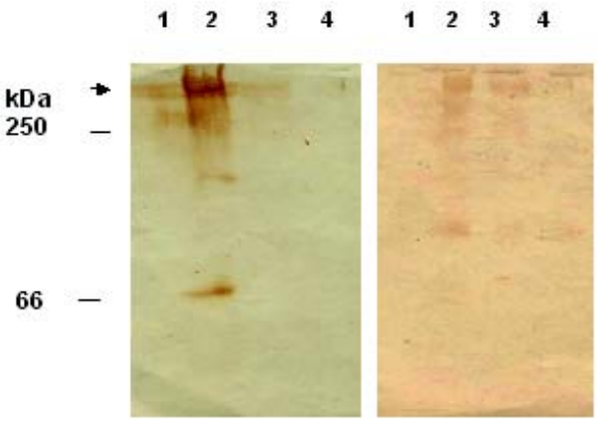


Fig. 4. Western blot analysis and lectin binding studies of recombinant glycosylated mouse OGP expressed by clone 4. Lane 1: Phenyl sepharose fraction, Lane 2: Ammonium sulphate fraction, Lane 3: Phenyl sepharose fraction of vector, Lane 4: Ammonium sulphate fraction of vector.

The band corresponding to mouse OGP was excised from the gel and used to immunize rabbits. The antiserum is currently being characterized.

Identification of Putative Protein Partners to OGP

OGP has been shown to be associated with sperm head and tail regions and could be either epididymal, testicular or prostatic. In an attempt to identify the sperm protein partner/s to OGP, a human epididymal cDNA library in λ uni-Zap XR vector (from Stratagene) was immunoscreened using the N-terminal region of monkey OGP and its specific antisera. Positive phagemids were analyzed by PCR amplification using vector specific T3 & T7 primers. Inserts of 1100bp and 1200bp were obtained. These are being sequenced. These studies will help unravel the role of OGP in fertilization,embryo transport and help improve the fertilization rates in IVF/GIFT.

Structure-Function Studies on Gonadotropins and their Receptors

Gonadotropins play a critical role in various reproductive processes both in males and females. Attempts are being made to understand gonadotropin-receptor interaction at the molecular level with the use of synthetic peptide strategy. This will facilitate the design of small molecules having gonadotropin agonistic or antagonistic activities, which could be used clinically.

Novel approach of using disulphide containing peptides to delineate the functional domains of gonadotropins has been developed. Studies carried out with human chorionic gonadotropin (hCG) and follicle stimulating hormone (FSH) suggest major differences in the receptor binding regions in the hormone-specific β-subunit of these hormones though their crystal structures are very similar. Major receptor binding region around the disulphide bonds cys (28-82) and cys (38-84) in the β-subunit of FSH has been identified (Fig. 5). Information obtained will form the basis for the development of more potent inhibitors of specific hormone action.

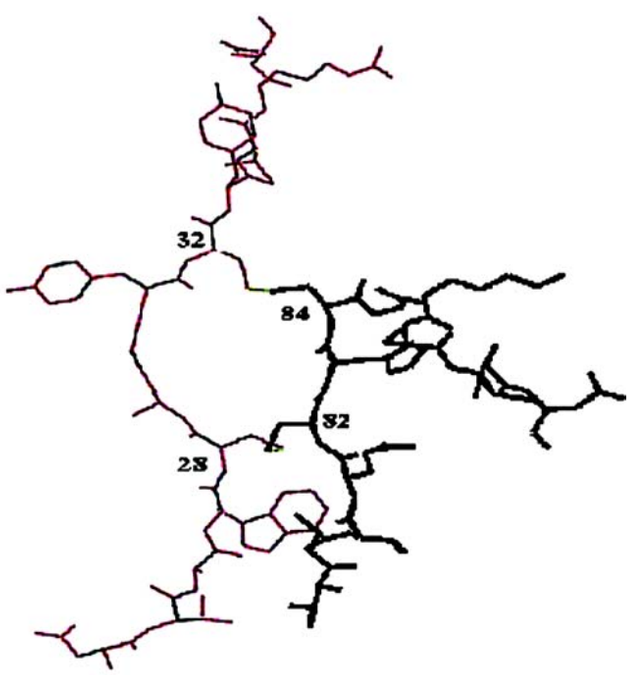


Fig. 5. Major receptor binding region of hFSH showing the region β 24-36 (in red) and β 78-90 (black) connected by disulfide bonds 28-82 and 32-84.

CLINICAL/OPERATIONAL RESEARCH

Clinical trial with once a month combined injectable Contraceptive "Lunelle" (medroxyprogesterone acetate (MPA)-25 mg + ethnyl oetradiol (EE2) cypionate-5mg)

Injection Lunelle , a monthly injectable contraceptive, is being offered to women seeking family planning services at 16 HRRCs located in the department of Obstetrics and Gynecology of the medical colleges. The study envisages enrolment of 1200 women to assess the relative acceptability, safety, efficacy and continuation rate of Lunelle when offered through cafeteria approach. A total of 806 women have been enrolled so far and of these 200 have completed 6 months of use. The life table cumulative discontinuation rate was 17.7 per 100 users at 6 months. Discontinuation rate due to menstrual abnormality was 7.6 and due to personal reasons, it was 5.8 per 100 users. No pregnancy has been reported till date. About 46.0% women experienced menstrual irregularities during six months of use.

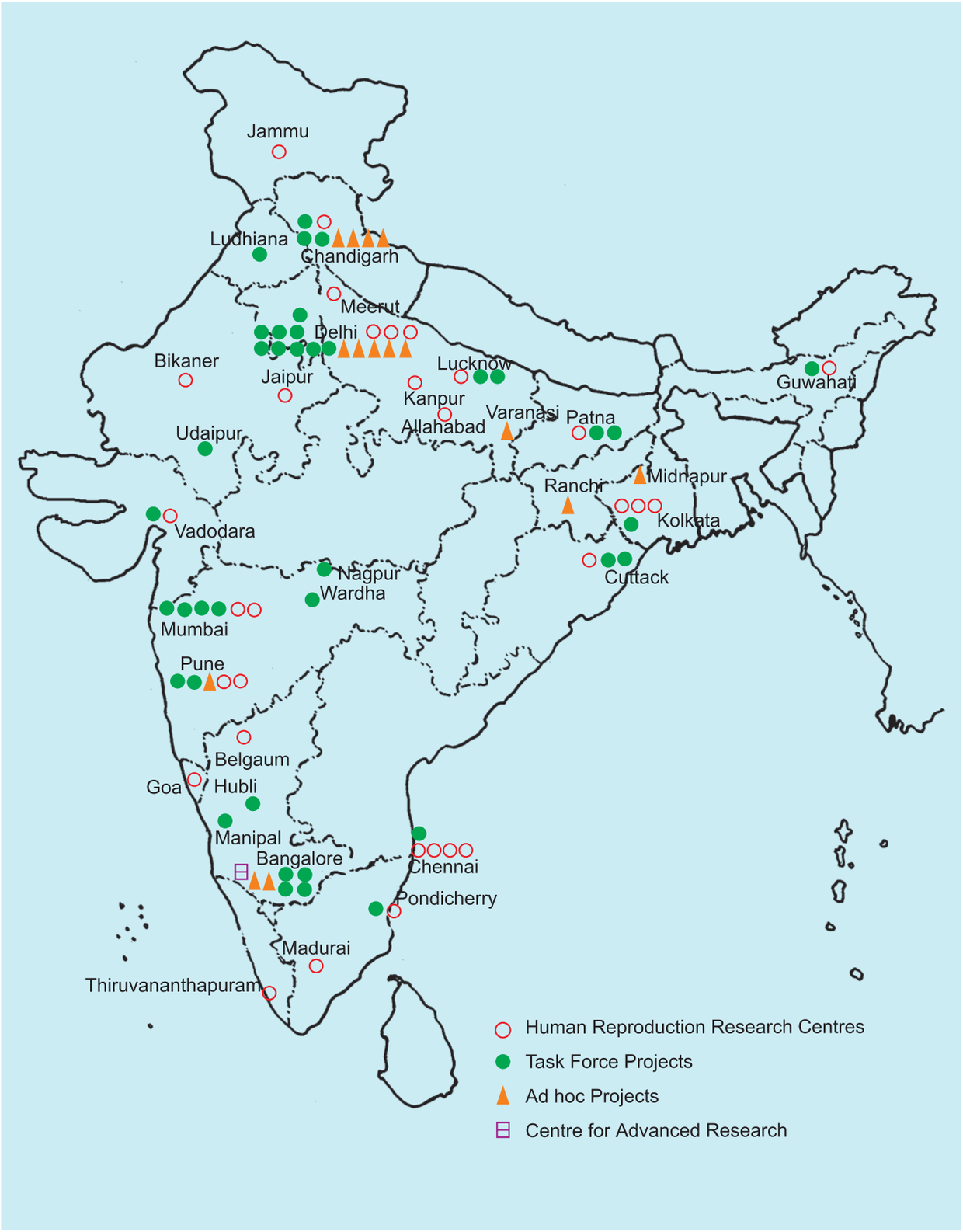
Acceptability and Continuation Rates of Norethisterone Enanthate (NET EN)

A pre-programme introduction study with two-monthly injectable contraceptive NET EN (200mg), involving 1200 subjects, has recently been initiated at 10 HRRCs to assess (i) user acceptability and continuation rates of NET-EN; (ii) the incidence of menstrual irregularities and other side effects; (iii) socio-behavioural aspects of users of NET-EN from different regions/cultural settings; and the return of fertility. A total of 457 women have been enrolled so far of which 194 have completed 6 months of use. Preliminary observation indicated discontinuation rate of 10.3%, 18.1% and 21.1% at the end of 2, 4 and 6 months of use respectively.

Emergency Contraception with Levonorgestrel and Cu T 200B

Emergency contraception provides an attractive option for preventing unwanted pregnancy after unprotected coitus i.e. unplanned or accidental sexual exposure as well as in cases where regular contraceptive is either missed or there is slippage/breakage of barrier method. A judiciously-used emergency contraception (EC) can prevent between 75% - 99% of unwanted pregnancies. Several methods are available now for EC and most of these are considered safe and effective. However, EC should only be considered as an emergency procedure . It is effective only if taken within 5 days of the first unprotected sexual act after the last menstrual period and no further exposure to unprotected sex in the same cycle.

Levonorgestrel 0.75 mg (oral) and Cu T 200B intra uterine device (IUD) were offered as methods of emergency contraception to women through HRRCs. A total of 1688 women came to the participating centres seeking EC. Of these, only 628 (35%) women could be provided EC . The remaining women were not eligible for EC due to various reasons viz came after the stipulated 3/5 days of unprotected sex (29.4%), overdue/pregnant (34.9%), more than one unprotected intercourse in the current menstrual cycle (14.3%) and did not meet the other eligibility criteria for the study (21.4%). This indicates the need for a strong IEC component so that beneficiaries are aware of who can avail of the method and when it can be availed. A total 560 women have been assessed in the study. The relative acceptance for levonorgestrel was 64.6% and for Cu T 200B, it was 35.4%. Reason for seeking EC included non use of regular contraceptive (44.3%), forgot to use condom (10.8%), breakage/ slippage of condom (27.0%), expulsion of IUD



MAJOR ICMR RESEARCH PROJECTS IN REPRODUCTIVE HEALTH

(6.3%), forced sex/rape (2.8%) and failure of natural family planning methods (8.8%), No serious side effects during use were reported with either of the two methods. Till date 6 pregnancies (3 method failures and 3 user failures) have been reported with levonorgestrel, *i.e.* a pregnancy rate of 1.66%. The number of pregnancies averted was 76.0% (prevented 19 out of 25 expected pregnancies). No pregnancy has been reported with Cu T 200B.

Clinical Trial with SMA, an Intravasal Injectable Male Contraceptive

Restricted phase - III clinical trial with male injectable contraceptive [reversible inhibition of sperm under guidance (RISUG)], developed by IIT Delhi, is being carried out at 3 centres in Delhi. The interim data analysis of 63 subjects, who had completed six months of follow up showed scrotal swelling in 82.5% subjects at one week follow up which persisted in 76.2% subjects up to one month. 43% subject's felt persistent pain in scrotal region, which persisted in 30.2% subjects for one month. Scrotal nodules were observed in 19% subjects at one week and increased to 24% subjects at one months of injection. Scrotal abscess, fluid collection around scrotum and inflammatory pathology were seen in one case each after one month of treatment. Albumin and sugar were noticed in urine in 6 and 1 subject respectively after six months of injection. Method failure (presence of motile sperm) was observed in 4 subjects and in one it resulted in pregnancy. After evaluating the data the Monitoring Committee and the Toxicological Review Panel has recommended that no new subjects should be recruited in this study till toxicity of SMA and the solvent dimethyle sulphoxide is evaluated. It was also recommended that all the trial subjects should be followed up for 2 years initially and in those interested in reversal, the drug should be flushed out from their vas. Also data on reversibility should be generated.

Contraceptive Knowledge, Practices and Utilization of Services in Rural Areas of India

To obtain information from rural women regarding their contraceptive knowledge, practices and utilization of services, a cross-sectional survey of 117,465 eligible women was carried out in the sample area of 29 districts from January 1996 to February 1997. All users of IUD, oral contraceptive (OC) and acceptors of a permanent method in the last one year (14,2760) were interviewed in detail. In addition a systematically selected sample of 17,082 non users was also interviewed.

Overall contraceptive prevalence was 45.2% of which 34.2% had used a permanent method. Among the current users, the contraceptive had been availed mainly from either PHC (31.5%) or hospital (42.1%). Around half the women (53.1%) received counselling and 20.3% information regarding other methods. Pelvic examination was done in 39.1%. Around 97% women expressed satisfaction with the method, provider and services. Almost all the women (98.8%) were using a contraceptive method with the knowledge of their husband and had his support for continuing the same. There was no concept of using any family planning method for either postponing the first conception after marriage or spacing between the two child births. A large majority of women (70.5%) used a family planning method for the first time only after completing their desired family size. (Fig.6). Among the never users, 73.5% mentioned at least one modern method of family planning available in the national programme and 64.3%

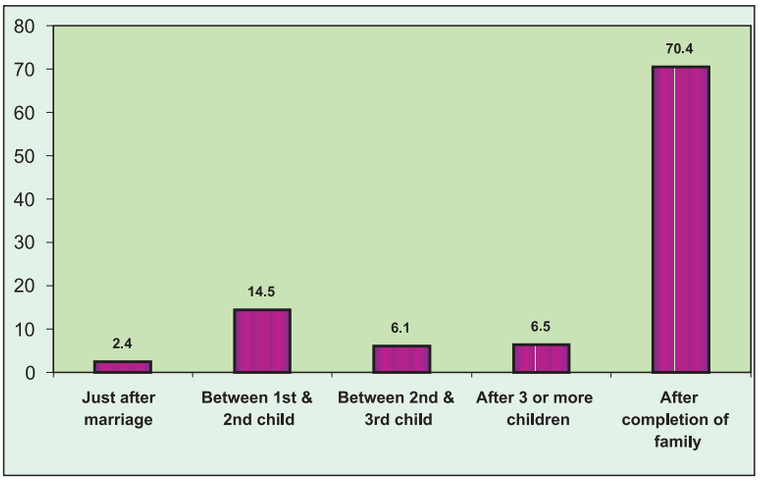


Fig. 6. First time use of any family planning method

mentioned the service source where it would be available. Fewer women in most of the districts mentioned spacing methods as compared to female sterilization. The main reason given for not using any family planning method was "family not complete" (34.6%). (Fig. 7).There is a need to promote spacing methods and motivate couples to accept them rather than only provide information since the study indicates that awareness regarding contraception is present in the rural areas.

INFERTILITY

Male Infertility

Evaluation of the Causes of Male Infertility

Retrospective data analysis was undertaken to study the causes of male infertility in a secondary referral centre so as to focus attention on the need-based research activities in this group of infertile subjects. The analysis in 335 infertile males indicated that 62% of the males who visited the clinic were >30 years of age and had more than 5 years of trying time. Longer trying time is known to be associated with decreased fecundity and higher incidence of chromosomal abnormalities. In these infertile males a high incidence of azoospermia was seen in 40% cases, and in 60% subfertility was due to varicocele, seminal infection, idiopathic and age related medical causes.

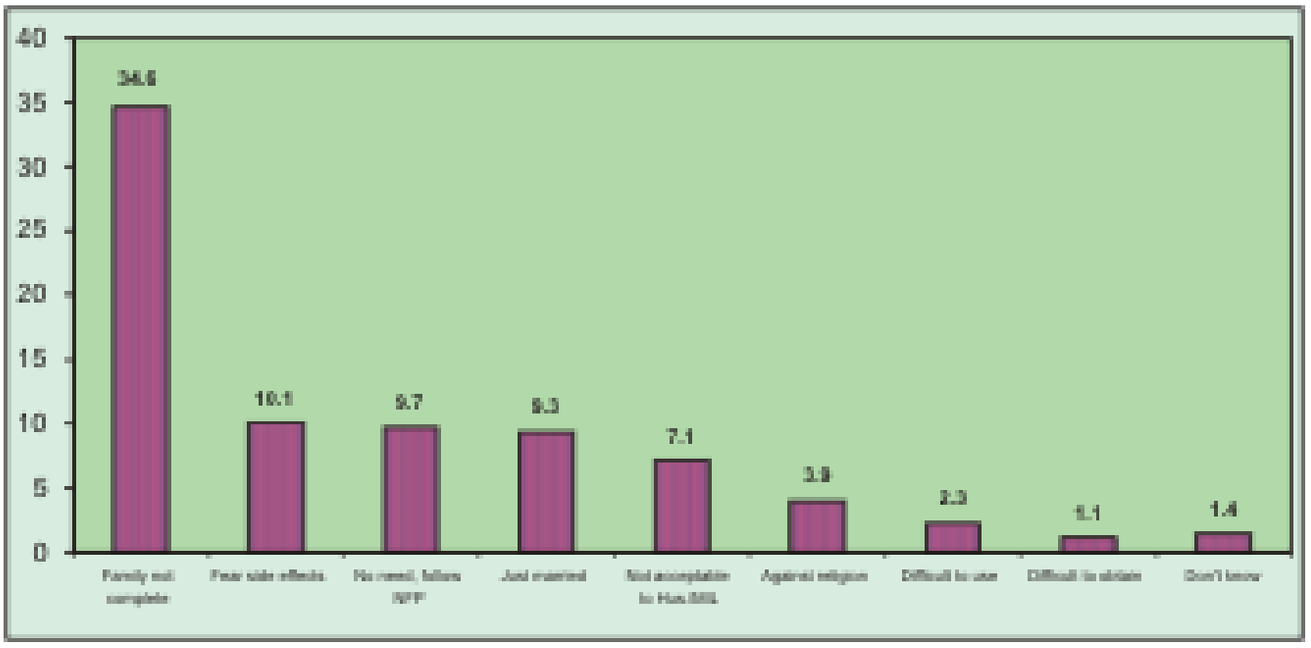


Fig. 7. Reasons for not using any family planning method

Genomic Study on Y Chromosome Microdeletion in Oligo-Asthenozoospermic and Severe Non-obstructive Azoospermic Males

Severe male infertility (non obstructive azoospermia/severe oligoastheno- zoospermia) has been associated with higher incidence of chromosomal aberration (structural/ numerical) and microdeletion of Y-chromosome. The important loci associated with spermatogenesis known as azoospermic factor (AZF) are situated on the long arm of the Y chromosome and constitute three distinct regions *i.e.* AZFa-c. Microdeletions in these regions have been reported to result in phenotype of Sertoli-cell-only-syndrome, maturation arrest at spermatocyte and spermatid level, respectively.

A study to evaluate the frequency and type of microdeletions in long arm of Y-chromosome has been initiated in 19 azoospermic males. Detailed history, clinical examination and estimation of FSH and testosterone levels and analysis of microdeletions in genomic DNA were carried out. PCR amplification of loci in AZFa region (sY84 and sY86) and of control male and female genes (SRY and ZFY) resulted in expected amplified product sizes of 326bp, 320bp, 472bp and 495bp fragments respectively (Fig. 8). The resulting control gene products confirmed the validity of the PCR protocol. Further enrollment of subject is in progress.

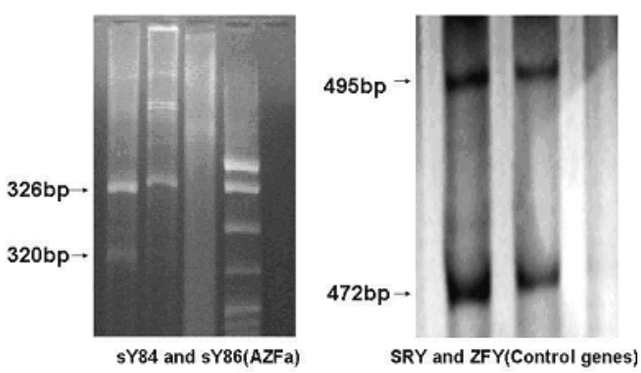


Fig. 8. PCR amplification of loci in the AZFa, *sry* and *zfy* gene.

Molecular Characterization of Human Sperm Progesterone Receptor

Limited information is available on the molecular characteristics and functional significance of progesterone (PR) receptors on human spermatozoa. In studies undertaken at NIRRH, Mumbai, PR transcripts were localized at the midpiece region of mature spermatozoa (Fig. 9) by *in situ* hybridization. These results were corroborated by RT-PCR analysis of sperm RNA in which transcripts for the C and N terminal regions were detected and found homologous to the corresponding regions of the conventional PR. Using specific monoclonal antibodies against the C and N terminal regions, PR was immunolocalized to the acrosome region of the spermatozoa. These results together suggest that the sperm PR is probably identical to the conventional PR.

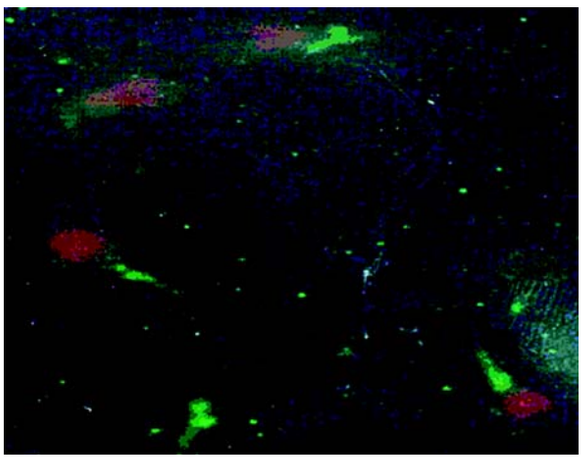


Fig. 9. Transcripts of progesterone receptor (arrow) are expressed in the mid piece of mature human spermatozoa.

To determine if sperm PR is an inherent protein or obtained during maturation in the epidydmis, the expression of PR protein was studied in the testis. Immunohistochemical and immunofluoroscence studies on human testicular sections and isolated germ cells revealed that the membrane bound PR is expressed in the secondary spermatocytes, round spermatids and testicular sperm suggesting that the sperm PR is an inherent

and not acquired protein during spermiogenesis.

Identification and Characterization of Fertility Associated Sperm Antigens

Attempts are being made to synthesize a molecular probe for diagnosis of infertility. Earlier studies indicated that lack and/or poor expression of 57 kDa protein may account for infertility in some men. To characterize the protein at the molecular level, a human epididymal cDNA library was screened using polyclonal antibody against 57 kDa protein. A 520 bp cDNA was sequenced and BLAST search showed 98 % homology with chromosome 17 (Fig. 10). The translated amino acid sequence did not show any significant homologies.

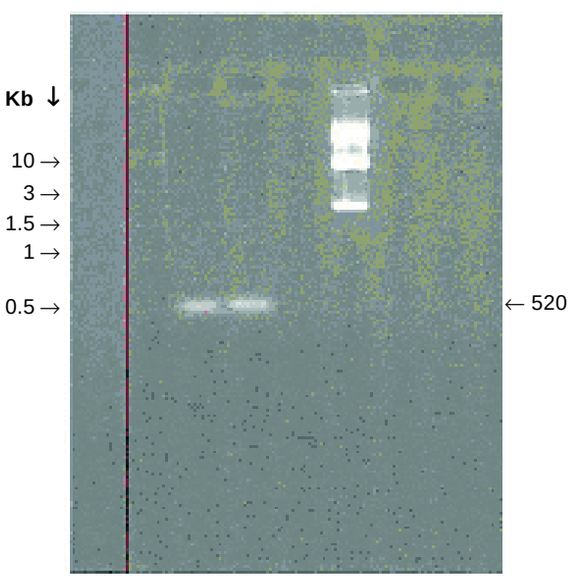


Fig. 10. Human epididymal cDNA library screening using polyclonal antibody raised against sperm antigen.

Female Infertility

Molecular Studies on Androgen Regulation in Ovarian Follicles

Studies were carried out using an intact antral follicle culture model to understand the role of local factors in the regulation of ovarian androgens. Fresh medium sized porcine ovarian antral follicles were cultured for 24 hrs. in a serum free medium containing the factors under study. The secretory capacity of follicles was estimated by assaying the androstenedione and progesterone in the culture supernatant. Expression of mRNA of genes was assessed in the theca cells isolated from the cultured follicles. An upregulation in androgen secretion corresponding to increase in CYP17 gene expression was seen with insulin, growth hormone and inhibin, whereas TGFβ, activin and melatonin showed down-regulating effect. Fig. 11 shows the results obtained with inhibin and melatonin. The results of these studies confirm significant role of local intra-ovarian factors in modulation of ovarian androgens mediated by regulation of ovarian gene expression.

Studies on Hyperandrogenicity using an Experimental Animal Model

Studies aimed at assessing the intraovarian regulation of genes in relation to hyperandrogenicity were undertaken in a rat model. Hyperandrogenicity was induced in adult female Holtzman rats by administration of a single injection of 2 mg estradiol valerate (E2V). Acyclicity was observed one month following the injection; enlarged follicles with large antral cavities (Fig. 12) and the granulosa cells showing fragmentation of the nuclei were seen indicating the effect of increased levels of androgens in circulation. The levels of ovarian androstenedione significantly increased in the E2V treated rats while reduction in the expression of two of the key steroidogenic genes *viz.* steroid acute regulatory (StAR) gene and CYP17 gene was observed.

Studies on Expression of Endometrial Function Markers in Fertile and Infertile Bonnet Monkeys

Study was undertaken for elucidating the molecular mechanism of endometrial

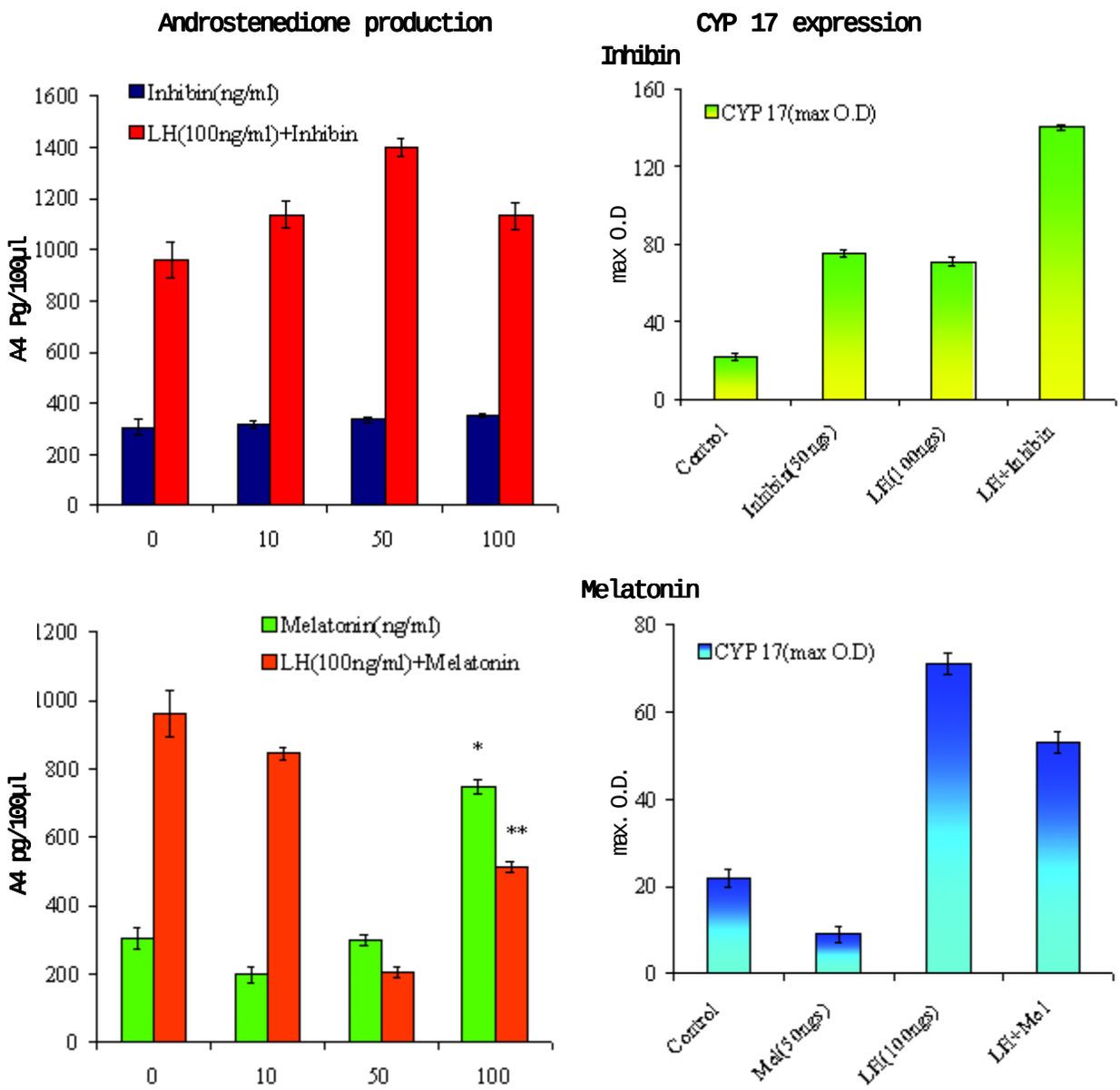


Fig. 11. Effect of inhibin and melatonin on androstenedione production and expression of CYP 17 gene in antral follicle cultures.

receptivity in primates. Studies will help in delineating the probable cause of unexplained infertility, IVF failures and recurrent abortions.

For identifying novel endometrial factors that may play a potential role in endometrial receptivity and implantation, differential display RT-PCR (DD-RTPCR) approach was used to screen endometria from fertile, infertile and mated female bonnet monkeys. Three cDNA fragments have been cloned showing differential pattern of expression in onapristone treated infertile animals. One of these fragments (DD2A) was found to be over-expressed. *In situ* hybridization using DD2A as a probe revealed predominant expression of this gene in the glandular epithelium of endometrium, expression was also observed in the stromal cell compartment during the luteal phase. Preliminary data also suggest that the gene is differentially expressed in the endometria during follicular

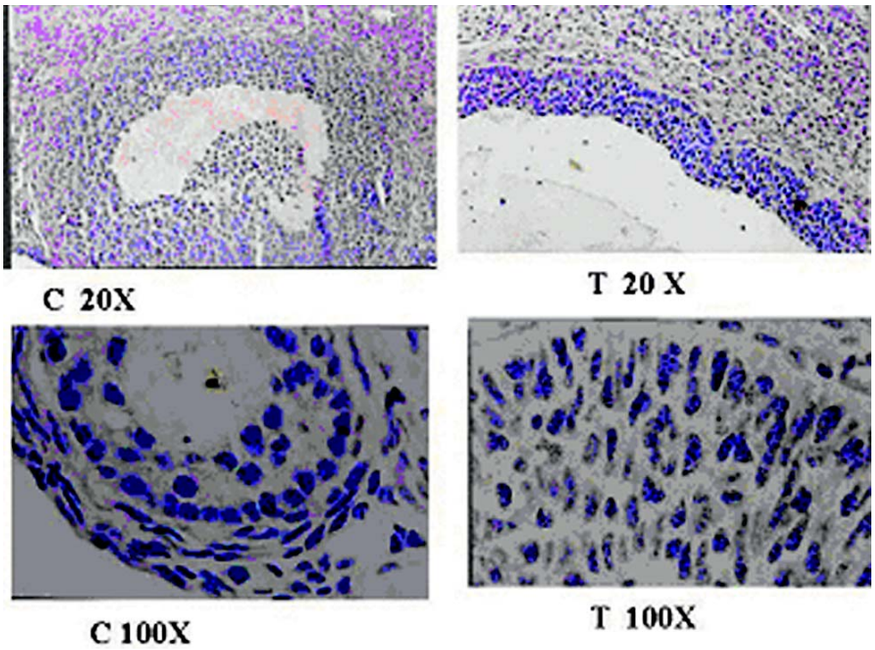


Fig. 12. Ovarian morphology in control (C) and estradiol valerate treated (T) rats.

phase as compared to the luteal phase. Fluorescent *in situ* hybridization (FISH) revealed that DD2A gene is a single copy gene. Using a bioinformatics approach, DD2A was identified to be a Rab binding protein that is involved in intracellular trafficking.

By DD-RTPCR analysis of endometria from mated and non-mated bonnet monkeys another differentially expressed cDNA fragment (gg1) was identified, cloned and sequenced (Fig. 13). BLAST search of this 600bp cDNA fragment revealed its homology to protein kinase A. Three hormone dependent molecules which may be involved in endowing receptivity to endometrium have been identified. Detailed characterization of these fragments and their regulation is currently underway.

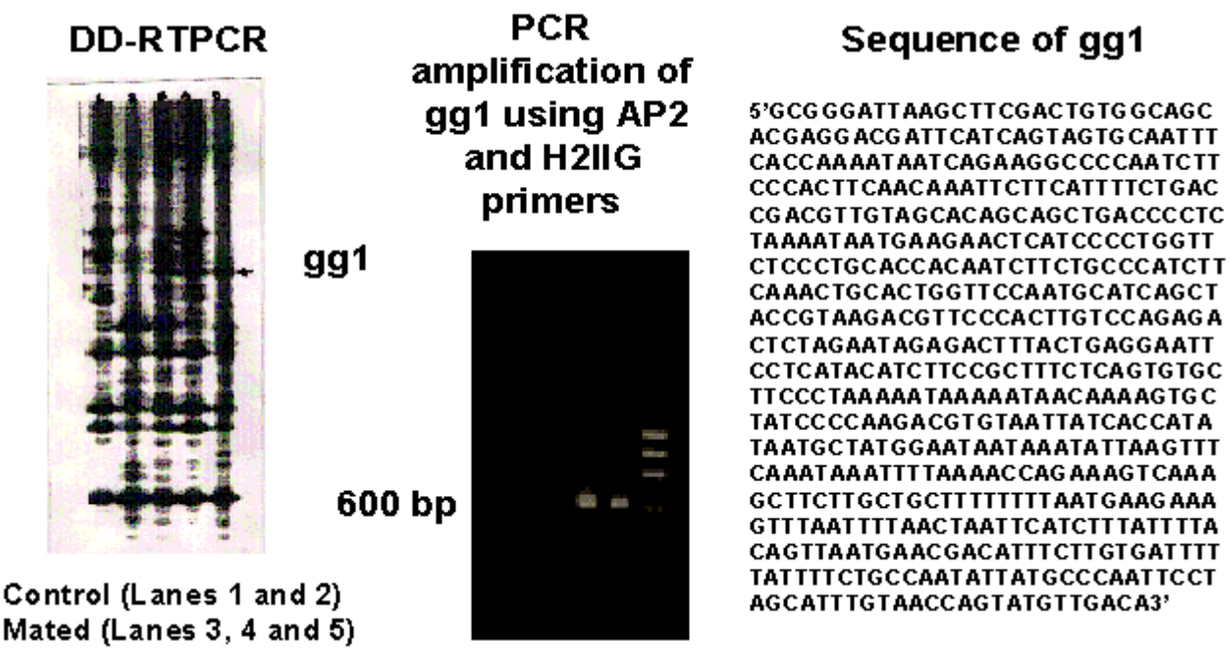


Fig. 13. Differential display DD-RTPCR analysis of peri-implantation phase endometria

National Guidelines for Accreditation, Supervision and Regulation of Assisted Reproductive Technology Services in India

The mushrooming of infertility clinics in India has been a matter of great concern. National Guidelines for Accreditation, Supervision and Regulation of Assisted Reproductive Technology (ART) clinics in India have been developed for regulating the ART services offered by large number of clinics, mainly in private sector. The guidelines describe requirements of ART clinics, essential qualifications of the ART team, ART procedures and their respective indications and cautions, precautions and concerns about ART practice. A three-tire system of Infertility Care Units has been proposed and efforts have been made to assist the physician or gynaceologist to refer the infertile patient to the respective Infertility Care Unit. The guidelines have covered various ethical and legal issues and provide future direction for research in this area and composition of National Accreditation Committee and its possible mechanism of operation.

To get the opinion of concerned people/ professionals/scientists/legal experts/ organizations etc. on these guidelines in general and especially on contentious issues, five public debates were organized by the Council in different parts of the country (New Delhi, Chennai, Kolkata, Jodhpur, Hyderabad, Bangalore). Suggestions emerging from these debates have been incorporated in the guidelines. The guidelines have also been approved by the National Human Rights Commission.

REPRODUCTIVE TRACT INFECTIONS

Chlamydia trachomatis Infection: Diagnosis, Prevalence and Immunopathogenesis

Some infections like *Chlamydia trachomatis*, human papilloma virus (HPV) are mostly asymptomatic and are the most common cause of infertility and cervical cancer, respectively. Their diagnosis is therefore important, and the need of the day is to have low cost, simple and reliable detection system. which are sensitive and

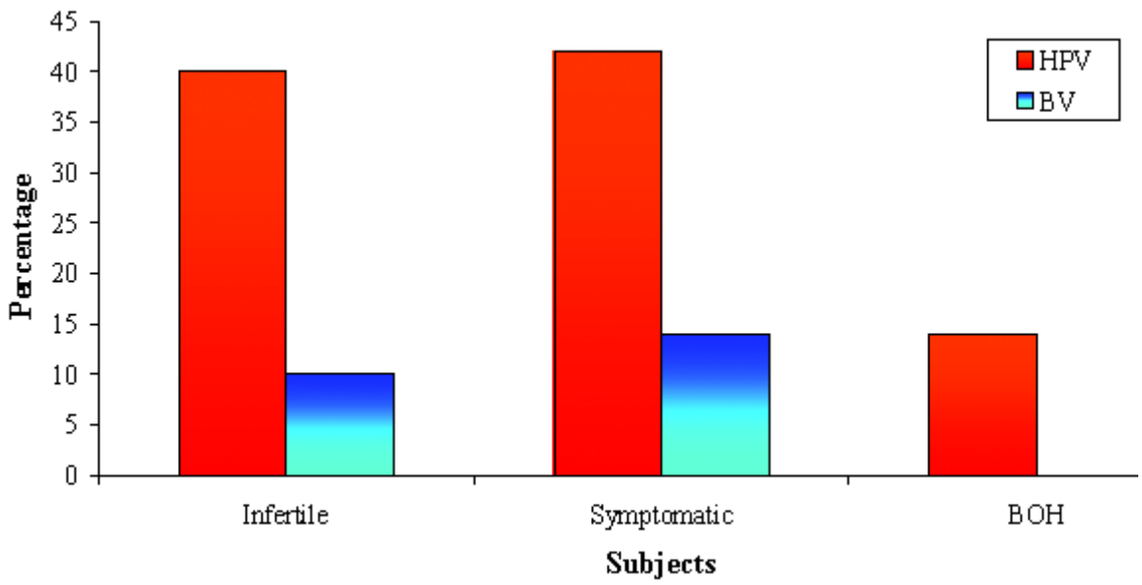


Fig. 14. Association of HPV and *B. vaginalis* with *C. trachomatis* infection among defined population.

specific. At the NIRRH, Mumbai, a specific test polymerase chain reaction (PCR) for diagnosis of these infections has been standardized and the amplified product confirmed by enzyme digestion, sequencing, blast-search and with the use of specific probe for diagnosis of *C.trachomatis* and HPV. The PCR system has also been evaluated using self collected (introital specimens) samples, cervical swabs and urine sediments of males with good sensitivity and specificity. This method is now being analyzed in clinic-based studies to evaluate the magnitude of RTIs/ STIs. Chlamydia infection is high (14%) among the infertile women whereas 12.5% of women with bad obstetric history manifest both the *C. trachomatis* and HPV (Fig. 14). Co-existence of multiple infections like *B. vaginalis*, *C. trachomatis* and HPV do exist among the infertile and symptomatic subjects.

Identification and Characterization of HIV Receptors on Spermatozoa

Using PCR, *in situ* hybridization, *in situ* PCR and electron microscopy, the presence of HIV has been detected on the membrane and in the cytoplasm of spermatozoa of infected men, as well as on the spermatozoa from seronegative donors preincubated with HIV. To identify alternate receptors for HIV on the spermatozoa, leukocyte free sperm preparation obtained by swim-up technique was used. A specific HIV binding protein of 160kDa has been identified on spermatozoa (Fig. 15). Further purification and characterization of this protein from sperm extract is in progress.

Nisin: The Antimicrobial Peptide for the Control of Fertility and STIs

Nisin, a 34 amino acid peptide (mol. wt 3.4 kDa), produced by *Lactococcus lactis* has been used as a food preservative for over half a century. The effect of nisin on sperm

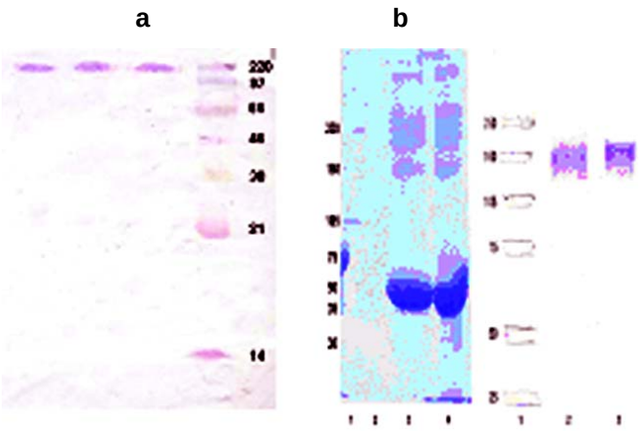


Fig. 15. Identification of HIV receptors on spermatozoa using viral concentrate. (a) SDS-PAGE and Western blot of 1% Triton-X 100 treated sperm extract. (b) Identification of HIV receptors on sperm by Western blot using gp 120.

motility in rats, rabbits, monkeys and humans was found to be time and dose dependent *in vitro*. Contraceptive efficacy of nisin was also evaluated in rabbits. Subacute toxicity studies did not show any adverse effect on vaginal epithelial cells (Fig.16), hematological parameters and serum biochemical profiles.

Studies indicated selective nature of nisin towards spermatozoa without affecting the vaginal cells. The mechanism of action of nisin on spermatozoa, RBCs, vaginal cells

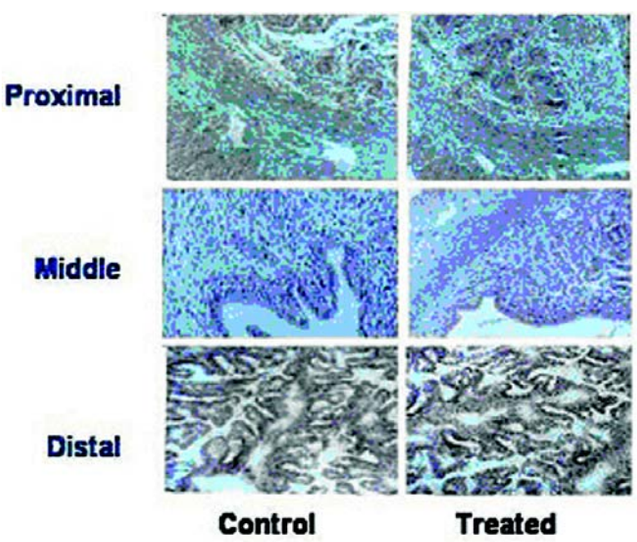


Fig. 16. Subacute toxic effect of nisin on vaginal epithelium in rabbits.

(ectocervical, endocervical and vaginal epithelial cells) and HeLa cells was studied *in vitro* using affinity driven peptide transfer and cell cytotoxic assays. The vaginal cell lines were successfully maintained and characterized using keratinocyte markers. The studies show difference in the affinity of nisin towards spermatozoa and vaginal cells, which could be due to variation in membrane charge.

The antibacterial activity of nisin was tested by measuring the zone of inhibition against three standard strains and clinical isolates of microorganisms. The results indicate the susceptibility of the organisms in the order of *E. coli* > *S. aureus* > *C. albicans* > *P. aeruginosa* > *C. tropicalis*. Studies suggest that nisin possesses dual properties of immobilizing spermatozoa and inhibiting microbial growth, making it a potential candidate for clinical evaluation.

Clinical trial on Praneem Polyherbal tablet for treatment of abnormal vaginal discharge

Vaginosis and cervicitis are the most commonly observed gynecological conditions hence it is necessary to have a wide range of effective and cost economic therapies in our country. Praneem containing neem, saponin and citrata oil, developed by Talwar Research Foundation, is undergoing evaluation at 6 centres to determine its efficacy and side effects in symptomatic women having abnormal vaginal discharge. An interim data analysis of 150 subjects indicated vaginal irritation and burning sensation in 31 and 47.7% subjects respectively. Difficulty in placement was reported in 3% subjects. Ninty five percent subjects reported being either fully (55.5%) or partially (39.8) satisfied with the treatment. On speculum examination, 69.7% subjects showed clinical recovery and laboratory diagnosis indicated full or partial recovery in 124 of the 128 subjects (57 women got complete and 67 partial relief). Only 4 women out of 128 experienced no relief on the basis of laboratory diagnosis. Overall nearly 75, 92 and 100% subjects have been cured from bacterial vaginosis, candidiasis and *Trichomonas vaginalis* infection respectively.

MATERNAL HEALTH

A Critical Appraisal of Cesarean Section (CS) Rates at Teaching Hospitals

Study was carried out with the objective to obtain an estimate of cesarean section rates and examine the indications and consequences of cesarean section at teaching hospitals in India. Information was obtained on total number of normal and cesarean deliveries during 1993-94 and 1998-99 from 30 medical colleges/teaching hospitals. In addition prospective data was recorded for a period of two months on 7017 consecutive cesarean sections on indications for cesarean delivery, associated complications and mortality. It was observed that the overall rate of cesarean section increased from 21.8 in 1993-94 to 25.4% in 1998-99. Among the 7017 cesarean section cases, 42.4% were primigravidas, 31% had come from rural areas, 20.8% were referred including 8% with history of interference, 66% were booked cases; period of gestation was less than 37 weeks in 21.7% and in 18% the surgery was elective. Major indications for cesarean section included dystocia (37.5%), fetal distress with or without meconium aspiration (33.4%), repeat section (29.0%), mal-presentation (14.5%) and PIH (12.5%). Maternal and perinatal mortality was 299/100,000 and 493/1,000 deliveries respectively and is high in spite of the increase in the cesarean section rates. There is need for standardized collection of information on all aspects of childbirth to ascertain the incidence

and indications of cesarean section nationally so that comparison and improvements of care can take place.

Risk Factors for Developing Meconium Aspiration Syndrome in Newborn Babies

An exploratory study was carried out at 31 HRRCs with the objective to assess the management practices of obstetric cases with meconium stained amniotic fluid (MSAF) and to study morbidity and mortality in new born babies with meconium aspiration syndrome, a major complication during delivery and child birth. An interim analysis of 7619 cases of MSAF indicated that 644 (8.5%) babies born to these women developed meconium aspiration syndrome (MAS). The mean age of the women with MSAF was 24.4±4.6 and in 52% it was their first pregnancy.

The risks of developing MAS in babies were studied in relation to obstetric profile and complications of mother during the present pregnancy. It was found that babies born to primipara mothers were at higher risk of developing MAS. Pre-eclampsia/PIH, post maturity, IUGR and prolonged rupture of membrane were the significant risk factors associated with the development of MAS in babies. Foetal distress at admission had significant risk in developing MAS. Oligohydramnios, chronic (not fresh), moderately thick MSAF, and thick MSAF were the highly significant risk factors for MAS. Fetal distress during labour and non-progress of labour were the other highly significant risk factors for developing MAS. Management of MSAF cases indicates large regional variation among participating centres. Amnio infusion was given in 16 out of 30 centres. About 50% of those who were given amnio-infusion had vaginal delivery and remaining had cesarean section.

Feasibility of using Misoprostol at the Peripheral Level for Prevention of Postpartum Haemorrhage (PPH)

Postpartum haemorrhage (PPH) and underlying anemia are the primary causes of maternal mortality in rural India and account for approximately 25-30% of maternal deaths. A community-based task force study has been initiated at five HRRCs to study the feasibility of administration of oral misoprostol for prevention of PPH by the paramedical workers at PHC level. The project is being carried out in collaboration with the DHO/CMO of the selected district, who is the co-investigator in the project. A total of 30 PHCs have been selected and randomly allocated as intervention or non-intervention areas. Misoprostol is being administered in the intervention PHCs whereas in the non-intervention PHCs the existing practice for prevention of PPH under the RCH programme is being provided. The preparatory phase including preparation of detailed manual of operations; developing linkages with the State and district health system; training of the research staff; orientation training to the medical officers and hands on skill-based training on management of third stage of labor to the ANM/LHVs of the selected PHCs has been completed. Implementation of intervention in the selected PHCs is ongoing.

Determinants of Antenatal Care Utilization in Rural Areas of India

To analyze the possible factors contributing to women's utilization of antenatal care services and to determine whether these services influence her decision regarding the place of delivery, a total of 7005 women who were pregnant at the time of a large cross sectional survey (of 117,465 eligible women from the sampled areas of 28 districts in 14 states) were interviewed in detail. As early reporting of pregnancy in rural areas is rare, further analysis on factors contributing to

antenatal care was carried out on 5344 pregnant women with a gestation of more than 4 months. Of these, 1390 (26.1%) women had no antenatal contact with the ANM and had also not visited any Government health facility during pregnancy for antenatal services or problems. There was a statistically significant reduction in the proportion of women obtaining antenatal care services with increasing age, parity and number of living children. However, no association was observed with other factors like outcome of previous pregnancy and health facility in the village.

There were large inter-district variations in perception about what needs to be done during pregnancy. In addition, majority of women who utilized (91.7%) as compared to those who did not utilize (61.7%) antenatal care services mentioned the need for taking tetanus toxoid injections and iron folic acid tablets (80% *vs* 50%) during pregnancy. Nearly one third of women without antenatal care expressed that nothing needs to be done when pregnant (Fig. 17). Need to register with ANM or to visit any health facility, primary or higher level was also mentioned by comparatively fewer women with no antenatal care. On the whole awareness about problems that could occur during pregnancy was significantly higher in women who had availed antenatal care services than in those who had not. More than half the pregnant women who had availed services mentioned at least one problem as compared to nearly one third of women with no antenatal care; fewer women in both groups mentioned complications that could impinge on the life of the mother and child namely bleeding or loss of foetal movements. In both the groups about 14% had not decided about place of delivery; 51.7% of women with antenatal care preferred institutional delivery as compared to 27.6% who had not availed antenatal care services (Fig. 18). The study indicates that there is a need for improving community awareness on maternal health and to motivate women to utilize maternal care services.

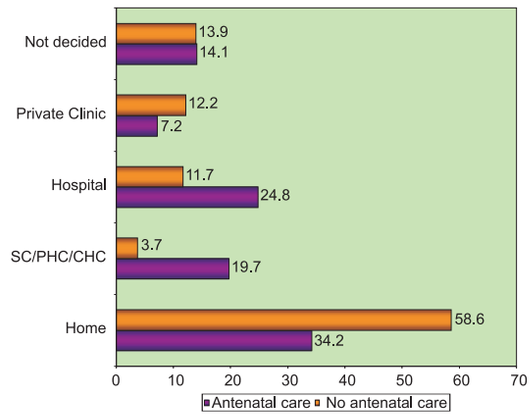


Fig. 17. Decision about place of delivery in relation to antenatal care services

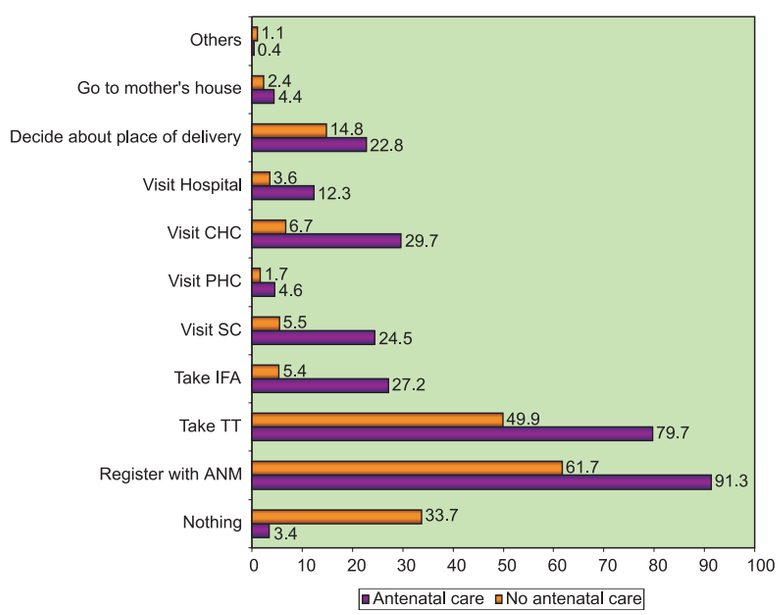


Fig. 18. Antenatal care services availed by pregnant women

Menopause

Prevalence of Osteoporosis in Indian Women

In post-menopausal women an accelerated bone loss occurs which ranges from 1 to 5% per year. Dual energy X-ray absorptiometry (DEXA) is the "gold standard" for measuring bone mineral density (BMD). Study has been initiated to determine the prevalence and develop norms for determining osteoporosis in Indian women. Bone density is being measured by ultrasonography (USG) of the foot (calcaneum bone) and DEXA of the hip and spine. To date 450 women between ages 25 to 75 yrs (100 women in each 10 year period and 50 women between 65-75 yr age group) have been enrolled. Sixty women diagnosed having osteoporosis have been offered either hormone replacement therapy (HRT) or bisphosphonates along with calcium and vitamin D or only calcium and vitamin D. They are also being monitored for bone turnover and associated markers including urinary carboxy terminal collagen telopeptide (CTx) levels, serum osteocalcin, vitamin D and plasma concentrations of intact parathyroid hormone. Interim data revealed significant correlation between the urinary CTx values and BMD. The levels of serum osteocalcin, vitamin D and plasma intact PTH levels were within the normal range. Women's acceptance of treatment, side effects and improvement in bone density, if any, are also being analysed. Individual and group counselling services regarding osteoporosis are held regularly at the "Elderly Women's Clinic".

Biochemical Markers for the Early Diagnosis of Osteoporosis

The biochemical markers of bone turnover include osteocalcin (OsC) and bone specific alkaline phosphatase (BSAP) which are the bone formation markers and urinary carboxy terminal collagen telepeptide (CTx) and pyridinium cross-links [pyridinoline (Pd) and deoxypyridinoline (Dpd)] which are bone resorption markers. These markers reflect the overall skeletal bone loss and are early indicators of response to therapy. Study was initiated to establish baseline data in Indian women for the biochemical indices of bone turnover. Serum OsC, urinary CTx and associated parameters [serum calcium, phosphorous and parathyroid hormone (PTH)] were estimated in samples from 206 healthy women in age group of 20-60 yrs and 62 menopausal women who received anti-resorptive therapy.

Preliminary data reveal that across every ten-year age group there was an increase in the levels of PTH, OsC and CTx indicating age related changes in the bone turnover markers. There was significant elevation in the CTx levels after the age of 35 yr. The calcium, phosphorous and PTH levels were, however, within the normal range. The bone turnover markers, OsC and CTx in women who received antiresorptive therapy showed significant drop (9-14%) within the first three months of therapy. CTx was observed to be a better indicator than OsC for assessing the response to intervention as it showed a significant drop (50%) at six months of therapy. The other two markers BSAP and Dpd are being estimated in these samples and data analysis is in progress.

Molecular and Cellular Mechanism regulating Osteoporosis and the Role of Pro Inflammatory Cytokines in Bone Loss

Cytokines are responsible for the accelerated bone loss following loss of sex steroids. To study the mechanism of action of accelerated bone resorption during menopause, immunoassays were standardized for interleukin 1β (IL1β), interleukin -6 (IL-6) and tumour necrosis factor (TNFα). The cytokine levels were estimated by ELISA in a small study population comprising 56

premenopausal, perimenopausal and post menopausal women. Initial results indicate that IL-6 is a better indicator of bone turnover in these women.

CHILD HEALTH

Home Based Management of Newborn and Young Infants

Current infant mortality rate in India is 70/1000 live births and two thirds of these are neonatal deaths. The single most important cause of newborn deaths in India is sepsis. Birth asphyxia, birth injuries and prematurity are the other major causes of neonatal deaths. According to the National Family Health Survey II (1998-99) almost two-thirds (65%) of deliveries take place at home. Thus, to bring further reduction in infant mortality, it is important to develop and deliver newborn care package at home level. The effectiveness study of a package of home-based interventions delivered by a trained community based newborn care workers (either *Anganwadi* worker or Community based worker chosen by community) in reducing mortality of neonates and young infants (<60 days) has been initiated in the rural communities through a multi-site field trial in collaboration with the existing primary health care system. The proposed package of home - based interventions will consist of: care of the infant at birth, care of normal and low birth weight babies, treatment of local infections, referral of sick infants, health education, provider-partnership and community participation.

National Neonatal-Perinatal Database

National Neonatal-Perinatal Database network was established and a protocol was developed for data collection on neonatal-perinatal morbidity and mortality from peripheral hospitals with the objectives: i) to generate and disseminate prospective data on neonatal-perinatal morbidity and mortality among intramural deliveries at the network institutions and district hospitals, ii) to describe the profile of morbidity and mortality of extramural neonatal admissions, iii) to use the data on neonatal-perinatal health for quality improvement of newborn care at the participating centres, and iv) to develop fetal growth charts for classifying babies as small for date, appropriate for date and large for date. As a capacity building project the Council is supporting 13 National Neonatology Forum (NNF) centres (for tertiary level hospitals), and 9 HRRCs (for secondary level hospitals) for collecting data on intramural deliveries, extramural births and maternal parameters on structured format. Data collection has begun at NNF centres from January 2002. The salient findings are:

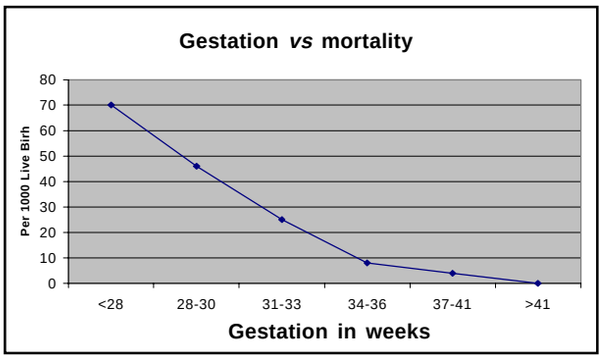
- Data on 16,611 deliveries were recorded at 10 centres. There was an unfavourable female to male ratio of only 855 females per 1000 males. 18.5% births were preterm, 35% low-birth weight, 9.7% small for gestational age and 3.2% multiple gestations (consisting of 489 twin-pairs and 44 triplet sets),

- Non vertex presentation was noted in 17% live births, Meconium stained liquor complicated 9.9% of all live births while fetal distress was detected in 6.3%; prolonged rupture of membranes was reported in 3.9%. Twenty seven percent deliveries were by cesarean section.

- Of the 16,611 live births for whom data on Apgar scores were available, scores of <7 at 1 min were documented in 7.7%, while 3.3% continued to have

scores of <7 at 5 min of life. Administration of oxygen was the most commonly used resuscitative measure in 10.1%, followed by bag and mask ventilation in 5.7%. Intubation for meconium was resorted to in 3.3% neonates while intubation for other indications was needed in only 1.9% babies. Chest compressions were used to resuscitate 0.84%, while use of medications was resorted to in just 0.73%.

- Cephalhematoma was the commonest (0.57%) birth trauma .Respiratory system morbidity figures indicate the incidence of hyaline membrane disease and meconium aspiration to be 1.49% and 2.28 respectively, while transient tachypnea was seen in 1.28% neonates. Amongst disorders of the central nervous system, hypoxic ischemic encephalopathy occurred in 2.28% neonates; seizures in 1.06% and intraventricular hemorrhage in 0.5%. The commonest congenital malformations were cardiac in nature (0.57%) followed by limb defects (0.35%). The incidence of hyperbilirubinemia, hypoglycemia, retinopathy of prematurity and polycyathemia was 5.1%, 1.4%, 0.11% and 0.98% respectively. Conjunctivitis was the most common superficial infection affecting 1.33% neonates.
- The incidence of systemic infection was 9%; of which 36.9% were culture positive sepsis. Septicemia (85.9%) was the commonest clinical category of systemic infection among the 1941 infected neonates, followed by pneumonia in 17.55 of them. Meningitis was diagnosed in 11.2% of them. There was no case of tetanus neonatorum.
- Just over a fifth (21.3%) of all infants received nursery care. Antibiotics were used in 8.1% neonates, and oxygen therapy in 6.6% while phototherapy was given to 4.8% of neonates. Assisted ventilation was provided to 2.1% and total parenteral nutrition to 1.3% of all neonates. While 94.5% of infants were discharged home, 3.2% died and 2.2% left against medical advice.
- There were 528 neonatal deaths amongst the 16,611 live-born, thus the neonatal mortality rate (NMR) was 31.7 per 1000 live births. Of those who died in the neonatal period, 62.9% died within one week and 37.1% died beyond the first week. NMR was associated with gestation at birth and birth weight (Fig.19).



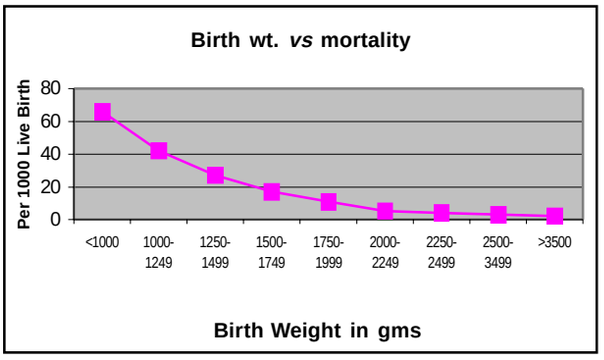


Fig. 19. Neonatal mortality in relation to gestation at birth and birth weight

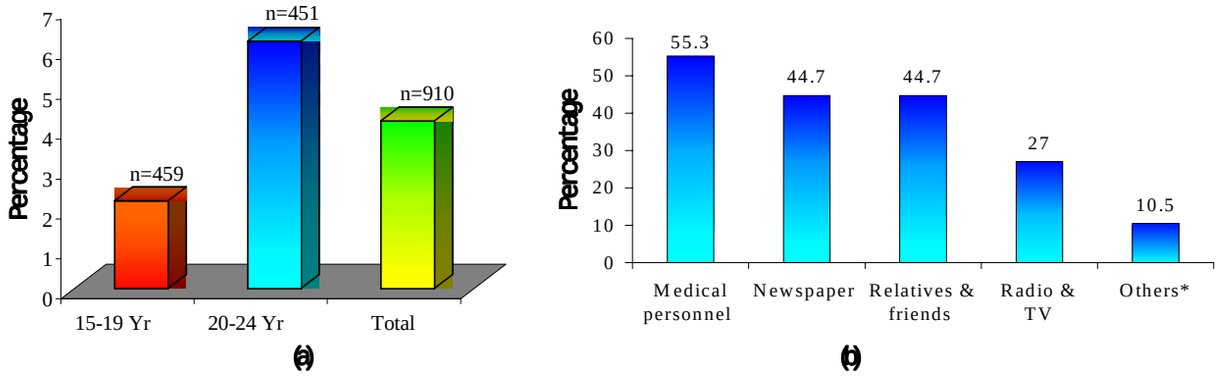


Fig.20. (a) Awareness of emergency contraception (EC) among adolescents and youth (b) Sources of EC information (*magazines and books).

ADOLESCENT REPRODUCTIVE HEALTH

Knowledge, Attitude and Felt Need of Emergency Contraception among Adolescents and Youth

A study has been initiated to assess knowledge, attitude and felt need for EC among adolescents and youth, health care providers, parents and teachers, women health advocates, NGO`s and drug store owners in and around Mumbai. The information was collected through quantitative and qualitative methods *i.e.*, questionnaires and focus group discussions through questionnaires. Information was obtained about attitudes towards sexuality, contraception, abortion, perception about EC; need, reasons for use and acceptability, benefits and risks, perceived advantages and disadvantages of EC; preferred strategies to disseminate information and need, means and feasibility to introduce EC in the family welfare services.

The results are based on data collected from 910 adolescents and youth (15-24 years). Adolescents and youth, males and females, were equally represented among the study population, and 98.2% were unmarried. About 84% were doing graduation, 11.8% higher secondary studies and 4.3% were in secondary school. Majority (43.7%) of them had monthly income of Rs 10,000/- and above. About 85% of adolescents and youth were aware of condom and 52.6% knew how to use it. More than two-thirds were aware of oral pills and 36.4% knew how it is used. Majority (75.8%) of adolescents and youth opined that in addition to married people, contraceptive services should be available to unmarried people also. About 65% of them felt that abortion affects the health of women adversely whereas 85.1% of adolescents and youth were not aware of MTP Act. The overall awareness about EC was low, (about 4.2%) (Fig. 20a). It was higher in sub-urban (6.1%) than urban (4.4%) and rural (2%) areas. Awareness of EC was higher among married adolescents and youth (12.5%) as compared to unmarried (4%). The main sources of information were medical personnel, relatives and friends, newspapers, radio and television (Fig. 20 b).

NUTRITION

Research in various fields of nutrition was continued at the National Institute of Nutrition (NIN), Hyderabad during the year. Need-based research has been the hallmark of the Institute's activities over the years. As in the past, several research projects have been undertaken to fulfill the requirements of the nutrition policy of the country. The National Nutrition Monitoring Bureau (NNMB) continued the assessment of major nutrient deficiency disorders of vulnerable groups and initiated estimation of serum vitamin A, haemoglobin and iodine content in salt in 10 states. Studies were also conducted on bone density in women, technology development for food fortification, postponement of cataract development by diet, diet and non-communicable diseases and food and drug toxicity. Molecular analysis of WNIN/ob rats and their genetic typing was continued at National Centre for Laboratory Animal Science (NCLAS), Hyderabad.

COMMUNITY STUDIES

Nutrition Profile of Indians in Uttar Pradesh

Assessment of nutrition profile of the rural community in 63 districts of Uttar Pradesh revealed that the average intake of cereals, millets and pulses in the population was satisfactory, while that of milk, sugar and jaggery was less than the recommended dietary allowances (RDA). The mean intake of all the nutrients except energy, protein and calcium was less than the RDA. Only about 64% of the households were consuming adequate amount of both energy and protein. In general, about 52% preschool children were undernourished (Fig. 1). The prevalence was >50% in 34 of the 63 districts surveyed. About 42% of adult males and 34% of adult females had chronic energy deficiency .

Health and Nutrition Status of Tribals in Orissa

A comprehensive assessment of health status and health care delivery was undertaken by RMRC, Bhubaneshwar in two primitive tribes, *Bondo* and *Didayi* in Malkangiri district of Orissa to obtain a first hand information on various health problems and diseases calling for specific medical intervention in order to augment the present health care delivery system. Anaemia was found to be the most important clinical finding (Fig. 2) in the population followed by fever and other diseases such as malaria. The nutritional status based on anthropometric indices revealed that 6.5% and 5.9% of children (0 - 14 yr) had severe stunting, 21.1% and 19.7% had severe wasting and 21.2% and 18.8% had severe underweight in *Bondo* and *Didayi* population respectively. Health care deliveries in these areas are very poor, situated in inaccessible

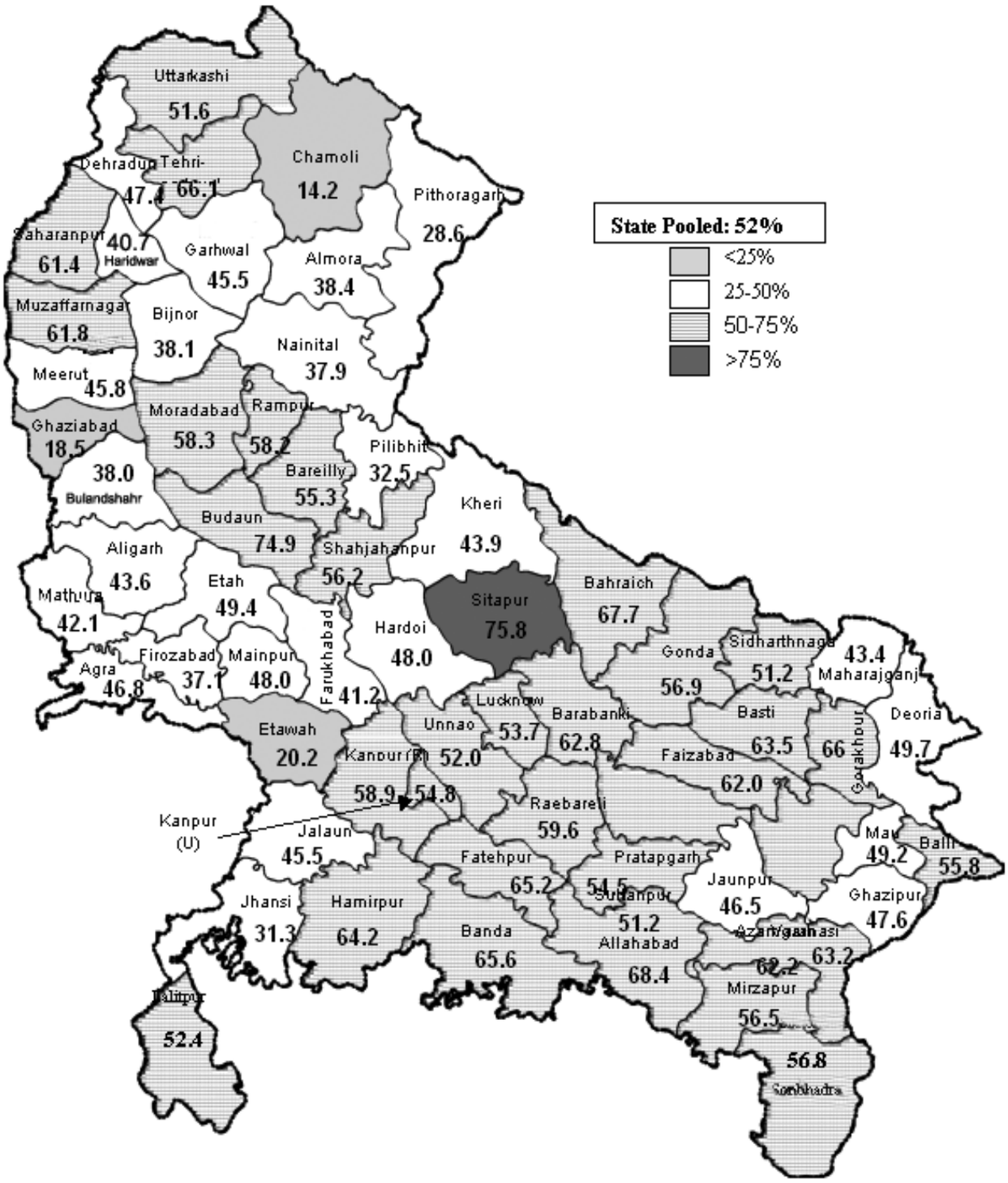


Fig 1. Map showing distribution (%) of prevalence of underweight (< -2SD weight for age) - among pre-school children in Uttar Pradesh and Uttaranchal.

forest and hilly areas which lack in basic infrastructure and amenities. The health culture and health related behaviour is still rudimentary in these areas/tribal communities. They still practise their own traditional belief, custom and practices.

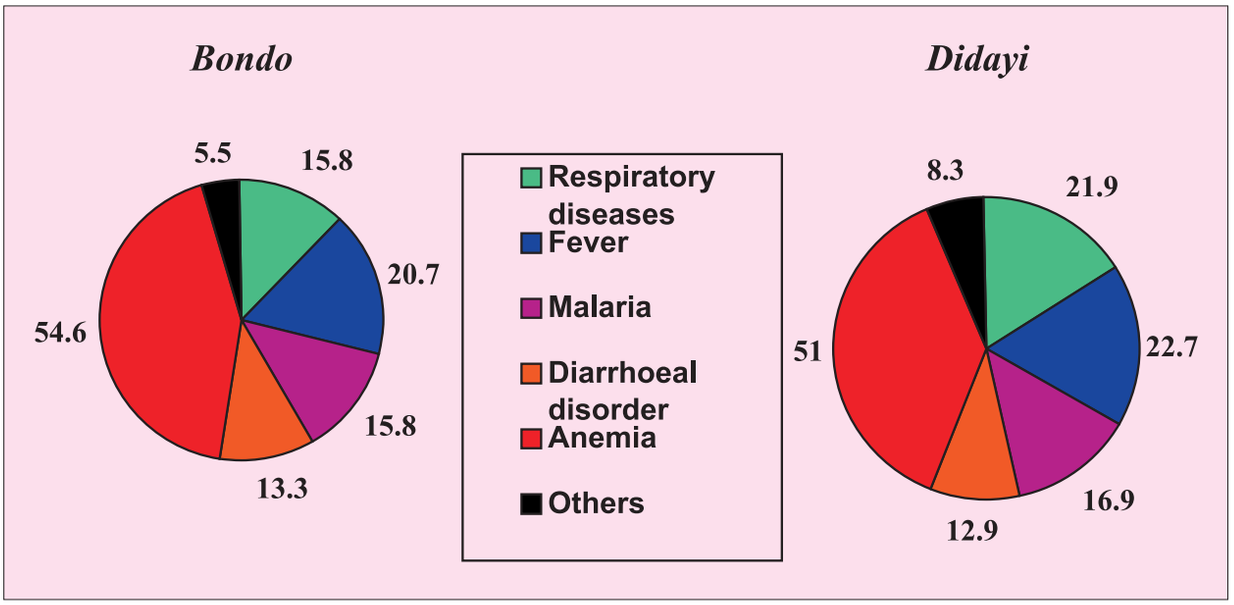


Fig. 2. Morbidity status in *Bondo* and *Didayi* tribes

Health and Nutrition Profile of Elderly Tribal Population of Orissa

Study was carried out by RMRC, Bhubaneshwar in elderly (>60 yr) population of three major primitive tribes, *Paudi Bhuniya*, *Kutia Kondh* and *Lanjia Saura* with the objectives to assess their socio-economic status, morbidity pattern, status of malnutrition, dietary habits and food intake patterns. The results revealed that these groups are socially weak , poor and illiterate with low living standards. Average intake of foodstuff and all nutrients (except vitamin A) was less than the recommended allowance (RDA). Anthropometric measurements indicated low nutritional status and chronic energy deficiency (CED). The prevalence of CED was 60% in *Kutia Kondh* and 70% in *Paudi Bhuniya*. Anaemia was observed in around 90% of the elderly population; females were found to suffer more with moderate and severe grades of anaemia compared to their male counterparts. About 20% of the elderly had different grades of hypertension. The confounding factors of malnutrition were found to be social isolation, illiteracy, poor communication and utilization of health care services and food insecurity, all of which need to be improved.

Nutrition Profile of Tribals of Madhya Pradesh

The *Baigas* are one of the most backward tribes of M.P. The RMRC, Jabalpur conducted study for assessment of nutritional profile of children in this tribe. The data indicated that 28.9% children in the age group 1 - 3 yr are severely malnourished (Fig. 3). Only 5.5%

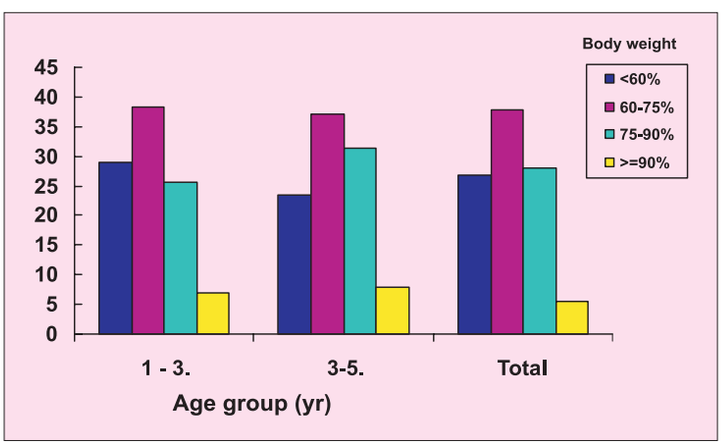


Fig. 3. Nutritional status of *Baiga* children (n=217)

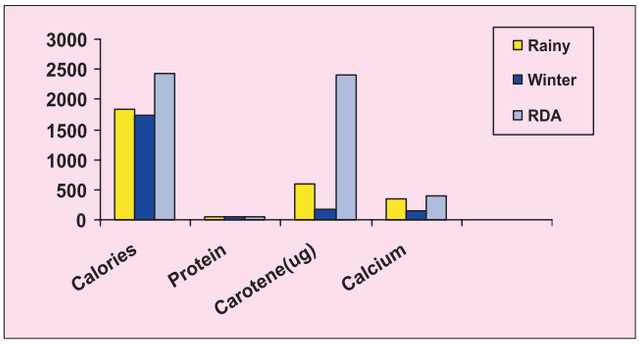


Fig. 4. Average nutrient intake (per day) by tribal children

children were found normal in this tribe. About 77.3% adult population had chronic energy deficiency, only 0.33% adults had body mass index>25 and about 8% had vitamin A deficiency (Bitot's spot, night blindness and conjunctival xerosis). Vitamin B complex deficiency was found in 0.5% individuals. The prevalence of severe anaemia was found to be 3.2%. Fig. 4 and 5 depict the intake of calories, iron, carotene, riboflavin, fat and zinc which is less than the RDA.

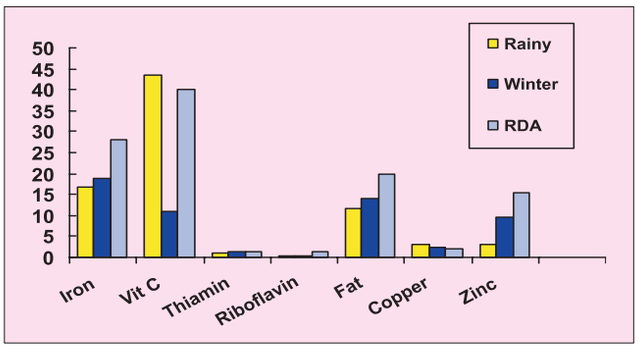


Fig. 5. Average nutrient intake (per day) by tribal children

Health and Nutritional Status of Saharia Tribals of Madhya Pradesh

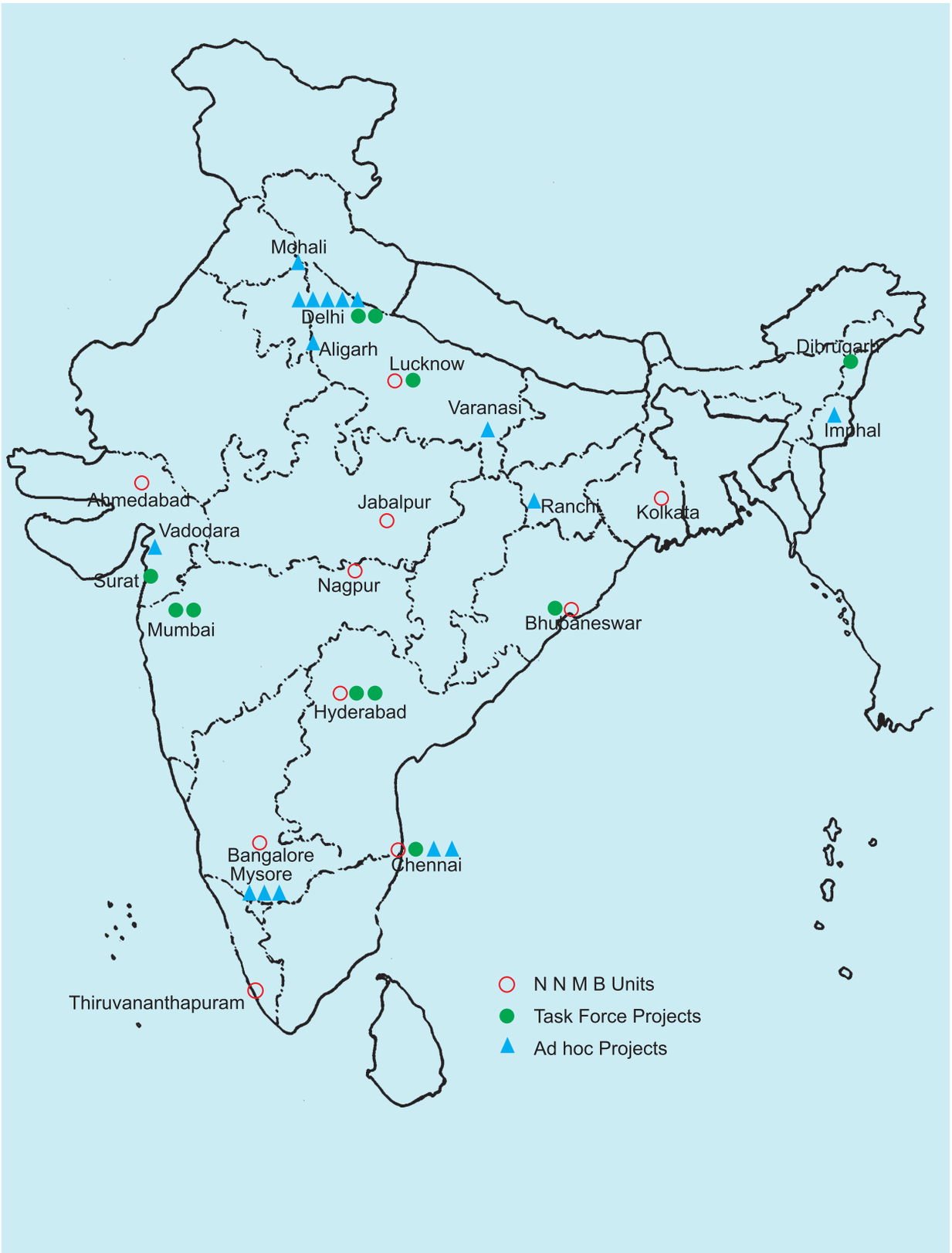
Study was undertaken by RMRC, Jabalpur in *Saharia* tribals for determining of their nutritional status. The study indicated that majority of the preschool children (93.5%) are under-nourished. Moderate to severe under-nutrition was seen in 59.5% children. Severe under-nutrition was observed in 15% children. Prevalence of under-nutrition in preschool children (Fig. 6) in terms of under-weight, stunting, and wasting (weight for age, height for age and weight for height below -2SD respectively) was 74.3%, 75.4% and 20% respectively. Forty-four percent of the surveyed population had signs of anaemia. Vitamin A deficiency was observed in 8.2% children while vitamin B complex deficiency was observed in 2.6% and vitamin D deficiency in 7.8% children.

Fig. 6. An under-nourished *Saharia* child

CLINICAL STUDIES

Women's Work and Bone Health

Bone-loading postures adopted during exercise are recommended for bone density improvement. However, the stimulation of bone turnover during prolonged bone loading postures in the absence of calcium intakes might prove to be deleterious for bone health.



MAJOR ICMR RESEARCH PROJECTS IN NUTRITION

Earlier studies showed that despite low calcium intakes standing or standing with load bearing/bending postures are better for hip densities when compared to the sitting postures at work. However, in the case of spine, standing and bending postures significantly reduce bone at the spine, but sitting postures do not worsen the spine bone densities. Using the WHO classification for diagnosis of osteoporosis, the onset of osteoporotic changes around 40 yr of age in the low socio-economic group was seen in spine (-2.27), hip (-1.7), forearm (-1.53) in this order. All the women from the low socio-economic group were found to have increased osteoclastic activity (indicated by acid phosphatase), but those with spinal osteoporotic changes are worse off on all the biochemical indicators of bone loss.

FOOD FORTIFICATION - TECHNOLOGY DEVELOPMENT

Food fortification is one of the important strategies accepted in the National Nutrition Policy to achieve the goals of controlling anemia in the country. The NIN has made considerable progress towards realizing this goal by developing new technology.

Double Fortified Salt

Encapsulated source of iron (MI formula) was found to keep iodine in a stable form in double fortified ordinary common salt, while the NIN formulation, using sodium hexa meta phospate as the stabilizer, required high quality salt for providing adequate iodine content of 15 ppm in double fortified salt.

Double Fortified Sugar

A laboratory based technology for fortification of sugar with iron and iodine has been developed. This technology showed good stability of iodine in the presence of various chemical sources of iron.

Double Fortified Wheat Flour

A laboratory based technology for fortification of whole-wheat flour (as per the Prevention of Food Adulteration Act) with iron at 25 and 50 mg/kg and folic acid at 220 µg/kg was developed. The two indigenous sources of iron that met the criteria as a chemical source of iron were anhydrous ferrous sulfate and H-reduced iron powder. The percent *in vivo* bioavailability in adult male human volunteers was three times higher with anhydrous ferrous sulfate compared to H-reduced iron powder.

STUDIES ON MICRONUTRIENTS

Nutrient Composition of New Varieties of Rice

Eleven varieties of rice obtained from the Directorate of Rice Research, Hyderabad were analyzed for proximate composition. The protein content in them was higher than 8g as against 6.8g found earlier (Nutritive Value of Indian Foods). In one of the varieties, it was about 12g. Consumption of such high protein rice could increase the protein intake of individuals by 8 to 9 g/day. This perhaps explains the gradual improvement in protein energy malnutrition status in the country, despite little changes in Indian dietaries intake.

Dietary Micronutrients in Ageing and Chronic Diseases

Studies conducted on WNIN female rats have shown a correlation between maternal micronutrient status and predisposition of the offsprings to insulin resistance in later life.

In another study on rats, it was found that restriction of both dietary micronuteints as well as calories had adverse effect on fasting

glucose and insulin and homeostasis model of assessment of insulin resistance (HOMA IR index) as compared to group with calorie restriction alone. It was also found that antioxidant status was better and oxidative stress low in rats of 'calorie restricted' group as compared to calorie and micronutrient restricted group. The results of the study confirmed the role of micronutrients in modulating oxidative stress.

Postponement of cataractogenesis by diet restriction is in part due to improved antioxidant status and/or enhanced protein editing. In a study the effect of long term restriction of diet/food, protein and vitamin on the aggregation of crystallins and α-crystallin chaperone activity in rat lens *vis a vis* cataractogenesis was assessed. Food and protein restriction lowered the susceptibility of α - and γ-crystallins towards aggregation while vitamin restriction tended to increase the aggregation of crystallins (Fig. 7). Interestingly, vitamin restriction improved chaperone activity of α-crystallin.

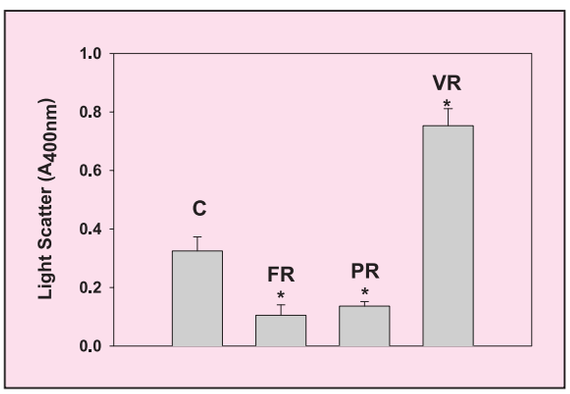


Fig. 7. Oxidation-induced aggregation of α_L-crystallin. 0.5 mg/ml α_L-crystallin from control (C), food restriction (*FR*), protein restriction (*PR*) and vitamin restriction (*VR*) groups.

DIET AND NON-COMMUNICABLE DISEASES

ARI Activity in Foods and Cataract

Diabetes mellitus advances onset and progression of cataract probably by modulating oxidative stress and glycation. Aldose reductase is important in diabetic cataractogenesis. Aldose reductase inhibitors (ARI) are valuable in delaying/preventing it. Screening of extracts of curcumin, *amla*, bitter gourd, fruits and *tulsi* leaves revealed significant ARI activity of the plants extracts. Curcumin appears to inhibit AR in a non competitive manner. Ongoing studies have shown that extract of black tea (but not green tea) significantly inhibited the glycation of purified bovine lens α- crystallin *in vitro*. Significant anti-platelet aggregation activity was also observed in water extracts of eight varieties of green leafy vegetables.

Dietary Fatty Acids and Insulin Resistance

Dietary fatty acids are known to affect the risk of chronic diseases particularly of diabetes and cardiovascular diseases. Adequate intake of essential poly unsaturated fatty acids (PUFA) namely linoleic (18:2n-6) and α-linolenic acids (18:3n-3) and their optimal balance (n-6/n-3 ratio ~ 5-10) is considered necessary for healthy heart. Studies were undertaken to investigate the effect of dietary fatty acids on membrane lipid composition and insulin sensitivity in target tissues (skeletal muscle and adipose tissue) of experimental rats.

Dietary saturated fatty acids (SFA) and trans fatty acids (TFA) were found to reduce insulin sensitivity in target tissues (skeletal muscle and adipose tissue). The effects of TFA were more marked than SFA. The current evidence indicates that the atherogenic effects of TFA can be prevented by increasing dietary linoleic acid. However, studies show that increasing dietary linoleic acid did not prevent TFA induced decrease in insulin sensitivity. On the other hand, increasing dietary α–linolenic acid and decreasing n-6/n-3 ratio to 2 increased insulin sensitivity in target tissues in diet induced insulin resistant rat model.

Resistin as a Molecular Link between Diabetes and Obesity

Obesity has a strong patho-physiological association with non-insulin dependent diabetes mellitus. However, the molecular link between obesity and diabetes remains to be resolved. Resistin, a cysteine-rich secretory protein, identified from mouse adipocytes, is down- regulated by anti-diabetic drugs like thiazolidinediones. Mouse and human resistins differ greatly not only in their sequence and structure but in their regulation and function also.

To understand the molecular features of resistin genomic counterpart of resistin encompassing the transcriptional start and translational stop from mouse and human was amplified and sequenced. Exon/intron boundaries of mouse and human were demarcated using DIALIGN algorithm. The mouse sequence was found to have an additional intron of 2279 bp (intron X), which is absent in human resistin. *In silico* analysis revealed a number of transcription factor binding sites. Of particular importance was the presence of PPAR responsive element (PPRE) along with the binding sites for other transcription factors like Ap1, NFkB and C/EBP. The binding of PPAR/RXR complex to PPRE present on intron X was shown by gel shift assays. Functional relevance of this DNA-protein interaction was demonstrated by transient transfection assays using luciferase as a reporter.

To address the structure-function relationship, human resistin was cloned, expressed and purified from *E.coli* system. The recombinant protein, although showing single band on MALDI TOF, displayed a concentration-dependent oligomerization as evident from size exclusion chromatography. The oligomeric structure was SDS-insensitive but ß-mercaptoethanol sensitive, pointing to the importance of disulfide linkages in resistin oligomerization. Intrinsic fluorescence remained unchanged in presence or absence of 8M urea. However, a significant shift was observed in presence of 20% β-mercaptoethanol. CD spectrum, very interestingly, revealed a concentration dependent reversible shift from alpha helical to beta sheet structure. These results indicate that cysteine residues involved in disulfide bond formation stabilize the native structure even in presence of 8 M urea.

FOOD AND DRUG TOXICITY

Application of Hazard Analysis Critical Control Point (HACCP) to Animal Products

HACCP is a preventive system to reduce microbial hazards. A study on HACCP was carried out in prawns. The samples were found to be contaminated with pathogenic microorganisms immediately after harvest and also at the market place. However, recipes prepared from prawn were free from pathogenic organisms. While pond water samples were contaminated with microorganisms including *Vibrio* sp., feed and ice samples used for preserving were free from pathogenic organisms. Every step in food chain has to be thoroughly investigated for identifying the source of contamination to ensure food quality and safety. The significance of the present study is that the pond water is the source of contamination. Hence, HACCP needs to be practiced during the entire food chain from pond to plate and not only at the export processing units.

Utilization of Mouldy Sorghum for Animal Consumption

A study was conducted to assess the feasibility of utilizing lactic acid bacteria, through natural fermentation, to detoxify contaminated sorghum and convert it to a value added animal feed ingredient.

The laboratory trial of production of *Lactobacillus* fermentation of mouldy sorghum with addition of locally available resources (e.g. *Casia tora* seeds) was tested at village level by feeding it to cattle. The acceptability was monitored in terms of feed consumption which was correlated with milk output.

NUTRITION AND CANCER

Studies on Ginger

Non nutrient components of diet have been shown to inhibit carcinogenic process by enhancing the intracellular levels of xenobiotic metabolism enzymes which play an important role in detoxification pathway. Spices and their active principles have been shown to possess chemopreventing properties. Studies done at NIN on modulation of xenobiotic metabolism by ginger showed that its feeding to rats resulted in stimulation of glutathione-S-transferase in liver, intestine, lung and kidney suggesting that regular intake of ginger can enhance the detoxification enzymes and thereby afford protection to host against tissue damage induced by exposure to xenobiotics.

Effect of Vitamin Restriction and Supplementation on Rat Intestinal Mucosal Cell Apoptosis

50% vitamin restriction was found to increase the oxidative stress and decrease the anti-apoptotic protein (Bcl-2) expression thereby enhancing the apoptotic rates while vitamin supplementation reversed the changes caused by vitamin restriction. Among the individual vitamins, vitamin E showed maximum decrease in oxidative stress, as well as decrease in apoptotic rates.

OTHER STUDIES

Molecular Analysis of WNIN/Ob Rats

The study on the candidate gene involved in obese rats was conducted at NCLAS, Hyderabad in collaboration with IISc., Bangalore . It showed that leptin receptor gene was not altered in these rats, as per the evidence on coding regions as well as m-RNA levels of various splice variants of the Ob-R gene.

Genetic Typing of Obese Rats Using Micro-Satellite Markers

A study has been initiated at NCLAS for genetic typing of WNIN/Ob and GR-Ob strains using micro-satellite markers. These markers span all the 22 chromosomes (including sex chromosomes) of the rat and the mutants will be typed along with the parental strain WNIN, related strain WKY and unrelated strain Fischer 344. Out of 100 markers selected for the study (4 markers/ chromosome), 22 markers were completed and unique markers typical of each strain could be observed.

PCR based DNA Fingerprinting in Obese Rats

The PCR based DNA fingerprinting using random primers was done at NCLAS in obese rats. The results yielded a unique DNA fingerprinting profile for homozygous obese rats which is different from its other phenotypes and other standard reference strains. This has been submitted for patenting.

ENVIRONMENTAL AND OCCUPATIONAL HEALTH

The Council's National Institute of Occupational Health (NIOH), Ahmedabad and its two regional centres at Bangalore and Kolkata are engaged in identifying and mitigating the occupational and environmental health problems in the country. The tools used for this purpose are research, education and development of the trained manpower and information dissemination. During the year under report, studies were undertaken to evaluate the effect of lead on puberty, development, pesticide poisoning resulting from repeated consumption of contaminated food in MP and Gujarat, usefulness of gloves for tobacco harvesting processes in Gujarat and Andhra Pradesh and health problems of women workers of fishing industry, child labour in gem polishing industries and rickshaw pullers of eastern India.

Effect of Lead on Adolescent Development and Puberty

An Indo-US collaborative long-term follow-up study was carried out in school children of Ahmedabad and Kolkata from 1997 to 2001 with the objective to investigate the effect of lead on growth and adolescent development and puberty in children exposed to auto exhaust pollution in Ahmedabad and due to pollution from smelting plant in Kolkata. Medical examination and anthropometric measurements were done in 1206 school children (10-14 yr old) in Ahmedabad and 705 children (9-15 yr old) in Kolkata. Special investigations like lead in blood, haemoglobin estimation and sexual maturation rating (SMR) was also done and these children were followed up for 3 years. During the first year (collection of base-line data) overall lead in blood was observed to be more than 10 µg/dl in 38.4% children in Ahmedabad and 30.6% in Kolkata. With the introduction of unleaded petrol in the country, a decreasing trend in blood lead levels was observed in follow up studies at Ahmedabad. Multiple regression analysis after controlling for confounding variables such as age, body mass index (BMI), height, skin fold thickness, blood haemoglobin levels and parental education showed that mean score of SMR is negatively associated with blood lead levels. Significant association was found between blood lead levels and SMR on segmental regression analysis.

Biological Markers of Manganese Exposure and Effects in Manganese Miners

An environmental-cum-epidemiological study was undertaken to evaluate exposure and health effects in miners exposed to manganese and to find out whether or not there is a link between chronic low level environmental/occupational exposure (Fig.1) and development of neuro-degenerative changes.

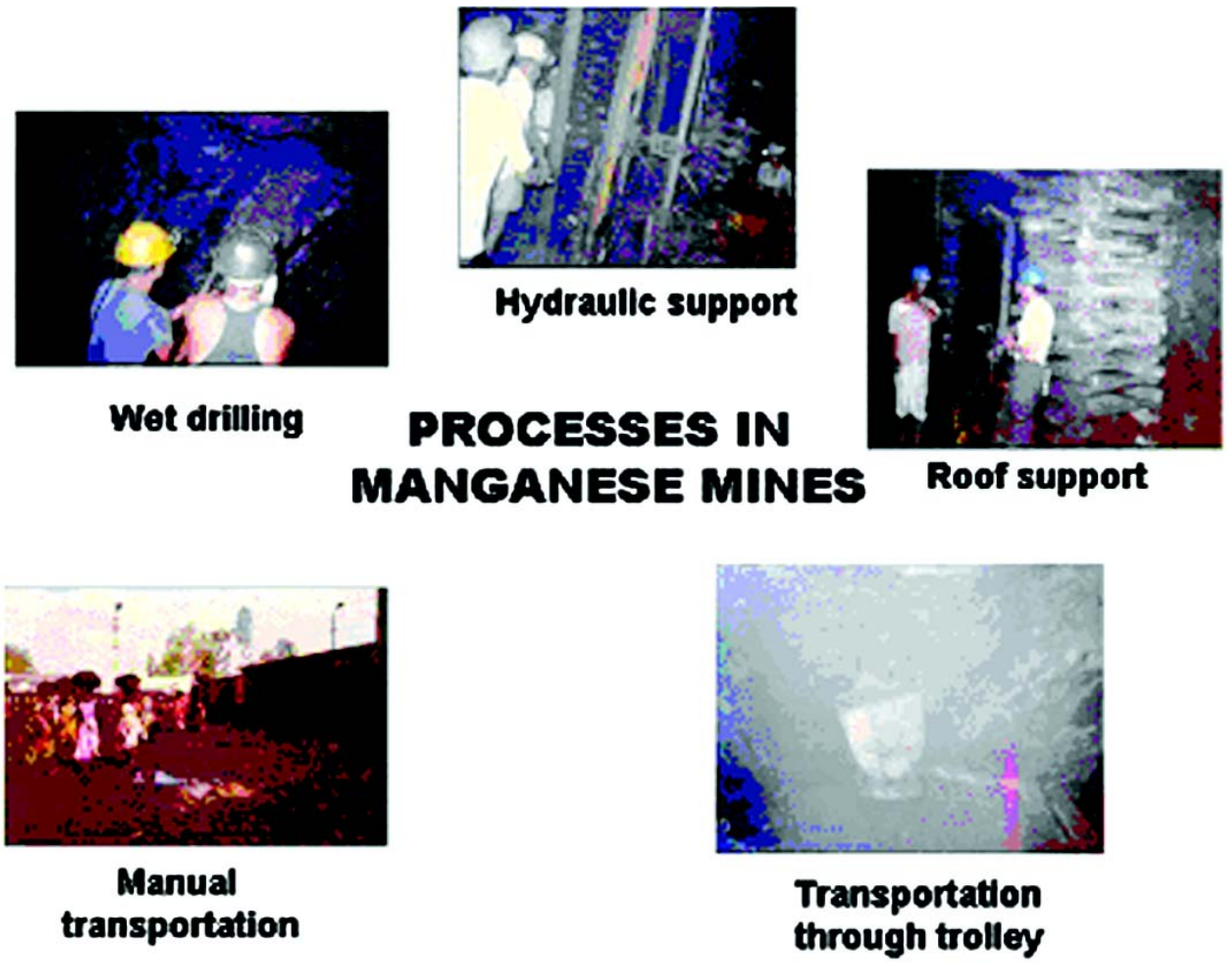


Fig.1 showing various processes in manganese mines

Of the 465 miners (age 35-45 yr.) exposed to manganese for 10-20 yr., 348 were followed up. They were subjected to complete clinical examination, biochemical analysis such as blood manganese levels, SGPT, SGOT, alkaline phosphatase, gamma GT, albumin and pulmonary function testing. Tingling, numbness and headache were the common neurological complaints present in 20% miners only while psychological symptoms such as losing temper easily, worrying without cause and regular insomnia were noticed in about 34% of them. "Draw a line test" revealed that 15.5% had tremors while drawing straight line between two parallel lines. About 70% miners had ≥ 2 μg/dl blood manganese levels.

Popularization of Gloves among Tobacco Harvesters

During the various agricultural processes in tobacco cultivation like topping of plant, disbudding of axillary buds and harvesting of plant and leaves, hands of the workers are soiled with thick gummy plant sap leading to absorption of nicotine through dermal route. Nicotine is known to cause acute toxicity among the tobacco harvesters and repeated small doses may cause chronic toxicity also. To prevent absorption of nicotine, various types of seamless knitted gloves were evaluated. The use of gloves significantly decreased the urinary levels of nicotine and cotinine (Fig.2 & 3).

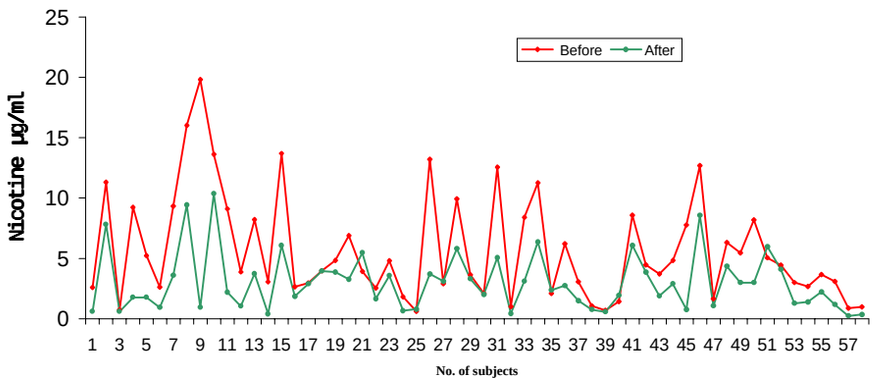


Fig. 2. Urinary levels of nicotine before and after use of gloves

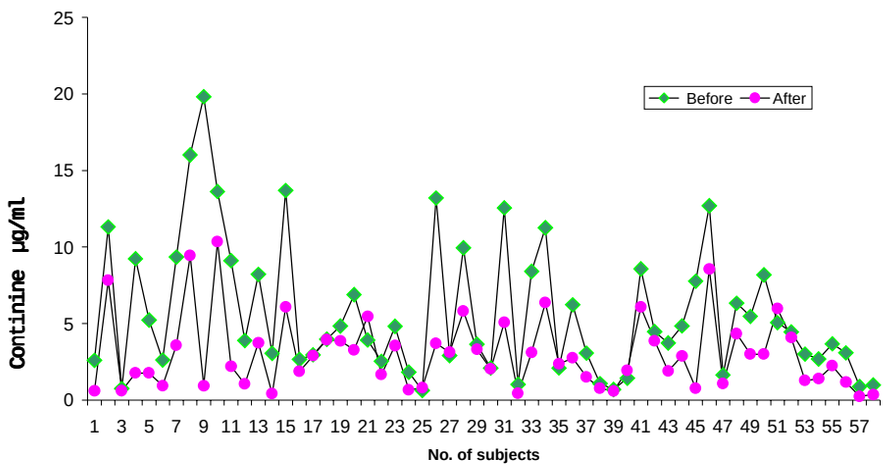


Fig. 3. Urinary levels of cotinine before and after use of gloves

Smearing of gummy plant sap on the hands, abrasions on the palm, peeling of the skin around the nails, bitter taste in food due to plant sap and work related symptoms like headache and giddiness were completely prevented. Among all the varieties of gloves, seamless knitted nylon gloves were found best from the viewpoint of effectiveness as well as durability and suitability (Fig.4).

Fig. 4. Clean hands after the use of seamless knitted nylon gloves

To popularize the use of nylon gloves, their distribution was undertaken with the help of NGOs like Self Employed Women's Association (SEWA) and Tribhuvandas Foundation and Government agencies like Beedi Tobacco Research Station (BTRS) of Gujarat Agricultural University and Central Tobacco Research Institute, Rajahmundry (AP). Each of the 8121 workers has been provided 3 pairs of gloves.

Poisoning due to Endosulfan

During January-February 2002, many newspapers from Madhya Pradesh reported a mysterious illness affecting a group of villagers of Amarpur village situated near Jabalpur. The major signs and symptoms reported were vomiting, altered sensorium and generalized tonic-clonic convulsions followed by unconsciousness. Lack of treatment and superstitions resulted in the death of three children. In the third week, following the onset of illness, 5 adults and 4 children were admitted to Medical College Hospital in Jabalpur and thorough investigation was carried out. Blood samples from affected persons and cooked food samples were collected and analysis of pesticide residues carried out.

All blood samples showed the presence of α-and β-isomers of endosulfan in variable amounts. However, endosulfan sulphate levels (the major toxic metabolite of endosulfan) showed an interesting correlation with the occurrence of convulsive episodes. One of the sweet preparations (*ladoo*) prepared from wheat flour showed extremely high levels of α-endosulfan (676 ppm). This illness was, therefore, confirmed as acute endosulfan poisoning due to contamination of wheat flour. Due to extreme poverty the villagers were found to be using empty containers (Fig. 5) for storage of food materials.

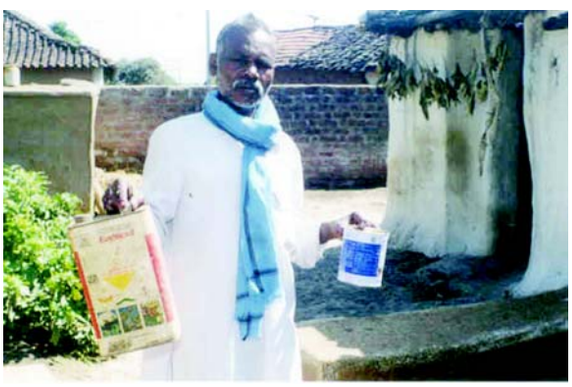


Fig.5. Villager carrying empty pesticide containers used for storage of food material

Thallium Poisoning among Villagers of Western Gujarat

During the year a report was received about the sudden loss of hair and nails of some villagers from Jasapar village of Jasdan *taluka* in Gujarat state (Figs.6 & 7). The affected subjects belonged to three families and all the members except the breast fed children were having loss of hair and nails. Poisoning by some chemicals or toxins, fungal or viral infection was thought of as the possible cause. But no cause for this sudden health effect could be satisfactorily ascertained. Finally, 26 subjects (12 men and 14 women) were examined for symptoms. Headache was the major symptom followed by fall of scalp and body hair. Pain in abdomen, tingling and numbness in the extremities, vertigo and lethargy, sleep disturbance, backache, prevalence of tremors in the fingers of the hand, joint pain and diarrhoea, constipation and hypersensitivity to sunlight and melanism and itching of the skin was reported.

Most had their nails eroded from the proximal end and few had whitish lunular stripes in the nails. The loss of hair and changes in nails along with paresthesia, tremors, weakness, abdominal pain and other gastrointestinal and musculoskeletal symptoms are widely reported in literature due to thallium poisoning. Blood, urine and hair samples obtained from a subject were analyzed for thallium. The thallium content was found to be 1.2063 ppm in blood (normal values 0.1 ppm). On detailed enquiry, it was found that these three families had consumed wheat collected from same point. After two weeks of continuous consumption of the wheat, the subjects observed the loss of hair

Fig.6. Alopecia following exposure to thallium.

Fig. 7. Complete erosion of proximal part of nails of fingers.

and changes in nails. From the clinical presentations and the history of wheat consumption, it was suspected that thallium could be the causal agent, which might have been used as a rodenticide. Accordingly, blood, urine and hair samples were analyzed for thallium content. Finally, the finding of thallium in significant amount in the blood and hair samples obtained from a subject confirmed it to be the causative agent.

Prevention and Control of Occupational Health Hazards among the Salt Workers of Gujarat

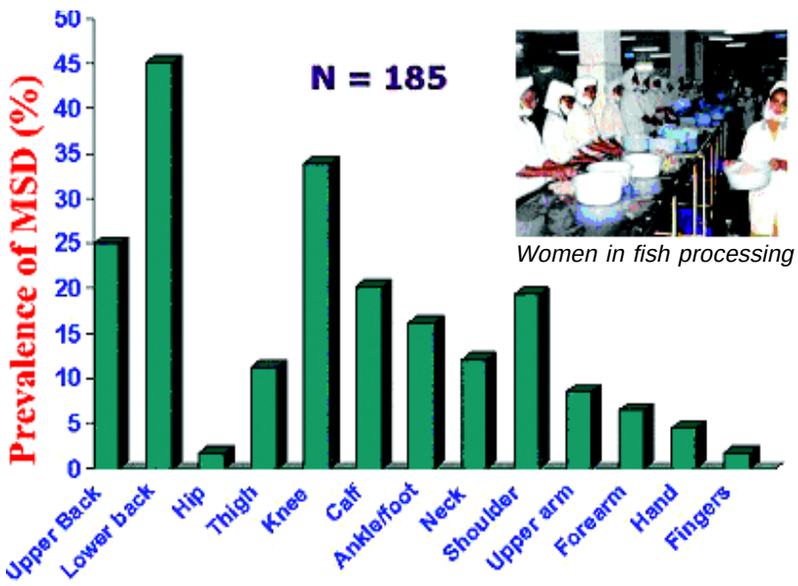
The subsoil brine in the desert areas of the Little Rann of Kutch in Gujarat contains very high salinity (15-20%) as compared to sea water (3.4%). The workers engaged in salt production under the unorganized sector have to stay and work in isolation at the remote sites in the adverse weather of the desert during the work season (October to June). The workers enter barefoot into the brine daily for 6 - 8 hr. during the process of crystal reshuffling. The hazardous effects of intense reflection of sunlight from the salt and a direct effect of sodium chloride dust on mucosa of the eye are responsible for various eye morbidities, whereas the direct contact of feet and hands with highly concentrated salt solution causes skin problems among them.

A study has been initiated by NIOH to find out the prevalence of occupational health hazards in salt workers in general and hypertension and various complications in particular and to identify the causative factor(s) responsible for these health hazards. A total of 441 salt workers (<40 yr) from Kharaghoda in Gujarat were studied. The general complaints like headache and joint and muscular pain were reported by the brine-exposed workers. Major dermatological symptoms (ulceration, palmar keratodermia and burning sensation) and eye complaints (burning of eyes, excessive watering and dimness of vision) were recorded in most of them. However, no evidence of hypertension was seen. Intervention studies after providing gumboots and goggles are ongoing.

Women in Fish Processing Industry - A Work Stress Analysis

Occupational health hazards were evaluated among 185 women workers engaged in four fish processing units. An interviewer-administered questionnaire was used to find out their health complaints.

High prevalence of pain and discomfort was noted among these women. Lower back was the most affected area followed by shoulder and upper back (Fig. 8). Improper hand tools, sustained standing work and poor working conditions are the main contributory



Women in fish processing

Fig.8. Musculo-skeletal discomfort among women in fish processing activities

factors for musculo-skeletal pain and discomfort. Survey reveals that women were exposed to cold environment, chlorinated water and fish meat related bio- agents. They experienced headache, eye irritation and watering of eye during their work. Respiratory irritation and cough during work possibly resulted due to the presence of respiratory irritant in the ambient atmosphere inside the units.

Hands were the most affected part in women who had repeated cut injuries in their fingers. 34% and 72% women reported numbness and blanching of fingers respectively (Fig. 9). Raynaud's phenomenon in fingers and dermatitis in hands and feet were identified among 31% and 9.3% women, respectively. The survey reveals that women in fish processing industry need to wear protective garments/gloves. The scope of work intervention is being explored. Awareness programs on good occupational safety and health practices are being planned. An improved ergonomic intervention may probably be effective in reducing these problems.

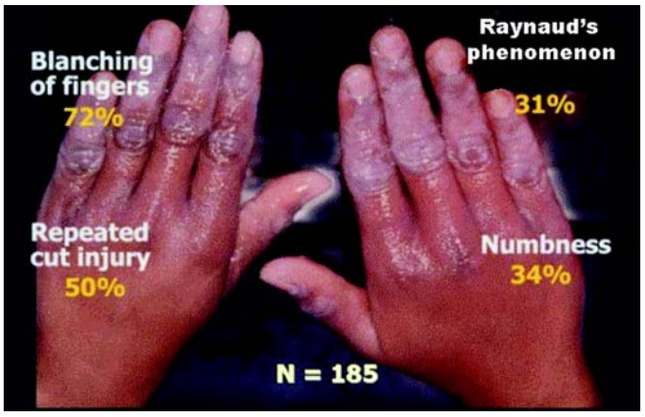


Fig. 9. Raynaud's phenomenon in fingers of women in fish processing activities

Occupational Health Problems of Child Labour in Gem Polishing Industries

In Jaipur, approximately 2 lac people are employed in the organized and unorganized sectors of gem polishing industry. About 10-15,000 children are working in unorganised units where processes expose the children to dust, chemicals and noise (Fig. 10). A study was carried out in these industries with the objectives to assess the health problems in 588 child labour and to evaluate the physical, chemical and ergonomic hazards of the working environment.

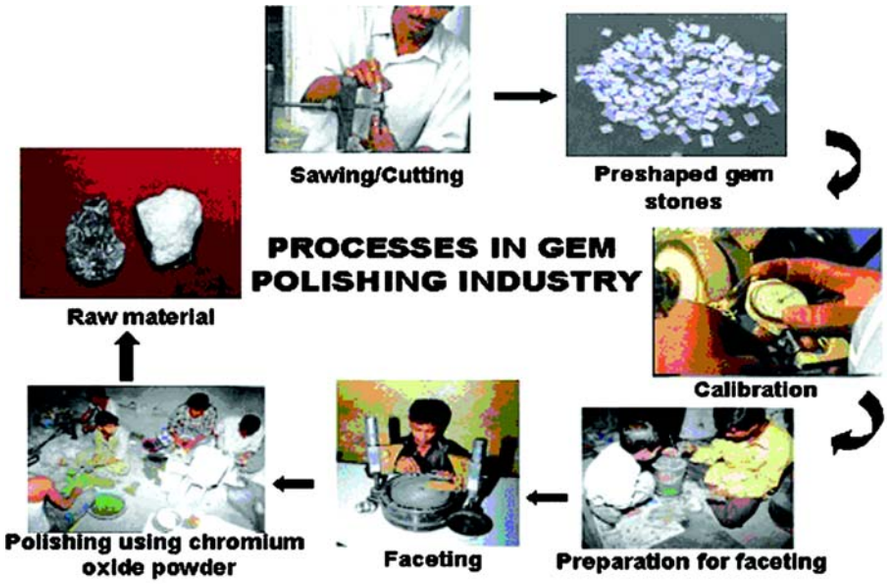


Fig.10. showing various processes in gem polishing industry

About 75% children had one or the other complaint. Respiratory symptoms were found in 27%, eyestrain in 29.5%, headache in 28.8% and repeated finger injuries during work in 37.5%. Exposure to noise and poor illumination was also noted. The respirable dust at

Shaping patio exceeded threshold limits values (TLV), while it was well within TLV at all other sites.

Occupational Health Problems of Cycle Rickshaw Pullers

About 8.5 lakh population is involved in rickshaw pulling in India out of which 2.60 lakhs are in West Bengal. This is the cheapest, non-polluting mode of transport available both in urban and rural areas. The rickshaw pullers are exposed to extremes of environmental conditions. The rate and depth of inspiration increases during rickshaw pulling resulting in increased amount of pollutant inhalation and its reaction with the lung tissues.

Health status of more than 1000 rickshaw pullers working in Kolkata and other urban centres was assessed. The main complaints of the subjects were found to be joint pain, weakness/fatigue, muscular pain, pain in abdomen, low back pain, breathlessness, sputum and cough. Some nutritional deficiency disorders like glossitis, angular stomatitis and anaemia as well as signs of respiratory tract infection were also noted. The PFT revealed restrictive, obstructive and combined type impairments. X-ray knee joint showed a number of cases with osteoarthritic changes. The chest X-ray revealed pneumoconiotic changes in the lungs of the subjects.

The results so far obtained indicate that benzene level were high in zones near rickshaw stands. Respirable dust level in different traffic zones in Kolkata indicated higher values (mean 274.3 $\mu g/m^3$).

The ergonomic study indicated that the design of the existing rickshaw did not match well with the body structure and dimensions of the rickshaw pullers. It has also been observed that the design of rickshaw all over the country is not uniform with the same pulling principle. Further redesigning studies have been taken up for acceptability and use by rickshaw pullers all over India.

Database Generation, Documentation and Information Dissemination for Hazardous Processes/ Chemicals

The NIOH is collecting information from various states on industries involved in these hazardous processes to provide likely estimates of workers exposed to these hazards. During the year under report data was collected from Mumbai (Maharashtra). There are about 9,779 registered industries in the city of Mumbai. About 1,913 (19.6 %) of them (with 62,798 workers) are involved in one or the other hazardous process. The top five physical and chemical hazards identified include explosion, excessive heat, fire, dust, noise (physical) and toxic gas, vapour, microorganism, radiation hazards and corrosive chemical. Data on hazardous industries from other states is also being obtained. The GIS will be used to identify exact location of the industries in the country for future use.

As one of the component of Hazchem Project three awareness programmes for NGOs and workers engaged in hazardous chemical industries were organized on "Safe Use of Chemicals and Pesticides" at NIOH, Ahmedabad, ROHC (E) Kolkata and ROHC (S) Bangalore.

NON-COMMUNICABLE DISEASES

Non-communicable diseases are now recognized as major cause of morbidity and mortality. The World Health Report 2001 has indicated that non-communicable diseases account for nearly 60% of deaths and 46% of the global burden of disease worldwide. Seventy five percent of the total deaths due to non-communicable diseases occur in developing countries. The council has major research programmes on epidemiological and clinical aspects of cancer, cardiovascular disorders, mental health, neurological disorders and ophthalmic diseases. Studies were also undertaken on molecular genetics of HPV infection, breast cancer and prevention of disabilities.

ONCOLOGY

The research on cancer addressed the issues related to pathogenesis through a multi-disciplinary approach. Cancer Registries continued to provide valuable data on cancer occurrence, which has its utility in development of hypothesis as well as for evaluation of intervention projects. Operational research projects to help in cancer control are also being undertaken. The Council's Institute of Cytology and Preventive Oncology (ICPO) at New Delhi is continuing its research and human resource development activities in the field of cancer of the uterine cervix and breast.

NATIONAL CANCER REGISTRY PROGRAMME

The National Cancer Registry Programme (NCRP), initiated in 1981-82, continues to collect authentic data on cancer occurrence in the country, through its network of six population based (including one in rural areas) and five hospital based cancer registries. The programme aims at generation of reliable data on cancer occurrence, conducting epidemiological studies and developing human resources in the field of cancer epidemiology and registration. Monitoring and evaluation of the programme is being undertaken by a Coordinating Unit (Bangalore) under the guidance of a Steering Committee. The data till the year 1998 have been finalized. In 1998 the crude incidence rate of cancer in different urban population based cancer registry areas varied between 54.0 and 86.7 per 100,000 males and 62.2 and 100.8 per 100,000 females. The crude incidence rate in the rural registry at Barshi (Maharashtra) was 37.3 per 100,000 males and 44.1 per 100,000 females. The age adjusted incidence rate in urban registries varied between 87.7 and 127.0 per 100,000 males and between 108.7 and 142.3 per 100,000 females. The age adjusted incidence rate at Rural Barshi was 43.9 per 100,000 males and 51.7 per 100,000 females. Delhi

registry showed the highest age adjusted incidence rate in both sexes. Most common cancer sites observed among males were those of lung, stomach, oesophagus, larynx, mouth, tongue, prostate and pharynx. The common cancers observed among females were those of breast, cervix, stomach, oesophagus, ovary, mouth, gall bladder and lung.

The consolidated report of the hospital cancer registries for the period 1994 to 1998 has also been finalized. Proportion of localized cases varied from 2.2% (Chennai) to 29.9% (Mumbai) among males, and from 3.8% (Chennai) to 28.3% (Mumbai) among women. Among the patients treated at the reporting institutions, radiotherapy was the commonest mode of treatment followed by surgery or chemotherapy except at Mumbai where surgery was the commonest modality of treatment among males followed by radiotherapy. The proportion of patients not receiving/accepting treatment at various centres varied from 23.7% (Thiruvananthapuram) to 49.4% (Bangalore) among males and 13.9% (Thiruvananthapuram) to 39.7% (Chennai) among females.

For development of an atlas of cancer in India data are being collected from the departments of pathology of medical colleges and major cancer hospitals (about 99 centres). So far information on about 100,000 cases has been received.

SURVEY ON PREVALENCE OF TOBACCO USE

The ICMR-WHO (SEARO) surveys on prevalence of tobacco use were carried out on representative samples in Karnataka and Uttar Pradesh, in a population of about 30,000 above 10 years of age in each state. The proportion of urban and rural population as observed from the census data from the specific district was used for allocation of cluster to urban and rural population. The difference between ever use and current use of tobacco was small suggesting presence of very few ex-users in the community. The prevalence of current use of tobacco in any form in Karnataka was 32.7% among urban men, 8.5% among urban women, 42.9% among rural men and 16.4% among rural women. The prevalence of current use of tobacco in any form in Uttar Pradesh was observed to be 45.0% among urban men, 8.2% among urban women, 51.0% among rural men and 9.2% among rural women. The prevalence increased with increasing age. The prevalence rates of tobacco use were higher in rural areas as compared to urban areas in most age-groups, except in teenagers, where reverse was true. Negative association between education and prevalence of tobacco use was observed in both the States. Similarly, higher family income levels were associated with a lesser prevalence of current tobacco use. Religion did not seem to have any association with prevalence of tobacco use. Tobacco use in smokeless form was predominant among women and men below 30 yr both in urban and rural areas, but smoking was the predominant form of tobacco use among men above 30 yr. Only a limited number of persons started their tobacco habit before 10 yr of age. The mean daily frequency of tobacco use was 14.9 times/ day among men and 7.5 times/ day among women in Karnataka and 10.0 times/ day among men and 7.9 times/ day among women in Uttar Pradesh. In Karnataka, 61.7% of tobacco users and 78.0% of never-users reported knowledge of at least one harmful effect of tobacco. In Uttar Pradesh, 90.8% of tobacco users and 88.7% of never-users reported knowledge of harmful effects of tobacco.

CERVICAL CANCER

Multidisciplinary Study on Cervical Cancer

A study has been initiated to understand the comparative role of genetic and environmental factors in cervical carcinogenesis. Of the proposed 50,000 target women 20,627 women attending Gynecology OPDs of four major hospitals of Delhi have been screened cytologically using Bethesda system of classification.

On screening of cervical smears about 7% cytological abnormalities were detected, majority of them were atypical squamous cells of undetermined significance (ASCUS) lesions and around 1.8% had epithelial cell abnormalities [low-grade squamous intraepithelial lesions (SIL), high-grade squamous intraepithelial lesions and malignancies]. The abnormal smears [ASCUS/ atypical glandular cells of undetermined significance (AGUS)] were further screened by repeat smear examination/colposcopic directed biopsy examination.

The ASCUS favouring reactive cases were followed up by repeat cytology after 3 months. On follow up 84% cases reverted to normalcy and 13% were persistent ASCUS lesions while 3% were SIL. The ASCUS favouring SIL were subjected to colposcopy. Colposcopically significant lesions were detected in 49% of cases, 12% of which on biopsy revealed cervical intraepithelial neoplasia (CIN) lesions.

AGUS reactive lesions on repeat cytology showed SIL in 8% cases, while colpodirected biopsy revealed CIN in 50% cases. Good cytohistocorrelation was achieved in high grade lesions and malignancies.

The follow up examination revealed that very few ASCUS lesions had underlying significant lesions. Very good cytohistological correlation was achieved in high grade lesions. The study provided significant insight about the role of ASCUS/AGUS lesions as the biological behaviour of these lesions among Indian women had not been reported in detail so far.

Comparative Evaluation of Cancer Detection using Multimodal Screening Tools.

Various alternative modalities for early detection of cervical cancer are being evolved at ICPO. Techniques like cytology and visual inspection aided (VIA) methods using acetic acid are being tested to assess their sensitivity and specificity. In this study, VIA was done in 871 women and human papilloma virus (HPV) screening in 312 women using hybrid capture II. The negative predictive values (NPV) were found to be around 99% with HPV screening and 90% with cytology. The sensitivity of VIA was 86.5% and specificity was 75%. A coloured pictorial manual on VIA and a calendar depicting differential diagnosis have been prepared for wide circulation at the national level.

Biological Behaviour of HPV Infection

Very limited information is available on the natural history of HPV infection of uterine cervix. Its prevalence, probability of acquiring this infection and the risk factors associated with it are not clearly known. The factors which govern its progression, regression and persistence are also poorly understood. A study has, therefore, been initiated to understand the prevalence and persistence of HPV infection. It is proposed to screen 5000 women with specific primers of HPV 6,11,16 and 18. Of the 580 women so far screened for HPV DNA using L1 primers. 24.4% have been found positive. During the process a low cost test for detecting common HPV types using RFLP method has been

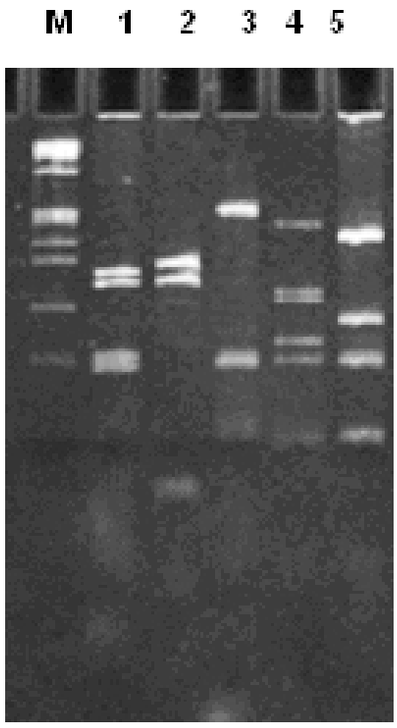


Fig.1. RFLP of the L1 amplicon (MY09/11) resolved on 8% PAGE, lane 1, 2, 3, 4 and 5 showing five different HPV types 6, 11, 16, 18 and 33 respectively

developed (Fig.1). HPV type 6 was found to be frequently present in different groups of cervical lesions. (Fig.2).

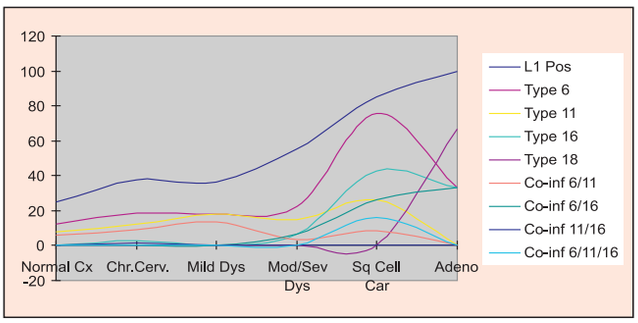


Fig.2. showing HPV infections in the females at different clinical stages

Transcriptional Control of Human Papillomavirus Gene Expression

Modulation of level of expression of specific genes is a prerequisite for the control of cellular growth and differentiation and it is generally regulated by the interplay of sequence-specific DNA binding proteins called transcription factors. The activator protein-1 (AP-1) which is formed either by a homodimer of jun proteins or heterodimer of jun and fos proteins derived from host cells has been found to play a central role in controlling expression of HPV oncogenes. *In vivo* analysis revealed differential expression of different members of AP-1 family as well as change in the dimerization pattern of the AP-1 family members, which might be playing a crucial role in the progression of cervical cancer. The antioxidative drugs are known to interfere with the redox status of eukaryotic cells. The role of a potent herbal antioxidative agent, curcumin, from *Curcuma longa* is under investigation.

Incubation of HPV 18 positive cervical carcinoma cells, HeLa with 100 µm curcumin resulted in a decrease in binding activity of AP-1. (Fig.3) Incubation of HeLa cells with 100 µm curcumin for 2 hr. showed a gradual decrease in HPV 18 expression which completely disappeared after incubation for 4-5 hr. The study on curcumin induced expression of individual family members of AP-1 showed a decreasing expression pattern of c-fos, which disappeared completely after about 2 hr of curcumin treatment. In

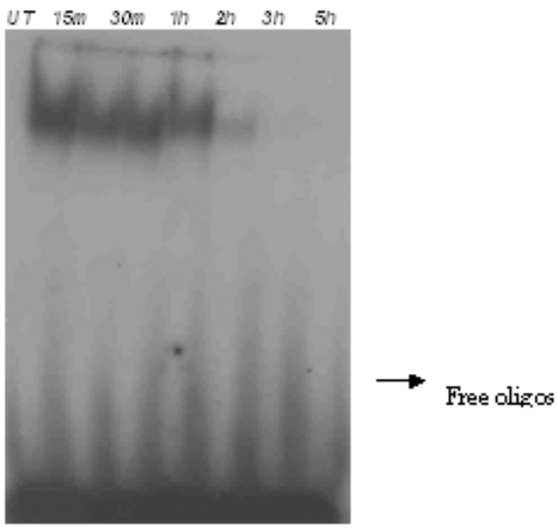
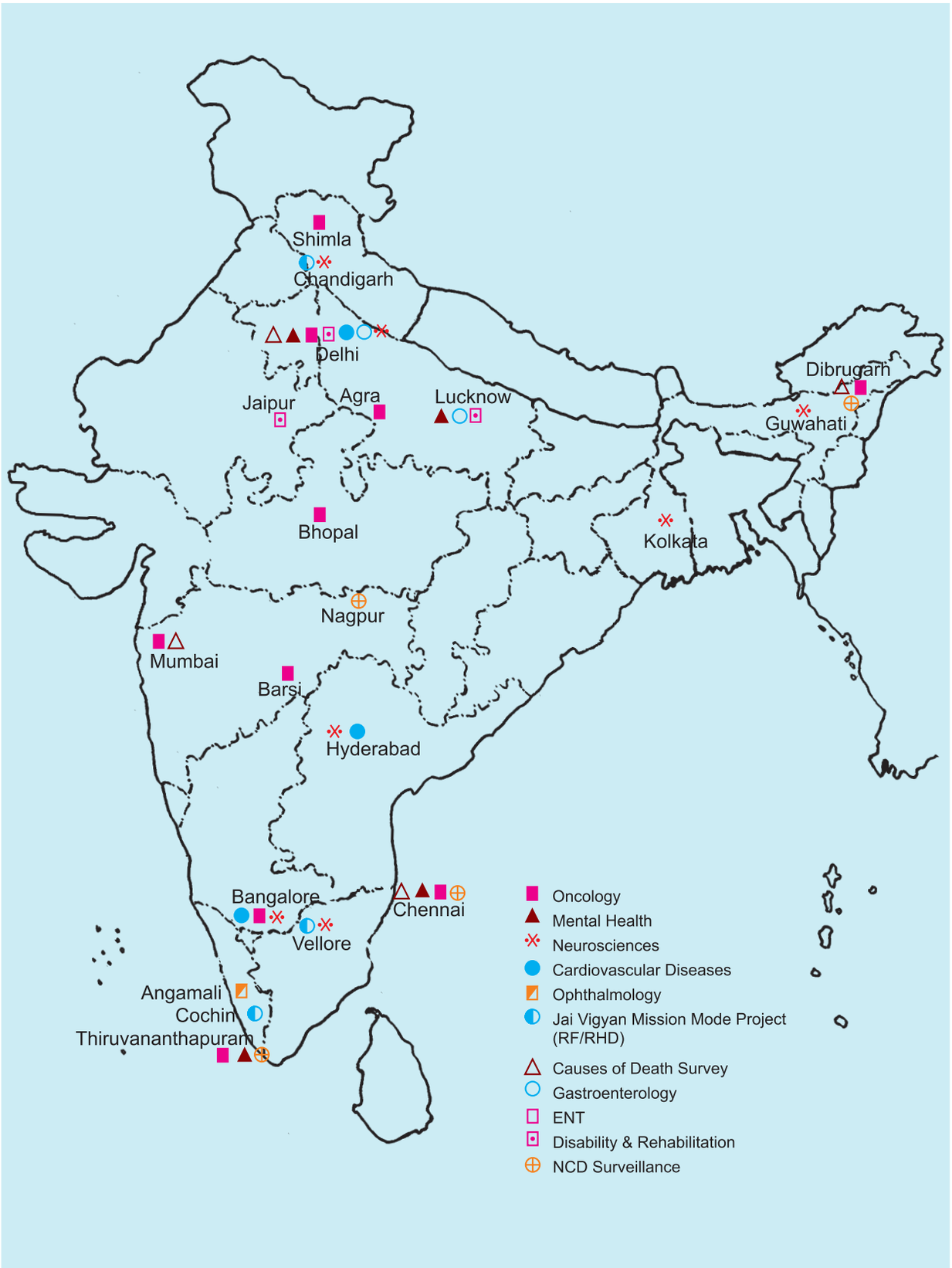


Fig.3. Electrophoretic mobility shift assay showing decrease in binding activity after 100µm curcumin treatment in HeLa cells.



MAJOR ICMR RESEARCH PROJECTS IN NON-COMMUNICABLE DISEASES

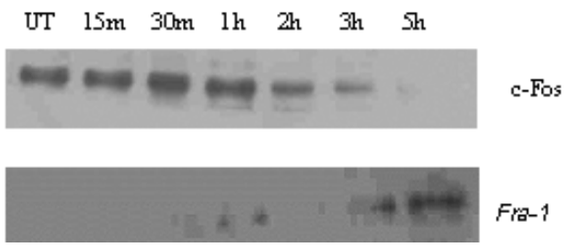


Fig. 4. Expression of c-fos and Fra-1 proteins after time dependent treatment of 100µm Curcumin in HeLa cells.

contrast Fra-1 showed an increasing pattern of expression after the above treatment (Fig. 4.) The protein expression also showed similar pattern of regulation. These data perfectly correlate with the observations in in-vivo tissue biopsy. Understanding of these steps would provide a basis for developing novel therapeutic approaches to effectively control HPV infection and cervical cancer using antioxidative drugs.

Genomic Instability and Genomic Deletion

Genomic instability and genomic deletion are considered important molecular events in the development of various human cancers. In a study 39 precancer cases of uterine cervix were studied for the status of microsatellite instability (MSI) with a panel of five internationally agreed primers (BAT25, BAT26, D2S123, D5S346 and D17S250) and loss of heterozygosity for 3p and 5p regions with another five set of primers (D3S1234, D3S1300, D3S1313, D5S208 and D5S406) along with status of HPV infection. Around 51% cases showed MSI (23% with mild dysplasia and 28.2% with severe dysplasia). Maximum instability was observed in the region 2p16 with D2S123 (20.5%). In addition to MSI, 8.6% cases showed LOH with the same primer (BAT 25) which amplifies the (A)n tract located in the intron of c-kit oncogene. The study revealed the role of MSI in the development of cervical cancer (Fig. 5).

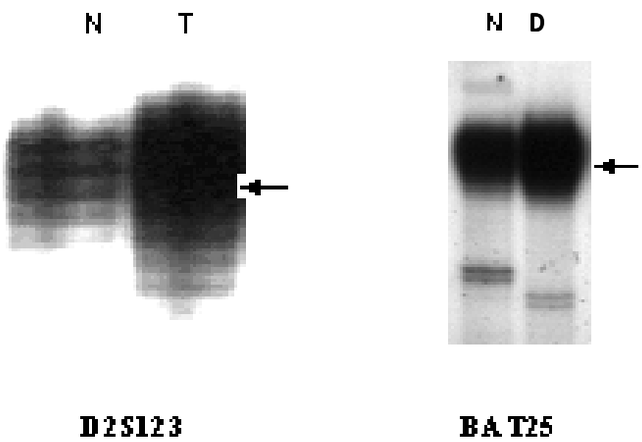


Fig.5. Showing genomic instability in the loci 2p16 (D2S123) and 4q12 (BAT25), indicated by arrows. D = dysplasia; N= DNA from corresponding normal tissue.

Glutathione S-transferase Polymorphism and Susceptibility to Develop Cervical Cancer

Multiple allelism at loci encoding detoxifying enzymes is associated with cancer risk. Glutathione S-transferase (GSTs) catalyzes the conjugation of glutathione to numerous potentially genotoxic compounds. A study was conducted to evaluate the influence of genetic polymorphisms of GST M1 and GST T1 on susceptibility to cervical cancer. A multiplex polymerase chain reaction method was used to detect the presence or absence of the GSTM1 and GSTT1 genes in genomic DNA isolated from 142 cases with cervical cancer and 96 normal controls .The results showed that the frequency of homozygous GSTM1 null genotype was significantly higher in cervical cancer cases (57.0%) as compared to controls (34.4%). The frequency of homozygous GSTT1 null genotype in cancer cases was 19.7% in comparison to 12.5% in controls. Significant difference in distribution of the null genotype of GST M1 was found in individuals above 45yr but this difference was not significant in individuals below 45 yr of age. No significant differences were found in cervical cancer cases and controls when data was analysed according to age

group for GSTT1 null genotype. Further, the combined analysis of both GSTM1 null and GSTT1 null genotypes did not appear to influence the susceptibility to cervical cancer suggesting that polymorphism of other detoxifying enzymes may play a significant role in cervical carcinogenesis. (Fig.6).

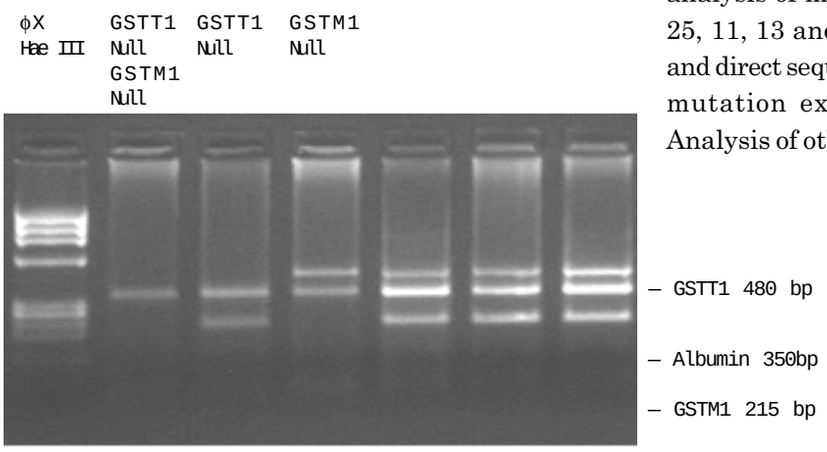


Fig. 6. Multiplex PCR showing amplification of GSTT1, GSTM1 and albumin genes segment, resolved on 3% agarose to detect polymorphism

BREAST CANCER

Multidisciplinary Study

The ICPO continued the multidisciplinary study on breast cancer in collaboration with Institute Rotary Cancer Hospital, AIIMS, New Delhi with the specific objectives of studying the epidemiological risk factors involved in cervical carcinogenesis, to study prognostic factors (clinical, morphological, hormonal, *etc*) involved in disease free survival/overall survival and to study status of breast cancer genes in the families of these patients.

During the year a total of 204 breast lumps collected at Maulana Azad Medical College, New Delhi were examined out of which 10% were found to be malignant cytologically. Based on the cytological diagnosis, the patients were recruited for the study. Detailed epidemiological information was recorded in the predesigned proforma and biological material was collected for analysis of lipid profile, hormonal assays and genetic studies. During the period under report, a total of 38 fine needle aspiration cytology (FNAC) samples were collected from women with sporadic breast cancer. No familial case of breast cancer was encountered. Mutation analysis of most commonly mutated exons 25, 11, 13 and 20 of BRCA1 by PCR-SSCP and direct sequencing revealed no deleterious mutation except some polymorphisms. Analysis of other exons is in progress.

Other Studies on Breast Cancer

In another study breast cancer samples from different places were investigated for BRCA1, BRCA2 and p53 gene mutations. Germline BRCA1, BRCA2 and p53 gene mutation analysis was performed on 24 familial breast cancer patients from two different distantly situated regions of India. Sixteen patients belonged to New Delhi and nearby regions and 8 to Goa. A total of seven mutations consisting of 4 deleterious and 3 amino acid substitutions with two novel missense mutations were detected in BRCA1 gene.

All 22 coding exons along with flanking intronic regions were analysed. Of the four protein truncating mutations, two were detected in North Indian population, one 57655insG leading to TGA at codon 1621 in exon 16 in a patient, and the other Gln→Stop codon at position 1395 in exon 12 in another patient. (Fig. 7). Of the three missense mutations two were detected in exon 7 at codon 110 and 114 to amino acid Lys→Thr and Ser→Pro in two other patients.

Eight familial breast cancer patients from Goa were analyzed for mutation in BRCA1 gene. Only one family out of 8 found mutated for BRCA1 gene. In this family two sisters

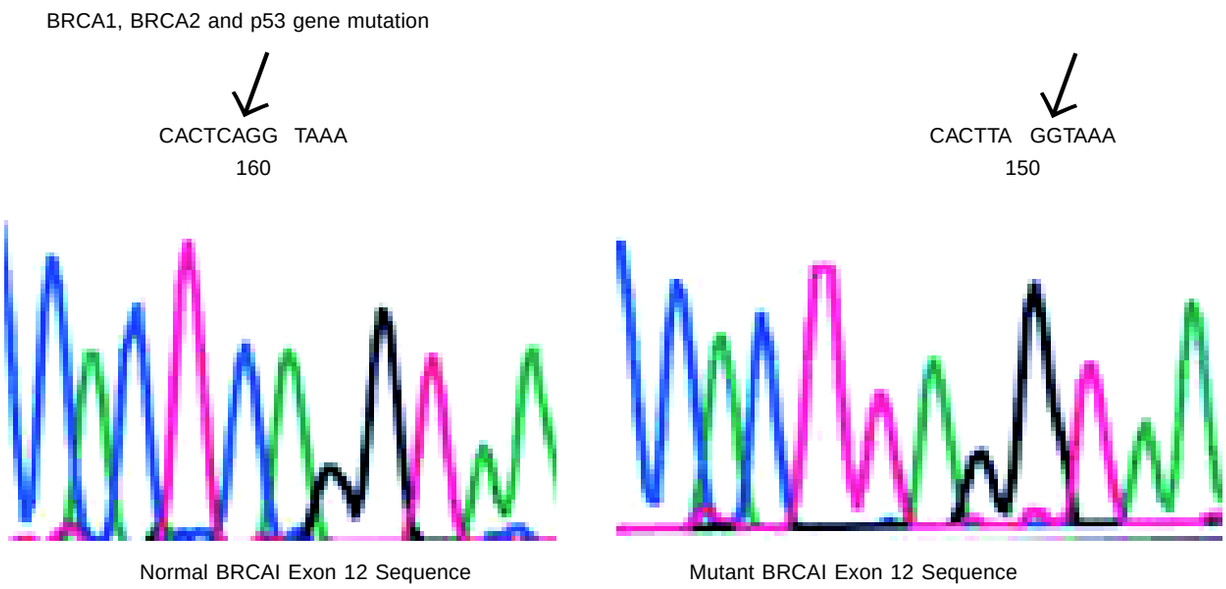


Fig.7. Showing mutation in BRCA 1 by sequencing analysis

1GF and 3GF showed protein truncating frameshift mutation 4665delA leading to formation of TAG at codon 22. Exons 2, 9, 11, 18 and 20 of BRCA2 gene were analysed for mutation. No significant sequence variation was detected in any of the familial cases except for two cases from Goa showing G203A substitution in 5' UTR of exon 2, a common population polymorphism.

Single transition missense mutation GTC →ATC was observed at codon 97 of exon 4 leading to amino acid change Val to Ile in only one familial breast cancer patient from North India which also showed 57655insG frameshift mutation in BRCA1 gene. No other p53 gene mutation was detected in any of the familial cases.

The overexpression of c-erbB-2 oncoprotein and epidermal growth factor receptor (EGF-R) showed an inverse association with estrogen receptor (ER) and a direct association with metastatic involvement of lymph node and high histological grade. Interestingly, the frequency of c-erbB-2 and EGF-R overexpression was significantly higher among postmenopausal cases in comparison with premenopausal cases. The investigated pathobiological factors indicate a difference between pre and post-menopausal breast cancer.

T-lymphocyte subsets (CD4+ and CD8+) were evaluated in breast cancer tissues as well as in the peripheral blood of breast cancer patients. Majority of tumor tissues showed a preponderance of CD8+ lymphocytes. On the other hand, peripheral CD4+ lymphocytes were found to be lower in breast cancer patients compared to controls. Moreover, T-lymphocytes (CD3+) showed a continued diminution during treatment for breast cancer.

STOMACH CANCER

Risk factors for Stomach Cancer with reference to Dietary Practices and Habits in Mizoram

In an ongoing project at RMRC, Dibrugarh, a total of 154 histopathologically confirmed stomach cancer patients (age 45+) registered in the Aizawl Civil Hospital, Aizawl till February 2003 have been enrolled and the detailed information regarding the dietary practices and habits has been recorded.

All the cases belong to Christian and indigenous community of Mizoram. More than 70% cases are educated up to primary and middle school level. 57% of them have income more than Rs.2500/- per month at the time of diagnosis. About 60% of the confirmed cases were physically active at the time of diagnosis. Occupation wise 15% of the cases are in service, 9.7% are skilled workers, 16.9% are unskilled workers, 32.5% have engaged in agricultural work and 9.2% are housewives. Amongst the agricultural workers, 48.0% had history of pesticide handling during cultivation. History of cancer was present in the families of 38.0% of the cases of which 71.0% had stomach cancer. History of malaria, dysentery and jaundice was recorded in 65.0%, 54.3% and 19.4% cases respectively. *H. pylori* infections were found in 58.5% of them.

CARDIOVASCULAR DISEASES

Cardiovascular diseases (CVD) are the commonest cause of death globally and account for approximately 12 million deaths annually. The disability-adjusted life years (DALY) attributed to CVD will rise to about 140-160 million with about 80% of this burden in developing countries. This unexpected increase in CVD reflects the demographic, economic and health transitions in these countries. In India, CVD is also the major contributor to the burden of premature mortality and morbidity and accounted for 85 million DALY's in 1990. By the year 2020, CVD will still remain the leading cause of mortality and disability in India. The most alarming health prediction for the new millennium is that heart diseases and stroke are going to top the list for morbidity and mortality.

Coronary Heart Disease

Hospital-based Study to Identify Risk Factors for Acute Myocardial Infarction in Indians

A multicentric case control study has been initiated at four centres - Bangalore, Delhi, Hyderabad and Lucknow to identify new risk factors and to find their association with coronary heart disease (CHD) in cases with newly diagnosed ischaemic heart disease (IHD). Four different sets of proformae for clinical, biochemical, dietary and stress related factors are being utilized for data collection. The study will seek to identify factor(s) positively or negatively associated with the risk of IHD. Till date 2304 subjects have been recruited. The data is being analyzed.

Hypertension

The RMRC, Dibrugarh, has been conducting research on hypertension in the north-east region of the country and on blood pressure levels in children.

Hypertension and Coronary Heart Disease

A study was carried out in an indigenous Assamese population wherein a cross section of 3180 people (30+ yr) from 28 villages in 5 districts of Assam were surveyed for the presence of hypertension and coronary heart disease. All the study subjects were interviewed through a specially designed pre-structured proforma for socio-demography, dietary habits and probable risk factors. Interviewed participants were clinically examined for blood pressure and anthropometric parameters. E.C.G was done for the presence of coronary heart disease.

Survey results and analysis in respect of 2011 subjects have already been reported. Overall, 45.3% of the 3180 study subjects were males and 54.7% were females, 78.8%

were married, 13.9% were either widower or widows, 32.5% were illiterates, 12.5% smokers and 36.4% alcoholics. Extra salt consumption was recorded in 54.2% of the study subjects. Age adjusted mean systolic blood pressure (SBP) was 135.5 in males and 137.1 in females, while diastolic blood pressure (DBP) was 83.6 in both males and females. The prevalence of hypertension in the study population was found to be 33.3%. Around 13% were found to have optimal systolic and diastolic blood pressure, while 25% had high blood pressure. Thirty three percent were on anti-hypertensive agents. Of all the hypertensives, 15.94% were in Stage 1, 10.82% in Stage 2 and 5.22% in Stage 3. Around 22% of the hypertensives were aware of their blood pressure. Biochemical analysis of lipid profile and blood glucose is in progress.

Blood Pressure Levels in Children

A pilot study on blood pressure levels in children (6 to 14 yr age group) was conducted in 13 schools of Dibrugarh district, Assam. A total of 889 children (male 475 and female 414) were surveyed of which 624 (male 317, female 307) were from Assamese community, 189 (male 112, female 77) from tea garden community and 76 (male 46, females 30) from other communities. Family history of hypertension, diabetes and heart diseases was recorded in a pre-structured proforma. The study subjects were interviewed, clinically examined for blood pressure level and anthropometric measurements were taken. The information on their family history for heart disease, diabetes and hypertension was collected. In children belonging to tea garden community the mean SBP was 107.58±8.78 in males and 107.46±9.72 in females. There was no significant change in SBP and DBP in male and female children from Assamese and other communities.

Jai Vigyan Mission Mode Project

Community Control of Rheumatic Fever/Rheumatic Heart Disease

The project was initiated under the PM's initiative in the mission mode. It has four main components - to study the epidemiology of streptococcal sore throat; to establish registries for RF/RHD; vaccine development for streptococcal infections and conducting advanced studies on pathological aspects of RF/RHD. The epidemiology component was taken up at Chandigarh and Vellore. The results of the field study were reported last year from the Chandigarh Centre. The Vellore Centre has screened 4,014 children in which 18.25/thousand had pharyngitis. They have lyophilized 1220 GAS strains for genotyping. In the cohort study the prevalence of GAS pharyngitis varied from 9.4 - 25.1/thousand children per month. The emm genotyping has just been started at Vellore Centre. The Chandigarh Centre has done emm typing of 17 strains of which the most common types are 77-1, 80-1 and 11.

Under the vaccine component 5 novel gene sequences have been identified which have been deposited in the gene bank. Peptides corresponding to 20 amino acids of amino terminal of M protein have been synthesized as 12 novel peptides. These peptides have been conjugated to tetanus toxoid for further immunological evaluation.

The registry component has been started at three centres; Chandigarh, Vellore and Cochin. The Chandigarh Centre has registered 202 patients of RF/RHD which are on secondary prophylaxis. Under the active surveillance component 7990 school children were screened of which 64 were suspected to have RF/RHD and were referred for echo-cardiography. Of these 34 children have reported for echo and 17 have been confirmed as RF/RHD. The Vellore Centre has examined 525 suspected cases of RF/RHD of which 112 have been confirmed as RHD and

22 as RF. Under the active surveillance 20,848 school children have been examined of which 321 have been suspected to have RHD. Of these 27 children have been examined by the cardiologists and 3 have been diagnosed as RHD. The Cochin Centre has conducted its first workshop for the medical practitioners in the district and has registered 27 cases.

OPHTHALMOLOGY

Prevalence of Glaucoma

The Global Initiative of Vision 2020 has identified glaucoma as one of the main causes of blindness all over the world. India is also a signatory to this document. However, there is a lack of data on prevalence of glaucoma in the Indian population. The Angamally Centre is collecting data on the prevalence of glaucoma in six blocks of this district. Based upon the data so far collected the prevalence of glaucoma has been found to be 2.7% (primary open angle glaucoma 1.15% and primary angle closure glaucoma 0.63%) in the population aged more than 35 yr. The highest prevalence of primary glaucoma was found in 44-64 yr. age groups. For the first time, community based data on prevalence of ocular hypertension has been found to be 1.65%. The data collection is ongoing.

MENTAL HEALTH

Total global burden due to mental health problems is approximately 12% and affects the quality of life. Mental and neurological disorders around the world accounted for 10% of the total DALYs lost due to all diseases in the year 1990 and are projected to increase by 15% by the year 2020. The ICMR is conducting various studies on mental health problems and services in the urban and rural areas of the country. Suicide is one of the important causes of death in most countries. The Council is also continuing a study on determining suicide behaviour in the Indian population.

Workshops on Urban Mental Health Care and Service Needs

In India the urban population was 17.3% in 1951, which increased to 25.73% in 1991. At present it is more than 30% and is expected to increase to 56% by the year 2025. The prevalence of mental and behavioural disorders was found to be 80.6% in urban population and 48.9% in rural population in India. A two arm study on urban mental health care and service needs was carried out to make an assessment of mental health services and needs. Current Situation Analysis (CSA) was done through regional Workshops at Mumbai, Chennai, Lucknow and Ranchi and one national Workshop at New Delhi (funded by WHO). The other arm addressed the project on Health Service Research at three centres (Delhi, Lucknow and Chennai). Both government and non-formal sectors participated in the Workshops and shared their data and experiences. Through these Workshops current and projected needs, availability and utilization of services and strategies for unmet needs were identified. It was reported that there is overburdening of in-patient and out patient facilities and under-utilization in special services in government settings. Current and projected needs identified were emergency treatment facilities, regular outpatient facilities, in-patient facilities for long term patients, short term and life time rehabilitation facilities, facilities for special population, de-addiction centres, child guidance centres, help lines *etc*. The Workshops also highlighted the need to increase awareness about mental disorders and mental health facilities with the help of media, public awareness programs, mental health camps, documentary films and small booklets.

Urban Mental Health Problems and Services Needs

India is a pioneer in providing mental health services in rural areas, but the urban areas have no such formalized system. The population in urban areas in India is growing very rapidly. The rapid growth without proper health services (especially on mental health) causes stress, pollution, noise and congested inhabitations. These have a direct correlation with mental health.

The ICMR has initiated a WHO funded study on urban mental health problems at three centres *viz.* Delhi, Lucknow and Chennai. The study aims to collect and collate data relating to existing mental health services -government, private and NGOs in urban areas, through mapping of these services in selected cities. The work carried out included mapping of specialized mental health services, assessment of diagnostic profile and pattern of utilization of services at five treatment centres and assessment of needs and services in the community. Instruments were developed and pre-tested. Mapping of the specialized mental health services and NGOs was undertaken. In-depth interviews were held with patients, informants and service providers. Key informant interviews, free listing and focus group discussions were also undertaken with general practitioners (GPs) and faith healers. As per the community perception, mental health problems were reported due to stress in majority of the patients and to medico-religious causes in a few patients. Interestingly, most of the faith healers reported that mental health problems were due to illness of brain. The burden of psychological and psychiatric problems in community was reported to be 30% as per the GPs. Fifty percent of them felt that mental health services were satisfactory.

Suicide Behaviour

Suicide is a major public health problem and is among the top ten causes of death in most countries. Indian data on this problem are very limited. Looking at the socio-cultural diversity of Indian population a task force project on suicide behaviour was developed with community and hospital component. The pilot study has been initiated at two centres *i.e.* Delhi and Thiruvananthapuram. The objectives of the study are to adapt/develop and pretest study instruments, to work out field work logistics and referral system for community settings, to establish project work logistics for hospital based study and prepare guidelines for intervention and manuals for training of research staff. The study instruments have been translated, tested and adapted. Community surveys were conducted in metropolitan areas at both centres and individual data were collected from families. The study has indicated wide acceptability without any negative effect of the project in the community. Hospital arm of the project were also undertaken in both the cities. Preliminary results indicated that mean scores on all the instruments had increasing trend with the grade of suicidal ideation.

ACCIDENTS, DISABILITY AND REHABILITATION

Avoidable disability is a major socio-economic and public health problem in India and other developing countries. The knowledge and technologies are available for their prevention and control. There is a clear need for a new strategy for integrated efforts to combat avoidable disability. The strategy for integration stems from the

recognition of a commonality of causative/ risk factors among groups of disabilities on the one hand, and the potential for delivering interventions against a group of disabilities using common channels within primary health care system on the other.

The task force project on prevention of disability among pre-school children has been initiated at 3 centres - Delhi, Jaipur and Lucknow. The aim of the project is to study the causes and risk factors of disability, epidemiology of disability prevention and development of basic rehabilitation services at PHC level. The base line surveys have been completed. The following have emerged as significant risk factors contributing to disability among young children (a) complications in child after birth, (b) delayed cry at birth, and (c) pre-term delivery. The following types of morbidity was found to be significantly higher among disabled children as compared to normal children-watering/ redness of eyes, pus discharge from ear, headache and earache. The study is trying to evaluate as to why the disability could not be prevented by right action at appropriate time. Training material has been developed for PHC doctors, paramedical staff and community leaders for prevention of disability among young children. The project is scheduled to continue intervention and subsequent evaluation during next two years.

CAUSES OF DEATH BY VERBAL AUTOPSY

Information on causes of death is essential for proper health care management, socio-economic planning and allocation of appropriate resources in the health sector. Existing systems of death statistics collection *viz.* the medical certification of causes of death in urban areas and the survey of causes of death in the rural areas do not provide complete data. The MOHFW requested ICMR to initiate short and long-term studies on causes of death due to selected major causes. A pilot study was, therefore, initiated at Institute for Research in Medical Statistics (IRMS) New Delhi and the National Institute of Epidemiology (NIE), Chennai. In the pilot study, five verbal autopsy schedules for ascertaining deaths in different population groups (neonates (0-28 days), post-neonates (29 days - 5 yr), adults (5+ yr), maternal and stillbirths were prepared and pilot tested. Algorithms were also prepared to arrive at the most probable cause of death in consultation with experts in the field of gynaecology, paediatrics and neurology. The Delhi centre validated the instruments on 47 hospital deaths. During 2001, IRMS covered 115 deaths in Bharatpur and NIE covered 224 deaths in Chennai. The study has been extended to five states representing the five geographical regions of the country.

BASIC MEDICAL SCIENCES

Research in basic medical sciences is being pursued intramurally in pathology and haematology through Institute of Pathology (IOP), New Delhi and Institute of Immunohaematology (IIH), Mumbai respectively and extramurally through Centres for Advanced Research, task force projects and open ended *ad hoc* research schemes and fellowships in the field of anatomy, biochemistry, cell and molecular biology, human genetics, immunology, pharmacology, physiology, toxicology, traditional medicine and the recently launched major initiative in genomics.

PATHOLOGY

TUMOUR BIOLOGY

Genetics of Breast Cancer in Indian Patients

At IOP, Delhi, 202 breast cancer patients and 45 age matched normal control individuals from North Indian population were registered for studying genetics of breast cancer. Of the total, 115 were < 40 yr (24 of them had family history of breast / ovarian cancer), 42 were between 41-45 yr (5 with family history of breast/ovarian cancer) and 45 were > 45 yr (14 had family history of breast/ovarian cancer). Interviews were held through specific questionnaire to examine interaction between genetic factors and social/environmental factors.

Screening of 100 patients for mutation in BRCA1 gene by heteroduplex analysis showed sequence variants among 28 patients. Thirty two percent patients with family history showed presence of a BRCA1 sequence variant. Sequence analysis of fragments showing heteroduplex variants has identified 4 splice site variants in BRCA1 gene, 3 recurrent frame-shift mutations, 4 missense mutations, one of which is likely polymorphism, as it has been found in 4 patients as well as controls and 2 missense variants of uncertain clinical significance in BRCA2 gene in more than one patient (two unrelated individuals each). Screening for mutations in the BRCA2 gene has been initiated. Sequence variants were found in Ex5, Ex13, Ex12, Ex18, Ex3, Ex7 and Ex10.

Molecular Biology of Prostatic Neoplasia

Cyclin Genes in Localized Prostatic Cancer

Studies of molecular genetic changes in prostate carcinomas are slowly improving our understanding of the biological process, which leads to a normal prostate epithelial cell becoming an adenocarcinoma cell with invasive and metastatic properties. Alterations in p53 function are infrequent in clinically localized prostate cancers but are more common in advanced cancers. Because the loss of normal cell cycle control

is an early event in the evolution of cancer, studies were undertaken at IOP, Delhi to determine changes in expression of the cyclin genes, *viz.*, mdm2, p16, p21^{waf}1, cyclin D and p34cdc2. Thirty cases of localized carcinoma prostate, 10 of prostatic intraepithelial neoplasia and 10 with benign prostatic hyperplasia (AAH) have been included in the study. Among prostate cancer cases, 40% were found positive for mdm2, 13% for p21^{waf}1, 16.6% for p16, 40% for p34cdc2 and 20% for cyclin D (Fig. 1). All cases of PIN were negative for mdm2 and p21^{waf}1 while 10% were positive for p16. Analysis of PIN cases for p34cdc2 and cyclin D is being done. All the patients of this cohort are on follow up. The observations would be correlated with clinicopathological variables.

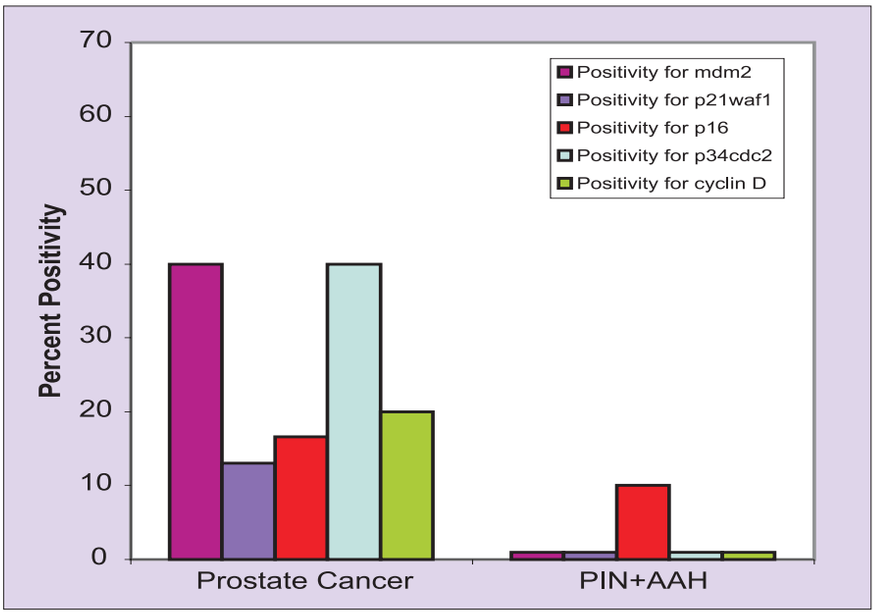


Fig. 1. Expression of cyclin genes in localized prostate cancer and PIN

Proapoptotic and Antiapoptotic Genes in Preneoplastic and Neoplastic Conditions of Prostate

Study has been planned to evaluate the role of apoptosis and genes (p53, bcl-2, bax and caspase-3) associated with apoptosis in preneoplastic and neoplastic conditions of prostate and their androgen dependent nature. Correlation of these genes with androgen receptor expression and clinical response is being studied. Eighteen cases of carcinoma prostate, 30 cases of high grade and 4 cases of atypical adenomatous hyperplasia (AAH) have been studied for immunohistochemical expression of p53, bcl-2 and bax. Expressions of p53 and bax proteins were found high (56 and 83% respectively) in carcinoma cases while expression of bcl-2 was more (42.4%) in preneoplastic conditions (PIN+AAH).

Lymphoid Haematopoeitic Malignancies

Apoptotic Cell Population as a Marker to Predict Induction of Remission in Patients with Acute Leukemia

Study was conducted to assess the spontaneous ability of acute leukemic cells to undergo cell death and to correlate spontaneous apoptosis with the clinical response of patients following induction chemotherapy. Peripheral blood samples of 31 patients of acute leukemias (15 ALL and 16 AML) were studied. Eighteen of them were followed up after induction chemotherapy. The mean live cell population in patients with complete remission (CR) was 40.2% as compared to patients who did not achieve CR (81.5%). The mean apoptotic cell

population in patients with CR was 59.8% as compared to 18.5% in patients who did not achieve CR. The findings suggest that patients who achieved CR had a significantly higher apoptotic cell population and a lower live cell population. Cell population with low apoptosis and high cell viability is found to be a possible predictor of a poor chemotherapeutic response in patients with acute leukemia.

PATHOLOGY OF LEISHMANIASIS

Development of Immunological and Molecular Diagnostic Tests for Kala-azar and PKDL

Comparative Potential of Amastigote and Promastigote Antigens, Recombinant Antigen and PCR for Diagnosis of Visceral Leishmaniasis Infection

Serological studies based on antigen prepared from amastigote stages of *L. donovani*, the stage of parasite that causes infection, are lacking. Studies were done at IOP, Delhi to measure by ELISA circulating antibodies to total antigen from the promastigote and amastigote stages of parasite as well as to recombinant K39 antigen and the results were compared with a PCR test for diagnosis of KA.

Samples of blood from 116 KA patients were examined; the sensitivity and specificity of ELISA test was found to be higher with amastigote antigen (92.3%) in comparison with promastigote antigen (89.0%). The diagnosis by ELISA was found to be comparable with PCR. The easy availability and low cost of indigenous amastigote antigen together with the simplicity of ELISA in comparison with PCR makes it a promising choice for the diagnosis of KA.

Cloning and Characterization of a Novel Gene (A-1) from L. donovani

Identification, cloning and sequence analysis of A-1 gene in *L. donovani* done at IOP, Delhi was reported last year. During the year 2002-03, further characterization of the gene was done.

Identification of Species-specific Polymorphism in Leishmania using A-1 Gene as a Probe

Attempts were made to determine the background of A-1 gene in *Leishmania* parasites to explore the possibility of using it as a tool to differentiate different strains/ species of *Leishmania*. Southern blot was carried out using genomic DNA from different strains of *Leishmania*. A comparative Southern blot of samples probed with the coding region of A1 ORF *L. donovani* Indian isolate displayed polymorphism with *Sac*I and *Bgl*II in comparison with *L. major* and *L. tropica* (Fig. 2).

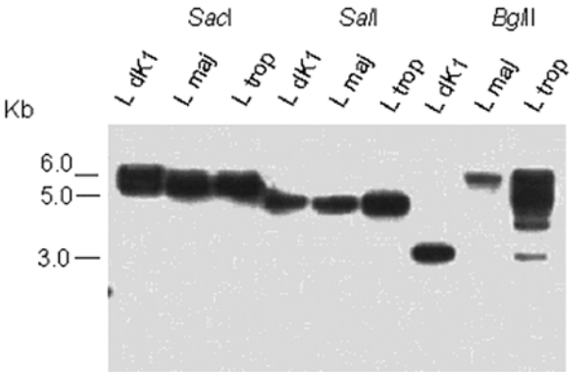


Fig. 2. Southern blot analysis of genomic DNA from *Ld India*, *L.major* and *L.tropica*

Copy Number of the Gene

To determine the copy number of *L. donovani* A-1 gene in the genome, Southern hybridization of the total genomic DNA from *L. donovani* promastigotes was done. A single band of ~7.0 kb or 5.2 kb was obtained on digestion with *Eco*RI and *sph*I respectively suggesting that A-1 is a single copy gene. The bands of similar intensity

obtained on digestion with a range of restriction enzymes *Bam*HI, *Hind*III, *Pst*I, *Sal*I and *Sph*I further supported this finding (Fig. 3).

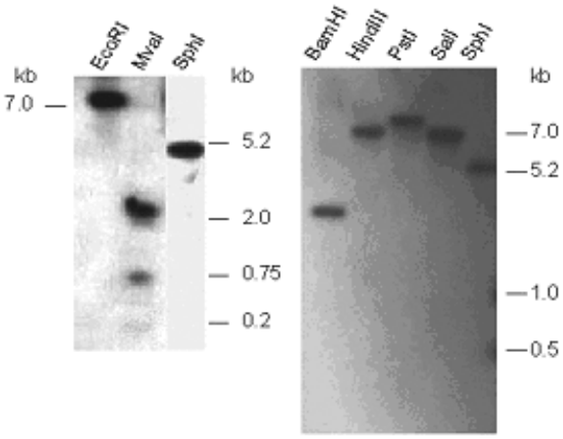


Fig. 3. Southern blot of Leishmania A-1: *LdK*1genomic DNA digested with the restriction enzymes.

Northern Hybridization of RNA Isolated from Different Growth Points

Northern hybridization of RNA isolated from different phases of growth at early, mid and late log phases was done using A-1 coding region as probe. A1 gene showed significantly higher expression in amastigote stage of parasite at all time points.

Centrin Knockout Mutants

Centrin exhibits growth regulated expression in Leishmania. Centrin lacking N terminal region had a dominant negative effect on growth of parasites. To confirm this, centrin gene was knocked out by homologous recombination. Mutant parasites lacking centrin gene showed a dramatic decline in amastigote stage though the promastigote stage had normal growth (Fig. 4). These mutants hold promise as attenuated vaccine candidates. It is planned to test these mutants in macrophages for growth and in animal model systems for immunogenicity and as attenuated vaccines.

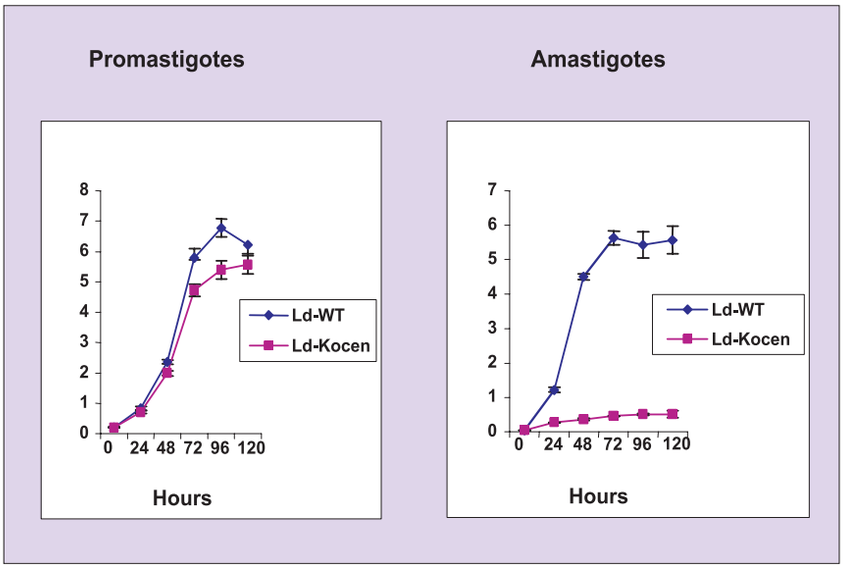


Fig. 4. Growth of *L.donovani* centrin knockout parasites

OTHER STUDIES

Pathophysiological Role of Estrogen in Males

Ongoing studies on the evaluation of seminal estrogens in fertility were continued during the year at IOP, Delhi. Investigations on the ejaculated human spermatozoa from proven fertile subjects demonstrated the presence of both estrogen and progesterone receptors.

Further studies with recently introduced epitope specific antibodies against estrogen receptors (ER) indicated gross differences in their localization in mouse spermatozoa. In contrast to the widespread localization of ER α, ER β was confined to the mid piece region of the mouse spermatozoa suggesting the possible role of estrogen in the motility of the spermatozoa.

In Vitro Cultivation of Differentiated Human Epidermis for Autologous Grafting in Burns

A method to culture multi layered differentiated epidermis was standardized during the year at IOP using Rheinwald and Green culture conditions. The cultured epidermis was verified histologically by light and electron microscopy and immunohistochemically. The growth conditions to obtain epidermal sheets for larger areas have been optimized. This was achieved by serial subculture of keratinocytes. In order to ensure that the cultured epidermis is free from any bacterial contamination, a microbiological quality control protocol has been established. The standardized epidermal culture was found to be free of bacterial and mycoplasma contamination. Expansion of keratinocytes from 5cm^2 to 4000 cm^2 by serial cultivation of cultured epidermal sheets was achieved (Fig. 5).

Fig. 5. An *in vitro* grown differentiated epidermis

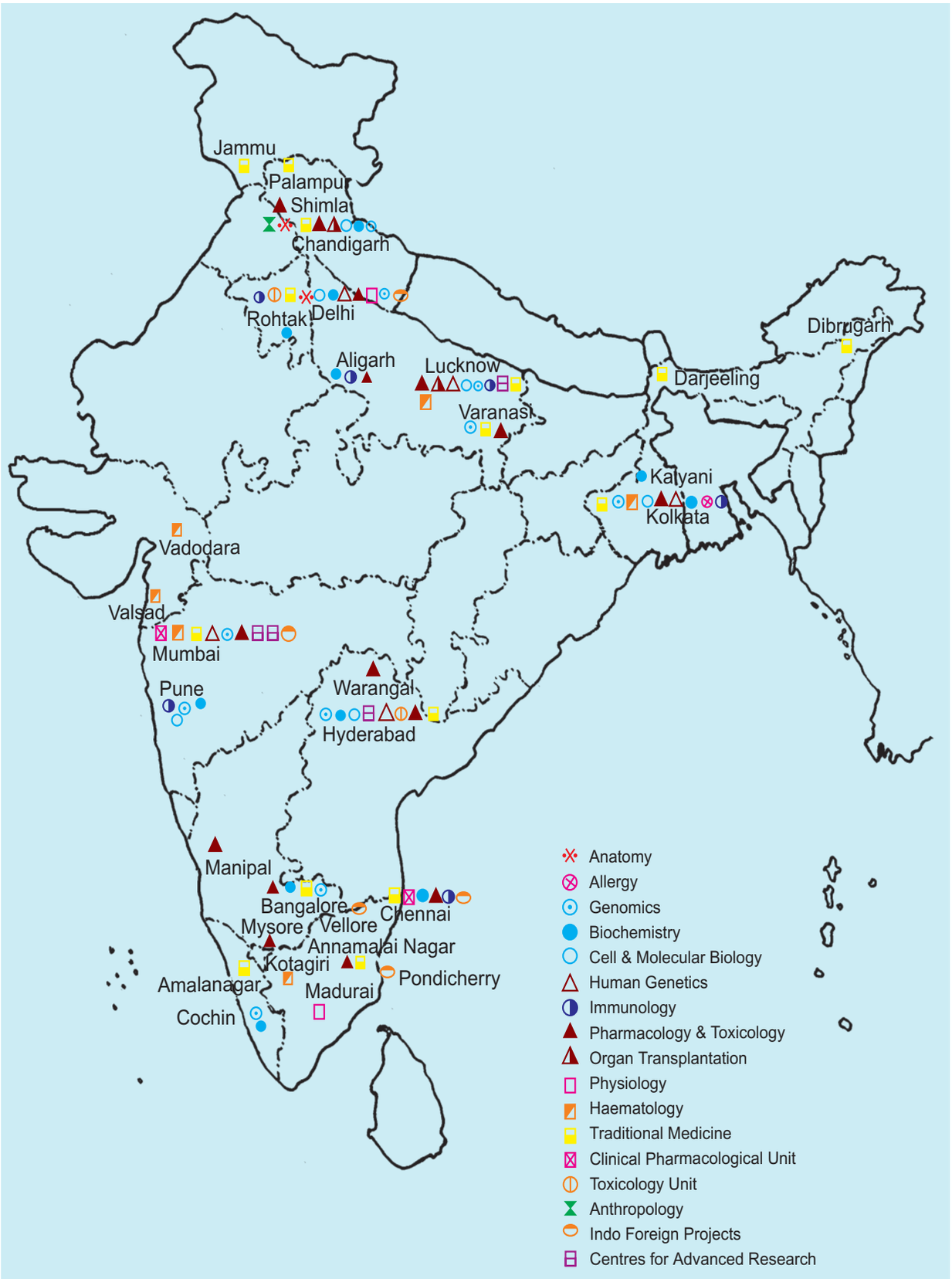
BIOCHEMISTRY

The Molecular Mechanism of Aging

The Advanced Centre for Biochemical and Molecular Correlates of Aging at University of Hyderabad, Hyderabad has been pursuing studies to understand the molecular mechanisms of aging process in brain through multi-pronged studies for examining the possibilities of establishing molecular markers for aging and intervention to retard the progress of aging and age associated diseases. The results have shown that the primer extension activity in a model oligo duplex (14 mer. 21 mer) by the rat neuronal extracts is lost with age. Protein synthesis studies carried out with the whole cells and cell-free extracts indicated that there is general decline in protein synthesis and impairment in translational initiation during aging. Topo II alpha and beta levels were estimated in cerebellum, cerebral cortex and midbrain of rats of different ages. The cerebellar regions showed higher topo II beta activity as well as higher protein levels. Age dependent decline in the topo II beta activity (with highest activity in young rats) was noted.

Role of Thyrotropin Releasing Hormone (TRH) in the Modulation of Surfactant Protein -A

The study was carried out at PGIMER, Chandigarh to isolate and characterize surfactant protein - A (SP-A) to assess its binding affinity, extent of its binding and internalization in different cell types (alveolar macrophages and alveolar type II cells) isolated from lungs of preterm and term rabbit pups. Effect of gestational age on SP-A binding and the effect of TRH administration was also studied. The results have shown that SP-A is actively bound and internalized by the lung type II cells/ macrophages of pups though there is certain degree of gestational age dependent variation in the level of SP-A incorporated. Prenatal TRH treatment resulted in an increase in the levels (bound/internalized) of SP-A in all the study groups.The results of the study are concurrent with the maturational response of the fetal lung to TRH.



MAJOR ICMR RESEARCH PROJECTS IN BASIC MEDICAL SCIENCES

Mechanism of Action of a Hypoglycemic Compound from Ficus bengalensis

Studies were carried out at University College of Medical Sciences, Delhi for studying the mechanism of action of hypoglycemic principle from water extract of bark of *Ficus bengalensis*. The compound produced 68% fall in fasting blood glucose levels and improved lipid profile in severely diabetic rabbits.There was significant fall in total and LDL+VLDL cholesterol and triacyl glycerol and increase in serum C-peptide levels after treatment with this compound in mild as well as severely diabetic rabbits. Levels of glycolytic (glucokinase) and lipogenic enzymes (glucose-6-phosphate dehydrogenase) increased while those of gluconeogenesis (glucose 6 phosphatase) decreased. Results of the study show that this compound can be used for treatment of diabetes in humans.

Role of DNA Fragmentation in Neuro-pathogenesis of Diabetes and Hypoglycemia

Studies were conducted at Guru Nanak Dev University, Amritsar for understanding the role of DNA fragmentation in neuropathogenesis of hypoglycemia and diabetes in experimental animals. A gradient of vulnerability in DNA fragmentation was observed among different brain regions. In hypoglycemic animals dentate gyrus and CAI regions of hippocampus and subventricular zone of hypothalamus were found to be the most vulnerable followed by thalamus and cortex. In biochemical studies diencephalon region showed most pronounced changes in mitochondrial lipid peroxidation as well as decline in primary antioxidant enzymes like Mn-SOD, catalase and GSH content. Deficiency in mitochondrial antioxidant system elicited spontaneous accumulation of reactive oxygen species (ROS) within the cells. The results revealed that enhanced ROS generation due to decline in antioxidant defense system may lead to DNA fragmentation and apoptosis in severe hypoglycemic and diabetic conditions. Efforts are on to unravel the mechanisms by which hypoglycemia induces permanent neuronal damage.

TRADITIONAL MEDICINE

Studies were continued at Centre for Advanced Research for Drug Development at CDRI, Lucknow on various identified plants. Phase III clinical trial has been initiated with *Picroliv* in liver cirrhosis patients and TB patients receiving multiple drug therapy at BYL Nair and KEM Hospital, Mumbai. The extract of *Centella asiatica* caused significant reversal of scopolamine induced deficit in passive avoidance test in mice indicating amnesic (potential antidementia) activity. The effect of *Terminalia chebula* (TC) and the compound K022 was studied on glucose and insulin secretion in acute, chronic and chronic unpredictable stress models in adult rats. *Panax ginseng* was taken as standard drug. Exposure to the acute stress resulted in a significant increase in plasma glucose and serum insulin levels while chronic (and chronic unpredictable stress) did not affect the levels of glucose or insulin. Pretreatment with *T. chebula*, K022 and *P. ginseng* effectively reverted increased glucose as well as insulin levels.

At the Centre for Clinical Pharmacology of Traditional Medicine at BYL Nair Hospital, Mumbai studies were continued to find mechanism of action of the anti-diabetic plant *Pterocarpus marsupium* (*vijayasar*), clinical and experimental evaluation of a medicated oral rehydration solution containing *Cyperus rotundus* (*Nagarmotha* - whole red kidney beans), *Zinziber officinale* (*Sunthi*) and *Cuminum cyminum* (*Jeerak*) in diarrhoea and evaluation of a *Neem* formulation for

wound healing *in vitro* and *in vivo*. *Vijayasar* was seen to induce angiogenesis significantly. Experimental and clinical evaluation of medicated ORS was done and compared with WHO ORS. Although number of motions per day and the character of the stools was found to be almost same with both preparations, the recurrence rate in the later phase was found to be lesser with medicated ORS; it was easy to prepare and its taste and odour accepted well. For evaluation of the *Neem* formulation for wound healing, clinical and *in vitro* studies are being carried out.

CLINICAL PHARMACOLOGY

Studies were continued at Clinical Pharmacology Unit at Seth GS Medical College and KEM Hospital, Mumbai on 14 day primaquine therapy as anti-relapse therapy for *P.vivax* malaria. Results revealed that 2-3% of 131 cases treated with primaquine for 14 days relapsed. Resistance to primaquine regimen in *P.vivax* malaria has been documented for the first time in India.

The Clinical Pharmacology Unit at TRC, Chennai undertook studies on diseases caused by mycobacteria. Bioavailability studies of ofloxacin when given alone and in combination with rifampicin, isoniazid and pyrazinamide have shown that the pharmacokinetics of ofloxacin is not affected by the presence of other anti-TB drugs and bioavailability of ofloxacin remains unaltered. In a study on HIV/TB which assessed the role of malabsorption in the uptake of anti-TB drugs, the results showed that absorption of xylose is similar in healthy volunteers and TB patients. Xylose absorption is significantly lower in HIV and HIV-TB patients compared to TB patients. Urinary excretion of rifampicine and isoniazid was found to be lower in HIV and HIV-TB patients compared to TB patients. In another study done for the assessment of vitamin A levels in pulmonary tuberculosis patients, poor dietary intake, impaired absorption, increased utilization during infection, abnormal loss in urine during infection and acute phase response was observed.

A survey on current status of teaching of clinical pharmacology in India with special reference to drug development was undertaken by the unit at Chennai. The survey indicated that the graduate curriculum needs updating, collateral synchronization and integrated teaching with concerned clinical departments. Other suggestions included need for replacement of pharmacy with clinical pharmacology and animal experimentation with problem based and computer aided simulating exercises and training to handle latest state-of-the-art equipment, exposure to clinical trials *etc*. It has been suggested that exposure to clinical pharmacology and safety evaluation and visits of students to drug industries for understanding drug discovery techniques will go a long way in developing the area of clinical pharmacology in the country.

PHARMACOLOGY

Antibody-mediated Drug Delivery in Visceral Leishmaniasis

In an ICMR funded study completed at Indian Institute of Chemical Biology, Kolkata, a parasite specific 51 kDa protein has been isolated from infected macophage membranes for developing a drug targeting system for visceral leishmaniasis.

PRECLINICAL TOXICOLOGY

At the Pre-clinical Toxicology Unit at NIN, Hyderabad studies were undertaken for

evaluation of *Chlorella E-25 vulgaris*, interferon and anti rabies DNA vaccine. Other studies being continued include toxicity and allergenicity evaluation of recombinant hepatitis B vaccine and safety /toxicity studies of ayurvedic *bhasmas*.

HAEMATOLOGY

HAEMOGLOBINOPATHIES

Prenatal Diagnosis of β-Thalassemia

At IIH, Mumbai circulating fetal cells have been isolated in maternal blood in first and second trimester of pregnancy and single cell PCR for the prenatal diagnosis of β-thalassemia has been established during the year under reoprt.

Jai Vigyan Science and Technology Mission Project on Community Control of Thalassemia

The project aiming at education, screening, counselling and identifying couples at risk of having thalassaemic children was continued in 6 states (Maharashtra, Gujarat, Assam, West Bengal, Punjab and Karnataka). IEC material (brochures, booklets, posters, consent forms and questionnaire) in regional languages as well as in English have been prepared to bring about community awareness about the disease. A total of 12231 cases (4950 college students and 7281 antenatal cases) have been screened so far. Twenty two percent college students and 17.8% antenatal cases have been found NESTROFT positive and the overall prevalence of β-thalassemia trait has been found to be 2.8%. The prevalence of HbE trait and disease was very high in Dibrugarh and Kolkata. The other haemoglobinopathies detected included HbD, HbS and HbQ. About 12% college students and 32.5% antenatal cases were found to be iron deficient.

BLEEDING DISORDERS

Von willebrand Disease (VWD)

VWD is an autosomally inherited bleeding disorder. Certain subtypes of VWD, especially type 3 have severe bleeding manifestations. Carrier detection and prenatal diagnosis is important in them for prevention of the disease. VWF gene is a large one (~186Kb). Hence, gene tracking of the defective VWF allele is the method of choice. At IIH, Mumbai prenatal diagnosis was done in two cases of VWD by using two polymorphic markers VWF 1 and VWF 2 in intron 40 of the VWF gene. Carrier detection was also done in nine families of VWD.

Hemophilia

A multiplex PCR which allows the amplification of all regions of factor IX gene in a single PCR tube has been established at IIH, Mumbai. Total and partial deletions are easily and immediately identified by analysis of PCR reaction on a conventional 8% polyacrylamide gel followed by ethidium bromide staining. This will help in carrier detection and prenatal diagnosis in sporadic families of hemophilia B and in female carriers in the absence of the proband.

Biochemical and Molecular Characterization of G6PD Deficiency in India

Some of the tribal populations have got very high incidence of G6PD deficiency. Two biochemical variants of G6PD Insuli were identified during population screening and were subjected to sequencing this year at IIH. The mutation in both cases was found in exon 9. G6PD Rohini showed the presence of the Kerala-Kalyan mutation and G6PD Insuli showed the presence of a novel mutation 989G→A (Fig. 6).

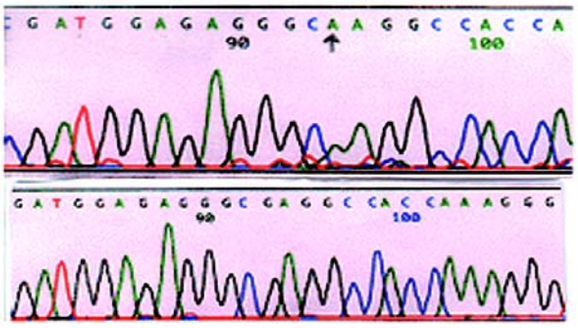


Fig. 6. G6PD Mutation

Study of Platelet Specific Antigens in Indian Population in Newborn

Neonatal alloimmune thrombocytopenic purpura (NAITP) occuring due to fetomaternal human platelet antigen-1 (HPA-1) system incompatibility is increasingly being detected worldwide in recent years. There is paucity of data on frequency of HPA-1 system in the Indian population as well as lack of confirmed diagnosis of the disease. At IIH, Mumbai two cases of NAITP were diagnosed during the year and treated successfully.

POPULATION GENETICS

Molecular Characterization of Bombay Phenotype

A rare blood group, Bombay phenotype, was discovered by IIH, Mumbai in 1952. Study has been initiated with the objective of characterizing molecular defects in the H gene in cases of serologically confirmed Bombay phenotype. Two mutations *i.e.* FUT1 and FUT2 are responsible for producing this phenotype-i) nucleotide 725T→G mutation in H gene and gene deletion of Se gene and ii) nucleotide 695G→A mutation detected in Japanese population. At IIH, 11 samples were analyzed of which 10 were found to be homozygous for 725 T→G mutation and one showed heterozygous pattern (Fig. 7). These samples will be checked for FUT gene deletion.

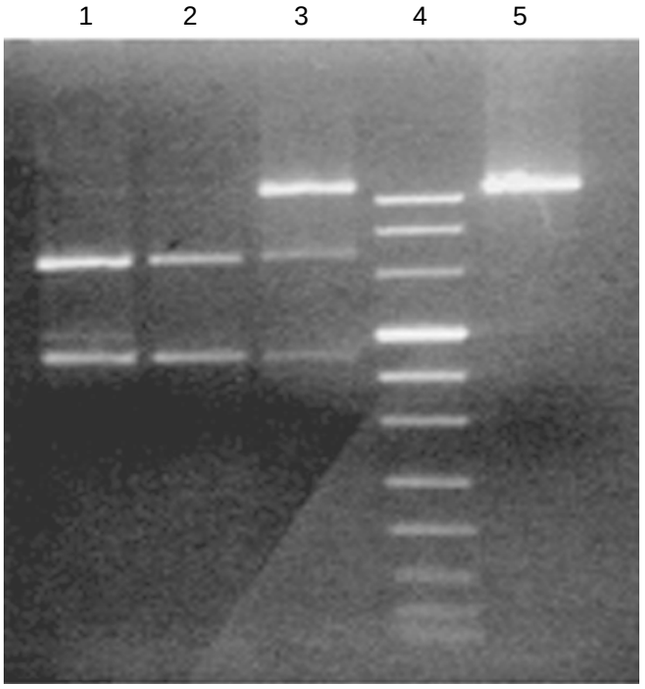


Fig. 7. Molecular characterization of H gene
Lane 1 & 2 : Homozygous for 725 T→G mutation
Lane 3 : Heterozygous for 725 T→G mutation
Lane 4 :Marker VIII (Roche) and
Lane 5 :Normal

STEM CELL BIOLOGY

Study was continued at IIH to standardize and assess the technique of long term cryopreservation at -80°c with mechanical freezer instead of liquid nitrogen. The cryopreservation of cord cells with 10% DMSO and hydroxyethyl starch was found to yield better results. CD34 positive cell recovery was found to be 85% after one year of cryopreservation.

HAEMOGLOBINOPATHIES / BLOOD DISORDERS AMONG TRIBALS

Nutritional Anaemia and Haemoglobinopathies amongst Tribal Populations of India

A multicentric project is ongoing in 4 states (Maharashtra, Gujarat, Orissa and Tamil Nadu) of India with the aim to assess

the nutritional and haematological problems of six ethnically and geographically different endogamous tribal populations on the verge of extinction. During the year health camps were organized and attempts were made to screen every tribal from the villages. A total of 5615 individuals from *Katkaris, Madias, Kotvadias, Kolchas, Irulas, Kurumbas, Mollukurumbas, Paniyas, Bondos* and *Didayis* were clinically examined. Anaemia was found to more common among the *Didayis, Bondos, Madias* and *Irulas* as compared to be other tribal groups. Females were more anaemic than males and children were found to be more anaemic than the adults. Severe anaemia was present in the tribals of Nilgiris.

Iron deficiency anaemia was more common among the *Didayis, Bondos, Paniyas* and *Irulas* followed by *Kurumbas, Kotvadias, Kolchas, Katkaris, Moolukurumbas* and *Madias*. Sickle cell gene was present in all the tribal groups. Maximum number of sickle cell heterozygotes and homozygotes were found among the *Paniyas, Kurumbas, Madias, Moolukurumbas* and *Katkaris*. β-thalassemia gene was also found to be present in all the tribal groups except *Kotvadias, Irulas* and *Moolukurumbas*. The prevalence rate of sickle cell trait varied from 1.5 to 28.9%. A very high prevalence of AS and SS was observed among the tribals of Nilgiris and Nagpur. β-thalassemia trait was mainly found among the *Katkaris, Kolchas* and *Didayis* and the prevalence rate varied from 0.9 to 5.6%. The prevalence of iron deficiency was found in 20 to 50% of AS and 5 to 30% of β-thalassemia cases. G6PD deficiency was found in all the tribal groups and the maximum number of cases were from *Madias*. Pallor, vitamin deficiency, night blindness, diarrhoea and malaria are some of the common health problems in these tribal groups. In Nilgris, not a single case of malaria was identified whereas diarrhoea was reported in 100% cases.

Intervention and follow up have been initiated in nutritional anaemia and sickle cell anaemia cases. Folic acid and fersolate tablets have been given to cases of nutritional anaemia and sickle cell disease with iron deficiency. Sickle cell anaemia patients have been advised to take electral powder and plenty of fluid during the vaso-occlusive crisis. An improvement in Hb and reduction in ferric erythropyrin phosphate levels has been observed in cases who are taking the tablets regularly. Hepatitis, influenza and pneumococcus vaccines were given to sickle cell anaemia cases in Nagpur. Report Cards were distributed to all the individuals whose blood was tested. Genetic counselling was given to the unmarried young individuals to avoid marriages between the carriers of haemoglobinopathies particularly HbS and β-thalassemia and young carrier couples have been advised to come for prenatal diagnosis.The study is in its final stages and results are being compiled.

Haemoglobinopathies among Scheduled Castes and Scheduled Tribes of Madhya Pradesh

A study is being carried out by RMRC, Jabalpur in scheduled tribes (*Korku* and *Gond*) and castes (*Mahar / Mehra, Katiya* and *Basod*) of district Chhindwara with the aim to find out the prevalence of sickle haemoglobin, β-thalassemia and G6PD deficiency.

The prevalence of sickle haemoglobin has been found to be 24% in SC population. Among the ST, *Korkus* have high prevalence of HbS (16.7%) compared to *Gonds* (3.6%). The prevalence of β-thalassemia trait varies from 2.2% (*Basod*) to 4.8% (*Korku*) and that of G6PD from 1.3% (*Katiya*) to 4.3% (*Basod*).

Eighty seven percent of these tribes are anaemic of which 1.8 are severely anaemic. Anaemia is more common among the adult females and children. Nutritional (iron deficiency) anaemia has also been found to be highly prevalent in these populations.

Hemolytic Disorders among Tribals of Orissa

A study was initiated at RMRC, Bhubaneshwar to estimate the nature and extent of hereditary haemolytic disorders (sickle cell disease, thalassemia and G6PD deficiency) in major tribes of Sundargarh district and to bring awareness among tribal communities.

The results indicated that haemoglobinopathies (7.9%) and G6PD deficiency (19.0%) were major public health problems in *Bhuyan* tribe. Both beta-thalassemia trait (10.2%) and sickle cell disorders (4.1%) were common in the community. For the first time, haemoglobin D (which is quite common in Punjab, Gujarat, Maharashtra, Uttar Pradesh and north-western states of India) has been encountered in trait form in *Khandyat Bhuyan* (1.2%). Further, for the first time in Orissa, *Paraja Bhuyan* was detected having hereditary persistence of fetal haemoglobin.

Since the prevalence of consanguineous marriages is high among the tribals and hemolytic disorders are genetically transmitted, they are highly prevalent among the tribal populations.

Studies on Molecular Variants of G6PD Deficiency in Malaria Endemic Tribal Population of Orissa

G6PD deficiency is the most common human enzymopathy spread all over the world where malaria is endemic. More than 90 molecular variants have been identified globally. Studies done by RMRC, Bhubaneswar in 8 tribes of Orissa revealed that all the variants belong to G6PD Orissa mutation (Fig. 8). The prevalence of the disease ranged from 3-11% in various tribes.

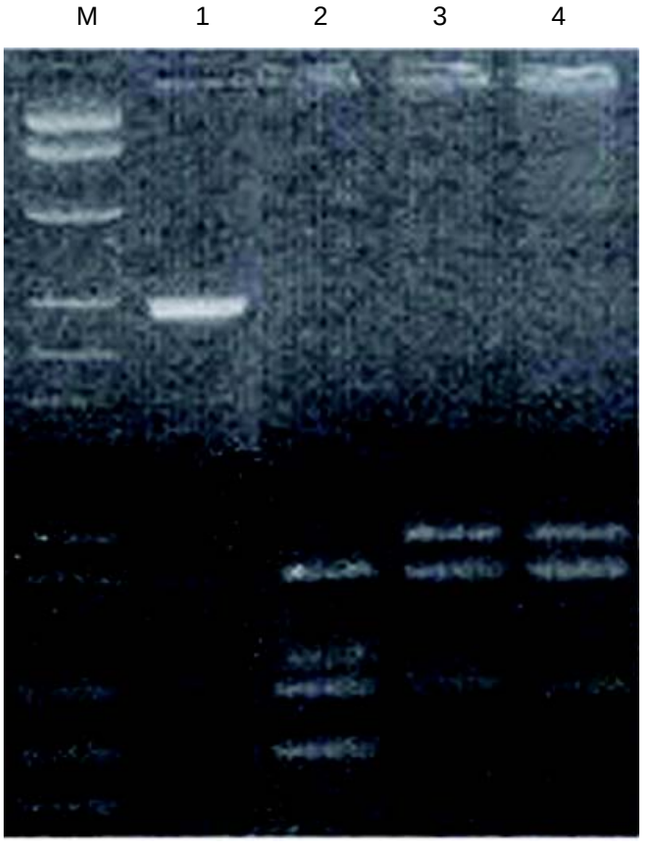


Fig. 8. Molecular analysis of G6PD variants
Lane M = ø X 174 DNA / I Digest,
Lane 1 = undigested PCR product of exop 3 and 4,
Lane 2 = Hae III digested amplified fragment of a non deficient sample,
Lane 3 & 4 = Hae III digested amplified fragment of G6PD, Orissa mutant

SUPPORTING FACILITIES

The Council's National Institute of Epidemiology (NIE) at Chennai and Institute for Research in Medical Statistics (IRMS) at New Delhi continued epidemiological studies and field trials in a number of areas of national importance. The IRMS conducted a study for assessing the usage and acceptability of Indian system of medicine and homeopathy among rural and urban population of India. A number of training programmes and workshops were conducted in biomedical statistics and public health for the benefit of researchers/field staff of various health/medical organizations. The NIE is continuing the two year Field Epidemiology Training Programme leading to Master of Applied Epidemiology degree.

NATIONAL INSTITUTE OF EPIDEMIOLOGY (NIE), CHENNAI

Field Epidemiology Training

The Institute continued the two year Field Epidemiology Training Programme (FETP) leading to the degree of Master of Applied Epidemiology. Nine scholars joined the third cohort (2003-04). The first contact session comprising basic concepts of epidemiology and bio-statistics has been completed for this batch of scholars.

Outbreak Investigations

The FETP scholars participated in an outbreak investigation of West Nile virus infection in three villages under Valavanthi PHC in Yercaud Block of Salem district. An outbreak of 55 fever cases including one death was reported from these villages in February 2003. Investigation of the outbreak by active case finding identified 77 cases. Clinical manifestations were high intermittent fever, severe prostration, headache, myalgia, arthralgia, backache, nausea, pain in the eye, redness of eyes and vomiting. Epidemic curve suggested intermittent transmission with an incubation period of approximately 6-8 days. Spot map showed scattering of cases in all three villages where no clustering pattern was evident. Both males and females were affected but there was no case below 10 yr. Differential diagnosis included dengue fever, Kyasanur forest disease, JE, leptospirosis and fever of viral origin. Sero immunology revealed two out of 70 samples to be positive for recent West Nile virus infection and two as indeterminate but indicative of West Nile virus infection. Using a revised case definition, 44 out of 77 cases showed clinical symptoms supportive of West Nile virus infection. Characteristics of the revised epidemic curve and spot map remained unchanged. When adjusted for sex, attack rates were significantly higher among those aged above 20 yr. Cases of West Nile virus fever have not been previously reported from this region. This outbreak appeared to be the first of its kind.

Clinical Trial for Chronic Hepatitis C

Study was conducted with the objectives to (i) assess whether combination therapies of (a) glycyrrhizin - interferon and (b) Rilivitin - interferon against chronic hepatitis C are effective to the level of 70% in Indian patients, (ii) evaluate the side effects/toxicity of the trial drugs, (iii) evaluate the cost-effectiveness of the two combination therapies and (iv) study the role of certain identified factors *viz.*, genotype, viral load and some host factors in deciding the outcome of therapy.

This multicentric study is being conducted at 9 centres -Chandigarh, New Delhi (3 centres), NOIDA, Lucknow, Kolkata, Mumbai and Hyderabad and is being coordinated by NIE. The duration of trial treatment has been reduced from 48 weeks to 24 weeks.

Leprosy Vaccine Trial

Based on second re-survey, two vaccine candidates (ICRC and BCG+ killed *M.leprae*) were found to provide protective efficacy of about 65% . The third re-survey of LVT was initiated during August, 1999 to know the sustainability of the immuno prophylactic effect of the candidate anti leprosy vaccines. It has been completed now and vaccine codes decoded. Interpretation of results is in progress to know the incidence and effect of vaccination on the general population. The ICRC is found to have given better protection than other vaccines.

Psycho-social Challenges faced by HIV Positive Persons

The Institute is conducting a study at the Institute of Venereology, Government General Hospital, Chennai to understand the impact of HIV positive status personally, emotionally and socially on the HIV infected individuals. Data collection has been done for 310 HIV infected persons through in-depth interviews.

Use of Simulation Model in National Leprosy Eradication Programme

The Institute has developed a simulation model in collaboration with the CDTDC, Erasmus University, Rotterdam. The epidemiological input for the development of the model was generated by NIE and the mathematical modelling aspects were done by the CDTDC. The internal mechanism of the model was reviewed; links between various parameters of the model were examined and possible reduction of input parameters identified. Capacity to modify the model was developed and modifications in the input screen are being done to make it user friendly. Once the modified version of the model is ready, it would be passed on to the State level managers for testing its use under routine programme conditions.

INSTITUTE FOR RESEARCH IN MEDICAL STATISTICS (IRMS), NEW DELHI

End-line Evaluation of India Population Project -VIII

The Ministry of Health and Family Welfare (MOHFW) has identified IRMS as nodal agency for providing technical advice and supervision to all the field agencies appointed by the states to ensure quality and consistency of the end-line surveys and to allow comparison across the project cities.

The objectives of the end-line evaluation are (i) to provide technical assistance to project cities and survey agencies selected to carry out the surveys of family welfare urban slum project in Bangalore, Kolkata, Delhi and Hyderabad. The areas of technical assistance specifically include sampling design, standardization of study

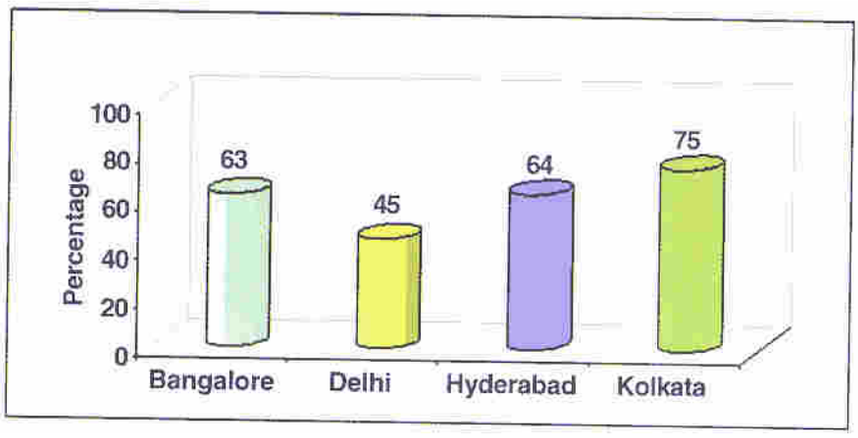
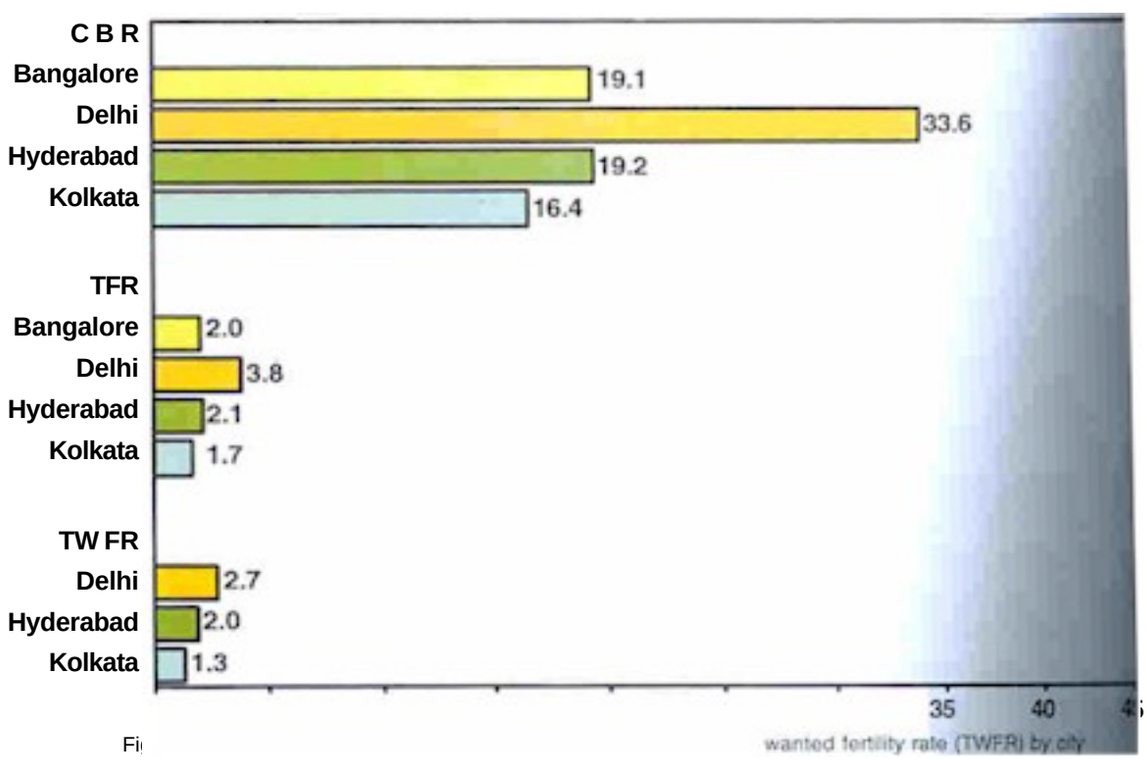


Fig. 1. Current use of family planning method in cities

instruments and methodology and ensuring quality during the various phases of study, (ii) to compile a consolidated end-line evaluation report for the project summarizing major findings, achievement of development objectives and highlighting the lessons learnt, and (iii) to cross check 5% of the households covered by the field survey agencies.

During the year key impact indicators studied were infant mortality rate, maternal mortality rate, total fertility rate, crude birth rate, contraceptive prevalence rate by method, mean age at marriage for women and men and utilization of maternal and child health services. Salient findings are presented in Fig 1-6. The results revealed that the current use of family planning methods in urban slums was highest in Kolkata followed by Bangalore. Crude birth rate and total fertility rate were highest in Delhi followed by Hyderabad and Bangalore. In Bangalore awareness about AIDS/ HIV was highest followed by Kolkata. In Bangalore 71% women from urban slums registered themselves with health services during first trimester of pregnancy while in Delhi only 31% women did so. Home delivery was preferred by about 70% women in Delhi while in Bangalore, Hyderabad and Kolkata almost all deliveries were conducted in hospitals.



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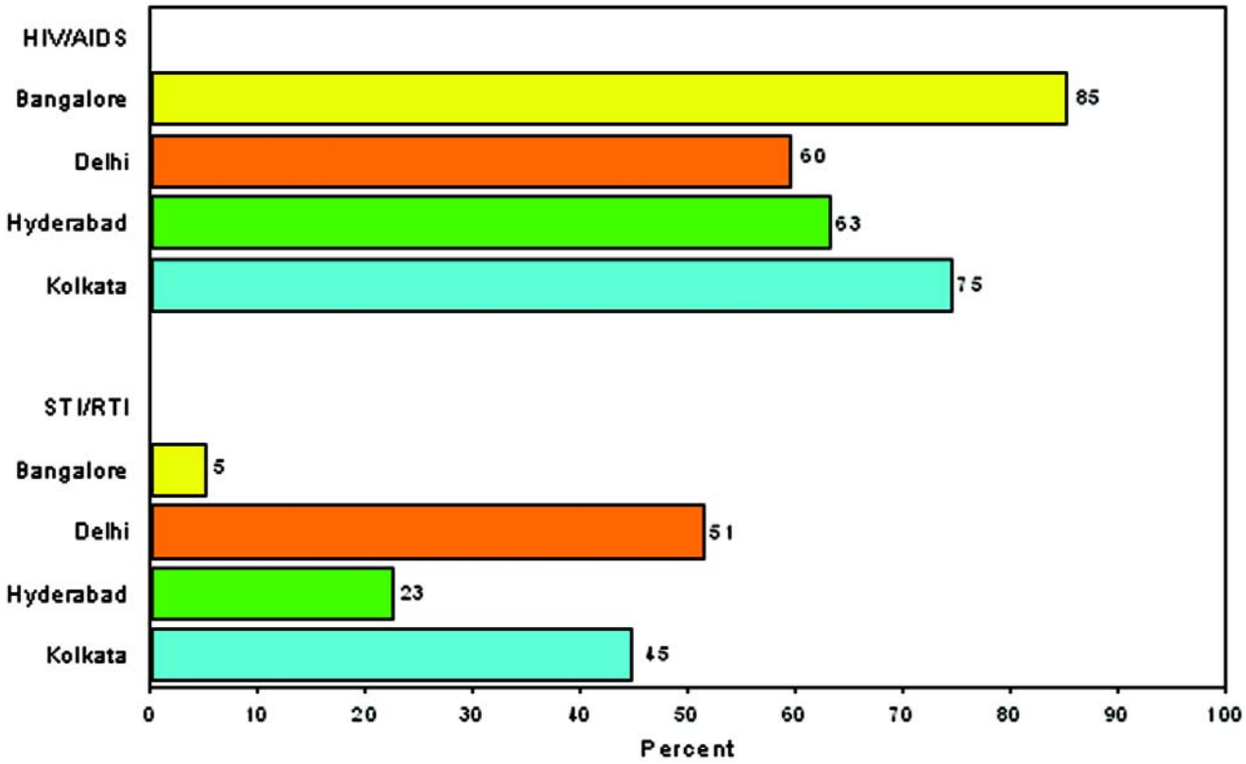

Fig. 3. Knowledge of HIV/AIDS and STI/RTI

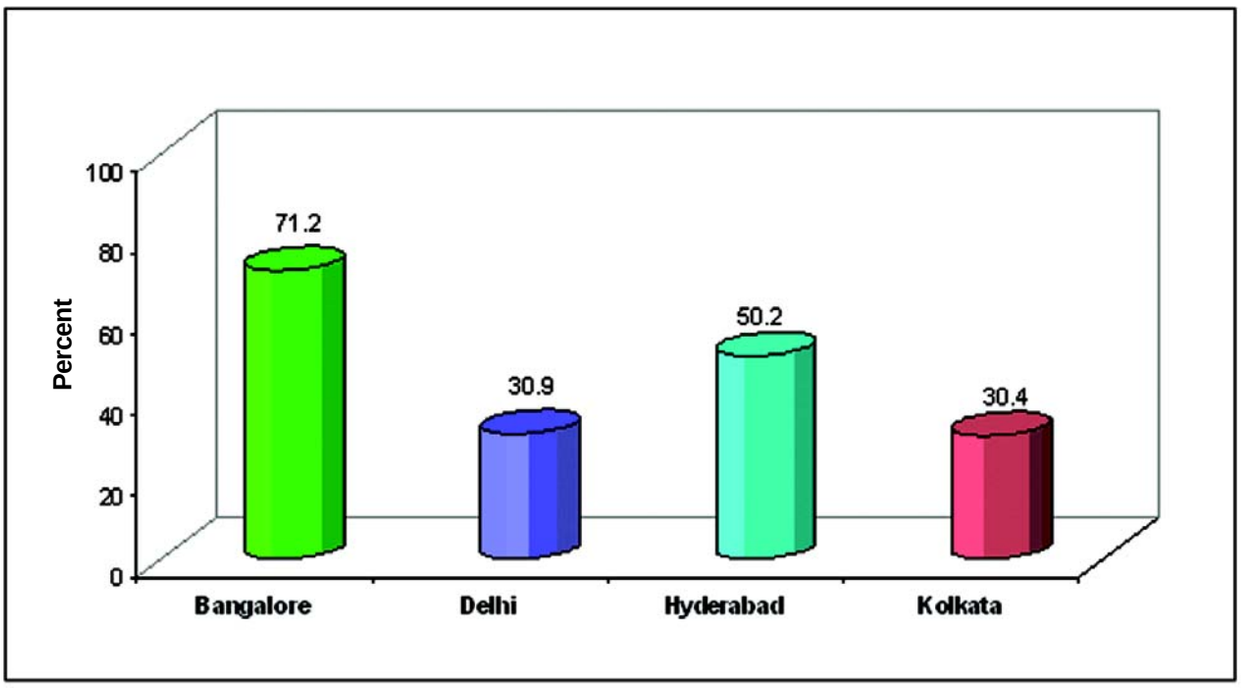

Fig. 4. Women who registered during first trimester in various cities in India

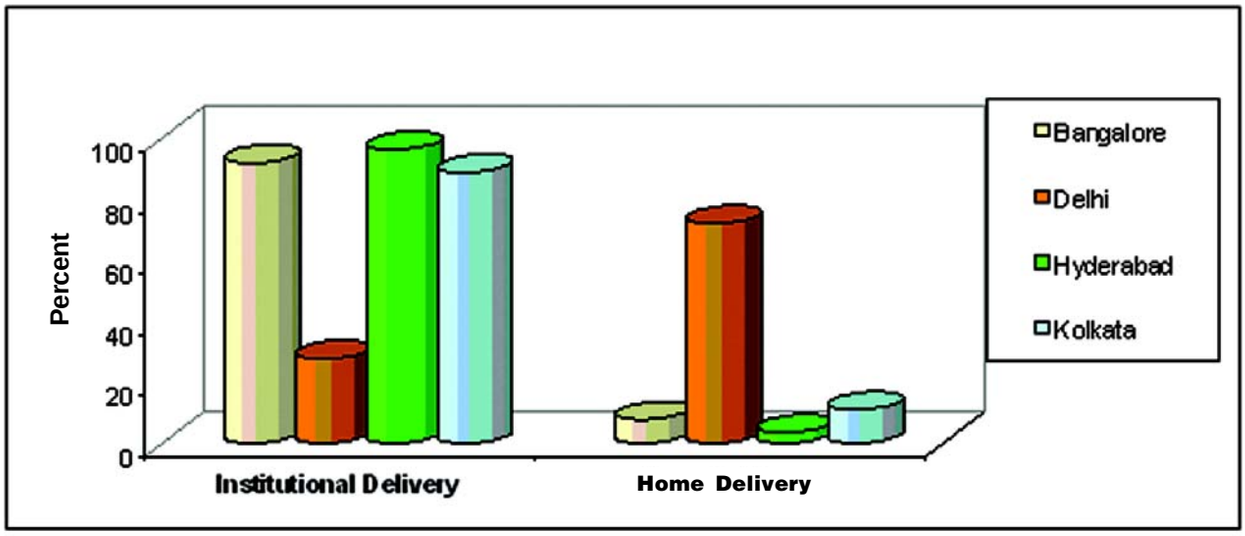

Fig. 5. Place of delivery in various cities in India

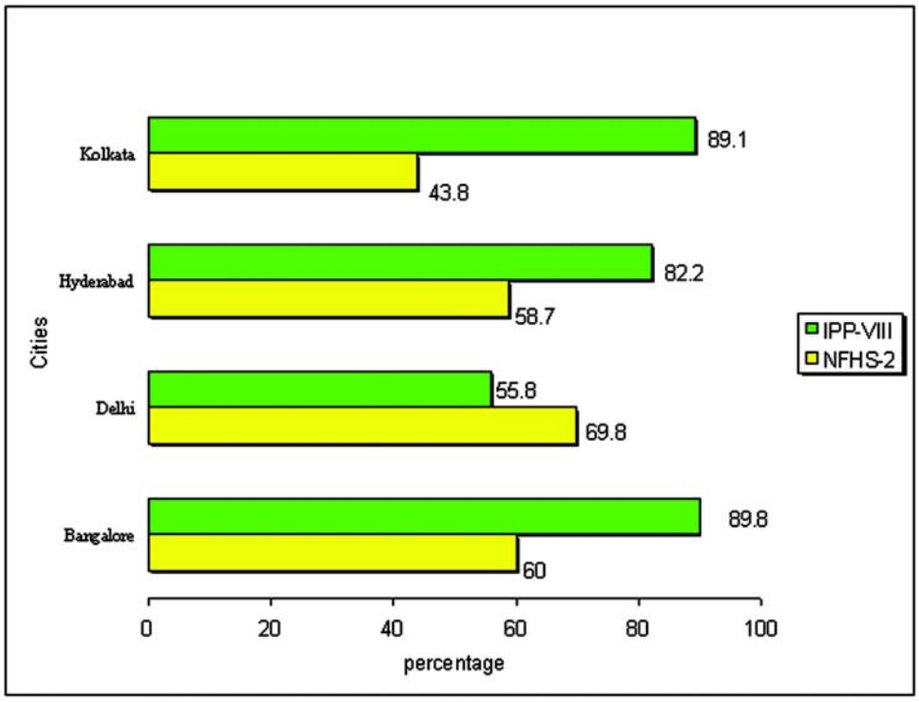

Fig 6. Percent of children aged 12-23 months who have received all vaccination. Comparison of results with NFHS-II

Usage and Acceptability of Indian Systems of Medicine and Homoeopathy

The Department of Indian System of Medicine and Homeopathy, MOHFW, entrusted IRMS, Delhi to undertake the study on usage and acceptability of Indian systems of medicine and homoeopathy (ISM&H). The study involved collection of information on availability of facilities alongwith the extent of utilization of these services from 35 districts in 19 states [in 420 hospitals and 840 dispensaries under ISM&H] giving due representation to rural/urban areas and also Government /non-Government sectors. Information on perception of 604 private practitioners and 5804 patients attending the dispensaries as well as 33,666 households with 44, 639 sick members availing ISM&H health care has also been collected in the study.

About 38% of households reported that they visit traditional healers for treatment (40 % in rural and 30 % in urban areas). The illnesses treated by traditional healers were mainly bone setting (30%), dog bite (16%), snake bite (19%) and jaundice (15%) (Fig. 7).

One third of the households preferred ISM&H for treating common ailments. Only 18% reported preference of ISM&H for serious ailments due to no side effects (31%), being cheap (30%) and effective (25%).

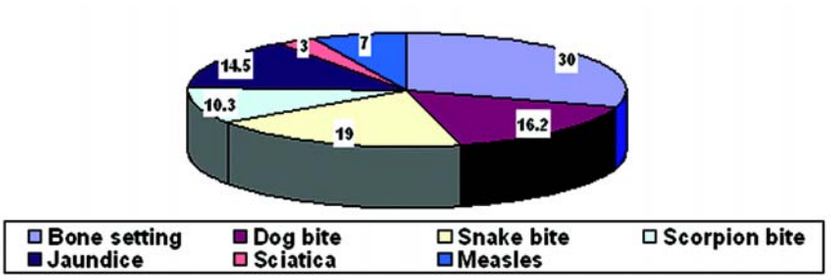

Fig. 7. Type of illness for which traditional healer is visited (%)

Almost all the allopathic users were aware of ayurveda and homoeopathy. Reasons spelt out by them for not using ISM&H were slow progress (28%), practitioners not available (27%) and no faith (12%).

The percentage of households availing ISM&H showed increase with income and literacy level. Most of the households wanted the Government to open new dispensaries under ISM&H and also to ensure sufficient supply of medicines.

INDO - FOREIGN COLLABORATION

The Council co-ordinates collaboration in biomedical research between India and other countries / international agencies. During the year 2002-03, the organization of following international meetings was facilitated (with financial support):

i. Indo-US Senior Advisors' Meeting on Occupational Health and Environmental Toxicology Working Group (New Delhi, May, 2002).

ii. Indo-Russian Working Group on Medical Sciences and Workshop on Immunomodulators in Russia (Moscow, August, 2002).

iii. Indo-US Joint Working Group on Maternal and Child Health (USA, October-November, 2002).

iv. Indo-US Workshop on HIV / STD - Behavioural Prevention Research (Agra, January, 2003).

v. ICMR-INSERM Joint Working Group (New Delhi, February, 2003).

vi. Indo-French Workshop on Neuroprotection in Early Life (Bangalore, February, 2003).

vii. Indo-US Joint Working Group on Environmental and Occupational Health (New Delhi, March, 2003).

The ICMR serves as the Secretariat for the Health Ministry's Screening Committee (HMSC), which considers research proposals involving foreign collaboration/assistance. During the year 2002-2003, three meetings of the HMSC were held wherein 60 projects for assistance/collaboration with WHO, National Institutes of Health, USA, Germany, Wellcome Trust, International Atomic Energy Agency, etc. were considered. Of these, 33 project proposals were approved by the Indian side.

Exchange visits of 75 scientists were arranged under joint projects and bilateral programmes in the field of biomedical sciences and public health between India and foreign countries such as Germany, France, Russia, USA *etc.* and also arranged the visits by Health Ministers of Bulgaria, Mozambique as well as Chinese Delegation to ICMR. From the country budget of WHO for biennium 2002-2003, support was sought for proposals made by ICMR Institutes / Centres and Headquarters for undertaking certain research projects and organizing training programmes in various fields of biomedical research.

INTELLECTUAL PROPERTY RIGHTS

The Intellectual Property Rights Policy was released by the Union Minister of Health and Family Welfare in May, 2002. An US patent has been granted for four hypoglycemic compounds isolated from *Eugenia jambolana (Jamun)*. A patent 'Species-specific PCR assay for detection of *Leishmania donovani* in clinical samples of kala-azar and post kala-azar dermal leishmaniasis' (IOP, New Delhi) has been filed at the United States Patent and Trademark Office (USPTO) in February, 2002. Two patents *viz.*, (i) a simple paper smear method for dry collection, transport and storage of cervical cytological specimen for rapid screening of human papillomavirus infection by PCR (ICPO, New Delhi) and (ii) obese mutant rat (NIN, Hyderabad) are being processed for filing at the USPTO. Attempts are being made to develop resource material on IPR and WTO issues, study the impacts of the IPR awareness programmes and to design and develop a database on literature, data and other reference sources on WTO and IPR issues.

BIOMEDICAL ETHICS

An ICMR -WHO intercountry meeting on ethics in health research and a Workshop on ethical issues in biomedical research was organized with the objectives to familiarize health scientists from south-east Asia with the essential principles and practice of ethics in biomedical research.

Besides these, a joint WHO-ICMR post launch interactive session on ethical, legal and social issues of genomics and an Indo-Canadian initiative (harnessing genomics to improve health in India) was conducted during the year.

TRAINING PROGRAMMES

All the ICMR institutes such as NIN, Hyderabad; NIRRH, Mumbai; IOP, and ICPO, New Delhi; TRC and NIE, Chennai; NICED, Kolkata; NIV, Pune and NIOH, Ahmedabad *etc.* organized training programmes and workshops in their areas of expertise for medical/health personnel - doctors, researchers, technicians and field workers.

PUBLICATION, INFORMATION AND COMMUNICATION

The Council intensified activities in the areas of biomedical information and communication during the year under report. Apart from bringing out the regular periodical and non-periodical publications of the Council, exhibitions, workshops, symposia, lectures and discussions were organized for dissemination of scientific knowledge among the target groups such as scientists, policy makers, school children and layman. The ICMR website (*http://www.icmr.nic.in*) gives useful information on health/biomedical research in India and is updated regularly.

PUBLICATIONS

PERIODICAL PUBLICATIONS

Indian Journal of Medical Research

The Indian Journal of Medical Research (IJMR) continued to be indexed and abstracted by all major global current awareness and alerting services. The journal is brought out with a new layout with structured abstracts. During the period under report many review articles on topics of current relevance were published.

ICMR Bulletin

The ICMR Bulletin entered 31st year of its publication and continues to be in great demand among biomedical scientists, health personnel including medical students and media.

Some of the topics featured in the Bulletin included Short-course Treatment of Leprosy: Present Status; Cholera Bacteriophages Revisited; Prospects of Elimination of Lymphatic Filariasis in India and what is New in the Diagnosis of Tuberculosis? The December 2002 issue of the Bulletin featured a special article on "Live and Let Live; Acceptance of People Living with HIV/AIDS in an Era where Stigma and Discrimination Persist" to commemorate the World AIDS Day (December 1, 2002).

ICMR Patrika

The monthly Hindi version of ICMR Bulletin was brought out regularly. Efforts were made to further simplify the language for layman. During the year articles on important health aspects such as *Haiza Bacteriophage: Punravalokan, Bharat mein filarial rog samapt karne ki sambhawanayen, West Nile vishanu ki mahamariyan: Bharat ke liye sabak, etc.* were published. On World AIDS Day, a popular article entitled *"Jiyen aur Jine Den: HIV/AIDS grast Vyaktiyon Ke Prati Laanchhan Evam Bhedbhav Nahin, Unhein Apnayen"* was published in the December 2002 issue of the Patrika.

Annual Report

The English and Hindi versions of the Annual Report of the Council for the year 2002-03 were brought out in 4-colour and on

art paper with improved layout design to make the report more attractive and informative with colour illustrations, lists of Council's research publications, ICMR funded research projects, fellowships, training programmes, *etc*. The Annual Report of the Council's Headquarters and Institutes can be accessed at the ICMR website (*http://www.icmr.nic.in*).

NON PERIODICAL PUBLICATIONS

Review Monograph on Medicinal Plants of India

The multidisciplinary data in respect of over 500 medicinal plants have been compiled, reviewed by experts and finalized for print as also draft monograph on another 250 species.

Development of Standards of Selected Medicinal Plants and Monographs Thereof

The first volume covering quality standards of 32 Indian medicinal plants has been reviewed by experts and is under print. This is an output of the programme on development of standards of important medicinal plants initiated at 5 institutions *viz.* NBRI, Lucknow; TBGRI, Thiruvananthpuram; BV Perd Centre, Ahmedabad and NIPER, Mohali. The programme has now been extended to two more institutions *viz.* R. N. Ruia College, Mumbai and University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh. The draft manuscript covering quality standards of another 30 medicinal plants is being prepared.

Medicinal Plant Monographs on Diseases of Public Health Importance

Draft Monographs have been prepared in the area of Malaria and Filariasis and are undergoing Expert Reviews. They cover leads from ancient knowledge, allopathic system of medicine as well as from scientific evidence.

INFORMATICS AND COMMUNICATION

BIOMEDICAL INFORMATION

The ICMR-NIC Centre continued to cater to the information needs of the medical community and during this period, 2980 searches were received by post/email which included 160 requests for full-text of journal articles (till January 2003). The web page (*http://indmed.nic.in*) crossed 38,000 hits since its launch.

IndMED database, has 23,567 records that can be accessed from the Centre's website (*http://indmed.nic.in*). The Centre also took up the task of developing an online full-text database of the biomedical journals, medIND with a proposal to cover full-text of journals covered in IndMED database in a phased manner. The prototype database covering the latest issues of 6 journals has been prepared and the Centre received signed MOUs from 18 journal editors who have shown willingness to have their journals included in the database. The Union Catalogue of Biomedical Periodicals was updated to include latest data from 31 libraries. This Catalogue was made web-searchable (*http://uncat.nic.in*) and the data was also released on CD format.

Three Workshops on "Biomedical Research and Internet" were held during this period at NIC, New Delhi, Bhaktivedanta Hospital, Mumbai and NIC, Bangalore. The participants were medical/library professionals and these 3-days Workshops included extensive hands-on sessions. One training programme "ONLINE Searching of Biomedical Databases" at NIC Hqrs., New

Delhi and two programmes on "Emerging Technologies for effective Management of Library and Information Services" were conducted. Two user awareness programmes were conducted at Goa Dental College, Goa and Department of Pharmacy, Annamalai University, Annamalai Nagar.

Scientometric Studies

The annual document - '2001 Research Output of ICMR Institutes' with analysis of publications from all institutes/centres was brought out during the year. The exercise of normalization of impact factor (IF) has been done for all the institutes. The scientometric analysis including citation analysis of research papers of NICED, Kolkata since inception has been initiated. A total of 325 papers were published by ICMR institutes during the year 2001. The MRC, Delhi topped the tally with 44 papers followed by IIH, Mumbai (34) and NICED, Kolkata (34). Of the total, 57.23% were covered by SCI/JCR. In this category, the IIH topped the tally with 28 papers. A total of 178 journals were used for publishing these papers. Out of 178 journals, 101 were covered by SCI/JCR. *Nature Genetics* had the highest IF (29.600) among the SCI/JCR covered journals whereas *Indian Veterinary Journal* had the lowest IF (0.043). There is a slight improvement in the average IF/paper of the Council from 1.456 to 1.661. The top five Institutes in terms of total IF were NICED (52.544), IIH (38.797), CJIL (33.998), MRC (26.894) and NIRRH (26.818). In all, 53 authors contributed 4 or more papers.

Bioinformatics Centre

The ICMR website *http://www.icmr.nic.in* is being updated regularly. The design of home page is changed and new features are added from time to time. During the year documents/features displayed on the website include National Guidelines for Accreditation, Supervision and Regulation of ART Clinics in India (open for public debate), National Health Research Policy (revised draft), National Cancer Registry Programme (Report of Population Based Cancer Registries (1990-1996)), National Cancer Registry Programme (1981-2001) - An Overview, ICMR Extramural Research Projects sanctioned during 2002-2003 and 1997-2001, Intellectual Property Rights Policy and Tenth Plan Document (2002-2007).

Databases pertaining to the extramural and intramural research projects of ICMR are updated regularly. During the year, several new databases were created and software packages developed for book-keeping.

Web portal for National Health Information Collaboration (NHIC) has been developed under Health Inter-network project of UNDP-WHO. The site will work as authentic web site pertaining to health research information for the country.

DISSEMINATION OF BIOMEDICAL INFORMATION

The Council and its various Institutes/ Centres continued to organize and participate in various activities for the dissemination of biomedical information to different target groups including layman.

To celebrate National Technology Day on May 11, 2002, the ICMR HQ organized a lecture on Creative Science for Innovation in Health Care Technology, by Prof. S.K. Basu, Director, National Institute of Immunology, New Delhi. Various ICMR Institutes/Centres also celebrated the National Technology Day by organizing lectures/discussions/open houses/exhibitions on this occasion. The ICMR HQ organized a lecture on "Strategies for Prevention of HIV in Asia" by Dr Roger Detels, Professor, University of California, Los

Angeles, USA on September 17, 2002 as part of the Council's Foundation Day celebrations.

The ICMR Headquarters and its various Institutes/Centres also celebrated the National Science Day in February/March 2003 with focus on the theme "50 years of DNA; 25 years of IVF-The Blue Print of Life", by organizing various events. The ICMR HQ organized a day long symposium on the theme. Eminent scientists in respective fields participated in the symposium.

On Hindi Day, a scientific debate on (i) *'Chikitsa anusandhan mein jantuon ke prayog per vivid: Uchit athwa anuchit'* and (ii) *Shakahar banam Mansahaar* was organized at the ICMR Hqrs. On 16th September 2002.

The NIN, Hyderabad celebrated the National Nutrition Week (September 1-7, 2002) by organizing extension lecture, nutrition education and awareness camps and nutrition extension programmes for various categories of people including women, children and tribals.

The Council participated in the S & T Exhibition "Pride of India Science Expo-2003" organized as part of the 90th Session of the Indian Science Congress at Bangalore during January 3-7, 2003. A large number of students and general public visited the exhibition and interacted with ICMR scientists. The ICMR was selected as one of the institutions/organizations for the best exhibitors Pride of India Award.

Appendix I

ICMR PERMANENT INSTITUTES/ CENTRES

1. Central JALMA Institute for Leprosy
   Taj Ganj
   Agra - 282001

2. National Institute of Occupational Health
   Meghani Nagar
   Ahmedabad - 380016

3. National Institute of Epidemiology
   Mayor VR Ramanathan Road (Spurtank Road)
   Chetput
   Chennai - 600031

4. Tuberculosis Research Centre
   Mayor VR Ramanathan Road (Spurtank Road)
   Chetput
   Chennai - 600031

5. Malaria Research Centre
   22, Sham Nath Marg
   Delhi - 110054

6. Food and Drug Toxicology Research Centre
   National Institute of Nutrition
   Jamia Osmania
   Hyderabad - 500007

7. National Centre for Laboratory Animal Science
   National Institute of Nutrition
   Jamia Osmania
   Hyderabad - 500007

8. National Institute of Nutrition
   Jamia Osmania
   Hyderabad - 500007

9. National Institute of Cholera and Enteric Diseases
   P - 33, CIT Road Scheme XM
   Post Box No 177, Beliaghata
   Kolkata - 700010

10. Centre for Research in Medical Entomology
    4, Sarojini Street
    Chinna Chokkikulam
    Post Box No 11
    Madurai - 625002

11. Enterovirus Research Centre
    Acharya Donde Marg, Parel
    Mumbai - 400012

12. National Institute for Research in Reproductive Health
    Jahangir Merwanji Street, Parel
    Mumbai - 400012

13. Institute of Immunohaematology
    13th Floor, New Multistoreyed Building
    KEM Hospital Campus, Parel
    Mumbai - 400012

14. Institute for Research in Medical Statistics
    ICMR Headquarters Campus
    Ansari Nagar
    New Delhi - 110029

15. Institute of Cytology and Preventive Oncology
    Maulana Azad Medical College Campus,
    Bahadur Shah Jafar Marg
    New Delhi - 110002

16. Institute of Pathology
    Safdarjang Hospital Campus
    Post Box No. 4909
    New Delhi - 110029

17. Rajendra Memorial Research Institute of Medical Sciences
    Agam Kuan
    Patna - 800007

18. Vector Control Research Centre
    Medical Complex
    Indira Nagar
    Pondicherry - 605006

19. National AIDS Research Institute
    Plot No 73, Block 'G'
    Post Box No 1895
    Bhosari Industrial Estate
    Pune - 411026

20. National Institute of Virology
    20-A, Dr Ambedkar Road
    Post Box No 11
    Pune - 411001

Appendix II

REGIONAL MEDICAL RESEARCH CENTRES

1. Regional Medical Research Centre
   Nandankanan Road
   P.O. Chandrashekharpur
   Bhubaneshwar - 751016

2. Regional Medical Research Centre
   N.E. Region, East - Chowkidinghee
   Post Box No - 105
   Dibrugarh - 786001

3. Regional Medical Research Centre for Tribals
   Medical College Campus
   Nagpur Road
   Jabalpur - 482003

4. Desert Medicine Research Centre
   New Pali Road
   Post Box No - 122
   Jodhpur - 342005

5. Regional Medical Research Centre
   Post Box No - 13
   Port Blair - 744101

6. Regional Medical Research Centre
   National Highway No 4
   Belgaum - 590010

Appendix III

ICMR CENTRES FOR ADVANCED RESEARCH

1. ICMR-NIC Centre for Biomedical Information
   National Informatics Centre
   A-Block, CGO Complex,
   Lodi Road
   New Delhi - 110003

2. Centre for Advanced Research for Clinical Pharmacology in Traditional Medicine
   Topiwala National Medical College and B.Y.L. Nair Charitable Hospital
   Dr A.L. Nair Road
   Mumbai - 400008

3. Centre for Advanced Research for Drug Development from Natural/Plant Products
   Central Drug Research Institute
   Chattar Manzil Palace
   Mahatma Gandhi Marg
   Lucknow - 226001

4. Advanced Centre for Cellular and Molecular Reproduction
   Indian Institute of Science
   Sir C.V. Raman Avenue
   Bangalore - 560012

5. Centre for Advanced Research on Clinical Pharmacology
   Seth G.S. Medical College and K.E.M. Municipal Hospital
   Parel
   Mumbai - 400012

6. Centre for Advanced Research on Aging and Brain
   University of Hyderabad
   Hyderabad - 500046

7. Centre for Advanced Research in Molecular Medical Microbiology
   Indian Institute of Science
   Bangalore - 560012

Appendix IV

TRAINING PROGRAMMES CONDUCTED BY ICMR INSTITUTES DURING 2002-2003

Diarrhoeal Diseases

At the National Institute of Cholera and Enteric Diseases, Kolkata:

- Training Programme on Molecular Epidemiology of Diarrhoeal Diseases with special reference to Cholera (August 12-21, 2002) (Sponsored by Japanese International Cooperation Agency).

Malaria

At the Regional Medical Research Centre, N. E. Region, Dibrugarh:

- Workshop on Operationalization of Insecticide Treated Bed Nets in Assam (April 24-26, 2002).
- Workshop for Laboratory Technicians on Assessment of Therapeutic efficacy of Antimalarials (May 28-29, 2002).

At the Desert Medicine Research Centre, Jodhpur:

- Workshop on Identification of Research Priorities of Malaria for its Prevention and Control (June 27, 2002).
- Training Programme on RS and GIS Application for Interpreting Vector Breeding and Preponderance (November 15-16, 2002) (WHO Sponsored).

Visceral Leishmaniasis

At Rajendra Memorial Research Institute of Medical Sciences, Patna:

- Workshop for the Investigators of Phase IV trial of Miltefosine for the Treatment of Visceral Leishmaniasis (May 26-28, 2002) (Sponsored by WHO/TDR/ICMR).

Vector-borne Diseases/Entomology

At the Vector Control Research Centre, Pondicherry:

- Regional Course on Comprehensive Vector Control (August –September, 2002).

HIV/AIDS

At the National AIDS Research Institute, Pune:

- Workshop on Laboratory diagnosis of HIV and STDs (September 2-4, 2002).

Reproductive Biology/Basic Health

At the National Institute for Research in Reproductive Health, Mumbai:

- Workshop on Development of Information, Education and Communication Material on Emergency Contraception (August 26-28, 2002).
- Training in Insertion and Management of Complications with IUCDs (January 10, 2003).
- Management Training in Basic Health Services for Officials of Department of Health, Madhya Pradesh Government (January and February, 2003).

Nutrition

At the National Institute of Nutrition, Hyderabad:

- M.Sc. in Applied Nutrition (June 17, 2002 – March 15, 2003).
- Postgraduate Certificate Course in Nutrition (January 1 – March 15, 2003).
- Training Course on Techniques for Assessment of Nutritional Anaemias (December 2-13, 2002).

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Certificate Course on Endocrinological Techniques and their Application (August 1 – September 13, 2002).

Occupational/Industrial Health

At the National Institute of Occupational Health, Ahmedabad:

- Training Course on Determination of Impact on Health and Vegetation due to Air Pollution (March 10-14, 2003).
- Certificate Course on Industrial Health for Medical Officers (August 12-November 20, 2003).

At the Desert Medicine Research Centre, Jodhpur:

- Training Programmes for Sandstone Quarry Workers on Occupational Health (October 4-13, 2002; December 3-9, 2002). (WHO Sponsored)

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 1-September 13, 2002 and February 17-April 4, 2003).

- Training Course in Blood Group Serology and Blood Bank Methodology for Blood Bank Technicians (August 1-30, 2002 and February 17-March 14, 2003).

- Training Course in Advanced Haematology and Immunohaematology (September 16-27, 2002).

Tissue Culture

At the National Institute of Virology, Pune:

- Training Course on Tissue Culture (May 20-June 30, 2002).

Pathology

At the Institute of Pathology, New Delhi:

- Workshop on Microwave Histoprocessing organized by Ms Labcon India (October 22, 2002).

- Basic Level Course for Laboratory Technicians (December, 2002).

- Advanced Level Course for Laboratory Technicians (March, 2003).

Laboratory Animal Technology

At the National Centre for Laboratory Animal Science, National Institute of Nutrition, Hyderabad:

- Training Course for Laboratory Animal Technicians (June 15-July 31, 2002).

- Training Course for Laboratory Animal Supervisors (September 4-November 30, 2002).

Biomedical Statistics/Epidemiology

At the Institute for Research in Medical Statistics, New Delhi:

- Training Course for Statistical Investigators Working in the World Bank Assisted ICDS Projects in Tamil Nadu (February 24 – March 1 and March 3-8, 2003).

- Workshops on Statistical Computing and Clinical Trials (April 15-19, 2002).

At the Institute of Epidemiology, Chennai:

- Workshop on Research Methodology (April 11-12, 2002).

At the Regional Medical Research Centre, Bhubaneshwar:

- Workshop and Training Programme on "Verbal Autopsy" for RGI Surveyors in collaboration with Institute of Health Systems, Hyderabad (January 1-6, 2003).

At the National Institute of Cholera and Enteric Diseases, Kolkata:

- Training in Epidemiology for Midlevel Health Professionals (November 6-26, 2002).

Publishing /Biomedical Communication

- Workshop on Promoting Excellence in Biomedical Research at the Desert Medicine Research Centre, Jodhpur (September 20, 2002).
- Workshop on Biomedical Communication in the Cyberage at Mahatma Gandhi University, Kottayam (June 20-22, 2002).
- Workshop on Information and Communication at National Institute of Occupational Health, Ahmedabad (June 25-27, 2002).
- Workshop on Proposal Writing at the National Institute for Research in Reproductive Health, Mumbai (November 20-22, 2002).
- Workshop on Accessing Information At Sikkim Manipal Institute of Medical Sciences, Sikkim (September 4-6, 2002)
- Workshop on Storage and Retrieval of Information at Mahatma Gandhi Institute of Medical Sciences, Sevagram (December 10-12, 2002).
- Workshop on Dissemination of Information at SV Institute of Medical Sciences, Tirupati (March 18-23, 2003).

Appendix V

SEMINARS / SYMPOSIA / CONFERENCES / WORKSHOPS

The following ICMR aided Symposia / Seminars / Workshops / Conferences were held during 2002 -2003

Title	Dates	Organisers
National Symposium on Tropical Diseases	April 2-3, 2002	Indian Institute of Chemical Biology Kolkata
Mobile Workshop on Human Genetics	April 4-6, 2002	School of Health Sciences University of Poona Pune
Workshop on Research Methodology	April 11-12, 2002	Padmashree Dr.D.Y.Patil Medical College for Women Pune
International Conference on Trends in Biotechnology: Stem Cells - Technology, Potential and Trends	May 2-4, 2002	All India Biotech Association Hyderabad
I International Conference in Medical Sociology - Health, Illness and Society in the New Millennium	May 5-6, 2002	Institute of Cardiovascular Diseases Madras Medical Mission Chennai
Seminar on Issues in Human Health	May 25, 2002	Inter Academy of Biomedical Science Forum Bangalore
National Seminar on Applications on Survival Analysis and Allied Models	June 21-22, 2002	National Institute of Mental Health and Neurosciences Bangalore
National Conference on Impact of Environment Pollution on Health: Problems and Solutions	August 29-30, 2002	International Development Centre New Delhi
II National Conference of the Indian Society for Sleep Research	September 6-7, 2002	National Institute of Mental Health and Neurosciences Bangalore

Title	Dates	Organisers
Orientation Course on Industrial Toxicology	September 9-30, 2002	Punjab Agricultural University Ludhiana
VI World Congress and XIV Indian Conference on Reproductive and Child Health Care	September 20-22, 2002	University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
National Seminar on the Use of Traditional Medicines in HIV Infections and AIDS	September 21-22, 2002	Amala Cancer Hospital and Research Centre Thrissur
III Annual Conference of Indian Leptospirosis Society	September 21-22, 2002	Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry
International Symposium on Bone Tumors	September 26-28, 2002	All India Institute of Medical Sciences New Delhi
National Conference on Management of Natural Resources for Our Sustenance	October 3-5, 2002	Loyola College Chennai
Seminar on Diarrhoea in Children	October 5, 2002	Indian Academy of Paediatrics (West Bengal Branch) Kolkata
Lancefield International Symposium on Streptococci and Streptococcal Diseases	October 6-11, 2002	All India Institute of Medical Sciences New Delhi
VIII General Conference and XIII General Meeting of the Third World Academy of Sciences and VII General Assembly of Third World Network of Scientific Organizations	October 19-23, 2002	Indian National Science Academy New Delhi
XXXII National Seminar on Crystallography	October 24-26, 2002	University of Jammu Jammu
III Annual Conference of Indian Society of Veterinary Pharmacology and Toxicology	October 24-26, 2002	G.B.Pant University of Agriculture and Technology Pantnagar
Symposium on Challenges in Malaria and Prospects for Research	October 29-31, 2002	Malaria Research Centre Delhi
XV International Congress of the International Association for Child and Adolescent Psychiatry and Allied Professions	October 29 – November 2, 2002	Postgraduate Institute of Medical Education and Research Chandigarh

Title	Dates	Organisers
XVI National Conference of Parasitology	October 31 – November 2, 2002	Rohilkhand University Bareilly
XXVII National Conference of Indian Society of Blood Transfusion and Immunohaematology	November 9-11, 2002	Indian Society of Blood Transfusion and Immunohaematology Jaipur
International Conference on Radiation Damage and Its Modification	November 13-15, 2002	Institute of Nuclear Medicine & Allied Sciences Delhi
V Congress of Asian Academy of Preventive Dentistry and XXIV Annual Conference of Indian Society of Pedodontics and Preventive Dentistry	November 14-16, 2002	Indian Society of Pedodontics and Preventive Dentistry Chandigarh
National Symposium and LXXI Annual Meeting of Society of Biological Chemists - India	November 14-16, 2002	Punjab Agricultural University Ludhiana
National Symposium on Venoms and Toxins	November 15-16, 2002	Acharya Shri Chander College of Medical Sciences & Hospital Jammu
Guha Research Conference – 2002	November 16-20, 2002	Jawaharlal Nehru University New Delhi
II International Society of Pediatric Oncology – Asia Conference and VI National Conference of Pediatric Hematology / Oncology	November 22-24, 2002	All India Institute of Medical Sciences New Delhi
Symposium on the Current Excitement in Biology	November 24-29, 2002	Centre for Cellular and Molecular Biology Hyderabad
XXXV Annual Conference of Indian Pharmacological Society	November 27-29, 2002	Defence Research and Development Establishment Gwalior
XXIX Annual Meeting of the Indian Immunology Society and Symposium on Immunoparasitology	November 27-29, 2002	Regional Medical Research Centre (ICMR) Bhubaneswar
V National Conference of Indian Academy of Allergy on Current Trends in Allergy and Applied Aerobiology	November 28-30, 2002	Bharati Vidyapeeth's College of Ayurved Pune

Title	Dates	Organisers
XXXII Annual Conference of the Indian Academy of Cytologists	November 28 – December 1, 2002	Postgraduate Institute of Medical Education and Research Chandigarh
Countrywide Awareness Compaign for Donation of Human Bodies/ Tissues to Science and to Develop Scientific Approach amongst the General Masses	December 2-3, 2002	Ganadarpan Kolkata
International Symposium on Cataracts - Molecular and Epidemiological Aspects	December 2-3, 2002	Science Centre Manipal Academy of Higher Education Manipal
XXI Annual Conference of Society of Toxicology	December 3-5, 2002	Regional Occupational Health Centre(ICMR) Kolkata
National Conference on Rural Health	December 5-7, 2002	Rural Medical College of Pravara Medical Trust Ahmednagar
Workshop to Frame Guidelines for Diagnosis and Management of Chronic Obstructive Pulmonary Disease in India	December 6-7, 2002	Postgraduate Institute of Medical Education and Research Chandigarh
OTAI-JOCS Asian Conference - 2002 and International Exhibition on Lipids, Fats and Oils	December 6-8, 2002	Oil Technologists Association of India New Delhi
Indo-German Workshop on Survey Methods	December 9-21, 2002	University of Poona Pune
XXXIV Annual Conference of Society of Nuclear Medicine India and Symposium of Indo-American Society of Nuclear Medicine	December 11-16, 2002	Indian Institute of Chemical Biology Kolkata
XIII National Congress of Veterinary Parasitology	December 14-16, 2002	West Bengal University of Animals and Fishery Sciences Kolkata
IRMS Silver Jubilee and XX Annual Conference of Indian Society for Medical Statistics	December 19-22, 2002	Institute for Research in Medical Statistics New Delhi
National Conference on Biomedical Materials – 2002 and XIII Annual Meeting of the Society of Biomaterials and Artificial Organs	December 20-21, 2002	Jadavpur University Kolkata

Title	Dates	Organisers
19th National Congress of Indian Institute of Homeopathic Physicians	December 27-29, 2002	Dr. A.C.Homoeopathic Medical College and Hospital Bhubaneswar
National Children Science Congress - 2002	December 27-31, 2002	Indian Institute of Science Bangalore
Conference on Recent Trends in Probability and Statistics: Theory and Applications	December 31, 2002 – January 2,2003	Gauhati University Guwahati
90th Indian Science Congress	January 3-7 2003	Indian Science Congress Association Bangalore
Workshop for Editors of Indian Biomedical Journals	January 12-13, 2003	All India Institute of Medical Sciences New Delhi
XVII International Symposium on Glycoconjugates	January 12-16, 2003	Indian Institute of Science Bangalore
VI International Symposium on Biochemical Roles of Eukaryotic Cell Surface Macromolecules	January 16-18, 2003	Indian Institute of Chemical Biology Kolkata
XXIV Annual Conference of Indian Academy of Forensic Medicine	January 18-20, 2003	Sri Krishna Medical College Muzaffarpur
National Conference on Recent Trends in Insect Control	January 22-24, 2003	Bharathiar University Coimbatore
XI Annual Meeting on Molecular Immunology Forum	January 31 – February 2, 2003	Centre for Cellular and Molecular Biology Hyderabad
International Symposium on Innovations in Pharmaceutical Sciences and Technology	January 31 – February 3, 2003	BV Patel Pharmaceutical Education and Research Development Centre Ahmedabad
Indo UK Symposium on Hot Topics in pediatrics	February 1-2, 2003	Maulana Azad Medical College and Associated Hospitals New Delhi
Special Symposium on Recent Development in NMR Methodology and National Symposium on Magnetic Resonance	February 3-6, 2003	Indian Institute of Science Bangalore
Brain Storming Session on Neurobiology in the Post-Genomic Era	February 4, 2003	Banaras Hindu University Varanasi

Title	Dates	Organisers
XXX National Conference of Indian Association of Preventive and Social Medicine : Life Style Makes the Difference	February 6-8, 2003	Jawaharlal Nehru Medical College Belgaum
National Conference on Recent Advances in Reproductive Health	February 6-8, 2003	University of Rajasthan Jaipur
XXVIII Annual Conference of the Indian Society of Human Genetics	February 7-9, 2003	University of Jammu Jammu
International Conference on Role of Free Radicals and Anti -Oxidants in Health & Diseases and II Annual Conference of Society of Free Radical Research	February 10-12, 2003	Chhatrapati Shahuji Maharaj Medical University Lucknow
XXI National Symposium on Reproductive Biology and Comparative Endocrinology	February 10-13, 2003	Banaras Hindu University Varanasi
Ramalingaswamy Memorial Symposium - Frontiers in Pathology	February 12, 2003	All India Institute of Medical Sciences New Delhi
XXVIII Annual Conference of the Environmental Mutagen Society of India and Special Symposium on Arsenic Contamination in Ground Water and Its Health Effects	February 14-16, 2003	Indian Institute of Chemical Biology Kolkata
XI Annual Conference of Indian Society of Hypertension	February 15-16, 2003	Central Drug Research Institute Lucknow
Conference on Ageing in Asia: Emerging Trends and Perspective	February 16-18, 2003	Heritage Educational and Research Society Hyderabad
IX Asian Congress of Nutrition - Nutrition Goals for Asia Vision – 2002	February 23-27, 2003	National Institute of Nutrition Hyderabad
XX Annual Conference of Indian Society for Comparative Animal Physiology & on Physiological Approaches to Conserve Biodiversity and to Tackle Environmental Health Hazards	February 26-28, 2003	Sri Venkateswara University Tirupati

Appendix VI

LIST OF RESEARCH SCHEMES FUNDED DURING 2002-2003

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
Epidemiology and Communicable diseases			
1	Field Programme for the epidemiological studies in leprosy at Ghatampur	Dr. Kiran Katoch Central JALMA Institute for Leprosy Agra	5.09
2	Recognition of nonstructural protein NS3 of Japanese encephalitis virus by antiviral cytotoxic T lymphocytes raised by intracerebral immunization	Dr. R.Manjunath Indian Institute of Science Bangalore	3.04
3	Centre for Advanced Study in Molecular Medical Microbiology	Dr. R.Nayak Indian Institute of Science Bangalore	8.12
4	Characterization of the human B and T cell immune response to the membrane capsid, NS1, NS2b and NS5 proteins of Japanese encephalitis virus	Dr. S.Vijaya Indian Institute of Science Bangalore	5.85
5	Multicentric study of interferon-glycyrrhizin combination therapy and interferon-ribavirin combination therapy in the management of chronic hepatitis-C	Dr. S.Dutta Gupta National Tuberculosis Institute Bangalore	2.67
6	Virulence markers in *Helicobacter pylori* isolated in Bangalore and its association with disease	Dr. Regini Macaden St.John's Medical College, Hospital & College of Nursing Bangalore	1.38

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
7	Intervention for hereditary common haemolytic disorders among the major tribals of Sundargarh district of Orissa	Dr. R.S.Balgir Regional Medical Research Centre Bhubaneswar	3.54
8	Study on the nutritional status of *Dongria Kondh* primitive tribal and *Domb* scheduled caste populations of Orissa	Dr. Gandham Bulliyya Regional Medical Research Centre Bhubaneswar	2.50
9	A comprehensive study on delivery of health care research for capacity building amongst the primitive tribes of Orissa	Dr. G.P.Chhotray Regional Medical Research Centre Bhubaneswar	3.38
10	Intervention programme for cholera, intestinal parasitism, vitamin - A deficiency disorders and scabies amongst some primitive tribal populations of Orissa - a pilot study	Dr. G.P.Chhotray Regional Medical Research Centre Bhubaneswar	20.27
11	Study of prevalence of nosocomial infection in a medical college hospital	Dr. S.S.Jigjinni B.L.D.E Association's Shri B.M.Patil Medical College Bijapur	0.92
12	Potential of polysaccharide - cholera toxin ß subunit conjugate for respiratory mucosal immunity	Dr. Sanjay Chibber Panjab University Chandigarh	1.45
13	Virulence of *P.aeruginosa* in relation to catheter-associated urinary tract infections	Dr. Kusum Harjai Panjab University Chandigarh	1.96
14	Effect of outer membrane proteins from *Salmonella typhi* grown under different stress conditions on macrophages	Dr. Praveen Rishi Panjab University Chandigarh	3.74
15	Studies on mutation of TGF-ß and INFγ genes in the pathogenesis of pulmonary fibrosis	Dr. Digambar Behera Postgraduate Institute of Medical Education and Research Chandigarh	3.90

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
16	Natural habitat of *Cryptococcus neoformans* var. gattii strains in the environment of north India and north Karnataka	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	2.03
17	Development of fluorescent labeled polyclonal antibody reagents for specific identification of *Aspergillus candida and Cryptococcus* in paraffin embedded tissue sections	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	2.11
18	An epidemiological survey of sporotrichosis among tea garden workers in and around Dibrugarh (Assam)	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	2.13
19	Molecular characterization of Group A Streptococcus	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	4.71
20	Molecular cloning, sequencing and expression of adhesin gene of enteroaggregative *E.coli* (EAggEC) towards development of a specific probe	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	3.31
21	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C	Dr. Yogesh K.Chawla Postgraduate Institute of Medical Education and Research Chandigarh	2.33
22	Monoclonal antibody based ELISA system to detect malaria antigen in cerebrospinal fluid for diagnosis of cerebral malaria	Dr. M.L.Dubey Postgraduate Institute of Medical Education and Research Chandigarh	0.99
23	Identification and characterization of a toxin from enteroaggregative *Escherichia coli*	Dr. Sujata Ghosh Postgraduate Institute of Medical Education and Research Chandigarh	2.32

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
24	Development of IFN ELISA and immuno - PCR based on *Mycobacterium tuberculosis* complex specific antigen (s) for the early and specific diagnosis of tuberculosis	Dr. G.K.Khuller Postgraduate Institute of Medical Education and Research Chandigarh	2.00
25	Molecular mechanism of malabsorption in *Shigella* induced diarrhoea in rabbit as experimental model	Dr. Safrunnisa Mahmood Postgraduate Institute of Medical Education and Research Chandigarh	2.05
26	Study on the pathophysiology of *V.cholera* induced diarrhoea : at transcriptional level and at translational level	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.35
27	Study on the cellular responses by a galactose specific adhesin of enteroaggregative *Escherichia coli*	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.35
28	Study on the cellular responses by a mannose sensitive adhesin of *Salmonella typhimurium*	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.20
29	Developing a verbal autopsy instrument and using it to measure cause - specific mortality in adults	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	1.66
30	Association of genital mycoplasma and *Chlamydia trachomatis* in neonatal infections	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	1.56
31	Intestinal antimicrobial peptides : Isolation, purification and characterisation	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	2.36
32	Identification of novel mutation pattern in the ParC and GyrA genes of ciprofloxacin resistant clinical isolates of *Neisseria gonorrhoeae*	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	1.50

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
33	Study of typhoid carriers through culture of bile specimen obtained during routine endoscopy and surgical procedures	Dr. Chetana Vaishnavi Postgraduate Institute of Medical Education and Research Chandigarh	2.03
34	A study of possible mechanism(s) for T cell anergy in lepromatous leprosy	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	1.04
35	Interactions of galactose-binding lectin of *Entamoeba histolytica* with immune-competent cells	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	0.70
36	Evaluation of newer diagnostic methods for detection and differentiation of *Entamoeba histolytica* and *E.dispar*	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	1.82
37	Study of clinical utility and effect of a tumour necrosis factor inhibitor (pentoxyphylline) on immune profile in patients with HIV infection	Dr. Ajay Wanchu Postgraduate Institute of Medical Education and Research Chandigarh	1.94
38	Studies on pulmonary opportunistic mycotic infection in immunocompromised patients	Dr. Usha Ananda Rao Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai	0.94
39	A study on the transmission pattern(s) of hepatitis B virus (HBV) / hepatitis C virus (HCV) in symptomatic / asymptomatic pregnant women and their impact on pregnancy outcome and on children born to them	Dr. S.P.Thyagarajan Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai	3.49
40	ICMR Reference Centre on Hepatitis Serology and Molecular Virology	Dr. S.P.Thyagarajan Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai	3.50

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
41	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - Coordinating Centre	Dr. M.D.Gupte National Institute of Epidemiology Chennai	0.90
42	Chemotherapy of tuberculosis in HIV-infected patients : an evaluation of intermittent short course (RNTCP) regimens	Dr. Soumya Swaminathan Tuberculosis Research Centre Chennai	10.09
43	Polymerase chain reaction for detection and genotyping of *Chlamydia trachomatis* in conjunctivitis	Dr. H.N.Madhavan Vision Research Foundation Chennai	3.39
44	Detection and molecular characterisation of myco-bacteria by polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP) and DNA sequencing technique from ocular and other clinical specimens	Dr. K.Lily Therese Vision Research Foundation Chennai	4.91
45	Integrated vector control of malaria, filaria and other vector-borne diseases	Dr. Sarala K.Subbarao Malaria Research Centre Delhi	10.79
46	Application of remote sensing and geographical information systems for decision support in malaria control	Dr. Aruna Srivastava Malaria Research Centre Delhi	3.25
47	The role of proinflammatory cytokines in the induction of nitric oxide from human mononuclear phagocytes of patients suffering from pulmonary tuberculosis	Dr. Mridula Bose Vallabhbhai Patel Chest Institute Delhi	1.98
48	Analysis of isoniazid and rifampicin resistance mutations in the clinical isolates of *M.tuberculosis* by sequencing and Dot-blot hybridization	Dr. Mridula Bose Vallabhbhai Patel Chest Institute Delhi	3.20

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
49	Oxidant - antioxidant balance in bronchial asthma : evaluation of the role of alpha - tocopherol in treatment	Dr. S.K.Chhabra Vallabhbhai Patel Chest Institute Delhi	1.73
50	Studies on epidemiology and aspects of immunodiagnosis of penicillosis marneffei	Dr. H.C.Gugani Vallabhbhai Patel Chest Institute Delhi	2.35
51	*In vitro* biointeractions between *Candida* species, *Aspergillus fumigatus* and some other human pathogenic fungi	Dr. H.S.Randhawa Vallabhbhai Patel Chest Institute Delhi	0.59
52	Molecular characterisation of clinical isolates	Dr. S.S.Thukral Vallabhbhai Patel Chest Institute Delhi	2.00
53	High resolution genotyping of *Mycobacterium tuberculosis* IS6110 low-copy number strains combining novel molecular approaches for global detection of tuberculosis epidemics	Dr. S.E.Hasnain Centre for DNA Fingerprinting and Diagnostics Hyderabad	6.01
54	Application of heuristic engine : a novel forecasting software tool to predict the outbreak of JE in Andhra Pradesh	Dr. U.Suryanarayana Murthy Indian Institute of Chemical Technology Hyderabad	1.12
55	Lactoferrin and antibodies to lactoferrin in tears of leprosy patients	Dr. Ebenezer Daniel Schieffelin Leprosy Research and Training Centre Karigiri	1.05
56	Viability of *Mycobacterium leprae* in leptomatous patients after completion of 12 month and 24 months multidrug therapy	Dr. Gigi J.Ebenezer Schieffelin Leprosy Research and Training Centre Karigiri	4.80
57	Role of C-C chemokines in regulating tumor immune responses in breast cancer	Dr. Utpala Chattopadhyay Chittaranjan National Cancer Institute Kolkata	3.21

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
58	A novel approach to control infection of macrophages by *Leishmania donovani*, the causative agent of leishmania	Dr. Rajyasree Bandyopadhyay Indian Institute of Chemical Biology Kolkata	0.22
59	Optimization of dendritic cell-based vaccination / therapy against murine visceral leishmaniasis induced by antimony-resistant and - sensitive strains of *Leishmania donovani*	Dr. Santu Bandyopadhyay Indian Institute of Chemical Biology Kolkata	3.92
60	Role of quercetin, a naturally occurring flavonoid in the alleviation of anemia in visceral leishmaniasis	Dr. Tuli Biswas Indian Institute of Chemical Biology Kolkata	2.37
61	An approach to develop DNA vaccine against experimental visceral leishmaniasis	Dr. Syamal Roy Indian Institute of Chemical Biology Kolkata	3.88
62	Genetic predisposition to antituberculosis drug-induced hepatotoxicity	Dr. Bidyut Roy Indian Statistical Institute Kolkata	2.79
63	Impact of domestic animals and food derived from animals on the epidemiology of enterohaemorrhagic *Escherichia coli (EHEC)* and shiga - toxin producing *E.coli* (STEC)	Dr. S.C.Das Indian Veterinary Research Institute Kolkata	1.97
64	Natural history of *Helicobacter pylori infection* and its outcome in India	Dr. Abhijit Chowdhury Institute of Postgraduate Medical Education and Research Kolkata	3.54
65	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C	Dr. Abhijit Chowdhury Institute of Postgraduate Medical Education and Research Kolkata	3.29

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
66	Studies on HIV/AIDS drug abuse in eastern and north eastern part of India	Dr. S.K.Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	20.00
67	Studies on HIV/AIDS and drug abuse in Dimapur, Nagaland	Dr. S.K.Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	6.00
68	Studies on HIV/AIDS and drug abuse in Aizwal, Mizoram	Dr. S.K.Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	7.00
69	Studies on HIV/AIDS and drug abuse in Imphal, Manipur	Dr. S.K.Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	15.00
70	Detection of *Entamoeba histolytica, Giardia lamblia* and *Cryptosporidium parvum* by molecular biological tools	Dr. Pradeep Das National Institute of Cholera and Enteric Diseases Kolkata	1.45
71	A multicentric study on surveillance and molecular characterization of human viruses (HuCVs) from cases of acute gastroenteritis	Dr. T.N.Naik National Institute of Cholera and Enteric Diseases Kolkata	3.59
72	Monitoring of multiple antibiotic resistance among clinical strains of enteric pathogens	Dr. T.Ramamurthy National Institute of Cholera and Enteric Diseases Kolkata	1.85
73	A correlative study of the prevalence of IgM immunoglobulins against TORCH infections in pregnancy, with congenital malformations	Dr. Zuhara K.F. University of Calicut Kozhikode	1.56
74	Factors affecting susceptibility / resistance of the host to hepatic amoebiasis	Dr. Sheela Ghoshal Central Drug Research Institute Lucknow	1.80

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
75	Validation and multicentric evaluation : *Leishmania donovani* freeze dried DAT antigen for the diagnosis of kala - azar	Dr. Suman Gupta Central Drug Research Institute Lucknow	0.40
76	Herpes simplex encephalitis in children	Dr. Rashmi Kumar Chhatrapati Shahuji Maharaj Medical University Lucknow	1.46
77	Role of bacteria in the pathogenesis of juvenile idiopathic arthritis	Dr. Amita Aggarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.78
78	Study of T-cell epitopes of human hepatitis E virus	Dr. Rakesh Aggarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	0.40
79	Development of an animal model for Indian strains of *Helicobacter pylori*	Dr. Archana Ayyagari Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	2.30
80	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C	Dr. G.Choudhuri Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.82
81	Fingerprinting of the causative bacteria in brain abscess using different magnetic resonance techniques in humans and animal model	Dr. R.K.Gupta Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.35
82	*Campylobacter* infection and Guillain - Barre syndrome	Dr. K.N.Prasad Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	2.22
83	Magnitude of intestinal taeniasis and systemic cysticercosis in pig farming community of north India	Dr. K.N.Prasad Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.97

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
84	Host parasite relationship: a study on host immunity to survival of *Mycobacterium tuberculosis* isolates	Dr. R.M.Pitchappan Centre for Advanced Research in Health & Behaviour Madurai	5.39
85	Establishment of a field station in south Arcot district, Tamil Nadu for control trials of Japanese encephalitis	Dr. K.Satyanarayana Centre for Research in Medical Entomology Madurai	8.98
86	Shiga toxigenic *Escherichia coli* (STEC) in foods of animal origin and clinical samples	Dr. B.Dhanashree Kasturba Medical College and Hospital Mangalore	1.41
87	Determination of amplification of multi-drug resistance gene(s) in *Leishmania donovani* selected for resistance to sodium m-arsenite	Dr. Chinmoy Sankar Dey National Institute of Pharmaceutical Education and Research Mohali	3.00
88	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C	Dr. Deepak N.Amrapurkar Bombay Hospital and Medical Research Centre Mumbai	2.95
89	To study the potential of Buddemeyer type radirespirometric assay based on CO_2 evolution from (1-14C) palmitic acid by *M.leprae* as a rapid index of viability	Dr. Vanaja P.Shetty The Foundation for Medical Research Mumbai	1.96
90	Study on impact of health programmes in Bihar state	Dr. Chakradhar Sinha B.R.Ambedkar Bihar University Muzaffarpur	3.37
91	A prospective evaluation of clinical profile and natural course of water borne viral hepatitis in adults and seroepidemiology of HAV in children in India	Dr. S.K.Acharya All India Institute of Medical Sciences New Delhi	1.14

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
92	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C - Clinical Coordinating Centre	Dr. S.K.Acharya All India Institute of Medical Sciences New Delhi	0.40
93	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C (Participating Centre)	Dr. S.K.Acharya All India Institute of Medical Sciences New Delhi	1.52
94	Natural history of *Helicobacter pylori* infection in a birth cohort in an urban slum setting : risk factors, rates of clearance and re-infection, immune response to first infection,impact of infection on physical growth	Dr. Rajiv Bahl All India Institute of Medical Sciences New Delhi	13.18
95	*Helicobacter pylori* infection in early childhood : characterization of isolates and determination of their ability to exert pathogenic effect in *in vitro* models	Dr. Shinjini Bhatnagar All India Institute of Medical Sciences New Delhi	6.07
96	A multicentric study on surveillance and molecular characterization of human viruses (HuCVs) from cases of acute gastroenteritis	Dr. Shobha Broor All India Institute of Medical Sciences New Delhi	5.11
97	A study of *Clostridium difficile* - an emerging nosocomical pathogen with special reference to epidemiological typing	Dr. Rama Chaudhary All India Institute of Medical Sciences New Delhi	1.94

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
98	Aerobic and anaerobic bacteriological profile of diabetic foot ulcers with special reference to methicillin resistant *Staphylococcus aureus*	Dr. Benu Dhawan All India Institute of Medical Sciences New Delhi	0.75
99	Typing of extended spectrum beta - lactamases (ESBLS) produced by *Klebsiella pneumoniae* isolated from AIIMS hospital, New Delhi	Dr. Arti Kapil All India Institute of Medical Sciences New Delhi	1.10
100	Evaluation of algorithms proposed by NACO for syndromic management of urethral and vaginal discharge in a tertiary care centre in northern India	Dr. Neena Khanna All India Institute of Medical Sciences New Delhi	1.10
101	Molecular analysis of cytokine gene polymorhism in leprosy	Dr. N.K.Mehra All India Institute of Medical Sciences New Delhi	7.09
102	Diagnosis of malaria by detection of *Plasmodium falciparum* HRP-2 antigen using antigen capture assay	Dr. D.Nageswara Rao All India Institute of Medical Sciences New Delhi	0.64
103	Protective efficacy of peptide immunogens between B and T cell epitopes of F1 antigen of *Y.pestis*	Dr. D.Nageswara Rao All India Institute of Medical Sciences New Delhi	3.50
104	T cell signaling pathways using *M.leprae* derived antigens in leprosy patient	Dr. D.Nageswara Rao All India Institute of Medical Sciences New Delhi	2.25
105	Phenotypic and molecular characterisation of ocular isolates of coagulase negative staphylococci : implications in colonization and virulence	Dr. Niranjan Nayak All India Institute of Medical Sciences New Delhi	0.92

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
106	Molecular characterization of VP3 gene of human rotavirus strains associated with severe diarrhoea and without diarrhoea in children	Dr. Pratima Ray All India Institute of Medical Sciences New Delhi	3.16
107	Molecular characterisation of *Streptococcus pneumoniae* isolates causing various infections in human beings	Dr. Gita Satpathy All India Institute of Medical Sciences New Delhi	5.25
108	Surveillance of anti - tuberculosis drug resistance	Dr. Pradeep Seth All India Institute of Medical Sciences New Delhi	0.62
109	PCR and cytokine assays for diagnosing latent infection of Leishmania in asymptomatic family members of kala-azar patients of Bihar	Dr. Sarman Singh All India Institute of Medical Sciences New Delhi	0.49
110	Identification of target genes of the devR-devS two-component system of *M.tuberculosis* and development of rapid assays to measure its activity	Dr. Jaya Sivaswami Tyagi All India Institute of Medical Sciences New Delhi	5.43
111	To study the role of host genetic factors in hepatitis B viral infection in family contacts of HBV related liver disease patients	Dr. S.K.Sarin G.B.Pant Hospital New Delhi	7.54
112	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C	Dr. S.K.Sarin G.B.Pant Hospital New Delhi	1.66
113	Involvement of the school children in total population coverage for surveillance of leprosy and MDT compliance in a cosmopolitan city	Dr. R.S.Misra Hind Kushth Nivaran Sangh New Delhi	9.09

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
114	Anti-Pol II anti-TBP antibodies as markers for scleroderma and mixed connective tissue diseases (MCTD)	Dr. Uttam Pati Jawaharlal Nehru University New Delhi	5.62
115	Detection analysis of food - borne parasites using molecular approaches	Dr. Jaishree Paul Jawaharlal Nehru University New Delhi	1.49
116	Molecular biotyping, epidemiological and fungal susceptibilities of oppurtunistic human pathogenic fungi	Dr. Rajendra Prasad Jawaharlal Nehru University New Delhi	6.99
117	Rapid diagnosis of dengue virus serotypes from clinical samples by reverse transcription polymerase chain reaction	Dr. Anita Chakravarti Maulana Azad Medical College and Associated Hospitals New Delhi	3.47
118	Surveillance of hepatitis E virus in sewage and drinking water : prevention strategies against infection in a resettlement colony of Delhi	Dr. Premashis Kar Maulana Azad Medical College and Associated Hospitals New Delhi	3.48
119	Detection of precore mutants of hepatitis B virus by ligase chain reaction (LCR) in patients of chronic liver diseases	Dr. Premashis Kar Maulana Azad Medical College and Associated Hospitals New Delhi	3.94
120	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C	Dr. Premashis Kar Maulana Azad Medical College and Associated Hospitals New Delhi	2.75
121	Role of polyketide syntheses in the biology of *Mycobacterium tuberculosis*	Dr. Rajesh S.Gokhale National Institute of Immunology New Delhi	3.03

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
122	Intracellular trafficking of *Salmonella* in macrophages to understand the mechanism of bacterial survival	Dr. Amitava Mukhopadhyay National Institute of Immunology New Delhi	3.64
123	Mechanistic studies on the defensive mechanisms of *Leishmania donovani* against oxidative stress : role of phase I and phase II defensive enzymes of the parasite	Dr. Chandrima Shaha National Institute of Immunology New Delhi	2.09
124	Protein tyrosine phosphatases from *Mycobacterium tuberculosis* and their role in pathogenesis	Dr. A.K.Tyagi University of Delhi South Campus New Delhi	4.87
125	Studies on the role of VIRS gene in the pathogenesis of *M.tuberculosis*	Dr. A.K.Tyagi University of Delhi South Campus New Delhi	12.68
126	Application for remote sensing in identifying and mapping sandfly distribution in endemic and non-endemic kala-azar	Dr. Kamal Kishore Rajendra Memorial Research Institute of Medical Sciences Patna	2.50
127	Application of remote sensing (RS) and geographical information systems (GIS) for epidemiology and control of lymphatic filariasis	Dr. P.K.Das Vector Control Research Centre Pondicherry	1.18
128	Molecular epidemiology and genomics of filariasis - a national network for molecular typing	Dr. S.L.Hoti Vector Control Research Centre Pondicherry	5.54
129	Operational feasibility and impact of co-administration of albendazole and DEC in controlling lymphatic filariasis	Dr. S.P.Pani Vector Control Research Centre Pondicherry	9.53
130	Prevention and control of hepatitis B infection among the primitive tribes of Andaman and Nicobar islands	Dr. S.C.Sehgal Regional Medical Research Centre Port Blair	4.41

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
131	Chemotherapy of tuberculosis in HIV-infected patients : an evaluation of intermittent short course (RNTCP) regimens	Dr S.P.Tripathy National AIDS Research Institute Pune	6.66
132	Microbial enzyme inhibitors : novel define against secondary fungal infection	Dr. Mala Rao National Chemical Laboratory Pune	2.03
133	Virological studies in relation to assessment of efficacy of drug therapies for chronic hepatitis B and C	Dr. Vidya A.Arankalle National Institute of Virology Pune	21.25
134	A multicentric study on surveillance and molecular characterization of human viruses (HuCVs) from cases of acute gastroenteritis	Dr. Gagandeep Kang Christian Medical College and Hospital Vellore	4.94
135	Establishing laboratory based surveillance network to monitor anti - microbial resistance	Dr. M.K.Lalitha Christian Medical College and Hospital Vellore	18.81

Reproductive Health and Nutrition

136	Alpha-2 macroglobulin in type-I, type-II and experimental diabetes: correlation of plasma and vascular endothelium levels with severity of the disease	Dr. Jamal Ahmad Jawaharlal Nehru Medical College Aligarh	2.20
137	Human Reproduction Research Centre	Dr. Gauri Ganguli Moti Lal Nehru Medical College Allahabad	11.22
138	Pilot study on emergency contraception with CuT 200β and 0.75mg levonorgestrel (2 doses)	Dr. Gauri Ganguli Moti Lal Nehru Medical College Allahabad	0.42
139	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Gauri Ganguli Moti Lal Nehru Medical College Allahabad	0.90

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
140	National Nutrition Monitoring Bureau	Dr. J.Sundaram Directorate of Health and Family Welfare Services Bangalore	9.40
141	Genomics of male infertility	Dr. Arun Kumar Indian Institute of Science Bangalore	15.48
142	Identification of estrogen regulated epididymal factor(s) involved in sperm maturation	Dr. A.Jagannadha Rao Indian Institute of Science Bangalore	4.47
143	Advanced Centre for Cellular and Molecular Reproduction	Dr. A.Jagannadha Rao Indian Institute of Science Bangalore	5.00
144	Significance of germ-cell localization of immunoreactive riboflavin carrier protein during sperm function : its role in fertilization	Dr. P.B.Seshagiri Indian Institute of Science Bangalore	6.95
145	National Neonatal Perinatal Database	Dr. Swarna Rekha Bhatt St.John's Medical College, Hospital & College of Nursing Bangalore	0.88
146	Human Reproduction Research Centre	Dr. B.S.Kodkany Jawaharlal Nehru Medical College Belgaum	7.34
147	Role of IEC/counselling in facilitating couples' informed choice between conventional and no-scalpel vasectomy procedures	Dr. Yogiraj Sharma Directorate of Health Services Government of Madhya Pradesh Bhopal	1.76
148	National Nutrition Monitoring Bureau	Dr. K.Satyanarayana Regional Medical Research Centre Bhubaneswar	9.40

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
149	Evaluation of oxidative damage, mitochondrial oxidant generation and antioxidant defenses in testis of rat during critical stageas of maturation and their modulation by thyroid hormone (T3)	Dr. G.B.N.Chainy Utkal University Bhubaneswar	9.40
150	Human Reproduction Research Centre	Dr. Sohini Kochhar S.P.Medical College and Associated Group of Hospitals Bikaner	7.00
151	A study of polymerase chain reaction using broad based primers in the diagnosis of perinatally acquired sepsis in newborns	Dr. Sourabh Dutta Postgraduate Institute of Medical Education and Research Chandigarh	6.45
152	Human Reproduction Research Centre	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	10.62
153	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	0.90
154	National Neonatal Perinatal Database	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	0.10
155	Reactive oxygen intermediates and reactive nitrogen intermediates with microbiological studies in copper intrauterine device users	Dr. Indu Gupta Postgraduate Institute of Medical Education and Research Chandigarh	3.13
156	Birth asphyxia, hypoxic ischaemic encephalopathy : aetiology, management and outcome	Dr. Anil Narang Postgraduate Institute of Medical Education and Research Chandigarh	2.43

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
157	National Neonatal Perinatal Database	Dr. Anil Narang Postgraduate Institute of Medical Education and Research Chandigarh	0.88
158	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	2.85
159	National Nutrition Monitoring Bureau	Dr. K.C.Viswanathan Directorate of Public Health and Preventive Medicine Chennai	9.40
160	A study of impact of counselling on coping behaviour of HIV positive cases in different states	Dr. Mini Jacob Dr. M.G.R.Medical University Chennai	1.86
161	Social stigma attached to HIV infection-implications for health care and social adjustment	Dr. N.M.Samuel Dr. M.G.R.Medical University Chennai	2.25
162	Human Reproduction Research Centre	Dr. M.Sakunthala Bharathi Government Kasturba Gandhi Hospital for Women & Children Chennai	14.03
163	Human Reproduction Research Centre	Dr. C.Meenal Government Kilpauk Medical College and Hospital Chennai	13.23
164	Human Reproduction Research Centre	Dr. R.Thirupurasundari Government R.S.R.M. Hospital Chennai	11.31
165	National Neonatal Perinatal Database	Dr. M.Kappulakshmi Institute of Obstetrics and Gynaecology and Government Hospital Chennai	0.10
166	Human Reproduction Research Centre - Regional Centre for Clinical Research	Dr. M.Kuppulakshmi Institute of Obstetrics and Gynaecology and Government Hospital Chennai	17.12

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
167	National Neonatal Perinatal Database	Dr. N.Saraswathi Institute of Obstetrics and Gynaecology and Government Hospital Chennai	0.88
168	Novel cardiovascular risk factors and preclinical atherosclerotic markers in subjects with glucose intolerance	Dr. Deepa Raj Madras Diabetes Research Foundation Chennai	5.71
169	Studies of the genetic variation in hepatocyte nuclear factor genes and glucokinase gene in relation to maturity onset diabetes of the young (MODY) and early onset diabetes in south Indians	Dr. Radha Venkatesan Madras Diabetes Research Foundation Chennai	2.89
170	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. Catherine Barnard Service & Research Foundation of Asia on Family & Culture Chennai	0.79
171	Human Reproduction Research Centre	Dr. S.K.Mahapatra S.C.B.Medical College Cuttack	6.40
172	Promoting male involvement under RCH strategy - an action research on adolescents in rural orissa	Dr. Saraswati Swain The National Institute of Applied Human Research and Development Cuttack	1.77
173	Home based management of young infants	Dr. Saraswati Swain The National Institute of Applied Human Research and Development Cuttack	28.09
174	Human Reproduction Research Centre	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	15.19
175	Pilot study on emergency contraception with CuT 200β and 0.75mg levonorgestrel (2 doses)	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	0.01

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
176	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	0.90
177	National Neonatal Perinatal Database	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	0.10
178	National Nutrition Monitoring Bureau	Dr. Nargis Naseem Directorate of Health, Medical Services and Medical Education Gandhinagar	9.40
179	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. M.C.Das Gauhati Medical College Guwahati	18.29
180	Central Reference Laboratory of the National Nutrition Monitoring Bureau	Dr. K.Vijayaraghavan National Institute of Nutrition Hyderabad	9.40
181	National Nutrition Monitoring Bureau	Dr. K.Vijayaraghavan National Institute of Nutrition Hyderabad	9.40
182	Survey of *khesari dal* consuming populations in India and Bangla Desh for detoxification of ODAP and metabolic derangements	Dr. M.P.Pratap Rudra Osmania University Hyderabad	1.57
183	Studies on the nutritional and microbiological quality of sun dried, semi-fermented and salt cured fishes of Manipur	Dr. W.Vishwanath Singh Manipur University Imphal	5.17
184	National Nutrition Monitoring Bureau	Dr. Tapas Chakma Regional Medical Research Centre for Tribals Jabalpur	9.40
185	Human Reproduction Research Centre	Dr. Anju Taly S.M.S.Medical College and Hospital Jaipur	14.09

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
186	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. N.K.Lohiya University of Rajasthan Jaipur	3.66
187	Human Reproduction Research Centre	Dr. Sadhna Sharma Government Medical College and S.M.G.S.Hospital Jammu	9.90
188	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Sadhna Sharma Government Medical College and S.M.G.S.Hospital Jammu	0.90
189	Human Reproduction Research Centre	Dr. V.K.Singh G.S.V.M.Medical College Kanpur	9.30
190	Human Reproduction Research Centre - Regional Centre for Clinical Research	Dr. B.K.Sau Institute of Postgraduate Medical Education and Research Kolkata	15.47
191	Human Reproduction Research Centre	Dr. Anita Roy Medical College and Eden Hospital Kolkata	13.48
192	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Anita Roy Medical College and Eden Hospital Kolkata	0.90
193	Human Reproduction Research Centre	Dr. A.K.Mondal R.G.Kar Medical College and Hospital Kolkata	12.89
194	Pilot study on emergency contraception with CuT 200β and 0.75mg levonorgestrel (2 doses)	Dr. A.K.Mondal R.G.Kar Medical College and Hospital Kolkata	0.32
195	National Nutrition Monitoring Bureau	Dr. A.Roy Chowdhury Regional Occupational Health Centre(Eastern) Kolkata	9.40

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
196	Human proacrosin-acrosin system and sperm-egg interaction	Dr. A.K.Bhattacharya University College of Science Kolkata	1.30
197	Hman Reproduction Research Centre	Dr. Vinita Das Chhatrapati Shahuji Maharaj Medical University Lucknow	14.05
198	Home based management of young infants	Dr. Vinita Das Chhatrapati Shahuji Maharaj Medical University Lucknow	28.09
199	National Neonatal Perinatal Database	Dr. G.K.Malik Chhatrapati Shahuji Maharaj Medical University Lucknow	0.88
200	Evaluation of the effects of immunotherapy with husband's lymphocytes on prevention of recurrent spontaneous abortion : a double blind randomized trial	Dr. Suraksha Devi Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.67
201	National Neonatal Perinatal Database	Dr. Manorama Verma Christian Medical College and Brown Memorial Hospital Ludhiana	0.44
202	Human Reproduction Research Centre	Dr. P.Meenambal Madurai Medical College and Government Rajaji Hospital Madurai	15.98
203	Quantitation of pathogenic *Vibrio* spp in seafoods using molecular methods	Dr. I.Karunasagar College of Fisheries Mangalore	3.10
204	National Neonatal Perinatal Database	Dr. K.K.Diwakar Kasturba Medical College and Hospital Manipal	0.88
205	Human Reproduction Research Centre	Dr. Usha Sharma L.L.R.M.Medical College Meerut	8.50

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
206	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Usha Sharma L.L.R.M.Medical College Meerut	0.90
207	Role of leaf extract of *Stephania hernandifolia (aknadi)* on fertility regulation in male : an evaluation for male pill of plant origin for 21st century	Dr. Debidas Ghosh Vidyasagar University Midnapore	0.54
208	Chracterization of angiotensin receptors in diabetic rats	Dr. P.Ramarao National Institute of Pharmaceutical Education and Research Mohali	0.54
209	Human Reproduction Research Centre	Dr. Rekha G.Dever Grant Medical College and Sir J.J.Group of Hospitals Mumbai	9.00
210	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Rekha G.Dever Grant Medical College and Sir J.J.Group of Hospitals Mumbai	0.90
211	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. Ravi Verma International Institute for Population Sciences Mumbai	3.52
212	Phase II clinical trial on Praneem polyherbal tablet for assessment of its efficacy in symptomatic women with abnormal vaginal discharge	Dr. Kamal Hazari National Institute for Research in Reproductive Health Mumbai	3.52
213	Social stigma attached to HIV infection-implications for health care and social adjustment	Dr. C.P.Puri National Institute for Research in Reproductive Health Mumbai	2.25
214	Women's work and child survival	Dr. C.P.Puri National Institute for Research in Reproductive Health Mumbai	1.48

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
215	National Neonatal Perinatal Database	Dr. Mina S.Bhattacharya Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai	0.10
216	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. Vinita Salvi Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai	10.87
217	A study of impact of counselling on coping behaviour of HIV positive cases in different states	Dr. Vinita Salvi Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai	1.86
218	National Neonatal Perinatal Database	Dr. R.H.Udani Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai	0.88
219	Development of nutraceuticals containing antioxidants and flavonoids for the prevention of coronary heart diseases	Dr. J.Hemavathy Central Food Technological Research Institute Mysore	2.30
220	Biological efficacy of antihypertensive peptides from cereals and pulses common to Indian diet	Dr. P.S.Rajini Central Food Technological Research Institute Mysore	1.00
221	National Neonatal Perinatal Database	Dr. V.S.Dani Indira Gandhi Medical College and Mayo General Hospital Nagpur	0.88
222	National Nutrition Monitoring Bureau	Dr. N.R.Khan Public Health Institute Building Nagpur	9.40
223	The effects of *ghee* (clarified butter) on the serum lipid profile	Dr. R.L.Bijlani All India Institute of Medical Sciences New Delhi	1.75
224	To study the temporal expression of angiogenic modulators during pregnancy and their regulation by steroid hormones	Dr. Chandana Das All India Institute of Medical Sciences New Delhi	2.50

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
225	Trophoblast biology : intracellular signaling mechanisms	Dr. Chandana Das All India Institute of Medical Sciences New Delhi	3.67
226	National Neonatal Perinatal Database	Dr. A.K.Deorari All India Institute of Medical Sciences New Delhi	0.88
227	Prevalence of multiple micronutrient deficiencies amongst pregnant and newly married non-pregnant women in a rural block, Haryana state	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	5.94
228	Genomics of male infertility	Dr. Kiran Kucheria All India Institute of Medical Sciences New Delhi	6.40
229	Immunogenetic and humoral profile of diabetes mellitus in asian Indians	Dr. N.K.Mehra All India Institute of Medical Sciences New Delhi	3.70
230	Human Reproduction Research Centre	Dr. Suneeta Mittal All India Institute of Medical Sciences New Delhi	15.30
231	National Neonatal Perinatal Database	Dr. Suneeta Mittal All India Institute of Medical Sciences New Delhi	0.10
232	National Neonatal Perinatal Database	Dr. V.K.Paul All India Institute of Medical Sciences New Delhi	1.97
233	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. Gulshanjit Singh Deen Dyal Upadhyay Hospital New Delhi	6.07
234	Central Co-ordinating Unit for Contraception Research	Sh. N.C.Saxena Indian Council of Medical Research New Delhi	20.00

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
235	Pilot study on emergency contraception with CuT 200β and 0.75mg levonorgestrel (2 doses) - Co-ordinating Unit	Sh. N.C.Saxena Indian Council of Medical Research New Delhi	20.00
236	Study on proper length and width specifications for condom in different regions of the country based on anthropometric measurements	Sh. N.C.Saxena Indian Council of Medical Research New Delhi	20.00
237	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Sh. N.C.Saxena Indian Council of Medical Research New Delhi	5.00
238	Home based management of young infants - Co-ordinating Unit	Sh. N.C.Saxena Indian Council of Medical Research New Delhi	10.98
239	Women's work and child survival	Dr. Padam Singh Indian Council of Medical Research New Delhi	5.04
240	National Nutrition Monitoring Bureau	Dr. Arvind Pandey Institute for Research in Medical Statistics New Delhi	9.40
241	Lipid profile, blood glucose and insulin levels of adolescents from affluent families	Dr. Santosh Jain Passi Institute of Home Economics New Delhi	2.82
242	Long term management of retinal and renal complications in experimental diabetes by vanadate and antidiabetic compounds	Dr. Najma Zaheer Baquer Jawaharlal Nehru University New Delhi	2.92
243	Urogynaecological complaints in postmenopausal women with particular reference to stress incontinence (evaluation and management)	Dr. Uma Goyal Lady Hardinge Medical College and Associated Hospitals New Delhi	2.00

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
244	Morphological changes of placenta in tobacco users and non tobacco users	Dr. Gayatri Rath Lady Hardinge Medical College and Associated Hospitals New Delhi	1.93
245	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. H.C.Das Lok Nayak Jaiprakash Narayan Hospital New Delhi	0.61
246	A study of impact of counselling on coping behaviour of HIV positive cases in different states	Dr. Sudha Prasad Maulana Azad Medical College and Associated Hospitals New Delhi	1.86
247	National Neonatal Perinatal Database	Dr. Siddarth Ramji Maulana Azad Medical College and Associated Hospitals New Delhi	0.88
248	Identification and characterization of spermatozoa surface proteins involved in binding to zona pellucida glycoproteins	Dr. Satish K.Gupta National Institute of Immunology New Delhi	2.82
249	Genomics of male infertility	Dr. Satish K.Gupta National Institute of Immunology New Delhi	9.69
250	Study to identify factors involved in paracrine modulation of testicular cells to increase our understanding about cellular regulation of spermatogenesis	Dr. S.S.Majumdar National Institute of Immunology New Delhi	3.18
251	Social stigma attached to HIV infection-implications for health care and social adjustment	Dr. R.B.Gupta ORG Centre for Social Research New Delhi	2.25
252	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. D.P.S.Toor Rural Medical Society New Delhi	4.33

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
253	Human Reproduction Research Centre	Dr. Sudha Salhan Safdarjang Hospital New Delhi	11.18
254	Human Reproduction Research Centre	Dr. Prasad Neurencar Goa Medical College Panaji	6.00
255	Human Reproduction Research Centre	Dr. Sushma Pandey Patna Medical College and Hospital Patna	13.19
256	Home based management of young infants	Dr. Sushma Pandey Patna Medical College and Hospital Patna	28.09
257	National Neonatal Perinatal Database	Dr. B.Vishnu Bhatt Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	0.44
258	Human Reproduction Research Centre	Dr. Syed Habeebullah Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	8.64
259	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Syed Habeebullah Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	0.90
260	National Neonatal Perinatal Database	Dr. Syed Habeebullah Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	0.10
261	Human Reproduction Research Centre	Dr. Aparna Shrotri B.J.Medical College and Sasoon General Hospital Pune	1.23
262	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Aparna Shrotri B.J.Medical College and Sasoon General Hospital Pune	0.90

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
263	Human Reproduction Research Centre	Dr. K.Coyaji King Edward Memorial Hospital and Research Centre Pune	6.70
264	National Neonatal Perinatal Database	Dr. K.Coyaji King Edward Memorial Hospital and Research Centre Pune	0.10
265	Health-disease-nutritional status of tribal and non-tribal pre-school children and their mothers : A study in the Jharkhand region of south Bihar Chhotanagpur plateau	Dr. M.R.Chakravartti Centre for Environmental and Developmental Research Ranchi	3.14
266	A study of impact of counselling on coping behaviour of HIV positive cases in different states	Dr. A.R.Singh Ranchi Institute of Neuro- Psychiatry and Allied Sciences Ranchi	1.86
267	Home based management of young infants	Dr. B.S.Garg Mahatma Gandhi Institute of Medical Sciences Sevagram	28.09
268	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. T.N.Rajalakshmi Medical College and SAT Hospital for Women & Children Thiruvananthapuram	0.90
269	Human Reproduction Research Centre	Dr. V.Rajasekharan Nair Medical College and SAT Hospital for Women & Children Thiruvananthapuram	13.98
270	Pilot study on emergency contraception with CuT 200β and 0.75mg levonorgestrel (2 doses)	Dr. V.Rajasekharan Nair Medical College and SAT Hospital for Women & Children Thiruvananthapuram	0.63
271	National Nutrition Monitoring Bureau	Dr. K.A.George State Nutrition Bureau Nutrition Research Centre Thiruvananthapuram	9.40

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
272	Home based management of young infants	Dr. S.D.Iyenger Action Research and Training for Health Udaipur	28.09
273	Obesity in school going children	Dr. Uma Mahadevan Iyer M.S.University Vadodara	2.69
274	Human Reproduction Research Centre	Dr. L.N.Chauhan Medical College and S.S.G.Hospital Vadodara	15.78
275	National Neonatal Perinatal Database	Dr. L.N.Chauhan Medical College and S.S.G.Hospital Vadodara	0.10
276	National Neonatal Perinatal Database	Dr. Dulari J.Gandhi Medical College and S.S.G.Hospital Vadodara	0.88
277	Poverty, under-nutrition and fertility nexus in rural eastern Uttar Pradesh	Dr. R.C.Yadav Banaras Hindu University Varanasi	5.01
278	Study of altered cell biology and signal transduction in platelets in pregnancy toxemia	Dr. Debabrata Dash Institute of Medical Sciences Banaras Hindu University Varanasi	0.50
279	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. S.K.Mishra Child in Need Trust 24-Parganas	3.52
	Non-communicable Diseases		
280	Mental health service needs and service delivery models in the disaster afected population,Ahmedabad Centre	Dr. A.P.S.Chouhan Hospital for Mental Health Ahmedabad	3.52
281	Cholinesterase and paraoxonase patterns in organophosphate (OP) poisoning	Sh. Ashwin B.Patel National Institute of Occupational Health Ahmedabad	0.81

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
282	Early detection of micrometastases in colorectal cancer patients using prolactin and cytokeratin 20	Dr. Neelam Girish Shah The Gujarat Cancer and Research Institute Ahmedabad	3.72
283	Epidemiology of glaucoma	Dr. S.T.Fernandez Little Flower Hospital and Research Centre Angamally	7.27
284	Development of sentinel health monitoring centres in India	Dr. K.Anand Comprehensive Rural Health Centre Ballabhgarh	2.00
285	National Cancer Registry Coordinating Unit (Technical Wing)	Dr. A.Nandakumar Kidwai Memorial Institute of Oncology Bangalore	57.02
286	Study of matrix metalloproteases in breast cancer	Dr. P.S.Prabhakaran Kidwai Memorial Institute of Oncology Bangalore	4.91
287	A prospective serial correlative study of neurocysticercosis by clinical and imaging methods	Dr. A.Nalini National Institute of Mental Health and Neurosciences Bangalore	3.98
288	Role of T cell and humoral factors in immune mediated damage in Guillain Barre' Syndrome	Dr. Shripad A.Patil National Institute of Mental Health and Neurosciences Bangalore	3.98
289	A multicentric study on prevalence of asthma	Dr. George D'souza St.John's Medical College, Hospital & College of Nursing Bangalore	3.51
290	Mental health service needs and service delivery models in the disaster affected population in Gujarat, Bhuj centre	Dr. Sanjeev Gupta Hospital for Mental Health Bhuj	5.98
291	Orbital blood flow studies in glaucoma	Dr. V.P.Munjal Government Medical College and Hospital Chandigarh	0.22

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
292	Detection of possible novel tumour markers for the early diagnosis of small cell and non-small cell lung carcinomas	Dr. R.C.Sobti Panjab University Chandigarh	2.00
293	Endothelin - 2 gene polmorphism in patients with essential hypertension and in patients with target end organ damage	Dr. Veena Dhawan Postgraduate Institute of Medical Education and Research Chandigarh	2.14
294	HLA typing in Vogt Koyanagi Harada (VKH) syndrome in Indian population	Dr. Amod Gupta Postgraduate Institute of Medical Education and Research Chandigarh	2.06
295	Cervical carcinoma : analysis of HLA polymorphism and its relationship to human papilloma virus type 16	Dr. Babita Jindal Postgraduate Institute of Medical Education and Research Chandigarh	2.00
296	A multicentric study on prevalence of asthma	Dr. S.K.Jindal Postgraduate Institute of Medical Education and Research Chandigarh	7.49
297	Role of resveratrol in colon and lung carcinogenesis	Dr. K.L.Khanduja Postgraduate Institute of Medical Education and Research Chandigarh	1.44
298	Molecular genetics of essential hypertension : role of genetic determinants in essential hypertension in Indian subjects	Dr. Madhu Khullar Postgraduate Institute of Medical Education and Research Chandigarh	2.80
299	Homocysteine and essential hypertension in Indian subjects : relation with folate, vitamin B12 and methylene tetrahydrofolate reductase (MTHFR) gene mutation	Dr. Madhu Khullar Postgraduate Institute of Medical Education and Research Chandigarh	3.17
300	Relationship between BCG vaccination and prevalence of atopic diseases specially asthma in school children	Dr. Lata Kumar Postgraduate Institute of Medical Education and Research Chandigarh	4.59

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
301	Analysis of parkin gene mutations in patients with autosomal recessive juvenile Parkinsonism (AP - JP) and young - onset Parkinson's disease (YOPD) and their clinical correlation	Dr. S.Prabhakar Postgraduate Institute of Medical Education and Research Chandigarh	2.18
302	The contribution of prothrombotic state to the etiology of ischemic stroke in young in the Indian population	Dr. S.Prabhakar Postgraduate Institute of Medical Education and Research Chandigarh	6.06
303	*Jai Vigyan* mission mode project on community control of RF/RHD in India	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	20.43
304	*Jai Vigyan* mission mode project on RF/RHD (Registry Protocol)	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	7.21
305	*Jai Vigyan* mission mode project on community control of RF/RHD in India	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	7.92
306	Assessment of severity of acute pancreatitis : role of inflammatory mediators and cytokines	Dr. J.D.Wig Postgraduate Institute of Medical Education and Research Chandigarh	1.57
307	A comprehensive retrospective immunohistochemical evaluation of axillary nodal status for micrometastasis and prognostic marker status in primary tumour in breast cancer patients	Dr. K.R.Rajalakshmy Cancer Institute (W.I.A.) Chennai	1.57
308	Urban mental health problems and their service needs	Dr. V.Palaniappun Institute of Mental Health Chennai	6.00
309	Causes of death by verbal autopsy - a pilot study	Dr. M.D.Gupte National Institute of Epidemiology Chennai	13.18

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
310	Development and evaluation of bioactive ceramic coating	Dr. S.Rajeswari University of Madras Chennai	1.13
311	Prognostic markers in uveal melanoma : an immunohistochemical study	Dr. Jyotirmay Biswas Vision Research Foundation Chennai	4.46
312	Mutational screening of rhodopsin gene in autosomal dominant retinitis pigmentosa and rpe65 gene in patients of childhood onset autosomal recessive retinitis pigmentosa and Lebers' congenital amaurosis	Dr. G.Kumaramanickavel Vision Research Foundation Chennai	2.82
313	Molecular biological and virological study of intraocular fluids from patients with viral retinitis and choroiditis - correlation with clinical features and visual outcome	Dr. H.N.Madhavan Vision Research Foundation Chennai	6.62
314	Development of molecular diagnostics for acute lymphoblastic leukaemia (ALL) and to study the influence of ALL - 1 protein on chromatin organisation	Dr. Vani Brahmachari Dr.B.R.Ambedkar Centre for Biomedical Research Delhi	1.34
315	Genomic studies of asthma in Indian population	Dr. Balaram Ghosh Institute of Genomics and Integrative Biology Delhi	14.69
316	A survey of burden and coping strategies of caregivers of patients with severe mental disorders	Dr. R.K.Chadda Institute of Human Behaviour and Allied Sciences Delhi	2.37
317	Urban mental health problems and their service needs	Dr. N.G.Desai Institute of Human Behaviour and Allied Sciences Delhi	6.00

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
318	Mental health service needs and service delivery models in the disaster affected population in Gujarat	Dr. N.G.Desai Institute of Human Behaviour and Allied Sciences Delhi	3.51
319	Potentiation of allergic asthma by air pollution : the ozone - allergen interaction and its modulation by dietary antioxidants, alpha - tocopherol and ascorbic acid	Dr. S.K.Chhabra Vallabhbhai Patel Chest Institute Delhi	8.48
320	Studies on foods as sensitizing and inducing factors of allergy disorders with special reference to bronchial asthma	Dr. Raj Kumar Vallabhbhai Patel Chest Institute Delhi	4.81
321	A multicentric study on prevalence of asthma	Dr. V.K.Vijayan Vallabhbhai Patel Chest Institute Delhi	2.25
322	A study on treatment seeking behaviour and reporting pattern of patients to health service centres especially with fever symptom	Sh. Himanshu Kumar Chaturvedi Regional Medical Research Centre Dibrugarh	5.35
323	Epidemiological evaluation of the impact of insecticide treated mosquito nets on occurence of Japanese encephalitis cases in two selected endemic PHC areas of Assam, India	Dr. Prafulla Dutta Regional Medical Research Centre Dibrugarh	6.55
324	Malaria control in a forest fringe village of Assam : a pilot study	Dr. Prafulla Dutta Regional Medical Research Centre Dibrugarh	3.39
325	Study on coronary heart disease and hypertension in Mizoram tribal health sub-plan scheme	Dr. N.C.Hazarika Regional Medical Research Centre Dibrugarh	8.24

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
326	Morbidity surveillance in Sikkim	Dr. N.C.Hazarika Regional Medical Research Centre Dibrugarh	3.63
327	Etiology of endemic goitre in north-east India : role of environmental goitrogens	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	3.29
328	Molecular epidemiological analysis of methicillin resistant *Stapylococcus aureus* in Assam,India	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	4.83
329	Development of sentinel health monitoring centres in India	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	2.00
330	Studies on paragonimiasis in hill tribes of Arunachal Pradesh	Dr. Kanwar Narain Regional Medical Research Centre Dibrugarh	11.59
331	Homocysteine and stroke	Dr. N.C.Borah Institute of Neurological Sciences Guwahati	5.26
332	Role of growth factors and receptors in cataract	Dr. Yogendra Sharma Centre for Cellular and Molecular Biology Hyderabad	2.89
333	Differentiation of embryonal carcinoma cells with curcumin and identification of differentially expressed genes that trigger differentiation	Dr. Usha K.Srinivas Centre for Cellular and Molecular Biology Hyderabad	1.15
334	Role of apoptosis in tissue damage and wound healing in corneal infections	Dr. Geeta K.V. L.V.Prasad Eye Institute Hyderabad	1.45
335	Etiology of endemic goitre in northeast India : role of environmental goitrogens	Dr. Kamala Krishnaswamy National Institute of Nutrition Hyderabad	3.41

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
336	Prevention of disability among pre - school children	Dr. Akhilesh Bhargava S.M.S.Medical College and Hospital Jaipur	4.51
337	Mental health service needs and service delivery models in the disaster affected population in Gujarat	Dr. Chitra Somasundaram Shri M.P.Shah Medical College Jamnagar	6.13
338	A multicentric study on prevalence of asthma	Dr. S.K.Katiyar G.S.V.M.Medical College Kanpur	2.45
339	*Jai Vigyan* mission mode project on community control of RF/RHD in India (Registry Protocol)	Dr. R.Krishan Kumar Amrita Institute of Medical Sciences and Research Centre Kochi	25.29
340	Epidemiology of major neurological disorders - a random sample survey in the city of Calcutta	Dr. Shyamal K.Das Bangur Institute of Neurology Kolkata	6.22
341	Role of integrin and lectin cell surface molecules in tumor metastasis	Dr. Amitava Chatterjee Chittaranjan National Cancer Institute Kolkata	3.00
342	Reversal of multidrug resistance (MDR) in cancer by the application of new resistance modifying agents (RMA)	Dr. Soumitra K.Choudhuri Chittaranjan National Cancer Institute Kolkata	3.42
343	Experimental evaluation of snake venom as an anticancer agent	Dr. Aparna Gomes Indian Institute of Chemical Biology Kolkata	2.05
344	Comparative evaluation of 99m TC - MAG3 in normal and chronic renal failure patients	Dr. Mridula Misra Indian Institute of Chemical Biology Kolkata	2.28

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
345	Feasibility of a screening program with abnormal cytology and oncogenic human papillomavirus and other infections in the *maria - gond* tribal women : reproductive health care study and apoptosis	Dr. C.Duttagupta Indian Statistical Institute Kolkata	1.50
346	Assessment of AgNoR technique as tumour marker in cervical carcinogenesis	Dr. Vinita Das Chhatrapati Shahuji Maharaj Medical University Lucknow	0.43
347	Evolving tobacco control strategy for India	Dr. Sandeep Kumar Chhatrapati Shahuji Maharaj Medical University Lucknow	1.45
348	Prevention of disability among pre - school children	Dr. J.V.Singh Chhatrapati Shahuji Maharaj Medical University Lucknow	4.29
349	Urban mental health problems and their service needs	Dr. S.C.Tiwari Chhatrapati Shahuji Maharaj Medical University Lucknow	6.00
350	Mode of action of calcium glutarate in skin tumorigenesis	Dr. K.P.Gupta Industrial Toxicology Research Centre Lucknow	0.37
351	A study of structural and functional correlates of movement disorders in Japanese encephalitis	Dr. U.K.Misra Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	0.85
352	Seroepidemiology of *Taenia solium* cysticercosis in India. a multi - population study	Dr. Gagandeep Singh Dayanand Medical College and Hospital Ludhiana	0.86
353	Studies on the genetics of inherited aniridia in Indian population	Dr. P.Sundaresan Aravind Eye Hospital and Postgraduate Institute of Ophthalmology Madurai	2.44

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
354	Genetic and structural analysis of myocilin protein involved in juvenile onset primary open angle glaucoma	Dr. P.Sundaresan Aravind Eye Hospital and Postgraduate Institute of Opthalmology Madurai	3.21
355	Investigations on hydroxyapatite coatings of Ti and Ti - 6A1 - 4V for dental implants	Dr. V.Surendra Shetty College of Dental Surgery Manipal	0.5
356	Lipoprotein(A) level and other lipid profiles in myocardial infarction	Dr. P.Gopalakrishna Bhat Kasturba Medical College and Hospital Manipal	0.8
357	Effect of long term endosulfan exposure on male fertility	Dr. N.Pratap Kumar Kasturba Medical College and Hospital Manipal	1.61
358	Comparative evaluation of *Triphala* and chlorhexidine as a mouthwash : a controlled clinical trial	Dr. Shobha Tandon Kasturba Medical College and Hospital Manipal	1.76
359	Identification of the markers for chronic infection with hepatitis B virus and their relation to hepatocarcinogenesis: detection of HBX transcripts and immune responses to HBX gene products in CHB and HCC patients	Dr. Shubhade V.Chiplunkar Cancer Research Institute Mumbai	3.41
360	Molecular cytogenetic studies in oral cancer	Dr. Manoj B.Mahimkar Cancer Research Institute Mumbai	3.71
361	Evaluation of carcinogenic potential and mechanism (s) of action of *pan masala / gutkha*	Dr. G.B.Maru Cancer Research Institute Mumbai	3.73
362	Evaluation of chemopreventive effects of polyphenolic components from Indian grapes	Dr. Asha G.Ramchandani Cancer Research Institute Mumbai	3.73
363	Studies on the molecular mechanism of tamoxifen - induced apoptosis of astrocutoma cells	Dr. Neelam V.Shirsat Cancer Research Institute Mumbai	5.54

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
364	Identification of constitutional and somatic deletion / alteration in the 3p 14 - p21 region by dual colour fish using yeast artificial chromosome (YAC) clones in human renal cell carcinoma (RCC)	Dr. Pratibha S.Amare Tata Memorial Hospital Mumbai	2.45
365	Development of MUC1 - single chain - MET - ETA recombinant antibody (SCFV) for *in vivo* imaging and targetted therapy in breast cancer	Dr. Dilip Bandyopadhyay Tata Memorial Hospital Mumbai	9.00
366	*In vitro* chemosensitivity of oral squamous cancer by histoculture drug response assay (HDRA) and its correlation with clinical response to chemotherapy	Dr. K.A.Pathak Tata Memorial Hospital Mumbai	1.44
367	Radioprotective effect of *Ocimum sanctum (tulasi)* in patients undergoing hemi body irradiation : a double blind randomised trial	Dr. Rajiv Sarin Tata Memorial Hospital Mumbai	2.23
368	Development of sentinel health monitoring centres in India	Dr. Prashant Joshi Government Medical College and Hospital Nagpur	2.00
369	Development and synthesis of UV lamp phosphors for phototherapy	Dr. C.P.Joshi Shri Ramdeobaba Kamla Nehru Engineering College Nagpur	2.39
370	To study the prevalence of chronic renal failure in India	Dr. S.K.Agarwal All India Institute of Medical Sciences New Delhi	3.78
371	Impact of isolation of hepatitis C positive patients on incidence of HCV positivity in haemodialysis patients	Dr. S.K.Agarwal All India Institute of Medical Sciences New Delhi	1.68

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
372	Childhood Hodgkin's disease : role of Epstein - Barr virus (EBV) association, cellular proliferation and apoptosis parameters in relation with the treatment outcome	Dr. L.S.Arya All India Institute of Medical Sciences New Delhi	5.28
373	A longitudinal study to estimate proportion of patients with dementia and cognitive decline in Parkinson's disease, its clinical correlates with reference to apolipoprotein E alleles	Dr. Madhuri Behari All India Institute of Medical Sciences New Delhi	2.30
374	Molecular genetic analysis of parkin gene among Indians with autosomal recessive juvenile Parkinsonism (ARJP)	Dr. Madhuri Behari All India Institute of Medical Sciences New Delhi	4.12
375	Evaluation of iatrogenic nerve injuries following orthopedic procedures and role of nerve stimulation in their management	Dr. Surya Bhan All India Institute of Medical Sciences New Delhi	0.61
376	Incremental predictive accuracy of transcranial magnetic stimulation (TMS) as prognostic indicators for motor recovery in patients with acute stroke	Dr. Manvir Bhatia All India Institute of Medical Sciences New Delhi	2.49
377	Role of intratympanic dexamethasone therapy in sudden sensorineural hearing loss (SSNHL)	Dr. R.C.Deka All India Institute of Medical Sciences New Delhi	1.57
378	Impact of multidisciplinary intervention on health related quality of life (QOL) in ambulatory older subjects	Dr. A.B. Dey All India Institute of Medical Sciences New Delhi	1.13
379	Urinary screening of school children of Delhi : a preliminary study	Dr. A.K.Dinda All India Institute of Medical Sciences New Delhi	2.80

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
380	The development and standardization of a comprehensive dementia assessment scale	Sh. Surya Gupta All India Institute of Medical Sciences New Delhi	1.13
381	Urban hospital-based case-control study to identify risk factors for acute myocardial infarction	Dr. B.L.Jailkhani All India Institute of Medical Sciences New Delhi	1.98
382	Feasibility of transporting blood dried on filter paper for the measurement of lipids, lipoproteins and markers of glycaemic index, glucose, glycosylated haemoglobin and insulin for cardiovascular diseases	Dr. B.L.Jailkhani All India Institute of Medical Sciences New Delhi	3.11
383	Presynaptic membrane receptor autoantibodies in myasthenia gravis	Dr. B.L.Jailkhani All India Institute of Medical Sciences New Delhi	3.05
384	Reactivity of muscle nicotinicavetyl choline receptors and nonreceptor antigens from different animals with myasthenic antibodies	Dr. B.L.Jailkhani All India Institute of Medical Sciences New Delhi	2.12
385	Risk factors of substance use and abuse in offspring of substance abuse patients	Dr. H.P.Jhingan All India Institute of Medical Sciences New Delhi	1.84
386	Prevalence, etiological factors and treatment of malnutrition by dietary intervention in patients with chronic pancreatitis	Dr. Y.K.Joshi All India Institute of Medical Sciences New Delhi	3.59
387	Effect of glutamine supplementation on clinical outcome and nutritional status in patients of acute myeloid leukaemia (AML)	Dr. Y.K.Joshi All India Institute of Medical Sciences New Delhi	2.15

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
388	Human paraoxonase gln-arg (q/r) polymorphism in Indians with acute myocardial infarction	Dr. R.Lakshmy All India Institute of Medical Sciences New Delhi	1.40
389	Comparison of recovery, and complications and recurrence rate after endoscopic *versus* open carpal tunnel release	Dr. Rajesh Malhotra All India Institute of Medical Sciences New Delhi	13.64
390	Development and dissemination of intervention strategies for specific learning disability	Dr. Manju Mehta All India Institute of Medical Sciences New Delhi	1.69
391	Determination of the therapeutic range of temperature for heat therapy for Indian patients - a preliminary study	Smt. Kanchan Mittal All India Institute of Medical Sciences New Delhi	0.79
392	Molecular alterations in human oesophageal cancer : potential prognostic implications	Dr. Ranju Ralhan All India Institute of Medical Sciences New Delhi	3.73
393	Role of genomic instability due to alterations of recombination factors p53 and BRCA1 in the pathogenesis of breast cancer	Dr. Ranju Ralhan All India Institute of Medical Sciences New Delhi	1.00
394	Evaluation of external fixation and internal fixation in fractures of distal radius in Indian patients	Dr. S.Rastogi All India Institute of Medical Sciences New Delhi	1.82
395	Evaluation of VEGF and p53 expression as prognostic markers in giant cell tumour of bone	Dr. Rajani Bhan Safaya All India Institute of Medical Sciences New Delhi	0.86
396	*C.pneumoniae* and coronary artery disease : use of polymerase chain reaction assay (PCR), agent detection and serology in investigating the association	Dr. Gita Satpathy All India Institute of Medical Sciences New Delhi	2.04

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
397	Role of genetic factors in tropical pancreatitis	Dr. M.P.Sharma All India Institute of Medical Sciences New Delhi	2.04
398	Telomerase activity in carcinoma cervix - role of HPV	Dr. Neeta Singh All India Institute of Medical Sciences New Delhi	0.34
399	Amniotic membrane transplantation in acute ocular burns : a randomised controlled clinical trial	Dr. Radhika Tandon All India Institute of Medical Sciences New Delhi	1.05
400	Role of CYP2D6 and glutathione S-transferase M1 (GSTM1) polymorphism in multiple sclerosis patients	Sh. S.Vivekanandhan All India Institute of Medical Sciences New Delhi	1.60
401	Development of sentinel health monitoring centres in India	Dr. Bela Shah Indian Council of Medical Research New Delhi	5.44
402	Plasma modification of polypropylene monofilament for biomedical application	Dr. Bhuvanesh Gupta Indian Institute of Technology New Delhi	1.82
403	Causes of death by verbal autopsy - a pilot study	Dr. Arvind Pandey Institute for Research in Medical Statistics New Delhi	12.88
404	Modulation of local innate and adaptive immune responses in lungs by environmental and occupational hazards with special reference to air borne diesel exhaust particulates	Dr. Rajiv K.Saxena Jawaharlal Nehru University New Delhi	13.63
405	Investigation into androgen - independent activation of androgen receptor in prostrate cancer	Dr. Rakesh Kumar Tyagi Jawaharlal Nehru University New Delhi	2.21
406	To study the effects of community based rehabilitation and training programme on the quality of life of the Indian elderly	Dr. Kamala Khetarpal Kamla Charitable Trust New Delhi	1.00

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
407	Role of IGF - 1 and TNF alpha in progress and treatment of neurodegenerative diseases	Dr. Kakoli Ghoshal National Institute of Immunology New Delhi	6.99
408	Prevention of disability among pre - school children	Dr. H.C.Goyal Safdarjang Hospital New Delhi	5.12
409	Risk of malformations in children of women with epilepsy - a prospective, controlled study	Dr. D.C.Jain Safdarjang Hospital New Delhi	4.27
410	Prevalence of STI in rural and urban community in Delhi	Dr. Krishna Ray Safdarjang Hospital New Delhi	6.47
411	Flow cytometric assays to evaluate prognosis and patient's response to chemotherapy in acute leukaemia	Dr. Sumita Saluja Safdarjang Hospital New Delhi	2.54
412	Mental health service needs and service delivery models in the disaster affected population,Rajkot Centre	Dr. M.J.Somani Government Medical College Rajkot	4.61
413	Control of cancer through multi-organ approach - a district level operational research project	Dr. H.L.Kapoor Indira Gandhi Medical College Shimla	111.41
414	Recent trends in role of diet and drinking water in urolithiasis	Dr. Y.M.Fazil Marickar Medical College and SAT Hospital for Women & Children Thiruvananthapuram	1.51
415	Evaluation of T-cell mediated signal transduction of oral cancer patients in relation to immune response	Dr. Prabha Balaram Regional Cancer Centre Thiruvananthapuram	2.92
416	Trivandrum quality of life study : a study on quality of life in breast cancer patients undergoing treatment with curative intent	Dr. Manoj Pandey Regional Cancer Centre Thiruvananthapuram	0.60

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417	Cellular and molecular manifestations of natural plant compounds on human papillomavirus infected cells	Dr. M.Radhakrishna Pillai Regional Cancer Centre Thiruvananthapuram	1.83
418	Prognostic evaluation of karyotypic changes and telomerase activity in preleukemic and leukemic conditions	Dr. A.Ravindran Regional Cancer Centre Thiruvananthapuram	1.16
419	Angiotensin II in the pathogenesis of myocardial lesions in magnesium deficiency	Dr. K.Shivakumar Sree Chitra Tirunal Institute for Medical Sciences and Thiruvananthapuram	3.70
420	Development of sentinel health monitoring centres in India	Dr. K.R.Thankappan Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram	2.00
421	Antitumour activity of isoquinoline alkaloid berberine and its mechanism of action	Dr. Ramadasan Kuttan Amala Cancer Hospital and Technology Research Centre Thrissur	1.17
422	Studies on energy deficiency in an animal model of hepatic microvesicular steatosis produced by inhibition of fatty acid oxidation	Dr. K.A.Balasubramanian Christian Medical College and Hospital Vellore	2.02
423	*Jai Vigyan* mission mode project on RF/RHD (Registry Protocol)	Dr. Vinohar Balraj Christian Medical College and Hospital Vellore	2.28
424	The value of intravesical oxybutynin, probanthine and capsaicin in the management of neuropathic bladders	Dr. Suranjan Bhattacharji Christian Medical College and Hospital Vellore	2.39
425	Quantifying the contribution of neurocysticercosis to the causation of seizures and study the seroprevalence of cysticercosis in rural and urban communities in vellore district of Tamil Nadu	Dr. Vedantam Rajshekhar Christian Medical College and Hospital Vellore	5.58

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
426	Organophosphate poisoning : the relationship of oxidative stress to the occurrence of intermediate syndrome	Dr. Anand Zachariah Christian Medical College and Hospital Vellore	1.18
Basic Medical Sciences			
427	Leprosy genomics : the genomic diversity of leprosy bacillus and expression of its genes in human host	Dr. V.M.Katoch Central JALMA Institute for Leprosy Agra	6.00
428	Immunogenicity of DNA damaged by singlet oxygen:implications for anti-DNA antibodies in autoimmune disorders	Dr. Rashid Ali Jawaharlal Nehru Medical College Aligarh	2.97
429	Studies on the reactive oxygen species damaged DNA : implications in the etiopathogenesis of SLE	Sh. Moinuddin Jawaharlal Nehru Medical College Aligarh	2.46
430	Role of DNA fragmentation and prolonged immediate early gene expression in the neuropathogenesis of diabetes and hypoglycemia in rat	Dr. Gurcharan Kaur Guru Nanak Dev University Amritsar	1.89
431	Development of new erythromycin derivatives	Dr. P.K.Manna Annamalai University Annamalai Nagar	0.40
432	Functional genomics of the proteins interacting with the bacterial cell division protein FTSZ in the proliferating and dormant *Mycobacterium tuberculosis* H37RV	Dr. P.Ajit Kumar Indian Institute of Science Bangalore	13.00
433	Molecular basis of rotavirus pathogenesis : comparative structural and biological functional studies on the rotaviral enterotoxigenic protein NSP4	Dr. C.Durga Rao Indian Institute of Science Bangalore	5.20
434	Redox reactivities of metal oxides and peroxides	Dr. M.S.Hegde Indian Institute of Science Bangalore	1.40

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
435	Functional and structural genomics of RecA intein of *Mycobacterium tuberculosis* and *M.leprae*	Dr. K.Muniyappa Indian Institute of Science Bangalore	13.69
436	Mechanism of transcription termination in mycobacteria	Dr. V.Nagaraja Indian Institute of Science Bangalore	3.01
437	Identification and functional characterization of genes modulated by bacterial components and/or proinflammatory cytokines in a hepatoma cell line, H6	Dr. Dipankar Nandi Indian Institute of Science Bangalore	5.65
438	Immunogenomics and pathogenomics of *M.tuberculosis* and *M.bovis* (BCG)	Dr. R.Nayak Indian Institute of Science Bangalore	3.00
439	DNA repair and susceptibility to cancer	Dr. M.R.S.Rao Indian Institute of Science Bangalore	12.5
440	Gene expression profiling of cisplatin sensitive and resistant cells using cDNA microarrays	Dr. K.Somasundaram Indian Institute of Science Bangalore	6.04
441	A functional genomics approach to understanding diarrhoeas mediated by the heat-stable enterotoxin	Dr. Sandhya S.Visweswariah Indian Institute of Science Bangalore	3.25
442	Molecular genetic basis of hot water epilepsy	Dr. Anuranjan Anand Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	12.75
443	Characterization of *Plasmodium falciparum* inosine monophosphate dehydrogenase (IMPDH) as a drug target	Dr. Hemalatha Balaram Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	1.37
444	Purification of anti-malarial compounds from Indian herbs and elucidation of their mode of action in *Plasmodium falciparum*	Dr. Namita Surolia Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	21.50

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445	Molecular diagnosis of common opportunistic infections in cancer	Dr. R.S.Jayshree Kidwai Memorial Institute of Oncology Bangalore	3.29
446	A molecular genetic study of special sub-groups of psychoses	Dr. Sanjeev Jain National Institute of Mental Health and Neurosciences Bangalore	1.50
447	Comparison of Parkin mutations in early *vs* late onset patients between familial and sporadic Parkinson's disease	Dr. Uday B.Muthane National Institute of Mental Health and Neurosciences Bangalore	1.00
448	Puerperal cerebral venous thrombosis: a genetic approach to etiology	Dr. D.Nagaraja National Institute of Mental Health and Neurosciences Bangalore	3.86
449	A genomic approach to the development of peptide based diagnostic assays for Japanese encephalitis	Dr. V.Ravi National Institute of Mental Health and Neurosciences Bangalore	6.15
450	Molecular genetics of neuro-muscular disorders	Dr. Anisya Vasanth National Institute of Mental Health and Neurosciences Bangalore	0.92
451	*Jai vigyan* mission project on community control of thalassaemia syndromes - awareness,screening,genetic counselling and prevention	Dr. Cecil R.Ross St.John's Medical College Hospital & College of Nursing Bangalore	9.27
452	Survey and designing of monograph on medicinal plants of Western Ghat situated in Karnataka state	Dr. F.V.Manvi K.L.E. Society's College of Pharmacy Belgaum	2.15
453	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. G.P.Chhotray Regional Medical Research Centre Bhubaneswar	5.03

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454	Characterization of serine/ threonine kinases of *Mycobacterium tuberculosis*	Dr. P.K.Chakraborti Institute of Microbial Technology Chandigarh	2.39
455	Effect of prenatal exposure of ethanol on the functional development of intestine in rats	Dr. Akhtar Mahmood Panjab University Chandigarh	1.60
456	Detection and identification of fungal pathogens in blood using molecular probes	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	6.98
457	Characterization of IgA protease gene of *H.influenzae* from children of different age groups by DNA based techniques	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	3.16
458	Characterization of virulent genes of enteroaggregative *E.coli* to correlate their role in disease progression	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	16.53
459	Genomics of glucose-6-phosphate dehydrogenase deficiency in north Indian population	Dr. Gurjeevan Garewal Postgraduate Institute of Medical Education and Research Chandigarh	4.79
460	Study on the effect of the disease specific sialo glycoconjugate specific lectin in lung carcinoma	Dr. Sujata Ghosh Postgraduate Institute of Medical Education and Research Chandigarh	6.15
461	Group A streptococcus, *S.pyogenes* subtyping by insertion sequences	Dr. Anil Grover Postgraduate Institute of Medical Education and Research Chandigarh	10.00
462	Study of genetic and molecular basis of angiogenesis in renal cell and prostate carcinomas : developing cancer therapy resistant to resistance	Dr. Vivekanand Jha Postgraduate Institute of Medical Education and Research Chandigarh	1.25

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
463	Phase II study of transcriptional regulation of human LDL-receptor gene by cholesterol	Dr. Deepak Kaul Postgraduate Institute of Medical Education and Research Chandigarh	2.21
464	Studies on the effect of chronic ethanol feeding on transport of folate and expression of its transporter in rat intestine	Dr. Jyotdeep Kaur Postgraduate Institute of Medical Education and Research Chandigarh	1.37
465	Genetic risk factors in adolescents and young adults for coronary artery disease : genetic polymorphism in apoA, ApoB, apoE gene loci and its influence on blood lipid levels	Dr. Madhu Khullar Postgraduate Institute of Medical Education and Research Chandigarh	2.59
466	Poly (lactide -coglycolide) microparticles as controlled release drug delivery systems for antitubercular drugs	Dr. G.K.Khuller Postgraduate Institute of Medical Education and Research Chandigarh	1.56
467	Immunoprophylactic properties of 30kda secretory protein of *M.tuberculosis* H37RA in different adjuvant systems and immunophenotyping during immunization/infection	Dr. G.K.Khuller Postgraduate Institute of Medical Education and Research Chandigarh	2.32
468	Protective efficacy of *M. tuberculosis* complex specific protein antigens against experimental tuberculosis	Dr. G.K.Khuller Postgraduate Institute of Medical Education and Research Chandigarh	1.25
469	Molecular mechanisms responsible for the defective allele of human hepatic cytochrome p4502c19	Dr. K.K.Kohli Postgraduate Institute of Medical Education and Research Chandigarh	0.80
470	Role of vitamin E in the regulation of surfactant synthesis, secretion and protection of the lung alveolar type II cells following hyperoxic injury	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	3.27

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471	Alterations in the phospholipid transfer protein (PLTP) gene expression in neonates with respiratory distress syndrome	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	2.90
472	Alteration in interleukin-6 (IL-6) and tumour necrosis factor -alpha (TNF alpha) gene expression in neonatal sepsis	Dr. Anil Narang Postgraduate Institute of Medical Education and Research Chandigarh	3.13
473	Molecular cloning of a gene encoding a novel major copper binding protein in Indian childhood liver cirrhosis diseases:genomic organization, structural and functional characterization	Dr. Rajendra Prasad Postgraduate Institute of Medical Education and Research Chandigarh	2.00
474	Genetic characterization of the spiral and coccoid forms of *H.pylori* and mutational analysis of the urease gene	Dr. Pallab Ray Postgraduate Institute of Medical Education and Research Chandigarh	9.00
475	Facial reconstruction of skulls	Dr. Daisy Sahni Postgraduate Institute of Medical Education and Research Chandigarh	1.20
476	Analysis of genomic variation in population with kidney stone disease	Dr. S.K.Sharma Postgraduate Institute of Medical Education and Research Chandigarh	3.32
477	Expression of estrogen receptor alpha and beta and progesterone receptor in normal, hyperplastic and carcinoma endometrium	Dr. Radhika Srinivasan Postgraduate Institute of Medical Education and Research Chandigarh	2.00
478	Antimycobacterial activity of human neutrophil peptide -1 (HNP-1) against drug resistant strains of mycbacteria and its role as antiresistance peptide	Dr. Indu Verma Postgraduate Institute of Medical Education and Research Chandigarh	1.63
479	A study on the efficacy of alcohol oxidase loaded erythrocytes in combating methanol toxicity	Dr. A.Namasivayam Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai	13.00

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480	Effect of vitamin-E supplementation on the function of RBC anionic binding protein in uraemic patients	Dr. P.Varalakshmi Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai	1.17
481	A survey of the medicinal plants of Western Ghats	Dr. S.Ignacimuthu Entomology Research Institute Chennai	2.09
482	Central Biostatistical Monitoring Unit for Traditional Medicine Research	Dr. M.D.Gupte National Institute of Epidemiology Chennai	16.77
483	Clinical Pharmacology Unit	Dr. V.Kumaraswami Tuberculosis Research Centre Chennai	11.16
484	Flexible dose open trial on *vijayasar* for known diabetes	Dr. P.K.Mishra S.C.B.Medical College Cuttack	5.50
485	Analysis of polymorphism and expression profile of genes of mammalian cell entry (MCE) operons in clinical isolates of *M.tuberculosis*	Dr. Vani Brahmachari Dr.B.R.Ambedkar Centre for Biomedical Research Delhi	4.09
486	Genetic markers:vulnerability to common neuro-psychiatric diseases	Dr. Suman Kapur Institute of Human Behaviour and Allied Sciences Delhi	1.66
487	Genetic diversity of *Plasmodium falciparum* and *P.vivax* in India using molecular markers	Dr. Hema Joshi Malaria Research Centre Delhi	7.73
488	Molecular characterization of *Anopheles fluviatilis* complex: development of species specific diagnostic markers and microsatellite markers	Dr. Sarala K.Subbarao Malaria Research Centre Delhi	6.00
489	Role of lipoprotein(a) and its phenotypes as a risk factor for premature coronary artery disease in Indian subjects	Dr. Jasvinder K.Gambhir University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	1.45

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490	Determinants of genetic and sociocultural aspects of health vis-a-vis the role of health providers among the tribes of coastal,desert and Himalayan regions	Dr. G.K.Kshatriya University of Delhi Delhi	2.12
491	Studies on mechanism of signal transduction during release of proinflammatory cytokines IL-1beta and TNF-alpha by alveolar macrophages in asthma	Dr. S.K.Bansal Vallabhbhai Patel Chest Institute Delhi	1.37
492	*Jai vigyan* mission project on community control of thalassaemia syndromes - awareness,screening,genetic counselling and prevention	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	16.71
493	Genetic analysis of pancreatitis in Indian population	Dr. G.R.Chandak Centre for Cellular and Molecular Biology Hyderabad	2.85
494	Gene expression profiling of skeletal muscle stem cells using DNA microarrays	Dr. Jyotsna Dhawan Centre for Cellular and Molecular Biology Hyderabad	3.50
495	Clinical and molecular manifestations of anophthalmia	Dr. S.H.Rao Centre for Cellular and Molecular Biology Hyderabad	1.50
496	Comparative and functional genomic approaches to discovering novel targets for drug screening against cancer	Dr. L.S.Shashidhara Centre for Cellular and Molecular Biology Hyderabad	15.00
497	Genetics of reproductive dysfunction in women	Dr. A.P.Singh Centre for Cellular and Molecular Biology Hyderabad	5.15
498	Genetic causes of male infertility in India	Dr. K.Thangaraj Centre for Cellular and Molecular Biology Hyderabad	8.74

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499	Immunotherapy against intracellular infections, using TLTF cDNA delivered as naked DNA	Dr. Tushar Vaidya Centre for Cellular and Molecular Biology Hyderabad	2.50
500	Computational analysis and functional characterization of mycobacterial protein(s) interacting with macrophage effector-apc functions - an approach to understand the molecular basis of pathogenesis of *M.tuberculosis*	Dr. Sangita Mukhopadhyay Centre for DNA Fingerprinting and Diagnostics Hyderabad	5.50
501	Molecular genetic analysis of some forms of inherited childhood blindness, and genetic counseling of the affected families	Dr. Chitra Kannabiran L.V.Prasad Eye Institute Hyderabad	2.50
502	PPAR mediated regulation of glucose metabolism and coronary heart diseases: understanding the mechanism of action	Dr. Nasreen Z.Ehtesham National Institute of Nutrition Hyderabad	2.50
503	Centre for Advanced Research for Pre-clinical Toxicology	Dr. B.Sivakumar National Institute of Nutrition Hyderabad	6.71
504	Centre for Advanced Research on Aging and Brain	Dr. K.Subba Rao University of Hyderabad Hyderabad	13.23
505	Manufacturing Unit in Standardization and Quality Control and Formulation of Natural Products/Selected Traditional Herbal Remedies	Dr. K.L.Bedi Regional Research Laboratory Jammu Tawi	11.71
506	Application of primary monolayer cultures of rat hepatocytes in the development of hepatoprotectives from medicinal plants	Dr. R.K.Johri Regional Research Laboratory Jammu Tawi	3.39
507	Development of a synergistic hepatoprotective formulation	Dr. O.P.Suri Regional Research Laboratory Jammu Tawi	1.68

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508	Development of DNA fingerprints as molecular marker in selected medicinal plants	Dr. V.Verma Regional Research Laboratory Jammu Tawi	1.94
509	Studies on oxidant-mediated activation of Ca2+ dependent proteases in pulmonary vascular smooth muscle membrane	Dr. Sajal Chakraborti University of Kalyani Kalyani	1.80
510	Protein kinase C-mediated activation of Ca2+ dependent phospholipase A2 in pulmonary vascular smooth muscle cells under oxidant stimulation : role of cAMP, cGMP and pertussin toxin sensitive protein	Dr. Sajal Chakraborti University of Kalyani Kalyani	5.25
511	Protein phosphorylation in *M.leprae* and *M.tuberculosis*- its role in metabolism and pathogenesis	Dr. Lavanya M. Suneetha Schieffelin Leprosy Research and Training Centre Karigiri	1.00
512	Rapid diagnostic test for c-reactive protein (CRP) based on whole blood agglutination by a conjugated protein of monovalent lectin and fab fragment of anti human c-reactive immunoglobulin	Dr. T.K.Maiti Indian Institute of Technology Kharagpur	1.64
513	Dopaminergic and serotonergic functional regulation of aldehyde dehydrogenase in alcoholism at the molecular level	Dr. C.S.Paulose Cochin University of Science and Technology Kochi	3.38
514	Adrenergic, gabaergic and serotonergic gene expression, their interaction on insulin secretion and pancreatic β-cell proliferation	Dr. C.S.Paulose Cochin University of Science and Technology Kochi	3.12
515	Functional genomics of *E.histolytica* to identify genes controlling growth and proliferation	Dr. Anuradha Lohia Bose Institute (New Campus) Kolkata	4.24

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
516	Genomics, proteomics and bioinformatics of some target genes of *M.tuberculosis* for drug development	Dr. Joyoti Basu Bose Institute (Main Campus) Kolkata	3.59
517	Antigens and immune response in tuberculous infections	Dr. Parul Chakrabarti Bose Institute (Main Campus) Kolkata	3.10
518	Experimental determination of suitability of cholesteryl oleyl carbonate in fluidizing cholesteryl oleate in atherosclerotic plaque	Dr. Pradip Das Bose Institute (Main Campus) Kolkata	1.59
519	Host cell signalling in relation to *Helicobacter pylori* pathogenesis	Dr. Manikuntala Kundu Bose Institute (Main Campus) Kolkata	1.55
520	Molecular characterization of cross-reactive IgE-binding components in three fish species and comparison of fish hypersensitivity in paediatrics and adults with T cells response in pathogenesis of the disease	Dr. B.P.Chatterjee Indian Association for Cultivation of Science Kolkata	1.80
521	Molecular and immunological investigation on endotoxin-mediated innate immunity of *Achantina fulica* snails and its clinical application in the detection of endotoxin	Dr. Chhanda Biswas Indian Institute of Chemical Biology Kolkata	3.45
522	Potential plant as antileishmanial drug	Dr. Sharmila Chattopadhyay Indian Institute of Chemical Biology Kolkata	5.53
523	Molecular mechanisms of virulence loss associated with laboratory maintenance of the enteric pathogen *Vibrio cholerae*	Dr. Rukhsana Chowdhury Indian Institute of Chemical Biology Kolkata	2.05

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
524	Antibody - mediated drug delivery in visceral leishmaniasis	Dr. P.K.Das Indian Institute of Chemical Biology Kolkata	3.17
525	Evaluation of naturally occurring indole alkaloids from *Tabernaemontana coronaria* for the treatment of opioid tolerance and dependence	Dr. Sumantra Das Indian Institute of Chemical Biology Kolkata	2.78
526	Molecular and immunological investigation of o-acetylated sialoglycoconjugates in childhood acute lyphoblastic leukaemia (ALL) and their biological significance	Dr. Chitra Mandal Indian Institute of Chemical Biology Kolkata	3.00
527	Role of sialoglycoconjugates in host-parasite interactions in visceral leishmaniasis	Dr. Chitra Mandal Indian Institute of Chemical Biology Kolkata	4.47
528	Study of protein histidine kinase in *L.donovani*: a potential new chemotherapeutic target against kala azar	Dr. Sucheta Mukherji Indian Institute of Chemical Biology Kolkata	3.87
529	Molecular characterization of Wilson disease in Indian population	Dr. Kunal Ray Indian Institute of Chemical Biology Kolkata	2.71
530	Characterization of cytokine gene polymorphism in *H.pylori* infected Indian population	Dr. Susanta Roychoudhury Indian Institute of Chemical Biology Kolkata	3.20
531	Studies on the antileishmanial properties of novel naphthoquinonoid derivatives and their therapeutic applications	Dr. Banarasi Hazra Jadavpur University Kolkata	2.32
532	Production of a functional antimicrobial peptide in order to study the potential bacterial resistance it may encounter	Dr. S.K.Pal Jadavpur University Kolkata	2.53

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533	*Jai vigyan* mission project on community control of thalassaemia syndromes - awareness,screening,genetic counselling and prevention	Dr. M.K.Ghosh N.R.S.Medical College and Hospital Kolkata	16.54
534	Rotavirus genomics	Dr. T.N.Naik National Institute of Cholera and Enteric Diseases Kolkata	3.50
535	Studies on the mechanism of oxidative damage to anaemic red blood cells and protection by anti-oxidants	Dr. A.G.Datta The Society for Research on Haematology and Blood Kolkata	0.76
536	Neuropharmacological studies in rats having d - galactosamine - induced hepatitis	Dr. Dipankar Bhattacharyya University College of Medicine Kolkata	1.14
537	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. K.S.Asokan Nilgiris Adivasi Welfare Association Kotagiri	5.30
538	Flexible dose open trial on *Vijayasar* for known diabetes	Dr. R.V.Jayakumar Medical College and Hospital Kottayam	5.57
539	Centre for Advanced Research for Drug Development from Natural/Plant Products	Dr. C.M.Gupta Central Drug Research Institute Lucknow	16.51
540	Identification and functional studies on potential drug targets from *M.tuberculosis*, *P.falciparum* and *L.donovani*	Dr. C.M.Gupta Central Drug Research Institute Lucknow	14.92
541	*Plasmodium falciparum* ORF470: investigation of structure-function relationship	Dr. Saman Habib Central Drug Research Institute Lucknow	2.50
542	Search for potent antifungal peptides using knowledge based combinatorial libraries of peptides	Dr. Bijoy Kundu Central Drug Research Institute Lucknow	2.97

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
543	Development of anti-osteoporosis molecule from plant sources	Dr. Rakesh Maurya Central Drug Research Institute Lucknow	7.46
544	Development of new antimalarial agents based on leads from natural products	Dr. Chandan Singh Central Drug Research Institute Lucknow	4.22
545	Design and development of new class of antimycobacterial agents	Dr. R.P.Tripathi Central Drug Research Institute Lucknow	1.77
546	Cellular and functional recovery of Parkinsonian rats after intrastriatal transplantation of para neural cells : carotid body and olfactory ensheathing cell transplantation	Dr. A.K.Agrawal Industrial Toxicology Research Centre Lucknow	2.28
547	Delineation of molecular mechanisms of developmental neurotoxicity of selected environmental chemicals : role of early response genes	Dr. P.K.Seth Industrial Toxicology Research Centre Lucknow	1.60
548	Neurochemical, reproductive and immunotoxicological evaluation of the pyrethroid based mosquito repellents exposed during developmental period	Dr. P.K.Seth Industrial Toxicology Research Centre Lucknow	2.68
549	Microsatellite variation in north Indian subpopulations	Dr. Suraksha Devi Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	2.37
550	Molecular epidemiology of human and animal hepatitis E viruses (HEV) in India	Dr. Rakesh Aggarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	9.34
551	Physiological and behavioural aspects of human circadian rhythms under prolonged socio-temporal isolation	Dr. G.Marimuthu Madurai Kamaraj University Madurai	0.76

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
552	Evaluation of the effect of topotecan in combination with radiation in cultured human fibroblasts	Dr. G.C.Jagetia Kasturba Medical College and Hospital Manipal	1.12
553	Azathioprine *versus* corticosteroids in the treatment of *Parthenium hysterophorus* induced air-borne contact dermatitis	Dr. S.D.Shenoi Kasturba Medical College and Hospital Manipal	4.55
554	ICMR Unit on Standardisation and Quality Control and Formulation of Traditional Medicine	Dr. K.K.Bhutani National Institute of Pharmaceutical Education and Research Mohali	2.11
555	Handigodu disease - phase II	Dr. S.S.Agarwal Advanced Centre for Treatment, Research & Education in Cancer Mumbai	4.65
556	A basic study on phytoestrogens from the plants used in the traditional medicine	Dr. Rama A.Vaidya Bharatiya Vidya Bhavan's Swami Prakashananda Ayurveda Research Centre Mumbai	3.34
557	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India - Technical Co-ordinating Centre	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	11.73
558	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	6.35
559	*Jai vigyan* mission project on community control of thalassaemia syndromes - awareness,screening,genetic counselling and prevention	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	15.40
560	Catalytic antibodies against factor VIII : structure, function and implications for therapy	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	3.77

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
561	Genomic imprinting: a paternal contribution to embryogenesis	Dr. Nafisha Huseni Balasinor National Institute for Research in Reproductive Health Mumbai	3.06
562	Genomic studies related to micro-deletion of y-chromosome in severe oligospermic and non-obstructive azoospermic males	Dr. Jyotsna S.Gokral National Institute for Research in Reproductive Health Mumbai	3.15
563	Mutational analysis of human gonadotropin receptor genes and its implications in physiology and pathophysiology of pituitary-gonadal function	Dr. Smita Dilip Mahale National Institute for Research in Reproductive Health Mumbai	6.35
564	Genomic studies in polycystic ovaries and congenital adrenal hyperplasia	Dr. Anurupa Maitra National Institute for Research in Reproductive Health Mumbai	6.84
565	Model to predict *in vivo* milk/plasma ratios of therapeutic drugs	Dr. Anurupa Maitra National Institute for Research in Reproductive Health Mumbai	4.50
566	Genomics studies in premature ovarian failure (POF)	Dr. P.K.Meherji National Institute for Research in Reproductive Health Mumbai	1.00
567	Cryptic chromosomal rearrangements amongst couples with recurrent abortions - molecular analysis	Dr. Zareen M.Patel National Institute for Research in Reproductive Health Mumbai	5.00
568	Endometrial maps of receptive and non-receptive uterus in primates	Dr. Geetanjali Sachdeva National Institute for Research in Reproductive Health Mumbai	5.00
569	Survey on medicinal plants of Western Ghat	Dr. Usha Mukundan Ramnirajan Jhunjhunwala College Mumbai	1.84

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
570	Centre for Advanced Research on Clinical Pharmacology	Dr. Nilima A.Kshirsagar Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai	32.59
571	Towards the development of therapeutic agents using information from malaria immune persons from endemic areas of Orissa	Dr. Shobhona Sharma Tata Institute of Fundamental Research Mumbai	5.22
572	Centre for Advanced Research for Clinical Pharmacology in Traditional Medicine	Dr. Urmila Mukund Thatte Topiwala National Medical College and B.Y.L.Nair Hospital Mumbai	14.55
573	Development of enriched / cocktail antivenin to the toxic principles of *Vipera russelli* venom of different regions of India	Dr. T.Veerabasappa Gowda University of Mysore Mysore	0.90
574	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. D.L.Jain Government Medical College and Hospital Nagpur	8.88
575	Flexible dose open trial on *Vijayasar* for known diabetes	Dr. A.C.Ammini All India Institute of Medical Sciences New Delhi	5.57
576	Ophthalmic drug formulations using polymeric nanoparticles as carriers	Dr. N.R.Biswas All India Institute of Medical Sciences New Delhi	2.28
577	Evaluation of *Centella asiatica* and *Celastrus paniculatus* in experimental models of Alzheimer's disease in rats	Dr. Y.K.Gupta All India Institute of Medical Sciences New Delhi	2.06
578	Simultaneous electroencephalography (EEG) and MRI studies of sleep-wakefulness in rat brain	Dr. N.R.Jagannathan All India Institute of Medical Sciences New Delhi	0.55

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
579	Genetic analysis in male infertility	Dr. Kiran Kucheria All India Institute of Medical Sciences New Delhi	2.49
580	Immunogenetics of mycobacterial diseases : a 13IHWC international study	Dr. N.K.Mehra All India Institute of Medical Sciences New Delhi	3.52
581	Developing epitope based immunogen using different stages of *P.vivax* using inbuilt immuno adjuvants and delivery in microspheres	Dr. D.Nageswara Rao All India Institute of Medical Sciences New Delhi	1.44
582	Quinolone binding to DNA : spectroscopic and computer modelling studies	Dr. M.R.Rajeswari All India Institute of Medical Sciences New Delhi	0.44
583	Gene expression profile analysis of human esophageal cancer using cDNA microarrays	Dr. Ranju Ralhan All India Institute of Medical Sciences New Delhi	13.00
584	A study of the expression and targeting of inhibitor(s) of apoptosis - an *in vitro* and *in vivo* study	Dr. Neeta Singh All India Institute of Medical Sciences New Delhi	2.65
585	Evaluation of topical cyclosporin A in prevention of corneal graft rejection	Dr. R.B.Vajpayee All India Institute of Medical Sciences New Delhi	4.33
586	Cellular and molecular mechanism of alcohol related organ damage : biochemical, immunological and genetic studies	Dr. Suman Vasisht All India Institute of Medical Sciences New Delhi	3.91
587	Azathioprine *versus* coticosteroids for the treatment of *Parthenium* dermatitis - a double blind randomized controlled trial	Dr. K.K.Verma All India Institute of Medical Sciences New Delhi	1.56

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
588	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India - Co-ordinating Unit	Dr. Vasantha Muthuswamy Indian Council of Medical Research New Delhi	3.04
589	Molecular genetic basis of cancer : analysis of genetic alteration and transcriptional profile of genes during cervical carcinogenesis	Dr. B.C.Das Institute of Cytology and Preventive Oncology New Delhi	7.50
590	Establishment of a reference laboratory for undertaking hematological, biochemical, histopathological and immunopathological evaluation of pre-clinical toxicological studies	Dr. S.Jayaraman Institute of Pathology New Delhi	1.10
591	Construction and screening of *L.donovani* genomic DNA microarray for identification of differentially expressed genes in parasite isolates from kala-azar and PKDL patients	Dr. Poonam Salotra Institute of Pathology New Delhi	9.07
592	Molecular analysis of refractoriness of mosquito *Anopheles culicifacies* to malaria parasite	Dr. R.K.Bhatnagar International Centre for Genetic Engineering and Biotechnology New Delhi	3.02
593	Structural and functional studies on the aspartate decarboxylase enzyme (panD) of *M.tuberculosis*	Dr. Anand Ranganathan International Centre for Genetic Engineering and Biotechnology New Delhi	2.50
594	Antigen-dependent lymphocyte activation thresholds in adaptive immunity	Dr. K.V.S.Rao International Centre for Genetic Engineering and Biotechnology New Delhi	6.50
595	Herbal constituents as metabolic interceptors of chemical carcinogenesis	Dr. Sarwat Sultana Jamia Hamdard (Hamdard University) New Delhi	1.82

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
596	Comparative genomics approach to identify pathogenesis - related genes in *Entamoeba histolytica*	Dr. Sudha Bhattacharya Jawaharlal Nehru University New Delhi	15.00
597	To investigate neurochemical regulation of REM sleep and cellular changes after REM sleep deprivation	Dr. B.N.Mallick Jawaharlal Nehru University New Delhi	4.25
598	Genetic engineering of edible crop plants with oxalate decarboxylase for removal of oxalic acid,an antinutritional stress factor for better human nutrition	Dr. Subhra Chakraborty National Centre for Plant Genome Research New Delhi	3.25
599	Innate immune recognition of filarial parasites by phagocytes	Dr. Vineeta Bal National Institute of Immunology New Delhi	2.54
600	Domestication and cultivation of characterized population of *Picrorhiza kurrooa* royle Ex.benth.in Indian Western Himalaya	Dr. Virendra Singh Institute of Himalayan Bioresource Technology Palampur	3.70
601	Genetic polymorphism of drug metabolising enzymes in south Indian population	Dr. C.Adithan Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	0.37
602	Immunological and molecular studies on the mosquito humoral factors involved in the susceptibility/regulation of *Wuchereria bancrofti* infection and development in *Culex quinquefasciatus*	Dr. K.P.Paily Vector Control Research Centre Pondicherry	2.50
603	HIV-1 subtyping and detection of HIV-1 recombinants in India	Dr S.P.Tripathy National AIDS Research Institute Pune	6.57
604	New natural products as human immuno-deficiency virus reverse transcriptase (NHRT) inhibitors from the genus *Calophyllum*	Dr. Debashis Mitra National Centre for Cell Sciences Pune	1.47

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
605	Multi cellular spheroids - a 3D *in vitro* model for studies on cellular and molecular aspects of tumour progression and metastasis	Dr. Padma R.Shastry National Centre for Cell Sciences Pune	1.75
606	New natural products as human immuno-deficiency virus reverse transcriptase (NHRT) inhibitors from the genus *Calophyllum*	Dr. M.K.Gurjar National Chemical Laboratory Pune	1.34
607	Development of polytope DNA vaccine against Japanese encephalitis virus	Dr. M.M.Gore National Institute of Virology Pune	5.40
608	Antioxidant vitamin supplements as palliative treatment of bone disorders	Dr. A.N.Sontakke Padmashree Dr.D.Y.Patil Medical College for Women Pune	0.55
609	Indigenous plant lectins and their use as reagents in immunology and pathology	Dr. Rekha A.Nair Regional Cancer Centre Thiruvananthapuram	1.63
610	Survey of medicinal plants of Western Ghats of Kerala	Dr. A.Banerji Regional Research Laboratory Thiruvananthapuram	1.35
611	Inhibition of tumour specific angiogenesis of endothelial cells by curcuminoid derivatives	Dr. Girija Kuttan Amala Cancer Hospital and Research Centre Thrissur	1.12
612	*Jai vigyan* mission project on community control of thalassaemia syndromes - awareness,screening,genetic counselling and prevention	Dr. R.Z.Patel Medical College and S.S.G.Hospital Vadodara	6.98
613	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Y.M.Italia Valsad Raktadan Kendra Valsad	8.51
614	Experimental evaluation of some *ayurvedic rasayanas* on peptic ulcer and gastric muscosal offensive and defensive factors	Dr. R.K.Goel Institute of Medical Sciences Banaras Hindu University Varanasi	2.76

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
615	Studies on the status of gastric mucosal defensive factors *per se* and on physical and chemical factor-induced gastric ulceration in experimental diabetic rats *vis a vis* some Indian medicinal plants	Dr. R.K.Goel Institute of Medical Sciences Banaras Hindu University Varanasi	0.69
616	Pharmacokinetics of enantiomers of profens in women during different phases of menstrual cycle	Dr. V.Venkateswarlu University College of Pharmaceutical Sciences Warangal	0.80

Medicinal Plants Unit

617	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. M.Rajani BV Patel Pharmaceutical Education and Research Development Centre Ahmedabad	5.63
618	Preparation of phytochemical profiles of extracts of selected medicinal plants - an atlas of chromatographic profiles	Dr. M.Rajani BV Patel Pharmaceutical Education and Research Development Centre Ahmedabad	12.5
619	Medicinal plant monographs on diseases of public health importance - Filaria	Dr. R.K.Shenoy T.D.Medical College and Hospital Alappuzha	0.10
620	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. Karan Vasisht Panjab University Chandigarh	6.10
621	Development of DNA marker system for authentication of selected therapeutically important medicinal plants	Dr. S.P.S.Khanuja Central Institute of Medicinal and Aromatic Plants Lucknow	9.47
622	Heavy metals and persistent pesticide analysis for quality assurance of selected therapeutically important medicinal plants	Dr. Poonam Kakkar Industrial Toxicology Research Centre Lucknow	9.29

Sl. No.	Title of the Project	Investigator/ Institute	Grant Released during the year (Rs. in lakhs)
623	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. Shanta Mehrotra National Botanical Research Institute Lucknow	4.97
624	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. K.K.Bhutani National Institute of Pharmaceutical Education and Research Mohali	2.53
625	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. R.T.Sane Ram Narain Ruia College Mumbai	6.52
626	Monographs on Medicinal Plants of India	Dr. Ashok Gupta Indian Council of Medical Research New Delhi	21.67
627	Medicinal plant monographs on diseases of public health importance - Co-ordinating Unit	Dr. Ashok Gupta Indian Council of Medical Research New Delhi	1.82
628	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. V.George Tropical Botanic Garden and Research Institute Thiruvananthapuram	2.50
629	Medicinal plant monographs on diseases of public health importance - anti-inflammatory drugs	Dr. R.H.Singh Institute of Medical Sciences Banaras Hindu University Varanasi	2.50

Publication and Information

630	Scientometric studies – an ICMR sponsored study	Dr. K.Satyanarayana Indian Council of Medical Research New Delhi	2.04
631	ICMR-NIC Centre for Biomedical Information	Smt. Naina Pandita National Informatics Centre New Delhi	20.33

Appendix VII

LIST OF RESEARCH FELLOWSHIPS FUNDED DURING 2002-2003

Sl. No.	Title of the Project	Name of the Fellow/Institute
	Epidemiology and Communicable Diseases	
1	Role of apoptosis in the pathogenesis of rabies. Correlation of virological, pathological and immunological parameters - a study in human, canine and rodent nervous system	Km. M.S.Suja National Institute of Mental Health and Neurosciences Bangalore
2	Development of an immunodiagnostic assay using recombinant p1 protein of *Mycoplasma pneumoniae*	Smt. Irum Tabassum National Tuberculosis Institute Bangalore
3	HPLC methods for the determination of antifilarial drugs and their metabolites in different body fluids and their applications in pharmacokinetic studies	Dr. Reema Sarin Institute of Life Sciences Bhubaneswar
4	A study of polymorphic regions of the genes encoding protective antigens of *P.vivax* and *P.falciparum* strains prevalent in north - western regions of India	Sh. Umar Farooq Gaur Postgraduate Institute of Medical Education and Research Chandigarh
5	Antibody mediated selective targeting of isonicotinic acid hydrazide (INH) entrapped in PLG microparticles specifically to *Mycobacterium tuberculosis* infected macrophages	Smt. Indu Mehta Postgraduate Institute of Medical Education and Research Chandigarh

Sl. No.	Title of the Project	Name of the Fellow/Institute
6	Rapid detection and identification of dengue virus by molecular methods	Km. Jayashri Mahalingam King Institute of Preventive Medicine Chennai
7	Analysis of molecular basis of pyrazinamide resistance in mycobacteria	Smt. E.Ezhilkatharine Tuberculosis Research Centre Chennai
8	Rapid diagnosis of tuberculosis using purified antigens	Km. K.R.Uma Devi Tuberculosis Research Centre Chennai
9	Awareness of HIV/AIDS and risk behaviour pattern in patients of primary opioid dependence	Dr. Versha E.Millicans Institute of Human Behaviour and Allied Sciences Delhi
10	Restriction analysis and cloning of plasmid from a clinical isolate of *Mycobacterium avium* - intracellulare	Km. Divya Venugopal Vallabhbhai Patel Chest Institute Delhi
11	Identification and pathogenesis of influenza virus in acute exacerbation of asthma	Sh. Pankaj Kumar Vallabhbhai Patel Chest Institute Delhi
12	The molecular pathobiology of membrane iron in erythrocytes during anaemia in visceral leishmaniasis	Dr. Gargi Sen Indian Institute of Chemical Biology Kolkata
13	Molecular mechanism of bile induced changes in *Vibrio cholerae* and their physiological relevance	Sh. Nilanjan Sengupta Indian Institute of Chemical Biology Kolkata
14	Evaluation of newer laboratory techniques for early diagnosis of extra pulmonary tuberculosis	Smt. Vandana Tiwari Chhatrapati Shahuji Maharaj Medical University Lucknow
15	Molecular typing of *Salmonella* strains isolated from cases of enteric fever	Sh. Dinesh Singh Chandel All India Institute of Medical Sciences New Delhi
16	Prevalence and molecular typing of enterotoxigenic *Bacteroides fragilis* (ETBF) in diarroheal diseases	Dr. Nidhi Sharma All India Institute of Medical Sciences New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
17	Revalidation of syndromic approach for the management of genital ulcer disease in northern India	Dr. Manjula Singh All India Institute of Medical Sciences New Delhi
18	Characterization of devR - devS and devS homologue (Rv2027C gene product) of *Mycobacterium tuberculosis* with special reference to their phosphorylation	Sh. S.Chakravorty All India Institute of Medical Sciences New Delhi
19	Study of chronic hepatitis B and C in patients co-infected with human immuno deficiency virus	Dr. A.K.Garg Army Hospital (Research & Referral) New Delhi
20	A comparative study of the role of flexible fiberoptic bronchoscopy and sputum examination in diagnosis of pulmonary infections in iatrogenic immunocompromised patients	Dr. Nitin Sood Army Hospital (Research & Referral) New Delhi
21	Neurological manifestation of HIV infection	Dr. Shibashish Bhattacharyya Army Hospital (Research & Referral) New Delhi
22	Imaging in AIDS	Dr. M.S.Krishnakumar Army Hospital (Research & Referral) New Delhi
23	Adrenocortical function in human immunodeficiency virus (HIV) infection	Dr. Amitava Mitra Army Hospital (Research & Referral) New Delhi
24	Study of mutation in the HBV genome in fulminant hepatitis patients and its clinical significance	Sh. Abdul Malik Jamia Milia Islamia New Delhi
25	Cytoadherence and receptor - ligand interactions of *Plasmodium falciparum* field isolates with different receptor specificities	Sh. Anup Kumar Biswas Jawaharlal Nehru University New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
26	Epidemiology, molecular typing strain characterization and drug resistance prifiling of candidial infections in burn patients	Dr. Nivedita Gupta Jawaharlal Nehru University New Delhi
27	Genital infection with human papilloma virus : correlation with pregnancy and neonatal outcome	Dr. Garima Chauhan Maulana Azad Medical College and Associated Hospitals New Delhi
28	Role of hepatitis E virus (HEV) infection in acute viral hepatitis and fulminant hepatitis during pregnancy	Km. Nishat Jilani Maulana Azad Medical College and Associated Hospitals New Delhi
29	Seroefficacy of hepatitis B vaccine administered in the expanded programme of immunization at 0,6 wks and 9 months (alongwith DPT and measles)	Dr. Ajay Kumar Jain Maulana Azad Medical College and Associated Hospitals New Delhi
30	Pathogenicity of *Yersinia enterocolitica* of human and animal origin	Sh. Itender Singh University of Delhi South Campus New Delhi
31	Epidemiology and pathogenesis of fungal infections of nose and paranasal sinuses	Dr. Gurparamjit Singh Gill Government Medical College and Rajendra Hospital Patiala

Reproductive Health and Nutrition

32	Role of oxidative stress on reproductive activity in mice	Km. Parminder Kaur Panjab University Chandigarh
33	Evaluation of hepatoprotective role of zinc in conditions of nickel toxicity induced in protein deficient rats	Sh. P.S.Sidhu Panjab University Chandigarh
34	Impact of maternal hypothyroidism on androgen receptor gene expression in the ventral prostate during pre-pubertal and pubertal period in rats	Km. P.J.Arokya Mary Sashi Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai

Sl. No.	Title of the Project	Name of the Fellow/Institute
35	Nutritional and hypoglycemic effect of fruit pulp and leaves of *Annona squamosa* (custard apple)	Sh. R.K.Gupta Dr.B.R.Ambedkar Centre for Biomedical Research Delhi
36	First trimester uterine artery doppler velocimetry and pregnancy outcome	Dr. Arifa Anwar Elahi University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
37	Evaluation of doppler ultrasonography and correlation with perinatal outcome in intrauterine growth restriction	Dr. Tuleeka Sethi University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
38	Longitudinal assessment of resistance, pulsatility and amniotic fluid index by ultrasonography in post term pregnancy and their correlation with fetal outcome	Dr. Aneesha Minocha University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
39	Long-term (2 year) effects of a reduced-fat diet intervention in type 2 diabetes mellitus	Km. Neelima Gundupallee The Nizam's Institute of Medical Sciences Hyderabad
40	Characterization of cadherin and catenin expressed during implantation and establishment of its role in embryonic attachment	Km. Deeksha Saxena Devi Ahilya Vishwavidyalaya Indore
41	Antifertility investigations on the partially purified fractions of the seeds of *Carica papaya* with particular emphasis on mode of action in male albino rats	Dr. Neelam Pathak University of Rajasthan Jaipur
42	Hormonal control of male fertility using testosterone buciclate (TB) and 7-alpha methyl-19-nor testosterone (MENT)	Sh. S.Panneerdoss University of Rajasthan Jaipur
43	A study of health and nutritional status in relation to some biosocial factors among the *kora* and *mahali* tribes of West Bengal	Dr. Bechuram Mondal Indian Statistical Institute Kolkata

Sl. No.	Title of the Project	Name of the Fellow/Institute
44	Studies on further development of progesterone releasing intrauterine device (IUD) to enhance its duration of release	Dr. A.K.Ghosh Jadavpur University Kolkata
45	Studies on structural and functional properties of nonglycosylated and glycosylated haemoglobins in diabetes mellitus	Sh. Subhrojit Sen University College of Science and Technology Kolkata
46	Studies on the antioxidative effects of sesame lignans in diabetes induced rats	Dr. Krishna Chattopadhyay University College of Science and Technology Kolkata
47	Studies on the mechanism of action of CDRI-84/35 (1-formyl-4-dichloroacetyl piperazine), a potent antispermatogenic agent in rat	Km. Priti Ojha Central Drug Research Institute Lucknow
48	Role of enzyme adenosine deaminase (ADA) in early pregnancy threatened abortion in women	Dr. Savita Srivastava Chhatrapati Shahuji Maharaj Medical University Lucknow
49	Modulation of morphological and biochemical changes associated with male infertility by Indian herbal preparations	Dr. Sanjeev Shukla Chhatrapati Shahuji Maharaj Medical University Lucknow
50	A study on the effect of various herbal hypoglycemic agents on oxidative stress and antioxidant status in diabetics	Km. Anu Chandra Chhatrapati Shahuji Maharaj Medical University Lucknow
51	Cellular and molecular mechanism of endometrial receptivity in women	Dr. Annu Makker Chhatrapati Shahuji Maharaj Medical University Lucknow
52	Studies on molybdenum in tissues and interaction with other trace elements	Km. Ratna Pandey Lucknow University Lucknow

Sl. No.	Title of the Project	Name of the Fellow/Institute
53	Diabetes associated male reproductive dysfunction: role of oxidative stress and its nutritional amelioration	Km. Shrilatha Balakrishnan Central Food Technological Research Institute Mysore
54	A computer application to analyse trace element inter-relationships in serum of normal, Alzheimer's and Parkinson's disorder : a relevance to diagnostic approach	Sh. M.B.Sanjay Pande University of Mysore Mysore
55	Modulation of integrin and cytokine expression in mouse blastocysts by steroid hormones : mechanism of embryo implantation	Km. Sayantani Basak All India Institute of Medical Sciences New Delhi
56	Nutritional status of diabetics	Dr. Sneh Arora All India Institute of Medical Sciences New Delhi
57	Detection of fetomaternal haemorrhage following 1st and 2nd trimester abortions by Kleihauer Betke test and rise in maternal serum alpha feto protein	Dr. Kaberi Banerjee All India Institute of Medical Sciences New Delhi
58	Efficacy and safety of tranexamic acid for dysfunctional uterine bleeding and its comparison with cyclical progesterone therapy	Dr. Vidushi Kulshreshtha All India Institute of Medical Sciences New Delhi
59	Role of assisted conception in management of infertile couples	Dr. Shalini Singh All India Institute of Medical Sciences New Delhi
60	Centchroman for emergency contraception	Dr. Nalini All India Institute of Medical Sciences New Delhi
61	Role of conventional radiography, computerized tomography, magnetic resonance imaging in the evaluation of pituitary gland and its abnormalities	Dr. Nilu Mehrotra Army Hospital (Research & Referral) New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
62	Clinical predictors of sickness in young infants (age 0-2 months)	Dr. Anuj Jain Deen Dayal Upadhyay Hospital New Delhi
63	Study of placental histopathology and foeto placental ratio in intrauterine growth retardation	Dr. Meenal Sharma Deen Dayal Upadhyay Hospital New Delhi
64	Lactational performance of the nursing mothers in Delhi	Km. Kajali Paintal Institute of Home Economics New Delhi
65	Nutrition knowledge of medical practitioners in hospitals : an assessment, intervention and impact	Km. Charu Institute of Home Economics New Delhi
66	Analysis of mutation in SRY gene and chromosomal anomalies in infertile patients and its clinical importance	Sh. Mohammad Shahid Jamia Milia Islamia New Delhi
67	Endometrial evaluation in Indian postmenopausal women	Dr. Saira Zafar Maulana Azad Medical College and Associated Hospitals New Delhi
68	The effect of ethinyl estradiol in clomiphene induced cycles on endometrial thickness and pregnancy outcome	Dr. Shalini Pal Maulana Azad Medical College and Associated Hospitals New Delhi
69	A study of socio-demographic and medical variables as predictors of severe acute maternal morbidity and mortality in a tertiary care hospital	Dr. Babita Sharma Maulana Azad Medical College and Associated Hospitals New Delhi
70	Antitoxidative effects of melatonin to counter damage induced by lipid peroxidation during pregnancy and post delivery : studies in rats	Dr. Kanchan Upreti National Institute of Health and Family Welfare New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
71	Potential of antioxidants in fruits and vegetables in prevention of oxidation stress related disorders prevalent in Indians with special reference to cataract	Smt Kirtan Vilas Tarwadi Agharkar Research Institute Pune
72	Potential of antioxidants and micronutrients from foods and herbal materials for treatment of type II diabetes	Km. Sangeeta Shashikant Mengal Agharkar Research Institute Pune
73	Role of micronutrients (vitamins and W-3 fatty acids) in foetal adaptations to undernutrition and implications for adult health using rat model	Dr. Sadhana Ramachandra Joshi Agharkar Research Institute Pune
74	Glycemic index of the cereal based traditional recipes of Rajasthan	Km. Nikita Bordia College of Home Science Udaipur
75	Effect of short and long-term feeding of some common Indian spices on male reproductive performance	Sh. R.K.Mishra Banaras Hindu University Varanasi

Non-communicable Diseases

76	Effect of nephrotoxic agents on kidney	Km. Sabiha Fatima Aligarh Muslim University Aligarh
77	Clinical trial assessing efficacy of single agent (cisplatin) chemoradiation protocol *versus* conventional primary surgery and post - operative radiotherapy in advanced resectable pyriform fossa cancer	Dr. Abhey Sood Kidwai Memorial Institute of Oncology Bangalore
78	Evaluation of the radiosensitizing effect of withaferin A and hyperthermia on a radioresistant mouse melanoma - cellular and subcellular studies	Sh. Guruprasad K. Jawaharlal Nehru Cancer Hospital and Research Centre Bhopal

Sl. No.	Title of the Project	Name of the Fellow/Institute
79	Carcinoma - associated mucin antigens (tn, s-tn and t) : efficacy in detecting and monitoring patients with squamous cell carcinoma of the head and neck, oral, oesophagus, lung and cervix	Sh. K.Sankaranarayanan University of Madras Chennai
80	Biochemical studies on vitamin E administration in radiation treated oral cavity cancer patients	Smt. Subramaniyam Chitra University of Madras Chennai
81	Etiological and clinical profile of seizure disorder in children (01 month - 05 years)	Dr. Pradipta K.Acharya Base Hospital Delhi
82	Clinical study of operative conditions and hemodynamic response in cholecystectomy in general anesthesia *versus* combined spinal epidural anesthesia technique	Dr. Pallavi Kwatra Hindu Rao Hospital Delhi
83	Role of hypertonic saline in initial resuscitation of patients with acute pancreatitis	Dr. Himanshu Arora University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
84	Studies on oxidative DNA damage induced by organophosphate pesticides, chlorpyrifos and parathion in rats and search of a suitable biomarker	Sh. Radhey Shyam Verma Jiwaji University Gwalior
85	Biochemical and molecular genetics of homocysteine metabolism in coronary artery disease	Sh. Vinukonda Govindaiah Centre For DNA Fingerprinting and Diagnostics Hyderabad
86	Comparative study on tobacco consumption among medical and non - medical male college students in Calcutta	Dr. Manas Kumar Barua All India Institute of Hygiene and Public Health Kolkata
87	Malignancy associated molecular changes in human breast tissue	Sh. Indranil Basu Chittaranjan National Cancer Institute Kolkata

Sl. No.	Title of the Project	Name of the Fellow/Institute
88	Studies on ceramide in relevance to synovial cell and fluid of rheumatoid arthritis to find a basis for recovery	Dr. Aditi Banerjee Indian Institute of Chemical Biology Kolkata
89	Study of crystals in osteoarthritis knee and the evaluation of colchicine as a disease modifying drug for osteoarthritis	Dr. Ragini Srivastava Chhatrapati Shahuji Maharaj Medical University Lucknow
90	Mib-1 immunocytochemical expression in normal and neoplastic epithelium of human uterine cervix	Dr. Anju Mehrotra Chhatrapati Shahuji Maharaj Medical University Lucknow
91	Immunomodulatory role of *aswagandha* (*Withania somnifera*) in patients of lung cancer	Dr. Neelu Gupta Chhatrapati Shahuji Maharaj Medical University Lucknow
92	Studies on correlation of chlorinated pesticide and heavy metal lead and cadmium residues with human semen quality	Km. Niraj Pant Industrial Toxicology Research Centre Lucknow
93	Evaluation of the antineoplastic and radiosensitizing activities agents in cultured hela cells	Sh. Shrinath M.Baliga Kasturba Medical College and Hospital Manipal
94	Influence of curcumin on the wound healing properties of artificially wounded mouse exposed to different doses of gamma radiation	Sh. G.K.Rajanikanth Kasturba Medical College and Hospital Manipal
95	Comparison of white on white and blue on yellow automated perimetry in ocular hypertension and primary open angle glaucoma	Dr. Vikas Gulati All India Institute of Medical Sciences New Delhi
96	Study on optical fibre evanescent wave immunosensor	Sh. G.Biju Kumar All India Institute of Medical Sciences New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
97	Generation of domain specific antibodies against HIC - 1,a putative tumour suppressor protein, with a long term perspective to study its expression in various grades of human glial and other tumours and cell lines	Sh. Abdul Matin Mondal All India Institute of Medical Sciences New Delhi
98	Studies on the interaction of endosulfan and malathion with serum complement and macrophages	Km. Sadia Ayub All India Institute of Medical Sciences New Delhi
99	Studies on BRCA1 and BRCA 2 gene mutations in breast cancer patients	Dr. T.M.Valarmathi All India Institute of Medical Sciences New Delhi
100	Cytokine profiles of peripheral blood lymphocytes in patients with oral cancer	Km. Abhilasha Agarwal All India Institute of Medical Sciences New Delhi
101	Study of angiogenesis in renal cell carcinoma and its correlation with biological and clinical behaviour	Sh. M.K.Govindan All India Institute of Medical Sciences New Delhi
102	Correlation of polymorphism of apolipoprotein E gene with dyslipidemia and body composition in northern Indian subjects : a case-control study	Km. Manjari Dwivedi All India Institute of Medical Sciences New Delhi
103	To assess the response of chemotherapy and radiotherapy in high grade malignant glioma and estimation of micronuclei in these radio-chemo exposed human population	Dr. Dilip Kumar Parida All India Institute of Medical Sciences New Delhi
104	Concomitant *versus* sequential chemoradiation in locally advanced stage carcinoma of the oesophagus :a comparative study	Dr. Siddhartha Nanda All India Institute of Medical Sciences New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
105	C667t and a1298c mutations in methylene tetra hydrofolate raductase gene in patients with myocardial infarction in comparison with healthy controls	Dr. Mukta Sharma All India Institute of Medical Sciences New Delhi
106	Effect of antioxidant supplementation on pain, antioxidant profile and oxidative stress in chronic pancreatitis	Smt. Payal Bhardwaj All India Institute of Medical Sciences New Delhi
107	Study of prevalence of hypertension in paediatric age group 6-14 yrs. And role of known risk factors in childhood hypertension	Dr. K.S.Chandrashekhar Army Hospital (Research & Referral) New Delhi
108	A critical study of clinicopathological features with ultrasound of neck in malignant neck masses	Dr. Nirupam Adlakha Army Hospital (Research & Referral) New Delhi
109	A comparative study of solid silicone tire *versus* silicone sponge application in inferior retinal detachment surgery	Dr. A.K.Rastogi Army Hospital (Research & Referral) New Delhi
110	Histopathological examination study of host cornea under going keratoplasty and its correlation with the preoperative diagnosis of the corneal disease	Dr. Radha Vasan Army Hospital (Research & Referral) New Delhi
111	Retinal effects of chloroquine: evaluation by eletroretinogram and computerized automated perimetry	Dr. Pankaj Kataria Army Hospital (Research & Referral) New Delhi
112	A study on foveal avascular zone in patients with diabetic retinopathy	Dr. Keerti Mundey Army Hospital (Research & Referral) New Delhi
113	Study of inflammatory response to normothermic cardiopulmonary bypass	Dr. S.N.Naresh Army Hospital (Research & Referral) New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
114	Study of low - dose bupivacaine with fentanyl in spinal anaesthesia for urologic surgeries	Dr. Pramod Patra Army Hospital (Research & Referral) New Delhi
115	An evaluation of hearing in new born children of high risk group as compared to normal new born children to find out the incidence of congenital and early acquired sensori neural hearing loss	Dr. Shilpi Arora Army Hospital (Research & Referral) New Delhi
116	Study of transient evoked otoacoustic emissions as a screening technique of hearing in neonates	Dr. B.S.Pandey Army Hospital (Research & Referral) New Delhi
117	A study of efficacy of ND : YAG laser (1064 nm) in thermal mode (free - running) for laser trabeculoplasty in controlling intra - ocular pressure in primary open angle glaucoma in three different situations	Dr. Pradip Kumar Army Hospital (Research & Referral) New Delhi
118	Comparison of combination of epidural buprenorphine and neostigmine with combination of epidural buprenorphine and ketamine for postoperative analgesia	Dr. Sanjay Choubey Army Hospital (Research & Referral) New Delhi
119	The comparative effects of propofol *versus* seroflurane in induction, maintenance and recovery in day care surgery	Dr. B.M.Nayyar Army Hospital (Research & Referral) New Delhi
120	A comparative study of bupivacaine and bupivacaine with fentanyl for post - op analgesia in oncosurgical patients through continuous thoracic epidural technique	Dr. Subrata Chakravarty Army Hospital (Research & Referral) New Delhi
121	A comparative study of different doses of propofol with fentanyl on tracheal intubating conditions, without muscle relaxants in children	Dr. Sushil Garg Army Hospital (Research & Referral) New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
122	Molecular studies on the BRCA2 gene and the p53 gene mutation in breast cancer	Sh. Neeraj D.Jain Jamia Milia Islamia New Delhi
123	Comparison of early and late pulmonary changes in inhalation burn injuries - a prospective study	Dr. Swaroop Singh Gambhir Lok Nayak Jaiprakash Narayan Hospital New Delhi
124	Role of caspases, bax, k ras and apoptosis in malignant and premalignant lesions of oral cavity	Sh. Navneet Saini Maulana Azad Medical College and Associated Hospitals New Delhi
125	Telomerase activity as tumor marker in cervical cancers	Km. Alpana Sharma Maulana Azad Medical College and Associated Hospitals New Delhi
126	Effect of topical anti - glaucomatous medication on human conjunctiva - an evaluation by conjunctival impression cytology	Dr. Simaljit Kaur Sethi Safdarjang Hospital New Delhi
127	Comparison of ossicular destruction by atticoantral disease in adults and children	Dr. Nimesh Kumar Gupta Safdarjang Hospital New Delhi
128	Enhancement of memory in the aged : an intervention study	Dr. K.Lalitha Sri Venkateswara University Tirupati

Basic Medical Sciences

129	Hepatoprotective effect of andrographolide on liver cancer	Smt. Neha Pravinbhai Trivedi Gujarat University Ahmedabad
130	Investigation into the role of dopamine and 5-hydroxytryptamine in glycemic control and central effects of hypoglycemia-induced convulsions	Sh. D.N.Umrani L.M.College of Pharmacy Ahmedabad
131	Regulatory mechanisms of insulin action by taurine in high fructose-fed rats	Km. A.T.Anitha Nandhini Annamalai University Annamalai Nagar

Sl. No.	Title of the Project	Name of the Fellow/Institute
132	Antihyperglycaemic effect of *Phaseolus vulgaris* l.(kidney bean) and *Coccinia indica* w.and a. (little gourd) in experimental diabetes: effects compared with troglitazone, a new oral antidiabetic agent	Sh. S.Venkateswaran Annamalai University Annamalai Nagar
133	The antihyperglycaemic activity of *Casearia ovata* (lam.) willd.root extracts in streptozotocin-induced diabetic rats	Sh. A.Prakasam Annamalai University Annamalai Nagar
134	Identification and role of intestinal lactase gene in hypolactasia in adult rats	Km. Jaspreet Kaur Panjab University Chandigarh
135	Role of neurofilament phosphorylation chronic aluminium neurotoxicity in rat	Km. Amarpreet Kaur Postgraduate Institute of Medical Education and Research Chandigarh
136	Investigation of the role of beta-amyloid peptide on nitric oxide release in Alzheimer's disease	Dr. K.Samuel Jesudoss Central Leather Research Institute Chennai
137	Mutational analysis of alpha-l iduronidase gene (IDUA) in South Indian population	Sh. K.Mahalingam Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai
138	Therapeutic efficacy of *Tinospora cordifolia* stem extract along with paclitaxel on 7,12-dimethyl benz(a) anthracene induced breast cancer in albino rats	Km. M.Sarumathi Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai
139	A study on the expression of tamm-horsfall glycoprotein under oxalate stress	Km. Sumitra Kamalanathan Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai
140	Construction of a novel shuttle vector system for enhanced expression of *Mycobacterium tuberculosis* antigens	Km. C.Mani Tuberculosis Research Centre Chennai

Sl. No.	Title of the Project	Name of the Fellow/Institute
141	Detailed studies on mechanism of action of the hypoglycemic compounds obtained from the bark of *Ficus bengalensis*	Km. Shweta Gupta University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
142	Adhesion mediated cell survival signals in normal and cancerous cells	Dr. Rajeswari Jinka Centre For Cellular and Molecular Biology Hyderabad
143	Search for antidiabetic agents from arid zone plants	Dr. Rekha Arora University of Rajasthan Jaipur
144	Anti-thyroid action of phenylhydrazine : studies on the hypothalamopituitary - thyroid axis in juvenile and adult male rats	Dr. Mitali Pramanik Bose Institute (New Campus) Kolkata
145	Studies on growth and melanization of epidermal cells by selected ceramides and cerebresides to compare the action of ceramides present in a human placental extract meant for vitiligo therapy	Km. Shampa Mallick Indian Institute of Chemical Biology Kolkata
146	Influence of black tea polyphenols on secretory and motor activity of gastrointestinal system	Dr. Saujen Basu Indian Institute of Chemical Biology Kolkata
147	Involvement of calcium in 1-methyl-4-phenyl-1,2.3.6-tetrahydropyridine - induced neurotoxicity	Dr. Supriti Samanta Ray Indian Institute of Chemical Biology Kolkata
148	Molecular basis of inhibition of experimental hepatocarcinogenesis by *Trianthema portulacastrum* linn	Km. Mitali Basu Jadavpur University Kolkata
149	Screening, characterization and production of novel antibiotics from marine actinomycetes isolated from the deltaic Sundarbans	Sh. Malay Saha Jadavpur University Kolkata

Sl. No.	Title of the Project	Name of the Fellow/Institute
150	Pharmacological and structural evaluation of toxins from the skin extract of snake head fish *Channa striatus*	Sh. Surajit Karmakar University College of Science and Technology Kolkata
151	*In vitro* model for evaluation of medical devices for biological hazards	Dr. A.B.Pant Industrial Toxicology Research Centre Lucknow
152	Study of longitudinal growth and bone radiography in relation to oral iron chelator deferiprone (kelfer)	Dr. Anita Saxena Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
153	Apoptosis during immune response	Sh. C.P.Winston Kasturba Medical College and Hospital Manipal
154	Investigation of purinergic neurotransmission in smooth muscle : effect of ATPase inhibition on synaptic potentials in the mammalian vas deferens	Km. Parakashtha Ghildyal Indian Institute of Technology Mumbai
155	Molecular genetic studies in glaucoma	Km. R.Vijaya All India Institute of Medical Sciences New Delhi
156	Cardioprotective effect of *Hibiscus rosa sinensis* : A biochemical study	Sh. K.Gauthaman All India Institute of Medical Sciences New Delhi
157	Role of the medical preoptic neurons in the regulation of sleep and brain temperature under different environmental temperatures	Dr. A.P.K.Mahapatra All India Institute of Medical Sciences New Delhi
158	Immunohistochemical studies of effect of prenatal sound overstimulation on synaptogenesis in chick brainstem auditory nuclei	Smt. Phalguni Anand Alladi All India Institute of Medical Sciences New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
159	Outcome of HBsAg positive renal transplant recipients	Dr. Durga Shankar Army Hospital (Research & Referral) New Delhi
160	Interplay of the coronary risk agents in pediatric group of young patients affected with coronary artery disease	Smt. Vibha Pagare G.B.Pant Hospital New Delhi
161	Production of bioactive gonadotropin by insect cell using baculovirus expression vector system	Km. V.Pooja Jamia Hamdard (Hamdard University) New Delhi
162	Formulation and evaluation of novel drug delivery systems for anti-acne products using tea tree oil	Sh. S.S.Biju Jamia Hamdard (Hamdard University) New Delhi
163	Effect of low level 2.45 and 16.5 ghz radiation on developing rats brain	Sh. R.Paulraj Jawaharlal Nehru University New Delhi
164	Effects of arsenic on cell growth and development of *Dictyostelium discoideum*	Dr. Sampati Mukhopadhyay Jawaharlal Nehru University New Delhi
165	Elucidation of the role of neuropeptide, neurokinin B and its analogues on molecular and biochemical correlates in aging brain functions	Sh. M.Anil Kumar Jawaharlal Nehru University New Delhi
166	Evaluation of the modulatory effects of some common dietary constituents on radiation induced damage	Dr. Ashu Bhan Tiku Jawaharlal Nehru University New Delhi
167	Assessment of the probiotic potential of pediocin producing natural isolates of *Pediococcus* sps	Smt. Baljinder Kaur Punjabi University Patiala
168	Molecular diagnosis of chronic myeloid leukemia and its relevance to clinical management	Dr. Anshuman Chaturvedi Armed Forces Medical College and Command Hospital Pune

Sl. No.	Title of the Project	Name of the Fellow/Institute
169	Development of floating drug delivery systems in the effective management of *Helicobacter pylori*	Km. R.B.Umamaheswari Dr.Hari Singh Gour Vishwavidyalaya Sagar
170	Osmotically regulated multi-drug oral delivery systems development and characterization	Sh. D.Prabakaran Dr.Hari Singh Gour Vishwavidyalaya Sagar
171	Estrogen receptor activation factor (E-RAF) of the goat uterus and proteins with which E-RAF interacts prior to its nuclear entry	Km. Anitha P.Govind Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram
172	Genetic polymorphism of glutathione S-transferase allele in myelodysplastic syndrome	Km. Roshini Thomas Regional Cancer Centre Thiruvananthapuram
173	Leucocyte and platelet deposition in atherosclerotic plaques: role of sugar specific adhesion to endothelial lectin galectin 1 and prospect of its inhibition by human erythrocyte membrane oligosaccharides	Km. S.R.Sangeetha Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram
174	Effect of coadministration of cyanoglycosides isolated from *Cassava* and alcohol on experimental animals	Km. R.G.Boby University of Kerala Thiruvananthapuram
175	Studies on the metabolism of extra cellular matrix components by hepatic non-parenchymal cells	Km. P.Pranitha University of Kerala Thiruvananthapuram
176	Biochemical investigations on the flavonoids from *Emblica officinalis* and *mangifera* indica	Km. L.Anila University of Kerala Thiruvananthapuram
177	Biodemography and longevity among tribal population of Kerala	Dr. T.Parvathi Kumara Reddy Sri Venkateswara University Tirupati

Sl. No.	Title of the Project	Name of the Fellow/Institute
178	Effect of algal toxins (*Ptychodiscus brevis*) on the spinal monosynaptic transmission *in vitro*	Sh. J.N.Singh Institute of Medical Sciences Banaras Hindu University Varanasi
179	Effect of hypoxia on monosynaptic and polysynaptic reflexes evoked in the isolated neonatal spinal cord	Km. Archana Jha Institute of Medical Sciences Banaras Hindu University Varanasi
180	Evaluation of biochemical changes of bile juice under the influence of a compound indigenous drug in biliary stone diseases	Dr. Pankaj Srivastava Institute of Medical Sciences Banaras Hindu University Varanasi
181	Studies on the cardioprotective actions of bradykinin and its signal cascade mechanism in rats with experimental myocardial infarction	Sh. V.Krishna Kumar Andhra University Visakhapatnam
	Expenditure on fellowships during the year Rs.	157.00 lakhs

Appendix VIII

LIST OF PUBLICATIONS OF ICMR INSTITUTES

Aggarwal, A. and Pandey, A. Gender disparity in food intake among children under age 18 years in Delhi. In: Biostatistical Aspects of Health and Epidemiology. (Eds. C M Pandey, U Singh and P Mishra) Prakashan Kendra, Lucknow (2002) 301.

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