

ANNUAL REPORT 2005-2006

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INDIAN COUNCIL OF MEDICAL RESEARCH NEW DELHI

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DIRECTOR-GENERAL'S MESSAGE

The Indian Council of Medical Research is the premier research organization of the country in the field of biomedical/health research. It performs its function through its various Institutes, Centres and Advanced Centres spread throughout the country. Some of the Council's Institutes were renamed during the year under report *viz*. National JALMA Institute of Leprosy and Other Mycobacterial Diseases (earlier named as Central JALMA Institute of Leprosy), Agra, National Institute of Medical Statistics (earlier known as Institute for Research in Medical Statistics) and National Institute of Malaria Research (earlier known as Malaria Research Centre), both located in Delhi.



During the year under report, the Council moved forward in its research efforts not only in national priority areas but also in basic research in the field of modern biology. Under the *Avahan* India AIDS Initiative funded by Bill and Melinda Gates Foundation, the Council's National AIDS Research Institute, Pune is collecting biological and behavioural trend data in Indian population. A Memorandum of Understanding (MOU) has been signed between ICMR and Merck for initiation of clinical trial of HPV vaccine in India.

There has been significant growth and development in national and international scientific collaborations between ICMR and other scientific agencies in India and abroad. A MOU for South-South collaboration was signed between MRC (South Africa), FIOCRUZ (Brazil) and ICMR to work together in areas of common interest. A total of 73 exchange visits of scientists to and from India were arranged during the year under report.

During the year the Council carried out surveillance for human influenza. Chandipura virus encephalitis and outbreak of Chikungunya was also investigated. A multi-centre site preparation activity to initiate vaccine probe study to estimate preventable burden of *Hemophilus influenzae* B meningitis and pneumonia was launched during the year,

The scientists of the Council published over 450 research papers during 2005. During the year 2005-2006, a total of 779 research projects and 372 fellowships were funded by the Council. The impact factor of Indian Journal of Medical Research increased to 0.869 in 2005 as compared to 0.600 in the year 2004.

A total of 8 patent applications were filed during the reported period. A patent has been granted to a process of mosquito larvicidal formulation from *Bacillus thuringiensis* developed by Council's Vector Control Research Centre, Pondicherry.

The Council's Bioinformatics Centre has completed networking of all ICMR Institutes, Centres and Headquarters which has greatly improved communication among scientists with enhanced work performance and efficiency of the staff. The website of the ICMR is updated regularly incorporating features beneficial to the scientific community and civil society. This has resulted in increased interaction between ICMR and other agencies, scientists and job applicants.

I am glad to present the highlights of research activities of ICMR for the financial year ρ 2005-2006.

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Nirmal Kumar Ganguly Director-General

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AN OVERVIEW

The Indian Council of Medical Research (ICMR) continued to forge ahead in the field of medical and health research. Three of the ICMR institutes have been renamed. The Central JALMA Institute of Leprosy, Agra has been renamed as National JALMA Institute of Leprosy and Other Mycobacterial Diseases (CJILOMD), the Malaria Research Centre, Delhi has been renamed as National Malaria Research Institute (NMRI) and the Institute for Research in Medical Statistics also located in Delhi has been renamed as National Institute of Medical Statistics (NIMS). During the period under report, construction of new building of the National Malaria Research Institute was started at Dwarka, Delhi. A devastating fire destroyed a portion of CJILOMD, Agra resulting in loss of equipments, consumables and civil works worth Rs. 5 crores.

Under the Avahan India AIDS Initiative funded by Bill and Melinda Gates Foundation, the Council's National AIDS Research Institute, Pune is collecting behavioural and biological trend data in populations before and after interventions in six high prevalence states of India *i.e.* Andhra Pradesh, Karnataka, Maharashtra, Manipur, Nagaland and Tamil Nadu.

Studies were conducted by Tuberculosis Research Centre (TRC) on *Mycobacterium tuberculosis* for defining phylogentic link existing in the TB genome, for comparing global pattern of disease transmission and for elucidating evolutionary biology of tubercle bacillus.

A multi-centre site preparation activity to initiate an vaccine probe study to estimate preventable burden of *Haemophilus influenzae* B meningitis and pneumonia was launched.

The first year of surveillance for human influenza was completed. Almost half of the isolates belonged to H_3N_2 and about a quarter each to H1N1

and type B. Avian influenza, due to H5N1 appeared in Navapura and Jalgaon, Maharashtra. The National Institute of Virology (NIV), Pune being the WHO's National Influenza Centre participated in screening of the individuals who had history of exposure. About 500 samples were tested using real time PCR system, nucleic acid sequence based amplification (NASBA) platform. None were found to be positive.

Chandipura virus encephalitis which had appeared in Andhra Pradesh in 2003 and Gujarat in 2004, re-appeared in Andhra Pradesh in 2005. The mystery of the Siliguri outbreak, which occurred in West Bengal in 2001 was finally solved. Investigations carried out in collaboration with CDC, Altanta, revealed it to be due to Nipah virus. The Indian strain was related to the Bangladesh and Malaysian strain.

There was a major outbreak of Chikungunya in the Indian Ocean in the early 2006. In India cases were reported from Rajasthan, Gujarat, MP, Orissa, Maharashtra, A.P., Karnataka, Tamil Nadu and Kerala. The NIV provided the diagnostic kit (MAC ELISA) to all the States in India. The genotyping of the viral isolates from several states showed that they belong to the African genotype in contrast to the earlier outbreaks which were due to Asian genotype. The African strain had caused severe morbidity.

During the year under report, in the project for home based management of young infants, training was imparted and comparison made in services delivered by trained village health workers called *Shishu Rakshaks* and *Anganwadi* workers.

During the year under report, on application from Vector Control Research Centre (VCRC), Pondicherry patent has been granted to a process for preparation of mosquito larvicidal formulation from *Bacillus thuringiensis var. israelensis*. Besides, eight patent applications were filed, five in India and rest abroad. The Council's Regional Occupational Health Centre at Kolkata redesigned and developed a cycle rickshaw based on ergonomic principles for which a patent application had been made.

A Memorandum of Understanding (MOU) has been signed between ICMR and Merck for initiation of clinical trial of HPV vaccine in different regions of the Country. The Institute of Cytology and Preventive Oncology (ICPO) located in NOIDA has been designated as National Coordinating Centre for Indian HPV Vaccine Initiative. The impact factor of Indian Journal of Medical Research increased to 0.869 in 2005 compared to 0.600 in the year 2004.

Around 450 research papers were published by scientists of ICMR during the year 2005. Overall 779 research projects and 372 fellowships were supported during 2005-2006.

Seventy exchange visits of scientists to and from India were arranged under international collaborative programme of the council. An MOU for South-South collaboration has been signed between the MRC (South Africa), FIOCRUZ (Brazil) and ICMR to work together on health issues of medical interest.



ICMR INSTITUTIONAL NETWORK

COMMUNICABLE DISEASES

Infectious diseases continue to remain a public health challenge in India. The handling of infectious diseases is further complicated by the emergence of new pathogens. As the country learns to handle the existing infectious diseases, a new face of infectious diseases is unveiled making the task of disease control in India unmanageable. The ICMR, however, continues to fight this untiring battle in addition to handling the existing killers like tuberculosis, malaria and other tropical diseases. The Council is also instrumental in investigation and control of JE, dengue and chikangunya outbreaks in different parts of the country. This has been made possible through basic, applied and operational research being funded by ICMR in its own institutes (intramural projects) and in medical colleges, institutions and universities through the extramural programme. The ICMR countinued to fund health research initiatives in the priority areas, identified as per the national programme, through its intramural and extramural research programmes. As many as 16 of the ICMR institutes and Regional Medical Research Centres (RMRCs) are engaged in research on one or more aspects of communicable diseases such as HIV/ AIDS, leprosy, diarrhoeal diseases, malaria, filariasis, leishmaniasis, leptospirosis, hepatitis and poliomyelitis. Besides striving to develop better diagnostic and research tools and vaccine candidates, ICMR is also geared up with the surveillance activities for pathogens like hemophilus influenza, influenza viruses and rotavirus.

BACTERIAL DISEASES TUBERCULOSIS

Tuberculosis continues to remain an important killer disease in the country. ICMR's Tuberculosis Research Centre (TRC) located at Chennai is engaged in research on various aspects of the disease such as evaluating newer treatment regimens, molecular and drug resistance studies, epidemiological and clinical studies. Besides, studies are also being undertaken at Council's National JALMA Institute for Leprosy and Other Mycobacterial Diseases, Agra.

Clinical Trials

Randomized Clinical Trial to Test the Efficacy of Revised National Tuberculosis Control Programme (RNTCP) Regimens for the Treatment of Tuberculosis in HIV Infected Patients

HIV infection is now the biggest risk factor for tuberculosis. There is concern that the RNTCP recommended 6-month regimen might be inadequate for the treatment of tuberculosis in those who are also HIV infected. A randomized clinical trial is in progress in collaboration with the Government Thoracic Hospital, Tambaram, Government Rajaji Medical College, Madurai and the Government General Hospital, Chennai, to, a) assess the efficacy of RNTCP treatment regimens among HIV-infected persons with pulmonary or lymph node tuberculosis and to study any additional benefit of an extended continuation phase, b) study the relationship between stage of HIV disease and response to anti-TB treatment and c) study the nature of recurrent tuberculosis by using restriction fragment length polymorphism (RFLP). Patients with pulmonary or lymph node tuberculosis are randomly allocated to either a 6-month Category 1 regimen (rifampicin and isoniazid for six months with pyrazinamide and ethambutol for the first two months, all drugs given thrice weekly), or to a 9-month regimen (rifampicin and isoniazid for nine months with pyrazinamide and ethambutol for the first two months, all drugs given thrice weekly). The study commenced in January 2001 and patient recruitment has been completed. Patients (267) with bacteriologically confirmed tuberculosis were randomized to the 6-month and 9-month regimens respectively. Sixty three patients who were culture negative with X-ray abnormalities and clinical suspicion of pulmonary TB and 42 patients who received Cat II regimen (as they had history of previous treatment for TB) were analyzed separately.

The interim findings show that favourable outcome of TB treatment among HIV positive patients is similar in the 6 and 9-month regimens. The results for 267 patients, who were initially culture positive, show similar and high cure rates in both the 6 month (95.5%) and 9 month (95.7%) regimens, among people who completed full course of therapy (Fig.1). However, the death rate was quite high, both during treatment and more so, during follow up, indicating the advanced



Fig. 1. Smear culture negative patients at end of treatment

nature of the disease in most patients. Deaths due to TB were more in the earlier period while death due to AIDS related causes was more common in later period. Drug resistance rates were low in newly diagnosed tuberculosis cases (MDR TB 3%). Relapse rates were similar in both arms. The follow up is ongoing.

Epidemiological Studies

Epidemiological Impact Study: Community Survey of TB Disease and Infection

Directly Observed Treatment, Short Course (DOTS), a global strategy for control of tuberculosis is being implemented in India in a phased manner since 1997. DOTS was implemented in Tiruvallur district of Tamil Nadu in May 1999. TRC is monitoring the programme in one TB unit of the district. To assess the epidemiological impact of DOTS strategy, TRC is carrying out a series of sample surveys to estimate the prevalence of disease and infection in this district.

Diagnosis of TB among adult population included in the disease survey was based on screening methods and subsequent sputum examinations. All children included in the tuberculin survey were tuberculin tested with PPD and the reaction sizes were read after 72-96 hr. Two disease surveys each with two and a half year duration were completed and the second resurvey is in the completion stage. Coverage in the current survey was above 90% for all investigations. The completed surveys have shown a decline in TB prevalence.

Based on the existing data generated from Tiruvallur and elsewhere, the burden of tuberculosis in India for the year 2000 was estimated to be 8.5 million of which 3.8 million were bacillary cases, 3.9 million abacillary cases and 0.8 million extrapulmonary cases. In the third tuberculin survey completed, the ARTI was estimated to be 1.2%. The ARTI estimates in the two tuberculin surveys conducted earlier were 1.6% and 1.4% respectively (Fig.2). There was a significant decline in the trend of TB infection. The annual decline estimated from the first to the third survey was 6%. Also, various operational studies on



Fig. 2. Prevalence of infection and ARTI in three tuberculin surveys conducted after DOTS implementation in a rural area, South India.

the key aspects of the control programme conducted during the period have documented valuable information. Thus the results revealed that DOTS implementation was associated with a substantial reduction in the prevalence of TB among adults and risk of TB infection among children.

Basic Studies

Construction of Luciferase Reporter Phages Expressing *FFlux* **Gene Driven by Dormancy Inducible Conditional Promoters**

Early diagnosis of tuberculosis among the HIV infected and general population is essential in reducing



Fig. 3. Kinetics of different LRP constructs in *M. smegmatis* mc2155

the morbidity and mortality due to TB. Over the past decade, luciferase reporter phages (LRPs) have been developed that show great promise

for diagnostic microbiology. Conventional luciferase reporter phages from lytic phages such as D29 and TM4 used in LRP assay, though highly specific, lack sensitivity. Hence it was hypothesized that a temperate phage infecting Mycobacterium tuberculosis if used in the construction of reporter phage system would bring about a sustained light output. Moreover, most of the TB cases among the HIV infected population result from the reactivation of latent bacilli and so LRP with a dormancy inducible promoter would identify viable, but not cultivable (VBNC) population of M. tuberculosis. LRP was successfully constructed using Che12 with isocitrate-lyase promoter expressing Fflux gene (phAETRC21) and it gave a fourdigit RLU reading with M. smegmatis mc²155 with integration time of 10 seconds. (Fig.3)

Molecular Epidemiology of *M.* tuberculosis

At TRC, Chennai efforts are being made to decipher the portable genotype patterns of *M.tuberculosis* from high prevalence regions such as India and to compare it with COMMUNICABLE DISEASES

global patterns of disease transmission. The resulting genetic information from high prevalence areas such as ours would prove useful for defining phylogenetic links that exist with TB genomes and for constructing models of genome evolution. This will also help elucidate the evolutionary history of ancient tubercle bacilli. Spoligotyping is a PCR-based method dependent on hybridisation patterns of in vitroamplified DNA with multiple spacer nucleotides. It interrogates the direct repeat locus of *M. tuberculosis* and has the potential to identify the global distribution of the major clades of the *M. tuberculosis* complex. At TRC, spoligopattern of all the isolates were decipherred



Fig. 4. Spoligopattern of *M. tuberculosis* isolates

and compared to Spol DB₃ available at www.pasteurguadeloupe.fr/tb/spol3 to determine whether each pattern has been previously reported. Overall 42 clusters with spoligotypes matching the Spol DB₃ were found. The results revealed that the major clade present in Tiruvallur, South India belongs to group IV of Baker's classification (1) that is of East-African Indian lineage and is close to the spoligo pattern of Manila isolates with the deletion at RD239 (Fig.4).

Overexpression of MSMEG3682, a Protein Kinase from *M. smegmatis*

TRC reported for the first time a functional kinase MSMEG3682 from *M. smegmatis* and revealed its role in cell division. The enzyme was overexpressed in *M. smegmatis* mc²155 under the control of an inducible acetamidase promoter and its effect on growth and viability was studied. Changes in cell morphology were analyzed by scanning electron microscopy (SEM). Three and 1.1 fold growth retardation was observed with the induced and uninduced merodiploid strain compared to the wild type strain. A corresponding difference in viability was found when plated on acetamide containing-LB plates. There was extensive

clumping and cell lysis when merodiploid strain was grown beyond 30hr. SEM revealed irregular cell structure marked with bulb-like protrusions along the length of the cells or at the end of the induced merodiploid strain. Control strains failed to show differences in growth, viability and cell morphology (Fig. 5).

Role of HLA-DR2 on Immune Functions in Pulmonary Tuberculosis

In this ongoing study the aim was to understand the role of HLA-DR2 gene in innate immune functions such as macrophage phagocytosis with live *M*. *tuberculosis* and perforin positive cells in pulmonary tuberculosis. The study suggested that HLA-DR1, especially HLA-DR1/DR2 combination is associated with higher macrophage phagocytosis. HLA-DR3 and –DR10 are associated with lower phagocytosis. DR2/DR3 combination is associated with lower phagocytosis in normal subjects. Moreover, HLA-DR2 positive pulmonary tuberculosis patients showed decreased perforin positive cells suggesting that HLA-DR2 influences the innate immunity to *M. tuberculosis* infection.

mc²4808 uninduced



mc²4809 uninduced



mc²4808 induced



mc²4809 induced



Scale bar represents 5µm

Fig.5. Detection of M.leprae genomic DNA isolated from soil

Development of Immunodiagnostic Test for TB

For the early and specific tuberculosis, diagnosis of development of IFN-y ELISA and immuno-PCR based on M. tuberculosis complex specific antigen(s) was undertaken at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh. A reporter DNA construct was prepared from pUC19 by biotinylating it using Klenow fragment. Overall 77.5% AFB positive and 65% of AFB negative TB patients were diagnosed on the basis of detection of multiple specific antigens simultaneously in sputum sample. However, 85-90% control samples did not show the presence of any of the M. tuberculosis - complex specific antigens indicating high

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specificity. Thus, immuno-PCR with its high specificity and sensitivity may emerge as a powerful diagnostic test for tuberculosis.

Identification of Target Genes of the DevR – DevS Two-component System of *M. tuberculosis*

Identification of target genes of the DevR – DevS two-component system of *M. tuberculosis* and development of rapid assays to measure its activity was undertaken at the All India Institute of Medical Sciences (AIIMS), New Delhi. Studies from several laboratories have described its crucial role in pathogenesis and adaptation to environmental signals such as oxygen limitation and nitric oxide. Suitable promoter-specific reporter assays were developed including those based on the DevR promoter for studying hypoxia-responsive *M. tuberculosis* promoters in *M. smegmatis*. Availability of this surrogate host will accelerate the understanding of the unique physiological status of *M. tuberculosis* within granulomas which is rather poorly understood at present.

Protein Tyrosine Phosphatases from M. tuberculosis

A study on protein tyrosine phosphatases from *M. tuberculosis* and their role in pathogenesis was recently completed at the University of Delhi, South Campus, New Delhi. The *mptpA* and *mptpB* mutant strains of *M. tuberculosis* were constructed by homologous recombination. An M. tuberculosis strain was also constructed in which the genes for both mptpA and mptpB were disrupted. This double mutant strain (mptpAB) was evaluated for its pathogenesis in guinea pigs and compared with the wild type strain as well as with the mptpA and mptpB mutants. The studies demonstrated essential requirement of these tyrosine phosphatases for establishment of disease by M. tuberculosis. The studies also showed that both MptpA and MptpB play a crucial role in the virulence of M. tuberculosis. The marked reduction in the survival of M. tuberculosis in guinea pigs, upon disruption of MptpA or MptpB suggests that both of these proteins can act as potential targets for the development of new anti-tubercular drugs.

Role of virS Gene in Pathogenesis of M. tuberculosis

Studies on the role of *virS* gene in the pathogenesis of *M. tuberculosis* were carried out at

the University of Delhi, South Campus, New Delhi. The results showed that disruption of *virS* leads to increased permeability of *M. tuberculosis* cell envelope to various hydrophobic drugs, further confirming alterations in the cell wall ultrastructure of *M. tuberculosis*. The involvement of *virS* in the persistence of *M. tuberculosis* together with its role in maintaining appropriate structure of cell envelope to resist antitubercular drugs indicates that precise targeting of *virS* or the *mymA* operon gene products may increase the effectiveness of combination chemotherapy and impede the mechanisms involved in the persistence of *M. tuberculosis*.

Rifampicin Resistance Mutations in Clinical Isolates of *M. tuberculosis*

Analysis of rifampicin resistance mutations in the clinical isolates of *M. tuberculosis* by sequencing and dot-blot hybridization was completed at the V.P. Chest Institute, Delhi. One hundred and seventy nine pulmonary tuberculosis patients from V. P. Chest Institute, Delhi and RBTB Hospital, Kingsway Camp were selected for the study. Susceptibility testing was done by BACTEC 460 TB system and the proportion method. Sequencing of nine out of 18 rifampicinresistant isolates showed mutations outside the region complementary to probe D (522-527 base pairs).

LEPROSY

The Council's Central JALMA Institute for Leprosy at Agra has been renamed during the year as National JALMA Institute for Leprosy and Other Mycobacterial Diseases (NJILOMD). The institute has improved its infrastructure over the years and has a modern hospital, well equipped laboratories and a vibrant field programme. While the Institute has added new generation flowcytometry and equipment for proteomics during the year, it has embarked upon establishing a model rural health unit at Ghatampur with satellite centres at Banda and adjoining areas. Current mandate of the Institute is to undertake research on leprosy, selected areas of tuberculosis, HIV and other infections like filariasis which could be associated with endemicity of leprosy and other mycobacterial diseases.

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MAJOR ICMR RESEARCH PROJECTS IN COMMUNICABLE DISEASES

Clinical/Clinicopathological Studies

Differential Gene Expression of *M.leprae* using Genomic Approaches

The studies using DNA chip technology have progressed significantly. Using indigenously developed DNA chip covering selected genes of *Mycobacterium leprae* several genes expressed in human host were identified during last year. This expression has been validated by using real time PCR. Some of the targets appear to be useful for detection of viable organisms. Patent application has been filed for these targets.

Application of Direct *in situ* PCR Procedure on Tissue Specimens

Study is being carried out to enhance the sensitivity of histological diagnosis of leprosy specially in specimens with non-specific features. The techniques are now been extended to tuberculosis as well. During last year, more application data about the application of biotinyl-tyramide system was generated. The results indicate that this assay is more sensitive as compared to standard *in-situ* hybridization procedure developed earlier.

Immunogenetics and Immunological Studies

Cytokine Gene Polymorphism

Studies have been carried out in collaboration with AIIMS, New Delhi to gain better understanding of immunopathology of leprosy for better management of leprosy cases. First phase of the study has been completed and data is being analysed.

Toll 2 Receptor Gene Polymorphism

Study is ongoing to gain better understanding of immune mechanisms in leprosy and tuberculosis. During the year, a real time PCR assay was standardized to detect polymorphism in the target genes.

Molecular Mimicry between Human Tissue Components and Mycobacterial Components, Autoantibodies in Childhood Leprosy Cases

During the year antibodies to keratin were studied in leprosy serum and higher levels in reactional cases (BT in reaction) were detected. The structural basis of various findings as well as its application value is being assessed.

Delivery of M. leprae Antigens and T Cell Anergy

A project undertaken at AIIMS, New Delhi with the objective to study the effect of delivery of *M.leprae* antigens in particulate form in liposomes and on the levels of second messengers and various transcription factors leading to T cell anergy of its reversal has been completed. The study confirmed that decreased apoptosis *via* caspase activity and decreased expression of TNFR markers using particulate antigen formulations containing immunomodulators is the result of proliferation of lymphocytes especially in BL/LL patients as the anergized state of the cells is being reverted.

Sero-assays using Newer Antigens

During the year following important findings were obtained. *M.leprae* 45kDa, *M.leprae* rCFP-10, *M.leprae* rESAT-6 antigens appear to be potential serological reagents. Incubating the reactants at 37°C followed by incubation at low temperature (4°C) significantly enhanced the sensitivity of anti-PGL-1 antibodies and ML flow test appears to be useful for smear positive leprosy patients.

Anti-cytokine Antibodies in Leprosy

Using recombinant IFN- γ , attempt was made to detect anti-IFN- γ antibodies employing inhibition ELISA. Assay samples from 69 leprosy patients (13LL, 53 BT, 2BB and 1 indeterminate) were screened for anti IFN- γ antibodies. Of the 69 leprosy patients only 2 were found positive. None of the samples from healthy as well as non leprosy patients (suffering from other skin diseases) was found to be positive. Further studies with refined approaches are in progress.

Search for New Antigens of *M.tuberculosis* Capable of Inducing Strong T Helper Type 1 (Th1) Response in Healthy Contacts of Tuberculosis Patients

Study is progressing to identify immunologically relevant antigens for better diagnosis of tuberculosis. During the year under report, 5 candidate antigens ESAT-6, Ag85 complex (a,b,c) and CFP-10 have been investigated individually and also using cocktail of these antigens. The findings indicate that antigen 85c is most immunoreactive among these antigens in paediatric samples while the cocktail may have its own advantages in terms of specificity.

Immunogenic Activities of Lipid and Glycolipid Antigens derived from *M.leprae*

Studies are being carried out to understand the effect of different antigens/ fractions of M.leprae on immune response in humans. Intracellular calcium levels were evaluated in the peripheral blood mononuclear cells (PBMCs) of leprosy patients. Majority of lepromatous leprosy patients (4 out of 5) had lower basal calcium levels in response to thapsigargine (Tg) treatment as compared to those in controls. Further, it was found that cells treated with Tg along with *M.leprae* soluble antigens (MLSA) were having decrease in intracellular calcium levels in a dose responsive manner. It was also noted that increase in intracellular calcium levels by ionomycin on Tg+MLSA treated cells was less as compared to those in healthy individuals (Fig.1). Significance of these findings is being analysed.



Fig. 1. Intracellular calcium levels in PBMCs from healthy individuals and LL leprosy patients showing effects of thapsigargine, MLSA and ionomycin.

Viability Studies/ Drug Resistance in Leprosy

Surveillance of Drug Resistance in Leprosy

In this multicentric study, biopsies from leprosy cases (non-responders, treatment failure, relapses) from different parts of country (Mumbai, Kolkata, Karigiri *etc.*) are being collected and transported to JALMA or Scheiffelin Leprosy Training and Research Centre (SLTRC), Karigiri for detection of drug resistant *M.leprae* in treated cases of leprosy using mouse foot pad as well as molecular assays. No rifampicin resistance in the samples analysed during last one year has been observed. The study is continuing to include more cases as per the defined criteria.

Molecular Epidemiology

Genomic Diversity in Leprosy Bacillus

Studies are progressing to generate data on different prevalent genotypes of leprosy bacillus. Results of study will be useful for monitoring the transmission and better management of leprosy cases at public health level. New genotypes among strains of *M.leprae* have been identified by using TTC repeats. During the year under report, interesting data about the evolution of strains of leprosy bacillus was obtained (Table 1, Fig. 2) which showed that the majority of

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	Ser	Glu	Asp	Ile	Asp	Ile	Asp	Ile	Asp	Ile	Glu	Ala
Guna -	GAG	GAC	ATC	GAC	ATC	GAC	ATC	-	-	GAA	GCC-	AGC
Hardoi -	GAG	GAC	ATC	GAC	ATC	GAC	ATC	GAC	ATC	GAA	GCC-	AGC
Kanpur -	GAG	GAC	ATC	GAC	ATC	GAC	ATC	GAC	ATC	GAA	GCC-	AGC
Asdhana -	GAG	GAC	ATC	GAC	ATC	GAC	ATC	GAC	ATC	GAA	GCC-	AGC
Saraiyan-	GAG	GAC	ATC	GAC	ATC	GAC	ATC	-	-	GAA	GCC-	AGC

Fig. 2. Sequence alignment of DNA fragment corresponding from 544-579 (4 repeats) or 544-573 (3 repeats) of the rpo T gene in *M. leprae* from patients of Uttar Pradesh.

Table 1. Variation in the tandem repeats of *rpo*T gene

		Three repeats	Four repeats
Ghatampur	(64)	62	2
OPD	(60)	50	10
Total	(124)	112	12

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strains of leprosy bacillus in North (mainly UP) belonged to ancient Indian type (3 copies of rpoT) as compared to Japanese/Korean type (having 4 copies of rpoT). Further, a new technique for determining the genotypic differences has been developed and appears to be promising. Studies on the identification of novel loci for development of new DNA chip are progressing.

Molecular Epidemiological Studies with *M. tuberculosis*

Studies were carried out to generate information about genotypes of *M.tuberculosis* to trace the transmission of tuberculosis (specially drug resistance) in selected geographical locations. During the year under report significant data about variation in spoligotypes as well as MIRU-VNTR types of isolates of *M.tuberculosis* from Ghatampur, Kanpur as well as North-East as a part of a collaborative



Fig. 3. Spoligotypes of *M.tuberculosis* isolates from North-East

project with RMRC, Dibrugarh (Fig.3, Table 2) has been generated.

Further, combined use of spoligotyping and MIRU-VNTR shows that MIRU-VNTR typing can be used quite successfully to sub-type important spoligotypes such as, CAS, Delhi and Beijing families. (Tables 3, 4). These findings have important public health importance.

Table 2. Different spoligotypes in isolates of *M.tuberculosis* from North-East

S No	RMRC No.	JALMA No.	Octal Code	Shared type/Class
1	AMC-64	NE1	00000000003771	ST1/Beijing
2	AMC-63	NE2	00000000003771	ST1/Beijing
3	AMC-71	NE3	777767757413371	Orphan
4	AMC-69	NE4	703777740003771	ST26/CAS
5	AMC-68	NE5	777776777760771	ST118
6	AMC-106	NE6	703767740003771	ST141
7	AMC-104	NE7	777776777760601	ST137
8	AMC-82	NE8	00000000003771	ST1/Beijing
9	AMC-81	NE9	NA	
10	AMC-103	NE10	777021360000331	Orphan
11	AMC-86	NE11	703700040003771	Orphan
12	AMC-75	NE12	703777600000771	Orphan
13	AMC-76	NE13	00000000003771	ST1
14	AMC-1684	NE15	703777747770371	ST27
15	AMC-60	NE16	703777740003771	ST26/CAS
16	AMC-79	NE18	777767777413700	Orphan
17	AMC-85	NE19	703777340003771	Orphan
18	AMC-77	NE20	777677777413700	Orphan
19	AMC-1512	NE21	703777740003771	ST26/CAS

Table 3. Different spoligotypes in isolates of <i>M.tuberculosis</i> from					
	SharedType /Family/Percentage	Orphan			
Kanpur Urban	ST26/ CAS1_Delhi (19 %), ST25/ CAS1_Delhi (7%), ST11/ EAI3_IND (13%), ST1/Beijing (7%), ST138/ EAI5 (5%), ST53/T1 (4%), ST126/EAI5 (4%), ST119/X1(2.4%), ST141/CAS1_Delhi (2.4%), ST34/S (2.4%)	12%			

ST 26/CAS1_Delhi (18.5%), ST25/

ST598/CAS (2%)

ST628/T1(3%)

EAI5(8.3%) ST1/Beijing (8.3%)

CAS1_Delhi (7%), ST53/T1 (6.5%),

ST1/Beijing (3%), ST298 EAI3_IND /(3%),

ST26/ CAS1_Delhi (39%), ST11/ EAI3_IND

(6%) **ST1/Beijing (~5%)**, **ST53/T1(3%)**, ST1401/ CAS1_Delhi (3%), ST1345/ CAS

(3%), ST138/ EAI5 3%, ST1093/CAS (3%),

ST26/ CAS1_Delhi (29.2 %), ST138/

ST11/ EAI3_IND (2%), ST1120/CAS (2%), ST1324/T1 (2%), ST1590/CAS1_Delhi (2%),

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Kanpur rural

Ghatampur

Agra urban

from North-East

18%

10%

8.3%

Table 4. Comparative analysis of Spongolyping and MIRO - VIVIR (VDin	Table 4. Comparative	analysis of Spoligotypin	g and MIRU - VNTR typing
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S No.	Isolate	Village	Octal Code	Shared Type	MIRU VNTR
1	KMW3	Sukhapur	0000000000377	1	234825
2	KMW19	Sukhapur	0000000000377 1	1	235525
3	KMW78	Barauli	70377774000377 1	26	276736
4	KMW80	Barauli	70377774000377 1	26	256726
5	DKR92	Ghuranpur	70377774000317 1	25	263725
6	DKR225	Ghuranpur	70377774000317 1	25	244325

has been felt. For this purpose, new assay formats have been designed and are being evaluated.

Molecular Methods for Drug Resistance in Leprosy and TB

Studies are continuing on the evaluation of a 7 probe assay system for detection of rifampicin resistance in M.tuberculosis. So far the results are promising with correlation of more than 85% with microbiological results. Efforts are being made to transfer the technology to industry. Multicentric studies on strains of *M.leprae* from different parts of the country are progressing so as to find mutations which could be used to develop rapid molecular methods for surveillance of drug resistance in future.

Comparative and Functional Genomic Approaches for **Identification** and **Characterization of Genes Responsible for Multidrug Resistance**

Studies employing DNA chip technology are ongoing to identify novel targets which may ultimately lead to product development (probe and assays systems) such as new generation diagnostics for detection of drug resistance and

Molecular Mechanisms of Drug **Resistance**

Quantitative Assessment of Mutations by Real Time PCR of Genes Encoding for Resistance

Using a known and well standardized assay procedure, application studies on clinical isolates as well as specimens have been carried out during the year. While the technique has shown promise to map the mutations within a defined gene region, the need to standardize other assays spanning wider gene region

also for improving the therapy of TB and other mycobacterial diseases. Studies are continuing to identify more targets associated with resistance against other drugs viz. quinolones, pyrazinamide, ethambutol and aminoglycosides.

Biochemical Studies

Studies on Lipid Biosynthesis

Studies are being carried out to identify novel targets in the pathways of lipid biosynthesis. Using M.bovis BCG as a model organism, all the four anti-mycobacterial drugs (Rifampicin, Dapsone, Clofazimine and Ofloxacin) were found to inhibit the incorporation of radiolabeled palmitic acid into PGL of *M.bovis* BCG. Mechanism is being investigated.

Drug Permeability and Pharmacokinetics

During the year studies were pursued to evaluate the kinetics of accumulation of ofloxacin in *M.kansasii*. It was observed that accumulation of ofloxacin in *M.kansasii* was less as compared to *M.smegmatis*. Further studies showed the non-involvement of efflux in the accumulation of ciprofloxacin in *M.smegmatis*.

Proteomic Approaches to Understand Mechanism of Intracellular Parasitization and Drug Resistance

Study is using proteomic approaches to identify novel targets/ molecules which may lead to product development for better management of leprosy/TB cases. Using 2D gels, several proteins associated with drug resistant organisms have been identified and are being investigated further.

Therapeutic Trials

ROM Trials in Field in Agra District

Studies are ongoing in leprosy patients of Agra. The follow up data at 18 months revealed that 81.4% cases were cured and 8 relapses (2.7%); [3.36% in ROM (Rifampicin, Ofloxacin, Minocycline) arm vs 1.99% in C-ROM (Clarithromycin plus ROM) arm] have been noted. The data generated from this study will be correlated with results of similar studies being conducted by others. The findings will be relevant for better management of leprosy cases.

In another study where 6 monthly ROM is being compared with 6 monthly WHO MDT, it was found that 80.8% had completed treatment. Four relapses were recorded, 2 in each arm. Similarly, in MB cases being followed up, 63% had completed 12 month treatment *vs.* 86.4% ROM treatment. In this component, 3 relapses have been recorded in MDT arm only. The follow up work is in progress.

Immunotherapy in Borderline Leprosy

Studies are being carried out in borderline patients of leprosy at the hospital and are based on an earlier successful trial of combined chemotherapy and immunotherapy regimen (developed at CJILOMD in highly bacillated leprosy patients). Intake of cases in the study has been completed. Follow up of the cases shows that there is a good clinical improvement in these cases. Histopathologically, significant decrease in granuloma fraction has been observed in BT cases following Mw vaccine + MDT as compared to control group.

U-MDT for All Leprosy Cases

Studies have been progressing in the field area of Ghatampur and are based on successful trial of this regimen (developed at this Institute) in the PB patients. This regimen has now been proposed by WHO as an uniform MDT for PB as well as MB leprosy cases. The significance will be availability of an universally applicable effective regimen for better management of leprosy cases. All the 324 cases included in the study have been followed up for 6 months and 275 for one year after release from treatment.

Comparative Study of High Dose vs Low Dose Oral Corticosteroid Therapy in Reversal Reactions in Leprosy

Studies were undertaken to gain knowledge for better usage of steroids in the treatment of leprosy cases. The observations over almost 30 months post steroid treatment (in small number of patients) indicate that steroid doses of 60mg per day prednisolone equivalent tapered over a period of 5 months showed better response.

Reconstructive Surgery

Different Surgical Intervention Studies

Various intervention studies are going on to prevent and correct deformities. These include decompression of peripheral nerve trunks, closure of heel ulcers by skin stretching, the effect of different surgical interventions on nerves and tendons for improving functional capability and JALMA flap for restoration of volume of first web space in muscle atrophy associated with ulnar palsy in leprosy. During the year, closure of heel ulcers by skin stretching has been completed. It was observed that 50% of the cases did not have any recurrence even after 36 months, 10% had major recurrence whereas the remaining had minor recurrence only. This technique eliminates donor defects, associated morbidity and enables closures with a good scar in heel ulcers which do not have calcanean involvement.

Epidemiological Studies

Epidemiological Studies on Leprosy in Agra District

The studies are continuing in field area of Agra district and are aimed at gaining knowledge about the epidemiology of leprosy in the district. Results of rapid survey conducted in Agra district showed an overall prevalence of 6.83/10,000 during 2004-2006 as compared to 16.4/10,000 during 2001-2003. The incidence rate of leprosy in Agra, based on 42113 persons resurveyed, was observed to be 6.2/10,000 person years (4.2 among non-contacts, 41 among PB contacts and 131 among MB contacts).

Studies on Different Epidemiological Aspects of Leprosy in Ghatampur

First phase of the study ongoing in Ghatampur (Kanpur) has been completed during the year. Second phase of the study has been started to follow trends for developing an hypothesis / model about factors responsible for high endemicity seen in this area. Resurvey has been completed in about 20% of population and trends indicate reduced total burden of disease. The role of ecological factors including the presence of *M.leprae* in the environment and other mycobacteria is also being studied. The presence of viable *M.leprae* in the environment as seen by DNA targeting PCR (Fig.4) has been observed in a section



Fig.4. Detection of M.leprae genomic DNA isolated from soil

of soil samples from this area. Besides epidemiological parameters genetic and immunological markers are being studied. Follow up is continuing to assess the effect of different interventions (conventional and newer regimens) started during the first phase.

Prevalence of Drug Resistance in Tuberculosis in Agra and Kanpur (Ghatampur) Areas

Studies have been completed in Category I tuberculosis patients in the field area of Agra and Kanpur districts. An overall prevalence of primary multidrug resistance (MDR) (4.4% in Agra and 3% in Kanpur district) has been observed in these surveys. No MDR has been observed in rural areas of Kanpur in two repeat surveys. This baseline data will be used to follow the trends in this population.

Surveillance of Leprosy in Community by School Children

Data collection has been completed at Indian Leprosy Association, New Delhi where school children were used for surveillance of leprosy alongwith monitoring the MDT compliance through information, education and communication (IEC) activities and bringing in newly detected patients under care of health providers for management of disease. A large number of undiagnosed (at par with local prevalence rate) cases so far not brought under MDT were detected and brought under regular MDT for full specified duration. The study highlighted the fact that school children remain unreported in regional prevalence due to their being absent from homes during PHC activities and surveys of population in the area. Children and adolescents had predominance of PB leprosy. The quantitative assessment of IEC activities in schools brought to surface much needed scope for creating

Agarose electrophoresis of PCR performed using primers targeted for *M. leprae* specific region in RLEP region in DNA samples extracted from soil. Lane 1-11: soil samples Lane 12: Negative Control, Lane 13-15: Positive Controls, M : 100 bp DNA ladder awareness with regard to leprosy amongst teachers, students and neighbouring community of the area. Properly motivated school children could act as sentinels in the community for suspecting leprosy and monitoring them on MDT. The pre-and post-IEC evaluation brought to notice a

distinct improvement with regard to knowledge of signs, symptoms, treatment and attitude toward leprosy post-health education. Except for IEC dissemination, the role of school students in detecting leprosy cases in their families and neighbouring community was poor.

DIARRHOEAL DISEASES

Diarrhoeal diseases are important causes of morbidity and mortality in India. On an average a child suffers three episodes of diarrhoea per year. As the majority of childhood diarrhoeas are caused by *V. cholerae*, *Shigella*, rotavirus and enterotoxigenic *Escherichia coli* which cause high morbidity and mortality, development of vaccines against these organisms is essential. The Council's National Institute of Cholera and Enteric Diseases (NICED), Kolkata and RMRCs are engaged in studies on diarrhoeal diseases.

Community Based Study

Acute Lower Respiratory Tract Infection and Diarrhoea in Rural Children

Acute lower respiratory tract infection (ALRI) and diarrhoea are two leading causes of mortality and morbidity in children below five yr. in the developing countries. There is lack of community-based information on the disease burden caused by different pathogens causing ALRI, and the epidemiological information regarding their magnitude in the community is also scanty. Breast feeding, particularly exclusive breastfeeding in infants up to 6 months of age and complementary feeding along with proper weaning are known to protect infants from diarrhoea as well as ALRI. However, there is very little information regarding extent of exclusive breast feeding in children <6months/ complementary feeding as well as weaning feeds given to children. Therefore, study was undertaken in rural children (below two years) suffering from ALRI and diarrhoea in relation to feeding practices with particular reference to breast feeding.

Study has been initiated in 11 villages of Kalikapur Gram Panchayat 1 and 2 area of Sonarpur block of South 24 Pargana district in a population of 29,000. A baseline demography of the families has been done. The West Bengal Government health staff and NICED field workers were given one day orientation training on ARI and breastfeeding, who in turn trained voluntary health workers. Newborn infants are being enlisted for weekly follow up. Anthropometric measurements of infants are continuing at the subcentres. So far 1297 infants have been identified for weekly follow up.

Clinical Studies

Impact of Lactobacillus in Children with Acute Watery Diarrhoea

A hospital based, randomized, double blind clinical trial to evaluate the role of lactobacillus (lactic acid bacteria) therapy in the outcome variables (stool output, duration of diarrhoea, consumption of fluid therapy) of acute watery diarrhoea in children was initiated during the year at the Dr. B.C. Roy Memorial Hospital for Children, Kolkata in double blind fashion. So far, 140 male children of all nutritional groups (except severe malnutrition) aged between 6-24 months suffering from acute watery diarrhoea (passage of more than 3 liquid stools within last 24 hr period) of < 3 days duration with some dehydration have been included in this study. Study is still in preliminary phase and data are being collected.

Vibrio cholerae

Molecular Epidemiology of Cholera in India

Resurgence of cholera has been reported in many countries with several sporadic infections and outbreaks. In India, several cholera outbreaks occurred recently and it appears that the trend in the prevalence of V. cholerae is very dynamic with constant change in the phenotypic and genotypic traits. V. cholerae O1 isolates (402) from cholera patients from 17 different areas were analyzed during 2004 and 2005. Among these, 43.2 and 56.7% strains were identified as Ogawa and Inaba serotypes respectively. Except for Delhi and Manipal, the serotype Inaba was exclusively identified in 5 cholera outbreaks. However, in Delhi and Manipal cholera outbreaks, Inaba was the predominant serotype with 66.0 and 67.0% respectively. During March-June 2004, Ogawa and Inaba serotypes were detected in Ahmedabad, Goa, Chennai, Madurai, Ludhiana, and Chandigarh. In Kolkata, there was a total replacement of Ogawa serotype by the Inaba from June 2005 onwards.

All the strains harbored *ctxA* and the El Tor allele of *tcpA* and *rstR* in the PCR assays. In the phage typing analysis, almost all the Ogawa as well as Inaba isolates included in this study belonged to type T4 and type 27 with new set of phages. Polymyxin B susceptibility test confirmed that the isolates are El Tor biotype. In the antimicrobial susceptibility pattern, isolates of Inaba were more resistant to chloramphenicol, streptomycin compared to Ogawa. Majority (91%) of the Inaba isolates showed reduced susceptibility for ciprofloxacin, whereas 32% of Ogawa isolates remained resistant to this drug.

Studies were done to detect the mutations in the *wbeT* gene of recent Inaba isolates and to find the uniformity in such changes with previous isolates. Inaba isolates from Tripura, Madurai, Ludhiana, Ahemedabad and Kolkata had identical sequence homology in the sequenced region of *wbeT*. Silent substitution of C for A at nucleotide position 553 prevailed in all the tested recent Inaba isolates. In addition, substitution of C for T at nucleotide position 538 lead to change in the amino acid from serine to proline The other mutations reported among previous Inaba isolates from India were not found in the recent Inaba isolates.

Ribotyping of 28 representative isolates (20 Inaba and 8 Ogawa) showed that most of the Inaba isolates of 2004 belong to the new ribotype RIV and isolates of Ogawa during the same period and old Inaba were identified as ribotype RIII. Prevalence of ribotype RIII was also detected among some of the 2004 Inaba isolates (VC187, GO13610, and DO1358). Twenty seven V. cholerae isolates (20 Inaba and 7 Ogawa) were tested by PFGE typing which consisted of 11 pulsotypes (A through K). Majority of the Inaba isolates belongs to 'H' type (12 isolates) or 'Ha' type (4 isolates), and 2 Ogawa isolates were identified as pulsotype 'Ha'. The new pulsotypes viz., L (Ogawa isolates DO5465, LU626), M (UP1/13.9-Inaba), N (K5919-Ogawa), O (CHN 5/04-Ogawa) differed with H type with 4 bands. In the other new pulsotype P (DO1272-Inaba), DNA band at about 242 Kb was absent and there was an additional band at about 290 Kb region compared to H type. In pulsotype Q (VC187-Inaba), an additional band at about 200 Kb was detected, which was absent in the pulsotype H.

The findings are congruent with earlier studies when the new serogorup *V. cholerae* O139 emerged in India. The phenomenon of seroconversion is a great challenge to the existing surveillance work, which needs careful monitoring. The study is in progress.

Studies on the Structure-function Relationship of *V. cholerae* Hemolysin

V. cholerae hemolysin (HlyA), an extracellular water-soluble membrane-damaging protein with a native molecular weight of 65,000, belongs to a unique class of dimorphic proteins that can exist in two stable states, a water-soluble monomer and an oligomeric amphipathic protein capable of spontaneous insertion into the membrane lipid bilayer. These proteins, commonly referred to as pore-forming toxins (PFTs) for their ability to lyse target eukaryotic cells by punching holes in the plasma membrane, interact with specific target membrane components and selfassemble by noncovalent interactions involving oligomerization domains into exceptionally stable and rigid β -barrel oligomers that eventually insert into the membrane by using amphiphilic β -hairpins as anchors to the nonpolar core of the lipid bilayer.

Experiments in the past year indicated that interaction of the pre-pore oligomer of the toxin with cholesterol-sphingolipid rich lipid microdomains played a decisive role in inducing its transition to an insertion-competent configuration. The fully active 65 kDa toxin and its 50 kDa variant, generated by a 15 kDa carboxy-terminal deletion, were incubated and fractionated in presence of the detergent. The results of the study reveal that truncated toxin was hemolytically100-fold less active but otherwise very similar to the 65 kDa toxin. The 65 kDa oligomer preferentially associated with the phospholipidcholesterol vesicles that were not solubilized by the detergent. In contrast, the 50 kDa toxin was completely solubilized suggesting a correlation between raft-association and efficiency of membrane permeabilization activity. Results of the study suggest that the survival of the hemolytically active quasi-stable monomer might depend on its association with a chaperone-like accessory molecule.

Shigella species

Molecular Characterization of Multi-drug Resistant Shigella flexneri in Kolkata

Shigellosis is a major public health problem in developing countries. Increased incidence of antibiotic resistance in *Shigella spp*. constitutes a major concern.

COMMUNICABLE DISEASES

High frequency of resistance of *S. flexneri* to many of the first line antimicrobial agents has been reported in recent years from Kolkata. Most of the conventional typing methods are based on the phenotypic properties of the micro-organisms and offer little strain discriminatory information. Study was undertaken with the objective to analyze clonal relationships among isolates of multi-drug resistant *S. flexneri* using different molecular typing methods to determine changes at the genetic level and to understand their implications in the epidemiology of the disease. During the period under study a total of 589 stool samples from Dr. B.C. Roy Memorial Hospital for Children were screened for detection of *Shigella* spp.

Out of 355 stool specimens 33 (9.2%) were positive for *Shigella spp*. Among Shigella strains 51%



Fig.1. PFGE pattern of isolated strain of Shigella

were *S. flexneri*, 9% *S. dysenteriae*, 30% *S. sonnei* and 9% *S. boydii*. All these isolates were tested for their antimicrobial susceptibility patterns to evaluate the possible mechanism of quinolone resistance. During the study period *S. flexneri* was the most prevalent serogroup and *S. flexneri* serotype 2a was the predominant serotype among the strains isolated. All *S. flexneri* were found to be multiple antibiotic resistant, few strains of *S. flexneri* type 2a were resistant to fluoroquinolone and the minimum inhibitory concentrations (MIC) of these strains were >256, 4-8, 10-16, and 12-16µg/ml for nalidixic acid, ciprofloxacin,

norfloxacin, and ofloxacin respectively. Few strains were also found resistant against gatifloxacin. However, all were found susceptible against azithromycin and ceftriaxone. All the tested strains uniformly harbored *ipa*H, *ial*, *Shigella* enterotoxin 1 genes. Digestion of chromosomal DNA with the restriction endonuclease Xba1 produced clearly resolvable restriction endonuclease analysis (REA) pattern after PFGE. Different pattern was identified amongst the isolated strains. (Fig.1.) All the *S. flexneri* type 2a originated from single clone.

Molecular Epidemiology of Shigellosis in Andaman and Nicobar Islands

A study was undertaken to understand the clonal relatedness of different species and/or serotypes of Shigella isolated from the islands during a 10 year hospital based surveillance, with each other and with those isolated from other parts of the country by employing of molecular tools. Random amplified polymorphic DNA (RAPD), enterobacteriaceae repetitive intergenic consensus (ERIC) sequence, repetitive extragenic pallindromic (REP) sequence and BOX-based polymerase chain reaction (PCR) was employed in conjunction with pulsed field gel electrophoresis (PFGE) assay to generate genetic fingerprints of each isolate (Fig. 2-4). Several genotypes were observed for each species and serotype of Shigella. Most of the serotypes and genotypes of S. dysenteiae isolated from these islands were during



Fig.2. RAPD fingerprint patterns of some S.dysenteriae isolates from Andamans

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Fig.3. ERIC-PCR fingerprints of Andaman S.dysenteriae isolates



Fig.4. PFGE pulsotype of representative isolates. Commonest genotype of *S.dysenteriae* from Andaman SH-123 (lane 3) was identical with that of OS-16, a Kolkata isolate (lane 7)

mid-1990s during an outbreak of bacillary dysentery. The study retrospectively revealed that the clone which caused the outbreak was exotic and may have been brought from Kolkata, where this particular clone was in circulation at that time. Two clones of S. dysenteriae 2 were also found, one of which was a Kolkata clone too. In S.sonnei, there were 2 commonly

circulating clones prior to year 2000 and this clone was found in Kolkata and Lucknow too during that period. The number of different genotypes of circulating *S. sonnei* had increased to 7 since 2001 when interestingly, *S. sonnei* replaced *S.flexneri* as the commonest isolate from the Islands in a scenario that is different from elsewhere in India or other developing countries. These new clones were not found in the mainland isolates. On the basis of the results obtained it is hypothesized that *S. sonnei* might have been brought to these islands some time back, perhaps from the eastern part of the country

and has started evolving into new genotypes recently as it starts to outnumber the endemic S.flexneri as the commonest isolate. S. flexneri presented the biggest group (84 strains) that had diverse (at least 39) genetic types. Most clones were represented by 2-3 isolates. The biggest clone was that of S.flexneri 2a (n=14) out of 41 strains representing this serotype. Genetic fingerprinting data revealed the presence of two of these clones in mainland (Manipal, Kolkata) also. However, the remaining 37 types were not found in the mainland isolates used in the study. The presence of a wide

range of genotypes of *S.flexneri* (even within the endemic 2a serotype) shown in the study suggests that these strains might have been brought to these islands at different times from different places and it is likely that these strains evolved further locally. The study further underscored the usefulness of PCR-based rapid fingerprinting methods for characterization of microbes.

Escherichia coli

Binding of *E. coli* Heat-stable Enterotoxin to the Intestinal Epithelial Cells and Brush Border Membranes

The principal objective of this study was to determine the presence and density of the STa receptor in intestinal epithelial cells and brush border membranes of different animals and to purify and characterize the receptor for STa from a high-density receptor system. During the reported period an attempt was made to clone the PCR amplified STa receptor gene into a suitable cloning vector. The 3.5kb amplified fragment (2-4µl) was mixed with TOPO-TA cloning vector and incubated at room temperature for 20 mins. Then 3µl of TOPO reaction mixture was added to *E.coli* (DH5 α) competent cell for transformation by following standard protocol. Transformed colonies of E.coli were selected by bluewhite selection procedure. For confirmation of cloning, plasmid DNA was isolated from the transformed *E.coli* cells and subjected to agarose gel

electrophoresis and shifting of bands compared to the control vector. Fur further confirmation restriction digestion by EcoR1 enzyme was performed. The digested product (STa receptor gene, size-3.5 kb) was partially sequenced by using M13 forward and reverse primers. Further studies are in progress.

Identification and Characterization of a Toxin from Enteroaggregative *E.coli* (EAEC)

EAEC is an important cause of diarrhoea in India. Various toxin genes of this pathogen have been characterized at protein level, however, many more remain to be characterized. At PGIMER, Chandigarh Indian clinical isolates of EAEC (strain T-8), procured from NICED, Kolkata were used for identification, purification and characterization of the toxin. The toxin showed complex carobohydrate specific HA activity. The binding efficiency of the toxin to GM1 was found to be greatest among all other gangliosides used. The toxin could induce cytotoxic activity on both HEp-2 and INT-407 cells and also induced fluid accumulation with histopathological changes in the rabbit small intestine. The toxin was found to interact with a 30kDa protein present on the INT-407 cells. It showed cross reactivity with the binding subunit of the classical cholera toxin pointing to the fact that the toxin is different from other reported toxins of EAEC.

Shiga Toxigenic *E. coli* (STEC) in Foods of Animal Origin and Clinical Samples

Siignificance of Shiga toxin producing *E. coli* as a cause of hemorrhagic colitis and hemolytic uremic syndrome has been established worldwide. The major reason for screening of STEC is to detect outbreaks and initiate public health interventions, limiting the number of deaths. In India very few studies have been undertaken to detect STEC in stools and food samples.

A study has recently been completed at Kasturba Medical College, Mangalore to assess Shiga toxigenic *E.coli* (STEC) in foods of animal origin and clinical samples. *E. coli* O157 was isolated and detected by PCR in one of the meat samples, however, it could not be implicated as a major causal agent of diarrhoea. The presence of STEC in food chains of Mangalore suggests that this enteropathogen is of public health importance. Hence, one has to be vigilant to trace this organism in diarrhoeal stool as a routine, should they become important enteropathogens in the not-too-distant future.

Helicobacter pylori

Characterization of the *cag* Pathogenicity Island of *H. pylori* isolated in Kolkata with reference to Interleukin-8 Secretion

CagA is a 120-145 kDa protein with a carboxy terminal variable region. Length polymorphism observed at the 3' end of *cagA* gene of *H. pylori*, which results in variation in the number of phosphorylation sites of the encoded protein (CagA), is of great interest in recent times since higher number of phosphorylation sites in CagA were described to be associated with stronger biological function and disease manifestation. To understand the length polymorphism at the 3' end of the cagA gene, one PCR assay was performed to amplify the 3' end region using two primers namely CAG1 and CAG2. A total of 75 strains, 40 isolated from duodenal ulcer patients, 20 from healthy volunteers (HV) and 15 from non-ulcer dyspeptics were included in the study. PCR results showed that all these strains carry *cagA* gene but yielded amplicons with different sizes.

Further analysis of the amino acid sequences predicted from nucleotide sequences of *cagA* 3' end revealed some distinct features present in this repeat region. *H. pylori* strains isolated from Kolkata carried *cagA* genes capable of coding proteins, which may contain EPIYA motifs as low as 1 to as high as 5 in number. All these EPIYA motifs were preceded and followed by distinct, short stretch of amino acid sequences.

The first EPIYA motif (termed in this study as Y1 to denote tyrosine phosphorylation site) in this CagA primary structure was preceded by a stretch of 10 amino acids which contain 6 successive asparagines in tandem and was termed as S1 to denote the starting sequence for the repeat region responsible sites for CagA phosphorylation. The first and the second EPIYA (termed as Y2) motifs are separated by a stretch of 13 amino acids in all CagA sequences included in this study that carry A-B-C or A-B-C-C or A-B-C-C type EPIYA motifs.

A very exciting observation has come out from this study while analyzing the intervening sequences of third, fourth and fifth EPIYA (termed as Y3, Y4 and Y5) motifs. These intervening regions, originally described as R3 contained shorter, discrete repeats. The sequence, termed in this study as I1 (QVAKKVNNAKIDRLNQIASGLGGVGQAAG) was present immediately after the second EPIYA motif (Y2) and unlike CagA sequences found in Japan was never repeated. This stretch was followed by another stretch of amino acids, termed as I2 (FPLKKHDKVDDLSKVGLS) and a very short domain of only 3 amino acid residues, termed as I3 (ASP), which was present just before the third EPIYA motif (Y3).

After the third EPIYA motif (Y3), another distinct domain was noticed and termed as W1 (TIDDLGGP), which was again followed by I2 and I3 in A-B-C-C and A-B-C-C-C type CagA. In A-B-C type CagA, though W1 and I2 were always present, I3 was replaced by another domain, termed as T1 having sequence REQQL (or REQNL in some strains). However, in A-B-C-C-C type CagA, I3 is repeated 3 times along with EPIYA motifs (at C positions) and after the last EPIYA at C position (Y5), I3 was replaced by T1. The comparative analysis of all the CagA primary structures revealed that this T1, which must be present after I2 (and in the place of I3) indicates the termination of this repeat sequences and after T1 no EPIYA site was observed in any CagA primary structure.

To check whether the above variation in the 3' end of the cagA gene has any effect in the expression of the CagA protein, representative H. pylori strains suspended in PBS, carrying different CagA primary structures were boiled, run on polyacrylamide gel and the total proteins were transferred to nitrocellulose membrane. After blocking with 3% bovine serum albumin, the membranes were incubated with blocking solution containing rabbit polyclonal anti-CagA and then anti-rabbit IgG. All the strains were found to express CagA including strain San77 (AB-C-C-C type), which was isolated from HV. RT-PCR assay was also performed to check the expression of cagA mRNA taking representative H. pylori strains with varying cagA 3' end structure using ureB as internal control. All the *H. pylori* strains expressed cagA, which means variable repeat regions at the carboxy terminal have little effect in the expression of the cagA gene. CagA was detected from the infected cell lysates by the Western blot analysis except for PCR24 where the intensity was significantly diminished.

The capacity of CagA to bind SHP-2 in different H. pylori strains containing variable 3' end structures was investigated. It was demonstrated that H. pylori virulence factor CagA, which is translocated from the bacteria into gastric epithelial cells, can perturb mammalian signal transduction machineries and modify cellular functions by physically interacting with a host cell protein, SHP-2. SHP-2 is known to play an important positive role in the mitogenic signal transduction that connects receptor tyrosine kinases and ras. Also, SHP-2 is actively involved in the regulation of spreading, migration, and adhesion of cells. Deregulation of SHP-2 by CagA may induce abnormal proliferation and movement of gastric epithelial cells, promoting the acquisition of a cellular transformed phenotype. Thus, the potential of CagA to disturb host cell functions as a virulence factor could be determined by the degree of SHP-2 binding activity. The results provide a molecular basis for the pathological actions of CagA on gastric epithelial cells.

Amino acid sequence diversity in CagA among different *H. pylori* strains from Kolkata was reproted. The phosphorylation of the EPIYA motif is located in the repeat region of CagA and is expanded by duplication. Accordingly, the number and sequence polymorphism of the CagA phosphorylation sites, which collectively determine binding affinity of CagA to SHP-2, may be important variables in determining the clinical outcome of infection by different *cagA H. pylori* strains. Study is ongoing to understand more closely the translocation of different types of CagA through type IV secretion system and its binding efficiency with SHP-2 by immunoprecipitation assay along with their roles in IL-8 production.

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

To study the natural history of *H.pylori* in a birth cohort in an urban slum setting a study was carried out at AIIMS ,New Delhi. The results of the study revealed that over three quarters of infants get infected with *H. pylori* as early as 10 weeks of age. However, there was no association of maternal and infant infection indicating that infant may be infected from sources other than the mother. Although there is higher diarrhoea prevalence among infected children during the first 6 months of life, infected children did not have lower weight or length gains or greater prevalence of anaemia.

Natural History of *H.pylori* Infection and its Outcome in India

Study was carried out at the Institute of Postgraduate Medical Education and Research (IPGMER), Kolkata on H. pylori infected duodenal ulcer patients with a regimen based on omeprazole, amoxycilin and clarithromycin for 2 weeks with follow up of the patient at defined time intervals to determine the frequency of eradication, the frequency of ulcer recurrence as well as reinfection in the eradicated group. H. pylori eradication rates were low (64.35%), compared to reports from Western countries as well as India. In order to find correlation, if any, with the putatitive genes of H. pylori and failure/success of eradication, alleles of the virulence genes vac A in the two groups (failure of eradication/eradication)were looked, as well as cag A status. It was found that organisms bearing vac A genotypes m1 s1 are more difficult to eradicate.

Entamoeba histolytica

Cloning and Characterization of Collagenase Genes of *E. histolytica*

Isolated electron dense granules (EDG) were characterized by biochemical and immunological parameters. The purified EDG showed 8 times more collagenolytic activity than the whole *E.histolytica* trophozoites. Purified EDG showed six polypeptide bands with apparent molecular weights of 108, 106, 104, 97, 68 and 59 kDa that were not detected in whole *E.histolytica* extracts. Similarly, two protease activities with apparent molecular weights of 40 and 85 kDa were detected only in EDGs. Scanning transmission electron microscopy demonstrated that EDGs were highly complex molecules, mainly made of cations. Maximum collagenolytic activity was observed in fraction 16. Collagenolytic activity of soluble fraction revealed a broad single clear zone compared to parent EDG at 85 kDa by zymography technique.

The recombinant protein was purified and eluted. Overexpressed band appeared in 64 kDa on SDS-PAGE analysis. After expression, affinity purification and proteolytic removal of maltose binding protein, bands appeared at 42kDa and 22kDa in SDS-PAGE. This 42kDa and 22kDa protein represented maltose binding and grainin 1 protein respectively. Further characterization of recombinant purified protein done using ELISA and Western blot confirmed that recombinant protein has similar epitopes with that present in the parasite. On confocal microscopy, grainin 1 protein was found to be localized on the surface and in vesicles of the *E.histolytica* trophozoites.

The antibody raised against the recombinant purified protein showed a single immunoreactive band at 22kDa position against both EDG and recombinant protein, thereby confirming that recombinant protein has epitopes similar to those in EDG.

Rotavirus

Molecular Characterization of a Porcine Group A Rotavirus Strain with G12 Genotype Specificity

A porcine group A rotavirus strain (RU172) was detected and molecularly characterized during a surveillance study conducted for rotavirus infection in a pig farm located in suburban area of Kolkata. The G12 genotype specificity of RU172 was revealed by PCR based genotyping assays following addition of a G12 type specific primer and was confirmed by sequence analysis of the VP7 encoding gene. RU172 strain exhibited maximum VP7 identities of 93.6 to 94.5% with human G12 strains at deduced amino acid level. In spite of its G12 genotype nature, RU172 appeared to be distinct from human G12 rotaviruses, and on phylogenetic analysis, formed a separate lineage with human G12 strains. Among the other gene segments analyzed, RU172 belonged to NSP4 genotype B, had a NSP5 and VP6 of porcine origin, and shared maximum VP4 identities with porcine P[7] rotaviruses (94.3%-95.4% at deduced amino acid level). Therefore, RU172 is the first report of detection of an animal rotavirus strain with G12 genotype specificity. Detection of strains like RU172 provides vital insights into the genomic diversity of group A rotaviruses of man and animals.

Genomic Diversity of Group A Rotavirus Strains in Eastern India

Rotavirus genotypes, G1-4 and G9 are important serotypes associate with childhood diarrhoea throughout the world. To determine G- and P- types of rotaviruses associated with dehydrating diarrhoea and to study the appearance and disappearance of

G- and P- genotypes during the study period, an active surveillance was conducted for elucidation of rotavirus infection in two leading hospitals in Kolkata, (West Bengal) and Berhampur, (Orissa) from May 2005 to February 2006. The rotaviruses was detected by RNA electrophoresis in polyacrylamide gel. G- and P- typing of the positive samples were accomplished by amplifying VP7 and VP4 genes by RT-PCR and genotyped by multiplex PCR methods. The genotypic distribution varied remarkably well from earlier study period (2002-2005). G1 was the most predominant strain (64%) followed by G2 (19%), G9 (11.1%) and G12 (5.5%) and not a single G3 or G4 was detected. On the other hand, 68% samples exhibited P[8] followed by mixed P-types (21.6%), P[4](5.4%), and P[6](5.4%). The three G9P[8] strains and one G9P[4] were identified by type-specific primes and then confirmed by nucleotide sequencing. In contrast to the earlier study, G12 strains were replaced by G9 rotaviruses as the third most predominant strain in this part of the country.

Molecular Characterization of VP3 Gene of Group-A Human Rotavirus

A study was carried out at AIIMS, New Delhi to elucidate molecular characterization of VP3 gene starting with genetic variation in rotavirus strains prevalent in India. Rotavirus strains of G1-G4 and G9 serotypes are the most prevalent in India. VP3 gene from G9P11 (116E strain) and G2 (clinical sample) rotavirus were cloned and sequenced. Along with them, 20 more VP3 sequences representing G1, G6, G3, and G7 including several clinical specimens representing G1 and G4 serotypes were analyzed from the database. Further RT-PCR was developed with NSPU genotype specific primers and a correlation between NSPU genotype and VP6 serogroup was also analyzed. The assay will facilitate further studies on molecular epidemiology of roravirus.

OTHER MICROBIAL INFECTIONS

Leptospirosis

Leptospirosis is the most common zoonotic disease in the world. The clinical spectrum of disease is highly variable ranging from mild fever to fatal disease with multi-organ involvement. Most diagnostic laboratories use conventional techniques which are cumbersome, time consuming and expensive and have to be imported. Development of indigenous rapid test is of utmost significance. The RMRC, Port Blair is conducting studies on leptospirosis for developing PCR for rapid diagnosis and for molecular characterization of leptospiral isolates.

Leptospiral Carrier Rate among Animals Slaughtered in Port Blair

Study is continuing at RMRC, Port Blair to isolate leptospires from various animals slaughtered like cattle and goats and to characterize the isolates by serological and molecular genetic techniques. A total of 184 cattle and 202 goat serum and kidney samples were collected from Port Blair slaughter house. Of the 184 serum samples collected from cattle 34% showed leptospiral antibodies. Icterohaemorrhagiae (37%) was the commonest serovar followed by hebdomadis (17%), grippotyphosa (16%), australis (11%), sejroe (10%), autumnalis (5%), pyrogenes (3%) and pomona (2%). Highest titre of 1:1280 was also observed against serovar icterohaemorrhagiae. These cattle belonged to different parts of Andaman Islands. There were 4 cattle isolates from kidney samples which were brought from Calicut locality within Port Blair city. All the four isolates belonged to serogroup *icterohaemorrhagiae* of serovar icterohaemorrhagiae.

Of 202 samples collected from goats 29% showed leptospiral antibodies. The *icterohaemorrhagiae* (24%) was the commonest serovar followed by grippotyphosa (16%), hebdomadis (14%),), sejroe (10%), pomona (9%), autumnalis and australis (5% each), ballum (3%) and pyrogenes (2%). Mixed equals were observed in seven samples collected from goats. The reactions were mainly among icterohaemorrhagiae and grippotyphosa, autumnalis and icterohaemorrhagiae, australis and grippotyphosa and autumnalis and ballum. One isolation was made from goat kidney samples. A maximum titre of 1:2560 was observed against serovar icterohaemorrhagiae followed by grippotyphosa.

Analysis of *OmpL1* and *LipL41* Genes among *Leptospira interrogans* Serovars and Development of Systems for the Expression of Recombinant *OmpL1* and *LipL41* of *L. autumnalis*

Study was carried out at RMRC, Port Blair to develop an ELISA system with recombinant leptospiral

COMMUNICABLE DISEASES

immunoreactive proteins, OmpL1 and LipL41 for diagnosis of leptospirosis. The genes for OmpL1 and LipL41 were amplified, cloned to appropriate vectors and transformed into E.coli. The expressed proteins were purified and coated on ELISA plates. A concentration of 30 ng was found to be the optimal. Fifty six paired serum samples from patients with leptospirosis, 37 from patients clinically suspected but found negative for leptospirosis and 132 single sera from other diseases (92 typhoid, 19 malaria and 21 hepatitis) were used to evaluate the test. The recombinant OmpL1 and LipL41 ELISA showed a sensitivity of 66.1% and 62.5% and specificity of 91.1% and 89.2% respectively during the acute phase. However, sensitivity increased significantly with both the recombinant proteins during the convalescent phase (91.1% and 89.3%). Cross reactivity when tested with sera from other infectious diseases ranged between 4.8% in case of malaria and 11.9% in case of typhoid fever. The test has the potential of being used in rapid screening for diagnosis of leptospirosis and can be exploited commercially.

Molecular Characterization of Leptospiral Isolates using RFLP

Certain sequences in the *Leptospira* genome exhibit polymorphism. Parts of the 23s rRNA and 16s RNA regions are few of such polymorphic regions in leptospires in the otherwise conserved ribosomal genes. Leptospiral reference strains and clinical isolates were characterized using PCR based RFLP in the 23s and 16s rRNA regions. Attempts were made to find these polymorphisms through selective amplification and subsequent restriction digestion of these polymorphic regions.

Last year results of 15 reference strains of leptospires representing 8 different genospecies alongwith 15 local isolates were presented. During the year 2005-2006 more strains of each genospecies of *Leptospira* have been included in the study to find out the polymorphisms among the strains of a particular genospecies. Ten different strains of genospecies *L.interrogans*, four different strains of each genospecies *L.kirschneri* and *L. santorosai*, three different strains of genospecies *L. borgpetersenii*, two different strains of genospecies *L.moguchii and* one representative of each genospecies *Lweilii*, *L.meyeri* and *L. biflexa* have been included. Thirty four more isolates of *Leptospira* from Andaman and mainland were also included in the study. Specific primers were used to amplify a 2300 bp and a 367 bp part of 23s rRNA and a 631 bp region of 16s rRNA. The amplified fragments were digested using 11 different restriction enzymes for studying the polymorphisms. Several types of restriction patterns were obtained with the PCR-amplified regions of the ribosomal genes, indicating the presence of RFLPs within these regions.

The 631 bp amplified product of 16 s rRNA region showed only 3 types of polymorphisms with Hin f1 restriction enzyme among the 8 genospecies studied. Among these *L. interrogans, L. borgpetersenii, L.welii* and *L.biflexa* showed similar type of RFLP pattern and could not be distinguished from each other, whereas *L. noguchii* and *L. meyeri* showed another type of pattern. However, *L. kirschneri* showed a unique pattern that did not match with the other genospecies and could be easily differentiated with this enzyme.

However, when 631 bp amplified products were digested with Dde1 restriction enzymes, it differentiated different strains of a particular genospecies. Among the ten different strains of *L.interrogans*, strain *ballico* and *swart* showed different patterns and these two strains could be distinguished separately from other strains. Strain *patoc1* and *andamana* of *L. biflexa* could be differentiated easily. Strain *butembo* also differentiates from other three strains of *L.kirschneri* in this region. Both the strains, *panama* and *LSU1945* of *L.noguchi* also showed differentiation. *L.meyeri* also showed unique pattern and could not match with other strains studied so far. However, with other enzymes, no further discrimination was found within this 631bp region.

Within the 2300bp amplified products of 23srRNA region digested with Dde1 enzyme, strain *ballico* could be differentiated from other nine strains of *L.interrogans*. Three strains of *L.kirschneri viz. buttembo, cyanopteri* and *moskova* showed different patterns of polymorphisms. Two strains of *L.noguchi* also gave different patterns and could easily distinguish within this region. *L. welii* showed unique pattern in this region while digested with Dde1. Two strains of *L.biflexa* gave different patterns also in this region. However, Dde1enzyme digest of 2300 bp could not differentiate among the three strains of *L. santorosai*.

Leptospiral isolates of Andaman did not reveal much polymorphism in the 16s region as shown within

the reference strains. These isolates, however, showed 3 types of polymorphisms by different enzymes in the 23s region. Hin1 restriction patterns of 3 mainland isolates were different from isolates from Karnataka, Tamil Nadu and Kerala. Comparative studies on RFLP patterns of more isolates and their genospecies are in progress.

Clinical, Bacteriological, Serological and Epidemiological Follow up of Leptospirosis

A total of 126 blood samples were collected from Manglutan PHC. Total number of paired samples was 70 and single samples collected were 56. Out of 70 paired samples 31% showed leptospiral antibodies, 32% of 56 single samples showed antibodies against Leptospira. Two leptospires were isolated during the year 2005. Serological and molecular characterization is yet to be performed. *Icterohaemorrhagiae* (15%) was the commonest serovar followed by *grippotyphosa* (6%), *hebdo* (3%) and *autumnalis* (2%). Highest titre of 1: 2560 was observed against serovar *icterohaemorrhagiae*.

Application of PCR for Rapid Diagnosis of Leptospirosis

An attempt has been made to find the correlation between PCR, MAT, isolation and lepto-dipstick as diagnostic tools during the acute stage of the disease. Of the 260 patients in whom all the results were available, 62 were diagnosed as leptospirosis cases serologically but 76 were identified as positive by PCR. Thirty two cases were dipstick positive and 19 were isolate positive. PCR and standard criteria was positive in 59 cases and in 181 patients both were negative. The sensitivity of PCR when compared to standard criteria was 95.2% and specificity was 91.4%. The sensitivity of PCR when compared to isolation was 78.9% and specificity was 91%, while dipstick showed low sensitivity of 38.7% and specificity of 96.6% compared to standard criteria. However, though PCR is expensive and requires expertise, its use in clinical samples particularly in outbreak situations where quick diagnosis is required, is indispensable.

PCR for Detection of Leptospires in Human and Animal Urine Samples

A Total of 82 paired human serum samples suspected to be leptospirosis cases, were collected from

Manglutan PHC. After a week 2nd serum samples were collected with urine samples of the same pateints. Leptospiral antibody was tested using MAT. Of the total serum samples 10% showed leptospiral antibody. Commonest was *icterohaemorrhagiae* (50%) followed by *grippotyphosa* (25%) and *australis* (13%). Maximum titre observed was 1280 against serovar *icterohaemorrhagiae*. In all, 16% urine samples were positive by PCR, while 4% samples were both PCR and MAT positive. Twelve per cent samples were positive by PCR but negative by MAT and 5 were MAT positive and negative by PCR. Seventy eight per cent were negative both by PCR and MAT.

Campylobacter jejuni

Role of Antiganglioside Antibodies and IgG FO-receptor Polymorphism in Development of *Campylobacter* related Guillain-Barre Syndrome (GBS)

GBS has emerged as an important cause of acute flaccid paralysis in the post-polio era. Several studies have established a strong link between GBS and C. jejuni infection. GBS is now regarded as an autoimmune disease affecting susceptible individuals, triggered by cross-reactive humoral and cellular responses to peripheral nerves. A study was recently completed at the Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow on role of antiganglioside antibodies and IgG FO-receptor (Fcy R) polymorphism in development of campylobacter related GBS. Results of the study revealed that antiganglioside antibodies were present in a significant number of acute phase sera of GBS patients as compared to controls. Multiple antiganglioside antibodies were detected in GBS patients who had microbiological evidence preceding C. jejuni infection. Anti-GM1 and Anti-GD1a antibodies (both IgG and IgM) were significantly associated with axonal subtype of GBS.

Pseudomonas aeruginosa

Virulence of *P.aeruginosa* in relation to Catheter – associated Urinary Tract Infections

P. aeruginosa is an opportunistic pathogen causing urinary tract infections (UTI) generally after

catheterization. It is resistant to many antibiotics and has an innate tendency to form biofilm on catheters which is difficult to eradicate. A study was carried out at Panjab University, Chandigarh to assess virulence of *P.aeruginosa* in relation to catheter –associated urinary tract infection. Acute model of ascending UTI was successfully induced in mice with planktonic and biofilm cells of *P. aeruginosa*. It was observed that renal bacterial load was significantly more when infection was induced with biofilm cells as compared to planktonic cells.

Staphylococcus aureus

Aerobic and Anaerobic Bacteriological Profile of Diabetic Foot Ulcers with Special Reference to Methicillin Resistant *S. aureus*

Foot ulceration is common in people with diabetes and is estimated to affect 15% of all diabetics during their lifetime. These ulcers are susceptible to infection. A study was carried out at AIIMS, New Delhi to assess aerobic and anaerobic bacteriological profile of diabetic foot ulcers with special reference to methicillin resistant S. *aureus* (MRSA). Results revealed that factors significantly associated with MRSA positive status were presence of hypertension, neuropathy and osteomyelitis Significantly more number of patients with MRSA infections required amputation. Findings of study will facilitate successful management and antibiotic usage and stem the spread of antibiotic resistant bacteria.

Clostridium Spp.

Development of Multiplex PCR for Detection of C. *perfringens* and C. *botulinum* in Food Samples

The incidence of *C. botulinum* and *C. perfringes* food poisoning is very high leading to paralysis and death. Present pathogen detection methods require culture and are time consuming. Therefore, less cumbersome methods are required. A study was carried out at AIIMS, New Delhi in which PCR for amplification of enterotoxin gene sequence of *C. perfringes* and BoNT gene sequence of *C. botulinum* was standardized. Multiplex PCR for detection of *C. botulinum* types A, B, E and F was also standardized.

PARASITIC DISEASES MALARIA

Malaria caused by *Plasmodium falciparum* is a disease with serious consequences. In view of the insecticide resistance developed by the vector species and emergence of drug resistance in *P. falciparum*, its control is a complex problem. The ICMR's National Institute of Malaria Research (NIMR) at Delhi, Vector Control Research Centre (VCRC) at Pondicherry and the RMRCs at Bhubaneswar and Jabalpur are actively engaged in multidisciplinary research for better understanding of the complex epidemiology of malaria and for finding solutions to the emerging challenges.

Integrated Disease Vector Control

Science and Technology project on Integrated Disease Vector Control of Malaria continued to provide scientific support in malaria control operations to the National Vector Borne Disease Control Programme (formerly National Anti Malaria Programme, NAMP). NAMP and NIMR, Delhi have jointly identified priority areas of research to realize the gains in malaria control.

All the field stations functioning under this project continued to interact with respective state health departments in planning and execution of activities to contain the malaria problem. Field units of the Centre actively participated in clinical drug trials, evaluation of diagnostic kits, new insecticides and insecticides treated nets. A study on the health impact assessment of Sardar Sarovar Narmada water resources development project on mosquito-borne diseases was initiated by Nadiad field unit. Project to develop strategy for integrated control of vectors of malaria, JE and dengue in Gujarat, Madhya Pradesh and Karnataka states has been completed by Nadiad, Jabalpur and Bangalore field units. Evaluation of botanical pesticides was carried out at Hardwar field unit and use of larvivorous fish was scaled up in five talukas and four districts and Mangalore city, Karnataka under the supervision of Bangalore field unit. In addition technical advice, consultancy services were provided to local/state health authorities and other governmental/non-governmental organizations.

Malaria Parasite Bank

Malaria parasite bank is supporting a large number of organizations working on various aspects of malaria. Biological material including nonhuman and human Plasmodia preserved/maintained at the Bank were supplied to various research organisations. The nonhuman parasites, especially P. berghei (both chloroquine resistant and sensitive) are being used for in vivo screening of extracts/ fractions of medicinal plants. A total of 48 P. falciparum isolates were supplied for studies on genetic variation of T-cell epitopes and another 20 isolates were supplied for molecular characterisation to Indian Institute of Science (IISc), Bangalore. Few of the isolates characterised for their chloroquine sensitivity status and erythrocyte invasion properties, were again cultivated in vitro to expand the number of vials cryopreserved at the Parasite Bank for future use/supply. One resistant isolate has been cloned this year. Eleven clones were separated from this isolate and these clones were given for checking their monoclonality by molecular analysis. After expanding, these clones were tested for chloroquine sensitivity. All the clones were found to be resistant in varying concentrations.

Vector Biology and Control

Synonymy of An. fluviatilis S with An. minimus C

An. fluviatilis S has been made conspecific with An. minimus species C based on homology in 335 base pair nucleotide sequence of D3 domain of 28S ribosomal DNA (rDNA) of An. fluviatilis S with that of An. minimus species C. In order to resolve the taxonomic status of An. fluviatilis S, the nucleotide sequences of a mitochondrial gene cytochrome oxidase II (COII) and complete internal transcribed spacer 2 (ITS2) region of rDNA of An. fluviatilis S were determined and compared along with already available 28S-D3 rDNA sequence, with other members and of the fluviatilis and minimus complexes.

Comparison of nucleotide sequences revealed that *An. fluviatilis* S differs from *An. minimus* C by 22 base substitutions in COII and by 13 substitutions and two indels in ITS2 region. However, this species differs from other members of fluviatilis complex (species T and U) by only 2 and 9-10 base pair substitutions, respectively,

for COII and ITS2 regions. In combined analysis a total of 1388 aligned base pair data were used including 328 base pair 28S-D3 sequence data where An. fluviatilis S and An. minimus C have identical sequence. In combined data analysis, An. fluviatilis S differs from An. minimus C by 35 base pair substitutions (2.6%) while it differs from species T and U by 15 (1.1%) and 14 (1%) base pairs only indicating that An. fluviatilis S is closely related to members of the fluviatilis complex as compared to An. minimus C. The neighbour joining (NJ) tree for members of fluviatilis and minimus complexes derived from combined set of data (COII, ITS2 and 28S-D3) shows that the fluviatilis complex (along with species S) forms a monophylatic taxon which is distinctly separated by minimus complex taxon (Fig. 1). The results clearly establish the specific status of An. fluviatilis S as one of the members of fluviatilis complex and revokes its synonymy with An. minimus C.



Fig. 1. Neighbour-joining tree inferred from combined sequences data of the three loci (COII, ITS2 and 28S-D3) from members of fluviatilis and minimus complexes. Numbers above the branches are bootstrap values. *An. varuna* and *An. aconitus* were taken as outgroup

Insecticide Susceptibility Status of An. culicifacies in Surat

Study was carried out in Ukalda PHC of Surat district in 2005 to assess the status of insecticideresistance in *An. culicifacies*. Base line resistance was determined using the standard WHO method and kit by exposing the mosquitoes to the designated WHO diagnostic doses of different insecticides. *An. culicifacies* was found resistant to DDT and malathion and was susceptible to other organophosphate, carbamate and pyrethroid insecticides. Synergistic bioassay studies with tri phenyl phosphate (TPP) a specific inhibitor of carboxyl esterase indicated complete synergism with TPP (10%) indicating the involvement of carboxyl esterase for conferring malathion resistance in this species.

The species composition of *An. culicifacies* indicated major sympatricity of species B and E. The proportion of species E was 59.4%, species B 39.2% and species C was only 1.2%. Prevalence of species E from this area is being reported for the first time. Identification of dead and alive mosquitoes in the insecticide bioassays to sibling species indicated differential susceptibilities to DDT and malathion. Species B was relatively less susceptible to DDT and malathion as compared to species E. Susceptibility of species C could not be determined due to its very low density.

Malaria in Rajasthan

Mapping of Insecticide Resistance in the Vectors of Malaria in Rajasthan

Studies were carried out by Desert Medicine Research Centre (DMRC), Jodhpur in 3 desert districts namely Barmer, Jaisalmer and Jodhpur and two vector species, An. stephensi and An. culicifacies were tested against 3 insecticides, DDT, malathion and deltamethrin. Both the species exhibited resistance to DDT and malathion but were totally susceptible to deltamethrin. The susceptibility data when analyzed in relation to the insecticide spray history of last 3 years, revealed that the susceptibility of the vector species increased with the gap of insecticide spray in case of both the vector species which indicates that the withdrawal of insecticide pressure increases the susceptibility of vector population against the insecticide withdrawn. Studies also revealed that continuous use of synthetic pyrethroids against malaria vectors reduced the density of the vector species and the proportion of the gravid females.

Plants for Vector Control

Larvicidal Potential of Active Solanum xanthocarpum against Mosquito Vectors

Susceptibility tests were carried out at DMRC, Jodhpur with larvae of four mosquito species viz. An. culicifacies, An. stephensi, Ae. aegypti and Culex quinquefasciatus. Larval susceptibility to methanol extracts of leaves, root, seeds and ripe fruits of this plant was determined. Results indicate that larvae of *An. culicifacies* are more susceptible to ripe fruit and seed extracts compared to other species of the mosquitoes.

Screening of Plant Extracts for Insecticidal and Repellent Activity against An. stephensi

In a multi-institutional collaborative project, a total of 727 samples were tested for their bioactivity, out of which 172 showed promising larvicidal activity (70-100% mortality) while 29 samples showed insecticidal activity against adult mosquitoes and 5 samples showed repellent activity for more than one hour. Of the various samples tested, 4 plants were identified for further development of plant extract based formulations.

Parasite Biology

Genetic Structure of Human Malaria Parasite P. falciparum

To understand the population structure of P. falciparum in India, field isolates from different geographical regions were analysed for surface protein markers-MSP-1 and MSP-2 for length as well as sequence variations. Three families of MSP-1 (K1, MAD20 and RO33) are prevalent in all the study sites with a few exceptions. K1 and MAD20 families have shown further allelic polymorphism while RO33 family was observed to be monomorphic with a single allele of 160 bp in all the study areas. In MSP-2, two families FC27 and 3D7 were observed in all the study sites and showed length variations. Fig. 2 shows the proportional prevalence of various families of MSP-1 and MSP-2. Further, DNA sequence analysis of various alleles of MSP-1 and MSP-2 families revealed that Indian P. falciparum isolates present a mixed allelic composition representing different global regions.

Genetic Structure of P. vivax

With an aim to understand the extent of genetic diversity in *P. vivax* populations, field isolates collected from different regions of the country were screened for polymorphisms in genomic sequence by PCR, RFLP and direct sequencing. Following marker genes were used for the study:

GAM-1 (Gene coding for transmission blocking antigen): Field isolates analysed from different geographical regions of the country, viz. Delhi, Tamil



Fig. 2. P. falciparum: Distribution of MSP-1 and 2 families among field isolates in India

Nadu, Goa, Car Nicobar, Gujarat, Madhya Pradesh, Uttar Pradesh, Bihar, Maharashtra, and Orissa revealed dimorphic nature of GAM-1 among Indian isolates. Both Belem and Chession type alleles were present with prevalence of Belem type allele (above 70%) in all the sites studied except Orissa. In Orissa isolates Chession allele was predominant (about 80%) which is similar to Thailand isolates, while isolates of other areas resemble Korean isolates. On the other hand, Indian isolates showed a totally different picture from Sri Lankan isolates which were highly polymorphic. Fig. 3 shows the proportional prevalence of two alleles (exclusively or on combination) among the Indian isolates.

MSP3 α : PCR characterization revealed three different fragment sizes (length variants) with predominance of 1.8 kb fragment (above 75%) in isolates studied from Delhi, Tamil Nadu, Goa, Car Nicobar, Gujarat, Madhya Pradesh, Maharashtra and Orissa. RFLP with *Alu* I and *Hha* I revealed a total of 19 different alleles among Indian isolates compared to 13 reported from Papua New Guinea (PNG) and Thailand. Sequence analysis of the PCR amplified fragments (all 3 variants 1.8, 1.4 & 1.2 kb) has revealed that 1.8 kb variant resembles



Fig. 3. Distribution of *P. vivax* GAM-1 alleles in different parts of India. Allele A – Chession type and Allele B – Belem type. Mix allele – presence of both Belem and Chession type together in the isolates



Fig. 4. Allelic distribution of MSP 3 α in India

closely to Korean and Thailand data while 1.4 kb variant resembles more to Venezuela data and 1.2 kb variant is

like Chession strain. Study further revealed that block-I region of MSP3 α was deleted in 1.2 and 1.4 kb fragments, in addition, 1.2 kb variant β -helix was also deleted thus creating a high degree of diversity among the isolates. Fig. 4 depicts the distribution of three size variants of MSP3 α among Indian isolates.

Pv SSUrRNA – Two subtypes: Isolates from different regions of India were analysed and results revealed presence of both old and new world type S-gene of SSUrRNA



P. vivax :18S small Old World : Type 1; New World : Type 2



Fig. 5. Global distribution of old and new world S-type allele of 18S small subunit rRNA

among the isolates with an even split of 60% old and 40% new world type. Similarly, isolates from PNG and Brazil also showed presence of both the types. In PNG isolates predominance of old world type (90%) was observed while among Brazil isolates predominance of new world type was noted (70%). This observation suggested the presence of both the S-type allele frequencies worldwide clearly demonstrating the global distribution of the two alleles and no geographical subdivision. Fig. 5 shows the prevalence of old and new world S-type allele of SSUrRNA among isolates of India and other global regions.

Development of Nuclear DNA Markers for Evolutionary Studies in *P. falciparum*

Estimation of genetic diversity in species populations and inferring evolutionary dynamics of different

genes is important in biomedical research, especially in finding new drug target genes and developing new effective drugs and vaccines. Recent researches in evolutionary genetics have revealed that estimation of genetic diversity is strongly dependant on the genetic markers used, thus making appropriate evolutionary inference both at species and gene level, difficult. Considering these facts, nuclear DNA markers in human malaria parasite P. falciparum have been developed using the published whole genome sequence information. Genetic fragments located in introns (noncoding sequences) are amplified by PCR technique by designing primers in the flaking exons (coding DNA sequences). Following this approach [(commonly known as EPIC (exon priming intron crossing)], a total of 170 putatively neutral fragments in the whole genome of P. falciparum have been developed (Fig. 6). In order to detect endemic mutations in different alleles in the *pfcrt* gene and to measure genetic diversity in both the resistant and sensitive varieties in isolates collected in different geographical populations in India, it is planned to sequence the whole *pfcrt* gene, instead of looking at the specific local mutations. Three



Fig. 6. Distribution of total number of introns and putatively neutral introns in *P. falciparum* genome



Fig. 7. Distribution of introns and exons and design of fragments for amplification by PCR of the Pfcrt gene in *P. falciparum*

primary primer pairs for amplifying the whole *pfcrt* gene and five nested primer pairs for sequencing the whole gene in short stretches have been designed (Fig. 7). The development of nuclear DNA marker would help in understanding the precise roles of demography and natural selection in evolution of *P. falciparum* in India.

Evolution of Introns in the Genome: Inference from the Whole Genome Scanning of *P. falciparum*

P. falciparum genome is unique in several aspects such as long proteins compared to homolog in other



Fig. 8. Bioinformatic approach of data retrieval from *P. falciparum* genome sequence database

organisms and it is AT rich genome (80.6 %). A genome-wide survey and study of *P. falciparum* for the understanding of genome organization was undertaken utilizing comprehensive datasets available in public databases, *viz*. PlasmoDB and NCBI combined with the availability of substantial sequence tracts from *P. falciparum*.

Data retrieval was done using web data source (PlasmoDB and EMBL) and collected according to analytical need (Fig.8). Most genes were small but the hypothetical genes were comparatively larger than the genomic average. However, functional genes were small in general

and clustered in the sub-telomeric regions of the chromosome. Introns in the functional genes were found to be smaller than average genomic length and small genes were considerably rich in GC content. The number of genes on each chromosome was marginally correlated to chromosome size. A statistically significant positive correlation was detected between the number of introns and chromosome size and the number of introns and number of genes along each chromosome. Generally, the number of introns was found to increase in the increasing order of the chromosome size. However, this pattern was found to be distorted for the two largest



Fig. 9. Distribution of introns of different classes in the two largest chromosomes of *P. falciparum*

chromosomes, chromosome 13 and 14 (Fig. 9). As evident in the figure, very large sized introns were found in chromosome 14, the largest of all chromosomes.

The other observed features in the present study, *e.g.* conservation of GT-AG splice site and presence of

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polypyramidine tail at 3' end suggest invasion of introns in eukaryotic genome after the separation from other lineages as suggested by intron late theory. The highly AT rich introns detected in this study seem to contribute much to the overall AT biased nature of *P. falciparum* genome. Most genes are intron-less and fall in the size range of 100-200bp in length.

Immunology and Host-parasite Interactions

Serum and Immunoglobulin Mediated Inhibition of Intraerythrocytic Growth of *P. falciparum in vitro*

Study was undertaken with the objectives to measure the level of antibodies developed during natural course of malaria infection in individuals of various age groups in different endemic areas. The study also aims to analyse the effect of immune pressure exerted by antibody on *P. falciparum* parasites by sera and immunoglobulin mediated growth inhibition *in vitro* and to determine the quantitative measurement of parasite invasion with variable level of antimalarial antibodies as a result of selecting subpopulation of parasites *in vivo* for maintaining parasite infection below threshold.

A total of 138 patients categorized into five epidemiological age groups were included in the study. *P. vivax* was detected in 35.5% and *P. falciparum* in 33.3% patients. Finger prick blood samples were collected by cross-sectional surveys during July to November of the years 2000 – 2004.

All the sera were tested for anti-malarial antibody by ELISA against defined peptides and crude erythrocytic antigens of P. falciparum. Sera of these patients demonstrated low, moderate and high level of antibodies against Pf-stage specific antigens-MSP1, AMA1, RAP1, EBA175 and infected erythrocyte lysate (Pf crude antigen). The effect of antibody positive pooled serum and immunoglobulin fractions with high ELISA O.D. values was assessed in P. falciparum culture by determining the merozoite invasion inhibition (MII) and parasite growth inhibition (PGI). The sera of responder group containing antibodies showed variable effect on parasite growth of two P. falciparum isolates. A positive correlation between MII and PGI of two isolates was observed. Sera containing high titre of antibodies reacted efficiently

in immunofluorescence assay. Reactivity was more pronounced with late trophozoite and schizont stages. Similarly, pooled antibody positive sera showed low to high intensity of colour development in dot blot assay.

Detection of Circulating Antigen, Antibody and Immune Complexes in Individuals of Endemic Area

Human blood samples collected from local malaria clinics, hospitals and by cross-sectional surveys in malaria endemic areas were tested by enzyme immunoassay for circulating malarial antigen, antimalarial antibody and antigen-specific circulating immune complexes. Assays were done in serum and finger-prick blood absorbed on filter paper. A total of 117 patients were screened for malarial parasite by microscopy; 54 were found positive and rest 63 were negative at the time of blood collection but they suffered from malaria in recent past. The ELISA tests for the detection of antimalarial antibody, circulating antigen and circulating immune complexes were done in 117 sera and FP eluates as a pilot study. The results of sera and FP eluates were comparable. Out of 54 malaria positive samples, 51 and 52 were detected positive for FC-Ag in sera and FP eluates, respectively indicating that the test has high diagnostic efficiency. Only 25-28% samples of negative group were detected FC-Ag positive due to very recent infection in these individuals. Antibody was detected in >90% malaria patients whereas in blood smear negative group about 86% showed sero-positivity for antimalarial antibody. The bound antigens in the form of CICs were detected more in malaria positive cases than the smear negative cases. The test parameters were



Fig. 10. Antibody, total circulating antigen, free circulating antigen and circulating immune complex profile in the study subjects (n = 240). The bar diagram is plotted with mean ELISA -log2 titre of each group
applied in 240 FP eluates collected from different age groups. The average antibody titre $-\log_2$ varied from 6–10. Both TC-Ag and CIC were found at lower level in younger age groups (Fig. 10). Although microscopic demonstration of malarial parasite in blood film is the method of choice to diagnose acute malaria, detection of circulating malarial antigens, antimalarial antibodies and immune complexes may help as supplementary tool for immunodiagnosis. When applied in a community-based study, these tests would be able to monitor infection dynamics.

Immune Responses to *P. falciparum* Antigens and Disease Susceptibility among Inhabitants Seasonally Exposed to Malaria

In malaria endemic areas, the acquisition of antimalarial immunity is progressive as observed by age wise gradual decrease of morbidity and mortality to malarial infection. This study was aimed to assess the relationship between *in vitro* immune responses and susceptibility to malaria based on a protective longitudinal study for one year. In the study, two groups of children, younger (1-<5 yr) and older (5-<15 yr) were enrolled in two areas (A-1 and A-2) of northern India where malaria is seasonal but the epidemiology is different. The frequency of humoral and cellular reactivity to six synthetic peptides (CSP, MSP1₁₉, AMA1, RAP1, EBA175 and PfG27) and crude blood stage antigen of *P. falciparum* was measured in the study subjects.

Individuals of A-1 showed very less number of malarial episodes compared to A-2 during one year. Clinical protection in children from A-1 was related to elevated levels of antibodies detected against CSP, MSP1₁₀, AMA1 and RAP1. However, anti-EBA175 antibody level was almost alike in two groups. Higher lymphocyte proliferation responses to MSP1₁₉, AMA1 and RAP1 peptides were observed in the study subjects of A-1 than A-2. The differences in T-cell reactivity as overall higher response rate of IL-4 and IFN-y but lower IL-10 and TNF- α to MSP1₁₀, AMA1 and RAP1 were observed in individuals of two areas. The immune responses among individuals of two ecotypes highlight the immunogenicity of the molecules, namely MSP1₁₀, AMA1 and RAP1 and their relation to clinical protection.

FILARIASIS

Applied and operational research for control/ elimination of filariasis is being continued at the Council's Vector Control Research Centre (VCRC) at Pondicherry and RMRC at Bhubaneswar. Major areas covered include development of microfilaricidal drugs, safety and efficacy of drugs for case management, mass drug chemotherapy, remote sensing, molecular biology and bioinformatics and estimation of disease burden.

Studies on Mass Chemotherapy

Comparison of Operational Feasibility and Impact of Co-administration of Albendazole and Diethylcarbamazine (DEC) and DEC Alone in Controlling Lymphatic Filariasis

The results of study revealed that it was operationally feasible to distribute the drugs to about 90% target population but the social mobilization was inadequate to improve the drug consumption rates up to the desired level of 80% in two districts in Tamil Nadu (Thanjavur and Thiruvannamalai). Supervised drug consumption has been only marginal. Compared to the baseline data, a significant reduction in mf density, prevalence, circulating filarial antigen (CFA) in the age group 6-10 yr and 20-25 yr and total geohelminth prevalence in both study districts in Tamil Nadu was noted. The relative change between the arms, however, was not significant in any of these parameters. In comparison to a significant decline in CFA prevalence, which was observed in the



Fig. 1. Change in circulating filarial antigen prevalence after 3 and 4 rounds of MDA with DEC alone



Fig.2. Change in circulating filarial antigen prevalence after 3 and 4 rounds of MDA with DEC+alb

co-administration district post-three rounds of MDA, it was observed only after 4th round in the DEC district, suggesting an edge of the co-administration as against DEC alone (Fig.1 and 2).

MDA Studies in Madurai

In studies undertaken at CRME, Madurai for evaluation of the role of vector control (VC) and MDA in filariasis elimination campaign, microfilaraemia prevalence (MFP) was found to be 0.58% and 3.02% in age group 2-5 yr and 15-25 yr respectively in MDA alone villages, while in MDA+VC villages nil MFP was noted in 2-5 yr age group. The antigenaemia prevalence (AGP) was 3 times lower in the MDA+VC arm as compared to MDA alone arm in both the age groups. In children MFP was maintained at zero level, while there was 71% reduction in AGP after 5 MDAs.

The vector control villages continued to demonstrate negligible vector density with nil transmission, both in resting and landing populations. In these villages, the per man hour (PMH) resting density during April 2005-March 2006 was 0.15. In villages without vector control the PMH density was 24.06 and the transmission intensity index (TII) was 0.1008.

In the WHO/TDR funded study at Tirukoilur, no MDA was carried out during the year. Longitudinal monitoring in the study villages indicated greater reduction in the prevalence and intensity of mf after 3 rounds of MDA in DEC+ALB arm compared to DEC alone arm. After one year of MDA IV, the cumulative COMMUNICABLE DISEASES

percentage reduction was similar (60%) in both the arms. But amongst the three age groups, 6-9 yr group showed higher MFP reduction in DEC+ALB arm alone. Decline in antigenaemia levels was observed in DEC+ALB arm, whereas age group 10-25 yr demonstrated 2 times higher reduction than the DEC alone arm. In a cohort of microfilaraemic survey, 85% and 79% subject were cleared of mf in DEC+ALB and DEC alone arms, respectively. Nil antigenaemia was recorded in DEC+ALB arm in children born after initiation of MDA (in 2 & 3 yr).

Vector mosquitoes, viz., *Cx. quinquefasciatus*, were collected resting in human dwellings (in 18 villages) and those landing on human volunteers (in 8 villages) every month. A total of 5826 and 5279 resting vector mosquitoes were dissected during the year following MDA IV in DEC+ALB and DEC alone arms respectively. There was an overall reduction of 90% and 88% in TII values after 4 MDAs. In landing collection, the average number of infective mosquitoes biting per month dropped from 4.6 to 1.9 after 4 MDAs in DEC+ALB and from 9.0 to 2.6 in DEC alone arm. In both arms transmission indices (TII & TP) were found to be low after MDA IV and the overall reduction of 90% and 88% was recorded in DEC+ALB and DEC alone arms respectively.

MDA Strategy in Urban Areas in Orissa

A study has been initiated by RMRC, Bhubaneswar to develop and test an innovative strategy for MDA to achieve high treatment coverage in urban populations. Initially formative research was undertaken to explore and identify opportunities in urban communities for development of strategy. A health services driven MDA strategy with community partnership and participation approach was developed and experimented in two endemic areas in Orissa. The intervention was evaluated by using several qualitative and quantitative methods during two rounds of intervention in 2004 and 2005. During first round of intervention, household coverage survey was undertaken in intervened urban area whereas in other urban and rural areas, MDA was done without such interventional strategy. Three indicators namely coverage (percentage of eligible people who received tablets), compliance (percentage of eligible people who swallowed tablets) and household coverage (percentage

of households visited by health worker during MDA) were used to evaluate the intervention. The intervened urban area recorded significantly higher coverage, compliance and household coverage than the nonintervened urban area, but nearer to that of the nonintervened rural area. Findings of the study.revaled that partnership approach involving various stakeholders is an innovative alternative method for addressing the problem of low MDA coverage and compliance in urban India. The MDA with local decision-making within the guidelines of program and local leadership is significantly more effective in urban communities than the department driven action. The innovative approach has potential to achieve desired levels of results in different strata of urban communities. It takes into account the specificity of the situation and thereby tries to address the socio-cultural peculiarities of different sub-groups and hence may be suitable for implementation in other urban areas in India.

Operational Research

Development and testing of new strategies for mass drug distribution (MDA) in urban areas was attempted in Chennai city. The first ever MDA of DEC in Chennai city was implemented in September 2004 by the Corporation. Evaluation of MDA in 20 randomly selected areas showed that 79.6% received DEC tablets and only 32.8% consumed it. About 19% of the people refused to consume the drug due to reports of side effects and deaths following DEC treatment.

The impact of annual mass administration of DEC alone or ivermectin alone, or co-administration of

DEC+ivermectin or DEC + albendazole on mf prevalence and vector infection rates was evaluated at community level. The impact of $\widehat{\mathfrak{g}}$ tenth round of mass DEC administration, weight (Mean <u>+</u> ninth round of ivermectin administration, seventh round of DEC+ivermectin administration and fourth round of DEC+albendazole administration was Disability evaluated in five villages each. The results suggest that even after 10 rounds of DEC, residual microfilaraemia and transmission continue to persist in the villages treated with DEC. Similar trend was observed after 7 rounds of MDA in DEC+ivermectin treated villages. The mf rate and intensity, which

increased in the absence of 9th round of MDA in ivermectin treated villages, declined after the 10th round of MDA. After four rounds of DEC+albendazole administration, the reduction in mf rate was 83% and no mosquito with infective stage larvae was found in any of the five villages. The results imply that (a) low levels of microfilaraemia continues to persist even after several rounds of MDA (b) the role of low density microfilaraemia needs to be understood in the resurgence of transmission and (c) progress from excellent control to elimination appears to be a long process.

Health Economics and Disease Burden Estimation

Disability weight is a key component of disability adjusted life years (DALYs), which quantifies the severity and burden of the disease. To assess and incorporate severity of the health condition, which varies with clinical manifestation, a descriptive system was developed from experts and patients using 7D5L instrument (7 health domains and 5 severity levels) for 7 health states of lymphatic filariasis. The patient had given higher scores than experts. According to experts, the disability weight for acute attack of adenolymphangitis (ADL) was found to be more than the disability weight for the chronic stages of lymphoedema and hydrocele. Disability weight was higher for lymphoedema than hydrocele. It increases with higher grades of lymphoedema and hydrocele. The community has given highest disability weight for lymphoedema grade IV (L4) as 0.85 and the least for hydrocele grade I (0.29). The disability weights for





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ADL, lymphoedema grade 1, grade II, grade III and hydrocele II were 0.74, 0.36, 0.44, 0.84 and 0.57 respectively (Fig. 3).

Estimates of burden of disease are important to prioritize health services, research and intervention measures in view of resource constraints. Estimation of national burden of disease (NBD) lymphatic due to filariasis (LF) was done using DALYs. The data on LF prevalence in 315 districts of which 269 are endemic, was



Fig. 4. DALYs' per thousand population in different states in India

available with National Filaria Control Programme. DALY was estimated state-wise using the descriptive epidemiological studies. The cases were distributed in 5 age groups in each gender. The DALY estimated using the disability weight given by the global burden of disease (GBD) study was 2.23 million, which is about 40 % of the global burden. Hydrocele contributed the maximum burden. The total DALY lost due to ADL was 0.01 million/episodes. The DALY/1000 population in each state is shown in Fig.1. DALY lost was maximum in the productive age group of 15-44 yr, contributing 54 % of total. DALY was estimated for each of the 7 manifestations of filariasis using the experts and community rated disability weights and it was 5.56 and 11.26 million respectively. Bihar recorded maximum DALYs followed by UP and West Bengal. These estimates are respectively 2.5 and 5 times higher than DALY estimated using GBD disability weight (Fig..4).

Molecular Biology and Bioinformatics

In order to determine infectivity rates of *Wuchereria bancrofti* in vectors for the assessment of transmission of filarial infection in endemic areas, infective stage-specific probes have been developed and validated at the VCRC. The stage specific RT-PCR

assay was found to be 98-100% specific and sensitive in detecting the infective (L3) stage in vectors. The assay will be an important and useful xenomonitoring tool for large-scale surveillance and monitoring of filariasis (Fig.5).



Detection of infective (L3) stage larvae of filarial parasite, *Wuchereria* bancrofti in its vector *Culex quinquefasciatus*

M - Molecular weight marker (100 bp); Lane 1, 3, 6, 9 & 10 - Positive s amples Lane 2, 4, 5, 7 & 8 - Negative samples ; Lane 11 - RT Negative ; Lane 12 -Positive control ; Lane 13 - Negative control.

Fig. 5. Detection of infective (L3) stage larvae of filarial parasite, W. bancrofti in its vector Cx. quinquefasciatus M-Molecular weight marker (100 bp); Lane 1, 3, 6, 9 & 10 - Positive samples Lane 2, 4, 5, 7 & 8 - Negative samples; Lane 11 - RT Negative;

Lane 12 - Positive control; Lane 13 - Negative control

In an attempt to develop a more sensitive immunodiagnostic tool that will also detect exposure to infection, monoclonal antibody (VCRC B5) has been developed at VCRC. The antigenic reactivity of this monoclonal antibody is being assessed by immunoscreening the infective (L3) stage cDNA library of *W. bancrofti*. Ten clones that showed antigenic reactivity are being sequenced.

Immunological Studies

Identification of a Novel Protective Antigen

GST enzyme was isolated from cattle filarial parasite, *Setaria digitata* to evaluate its role in human filariasis. IgG and IgM antibodies to GST were determined in individuals living in areas endemic for bancroftian filariasis. Ninety percent of infected individuals (asymptomatic microf-ilaraemic and chronic patients) demonstrated seropositivity for both the antibodies compared to only 20% of endemic normal population of a defined endemic community. IgE seropositivity of 80, 60 and 35% was observed in patients with chronic filarial disease, asymptomatic microfilaraemics and in endemic normals respectively. None of the sera collected from region non endemic for filariasis was found positive for any antibody isotype.

Innate Immunity in Filariasis

The association of TLR4 (Thr399lle) polymorphism with the parasitological status and chronic disease manifestations in filariasis was studied at RMRC, Bhubaneswar. TLR-4 (399) mutation frequency was significantly more in endemic controls in comparison to male patients with chronic disease indicating that TLR-4 mutation (Thr3999lle) could protect male human hosts from developing chronic filarial disease. Such an association of

TLR-4 (399) mutation was not observed in females. The study of such association of TLR4 mutation in common chronic disease manifestations *i.e.*, hydrocele (in male) and elephantiasis (in both male and female) indicated that mutation is associated with males only.

Development of Microfilaricidal Drugs

Out of 26 benzoyl piperazides, synthetic aromatic analogues of diethyl carbamazine, seven compounds were found to show promising activity *in vitro* against *Setaria digitata*, the cattle filarial adult worms. The compounds are being studied for *in vitro* and *in vivo* testing against human filarial parasites.

At VCRC, Pondicherry, two lead molecules exhibiting microfilaricidal activity have been identified from medicinal plants, *Plumbago rosea/indica* and *Trachyspermum ammi*. These molecules are currently being evaluated for *in vitro* and *in vivo* microfilaricidal activity at CDRI, Lucknow. The preliminary evaluation has confirmed the *in vitro* microfilaricidal activity of one of these molecules, naphthoquinone.

Glutathione *S*-transferase (GSTs) enzymes have been considered as good target for anti-parasitic drug



Fig.6.a The modeled 3D structure 1SJO of *bm*GST is given in Hex view

₩ GST MSYKLTYFPIRGLAEPIRLVLVDQGIKFTDDRINASDWPSMKSHFHFGQLPCLYDGDHQI BmGST MSYKLTYFPIRGLAEPIRLVLVDQGIKFTDDRINASDWPSMKSHFHFGQLPCLYDGDHQI

*WO*GST VQSGAILRHLARKHNLNGGNELETTHIDMFCEGIRDLHTKYAKMIYQAYDTEKDSYIKDI BmGST VQSGAILRHLARKHNLNGGNELETTHIDMFCEGVRDLHTKYTKMIYQAYDTEKDSYIKDI

##>GST LPVELAKFEKLLATRDDGKNFILGEKISYVDFVLFEELDIHQILDPHCLDKFPLLKAYHQ BmGST LPVEAAKFEKFLATRDDGKNFILGEKISYVDFVLFEELDIHQILDPHCLDKFPLLKAYHQ

Wogst RMEDRPGLKEYCKQRNRAKIPVNGNGKQ Brgst RMEDRPGLKEYCKQRNRAKIPVNGNGKQ

Fig. 6b.ClustalW sequence alignment of wbGST and bmGST. Comparison matrix: BLOSUM62; Gap open penalty: 12; Gap extension penalty: 4; Aligned score 98.1 % in 208 residues; Gap frequency 0.0%

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development. A model 3D-structure of the enzyme of the *W. bancrofti viz.*, *wb*GST, has been generated at VCRC by utilizing information on the amino acid sequences and applying automated comparative protein modeling and bioinformatics tools. The 3D structure of the filarial parasite *Brugia malayi* GST (Fig.6a) has been generated and compared with that of the modeled *wb*GST (Fig. 6b).

Developing Model Variants of LYMFASIM for Planning and Evaluation of Lymphatic Filariasis Programmes

LYMFASIM is a stochastic simulation model for lymphatic filariasis transmission dynamics of infection, disease and control. The model has been developed using data from an integrated vector management programme in Pondicherry. The validity of the model was tested against data from a different epidemiological



Fig.7. Observed and predicted trends in prevalence of microfilaria during and after 10 / 9 annual rounds of MDA with DEC/ ivermectin

setting in which 10/9 annual rounds of MDA with DEC/ ivermectin were carried out. The results of model fitting confirmed earlier findings in Pondicherry that immunity plays a role in regulating *W. bancrofti* infections in humans. Further, the model predictions indicated that 10/9 rounds of DEC/ivermectin based MDA with an average coverage of 65% will not lead to filariasis elimination (Fig.7). The predictions beyond the period of observation suggest that the trend will revert to the pre-MDA situation in about 15 yr.

Remote Sensing (RS) and Geographical Information System (GIS) for Control of Lymphatic Filariasis

A risk mapping of lymphatic filariasis has been created, based on geo-environmental risk model (GERM) in GIS domain. The 'risk map' created for Tamil Nadu region (Fig. 8) shows the areas where the transmission is likely or not. This will facilitate a geographically targeted approach for intervention



Fig. 8. Filariasis risk map for Tamil Nadu as predicted by the GERM

measures. Since the vector breeding potential at the micro level has been mainly due to man made features, and geo-environmental factors act as confounders, the level of agreement between the environmental variables and the risk of transmission is fairly good enough. The relationship between the model (predicted) and observed values was analyzed, using logistic regression and it was found that the model fitted well for the data indicating that the filariasis risk index (FRI) developed in this model was a significant predictor of "non-risk" status of filariasis in an area. The demarcation of the areas in terms of FRI, as being at 'risk' or at 'no-risk' derived from geo-environmental variables is highly advantageous, as one time exercise. This approach could be employed for delimitation purpose for any vast geographical area, in view of its rapidity, reliability and cost effectiveness.

Post-DEC Reactions in Human Bancroftian Filariasis: An Immunobiological Study in Orissa

A study was carried out at RMRC, Bhubaneswar to investigate the role of endosymbiont *Wolbachia* in mediating reactions after administration of DEC in infected human subjects. Three groups of patients [mf carriers (AS), subjects with chronic filariasis (CH) and cryptic infection (CR)] were treated with single dose of DEC to monitor reactions both clinically and subclinically by measuring inflammatory molecules *viz.*, TNF α , IL-6 and RANTES as well as to quantify *Wolbachia* to analyze correlation between them.

Concomitant Parasitic Infestation in Filariasis

The RMRC, Jabalpur conducted a study to look for concomitant parasitic infestation in filariasis. Stool samples (148) were collected from 338 subjects. About 27% individuals examined were found to be positive for filarial infection by Og4C3 ELISA and 29% showed filarial disease. About 41% inhabitants of the study area were suffering from filariasis. Of the total, 54 stool samples were found to be positive for at least one intestinal parasite. The commonest intestinal parasite found was roundworm. A higher percentage (42.6%) of individuals having intestinal parasites was positive for filarial infection compared to individuals without intestinal parasites.

LEISHMANIASIS

Visceral leishmaniasis (VL), transmitted by the bite of a sandfly, 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 the other states of the country. Research on various aspects of Kala-azar is being conducted mainly through the Council's Rajendra Memorial Resea]rch Institute of Medical Sciences (RMRIMS) at Patna.

Clinical Studies

Phase IV trial of Miltefosine in the Treatment of VL

The development of miltefosine (Impravido), the first ever-oral drug developed, is a historic landmark in the treatment of VL. An open, single-arm phase IV miltefosine WHO-ICMR sponsored study trial was conducted in field stations at 13 centres in Bihar to evaluate its use in patients with confirmed VL. At end of the 6-month post-treatment follow up period, 94% patients were free from signs and symptoms of VL while 6% showed relapse. Adverse reactions (vomiting and diarrhoea) occurred at a similar rate as in the prior phase-III trial with hospitalized patients. Most patients were without adverse event/reactions during the treatment period. The study demonstrated that oral miltefosine can safely and effectively be used in adult and paediatric patients under out-patient conditions.

Safety and Efficacy of Injectable Paromomycin in Patients with VL

Studies were continued to compare the safety of injectable paromomycin sulfate to amphotericin B when administered in the proposed dosage regimens and to compare the efficacy of injectable paromomycin sulfate to amphotericin B with regard to final cure rate at 6 months. A total of 667 patients (502 paromomycin and 165 amphotericin B) were randomized in 3:1 ratio, out of which 666 were treated. Initial cure was about 99% in both arms, whereas final cure was 94.6% in paromomycin and 98.8% in amphotericin B arm. Nephrotoxicity was observed in 5.3% subjects of amphotericin B arm only. In paromomycin arm, reversible ototoxicity was seen in 0.6% of the subjects.

Epidemiological Studies

Longitudinal Study of Asymptomatic Cases of VL in Bihar

To estimate the magnitude of asymptomatic cases of kala-azar in endemic area and long term follow up of the patients with estimation of self-cure, a total of 355 peripheral blood samples were collected from asymptomatic cases from endemic areas of kala-azar. During door to door visit, all individuals were subjected to clinical assessment. Peripheral blood was subjected to DNA isolation and PCR was performed from all isolated DNA samples for ITS region of the rRNA gene and a nested PCR was also done using the internal primers. A leishmania specific 600bp (approx) band was observed in positive cases. The PCR test was able to detect parasite DNA in 25 asymptomatic cases. DAT and rK39 tests were also positive in 39 and 24 asymptomatic cases respectively out of 355 samples.

Other Studies

Identification and Characterization of Intact Phosphoproteins of Leishmania donovani

Altogether 9 important proteins having molecular weight of 63, 42, 39, 32, 26, 24, 19, 17 and 13 have

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been identified with altered phosphorylation state. All these proteins showing intact phosphorylation gave strong reactivity against VL sera in Western blotting.These antigens are being studied with regard to their role in transmission of disease and also for their impact on immune response.

Field Evaluation of Novel Diagnostic Tests for VL

A study to evaluate the comparative efficacy of different immunological tests for the diagnosis of kalaazar, blood/urine samples from about 500 suspected VL cases from endemic areas were taken. The samples were subjected to freeze dried DAT, rK39, rK26 strip tests and KATEX. rK39 and DAT depicted acceptable sensitivity and specificity and can be useful immunological diagnostic tools for kala-azar in field set up.

Immunomodulatory Role of 63kDa *Leishmania* Antigen in the Promotion of IFNγ Response

The 63kDa stimulation of mononuclear cells from co-infection group of patients led to an increase in the CD4+ T cell counts from 6.37% to 15.60% (nearly twofold). There was an almost proportional increase in IFN- γ production from CD4+T cell population. The population of cells, other than CD4+ T-cells, secreting IFN- γ showed a slight decrease upon 63kDa stimulation. The results indicate that gp63 can inhibit HIV replication and can be a promising vaccine candidate.

Role of *Leishmania* Isolates from Responsive and Unresponsive Patients in IFN- γ and IL-4 Production by T-cells

In a study to evaluate host protective and disease promoter cytokines by sodium antimony gluconate responder and non- responder isolates *in vitro*, newly adapted non-responder showed faster growth and high peak mean density as compared to newly adapted responder parasites. The study characterized linkage between unresponsive strains of parasite with profound immunosuppression in VL patients compared to a responsive strain. The T-lymphocytes of unresponsive patients when stimulated with a responsive strain produced significantly higher IFNγ protective cytokines (Fig.1), which indicates presence of critical elements within a responsive strains, associated with protective immune response. On the other hand, unresponsive strains, when used to stimulate T-cells, resulted in production of more IL-4 from CD4 cells (Fig.2) establishing its linkage with disease progression.



Fig.1. Mean value of IFN-γ producing CD4+T-cells of nonresponder patients and healthy subjects by three categories of stimulations



Fig. 2. Mean value of IL-4 producing CD4+T-cells of nonresponder patients and healthy subjects by three categories of stimulations

Molecular Characterization of SAG Responsive and Unresponsive Kala-azar Isolates from Bihar

In order to assess the variation in SAG responsive and unresponsive isolates of kala-azar cases from Bihar, different clinical isolates (5 SAG responsive and 10 unresponsive) were mass cultured and DNA was isolated. ITS region of the rRNA gene was amplified from all the isolates. Amplicons were restricted with various restriction endonucleases such as *Taq* I, *Hha* I, *Hae* III, *Rsa* I, *etc.* Restricted fragments were hybridized with DIG-labeled probe. Hybridized bands were detected with non-radioactive detection digoxigenin kit. In PCR-RFLP analysis, out of 4 restriction enzymes *Taq* I demonstrated a band at 300 bp in SAG responsive cases but not in SAG unresponsive and PKDL strains.

PCR based Diagnosis of VLfrom Suspected Cases of Kala-azar in Bihar

Study was undertaken with objectives to develop a PCR based diagnosis of kala-azar from blood samples and to compare PCR results with conventional diagnostic methods. A nested PCR assay to detect parasite DNA in blood and aspirates from suspected kala-azar patients was done. Nested PCR primers encompassed approximately 600bp fragment internal to the ITS region of rRNA sequence. On amplification, the nested PCR primers could amplify parasite DNA from a significant number of samples that were negative in the primary reaction. Comparison of the results of PCR with of conventional diagnostic methods is in progress.

Determination of Amplification of Multi-drug Resistance Genes in *L. donovani*

Study was carried out at National Institute of Phamaceutical Education and Research, Mohali to determine the amplification of gene in arsenite resistant *L. donovani* promastigotes. Studies of the mechanistic aspects of resistance aimed at identifying certain key molecular targets for the reversal of the resistant phenotype were undertaken. However, no amplified gene could be detected in the arsenite resistant strain of *L. donovani* promastigotes. Further studies are needed to decipher molecular mechanism of resistance of *L. donovani* towards sodium m-arsenite.

Comparison of Treatment of Amastigote Macrophage Model of VL by Generic and Proprietary Amphotericin B

Study was undertaken to evaluate the efficacy of generic and proprietary amphotericin B for the treatment of VL. The peritoneal mononuclear cells from Balb/c mice, separated by Ficoll hypaque, were cultured and infected by *Leishmania* promastigotes (1:20) of different patients and subsequently treated with generic and proprietary Amphotericin B. Out of 12 *Leishmania* isolates in the culture wells of generic Amphotericin B, the amastigotes of 11 isolates were found negative while in the wells of proprietary

Fungizone and Amphotret all were found negative. The trend showed inferiority of generic product.

Remote Sensing and GIS for Identifying and Mapping Sandfly Distribution in Bihar

The distribution pattern of P. argentipes in endemic and non-endemic foci of kala-azar is very important from the disease transmission point of view. No attempt has ever been made to create a map of distribution of vector in Bihar. In this study, P. argentipes were collected from two study sites representing different types of eco-systems in Bihar. Eighteen villages in Patepur block in Vaishali district, one of the high endemic areas of kala-azar in North Bihar as endemic foci and 12 villages in Lohardagga block in Lohardagga district, as non-endemic foci, were selected for addressing and evaluating the use of satellite data for monitoring the macro-ecosystem, *i.e.*, specific vegetation cover and human settlement, and relating them with the changing conditions favourable for sandflies. Season wise data of temperature, humidity, vector density, incidence of VL cases and soil samples was collected through ground surveys carried out in the selected sites. Satellite data were analysed in silicon graphic image processing system using ERDAS software. The national differential vegetation index (NDVI) was used to distinguish the vegetative and non-vegetative areas. The preliminary analysis of both ground and satellite data sources included the construction of digital maps, which were overlaid on the digital environmental data and the relevant data for the collection sites using GIS software. Statistical analysis, showed significant correlation of vector density with variables like temperature, humidity, settlement, crop areas, moist fallow, dry fallow, minimum NDVI and standard deviation of NDVI. Multivariate regression analysis generated six models and the best model gave detailed mapping of sandfly density in both endemic and non-endemic sites. This model can produce a map of distribution of P. argentipes. Although, this model was based on data pertaining to two PHC/blocks of the state, it can be used for the prediction of vector density in other endemic areas of Bihar also. The map produced from the study could be of great use for planning and identifying areas of high vector abundance for vector control programmes such as localized and intensive indoor residual insecticide spraying.

VIRAL DISEASES

ENCEPHALITIS

Epidemic Investigations

Uttar Pradesh

Gorakhpur

In investigations done by NIV, Pune, cases of fever with CNS involvement were reported during July-August 2005 in Gorakhpur mainly in pediatric age group. IgM antibodies to JE virus could be detected in 42 out of 65 cases. JE virus was isolated from one patient by PBMC co-culture method and confirmed by MAb binding and RT PCR. MAb reactivity has revealed that the isolate has lost reactivity of one of the neutralizing MAb.

Raebareli

Outbreak of acute encephalitis was investigated from Raebareli (UP) in August, 2005. Majority were children but few adults were also infected. A total of 83% serum samples collected from 32 patients were positive for JE by MAC ELISA (22/28 sera and 10/13 CSF). Water stagnation and dry areas were interspersed in the region. This is the first report of JE from Raebareli.

Maharashtra and Andhra Pradesh

Four outbreaks of acute viral encephalitis (2 from AP and one each from Maharashtra and UP) among children were investigated. Association of Chandipura virus (PCR positivity) and presence of IgM antibodies to this virus was demonstrated in cases of acute viral encephalitis among children from AP and Maharashtra.

JAPANESE ENCEPHALITIS

Entomological and Serological Studies for Developing Forecasting Model for JE

Japanese encephalitis (JE) is the most important cause of viral encephalitis in eastern and southern Asia with 30,000–50,000 cases reported annually and JE epidemics occur in entire South East Asia regularly every year. However, at present, there is little national capability of facing JE outbreaks and most of the measures that are undertaken during the epidemics COMMUNICABLE DISEASES



Fig.1. Seasonal abundance and JEV infection in *Cx. tritaeniorhynchus* in Kurnool district

are of little consequence in view of high morbidity and mortality. There is, therefore, need of a reliable early warning system to forecast JE outbreaks. The Centre for Research in Medical Entomology (CRME), Madurai and Indian Institute of Chemical Technology (IICT), Hyderabad collaborated on a research project to develop a forecasting model for impending JE epidemics. This was accomplished through entomological and serological studies in Kurnool district which is one of the highly JE endemic districts in Andhra Pradesh. A total of 2235 female mosquitoes were collected in dusk collections in urban areas. Cx. tritaeniorhynchus was the dominant species comprising 74.9% of the total samples collected, followed by Cx. gelidus (20.1%), Cx. quinquefasciatus (2.75%) and An. subpictus (1.27%). In rural areas, a total of 6786 mosquitoes belonging to 4 genera and 9 species were collected in dusk collections: Cx. tritaeniorhynchus (84.8%), Cx. quinquefasciatus (7.5%) and An. subpictus (5.38%). Cx. gelidus, which was common in urban areas, constituted only 0.6% of the total catch in rural areas (Fig.1). Abundance (females /man hour) of major JE vector Cx. tritaeniorhynchus was lowest in hot summer months (May and July) but peaked in November in rural areas and in September in urban areas.

The per man hour (PMH) density of *Cx. gelidus* peaked in the month of September in urban area and November in rural areas. However, *Cx. gelidus* abundance was found to be very low in rural areas when compared to that in the urban areas. Natural JE virus infection was found in *Cx. tritaeniorhynchus* and *Cx. gelidus*. Two pools of *Cx. tritaeniorhynchus* in September 2005 and six pools in November 2005 were

found positive for JE virus. Cx. gelidus collections, one pool each in September and November 2005, were found positive for JE virus, indicating active transmission in the study area. Sera of school children (6 to 10 yr old) were examined by HI test for flavivirus antibodies (JE/West Nile/dengue). For this, 250 blood samples were collected prior to JE transmission season in November 2005; another 250 blood samples in post JE transmission season in March 2006 were collected which are being processed.

Vector abundance and JE virus activity was monitored longitu-dinally from the endemic villages of Cuddalore district, Tamil Nadu. Two peaks of abundance of Cx. vishnui subgroup mosquitoes were observed; the October 2005 peak being very prominent with 653.75 PMH and a comparatively less prominent in January 2006 (447.50 PMH). Overall minimum infection rate (MIR) decreased this year from 0.714 to 0.386. JEV infection was found in the vectors in all the alternative months from May 2005 onwards. MIR during the months of May and August was 6.667 and 2.105 respectively.

Total protein of Toxorhynchites splendens was resolved and blotting experiment was carried out. Virus overlay protein binding assay (VOPBA) was done with JEV antigens and JEV monoclonal antibodies. The JEV antigen was found to bind to a putative 32 kD protein



protein, immune serum was raised in rabbit. In order to examine the necessity of the receptor for virus binding, attempts are being made to block the Fig. 2. Detection of JE virus receptor protein of JEV

Tx.

(Fig. 2). Further, to

characterize the 32 kD

of

splendens

binding protein of Tx. with the rabbit immune splendens by virus overlay serum.

siRNA as an Antiviral against JEV

At NIV, a mixture of siRNAs directed against core, envelope and NS5 genes was found to be effective against JE virus when cells were treated with siRNA prior to exposure to virus. Considering earlier data,

siRNA treatment proved to be effective against acute and persistent infection of cells with JEV.

Tissue Culture Inactivated Vaccine against JE virus

An Indian strain of JE virus (014178) obtained earlier from Lakhimpur-Kheri (UP) was successfully adapted to Vero cells at NIV, Pune. The inactivated vaccine developed using this strain induced protective immunity as revealed by lethal challenge both by peripheral and intracerebral route. The vaccine induced the neutralizing antibodies.

In silico Sequence and Structure-based Antigenic Analysis of the Envelope Glycoprotein of Indian **Strains of JEV**

Prediction of the 3-D structure of the envelope glycoprotein of the JEV (Bankura & Vellore strains) in its native dimeric form was carried out at NIV using homology-based modelling. The dengue type 2 envelope protein crystallographic structure was used as a template. Further modelling the E138K in the Bankura strain resulted in change of the surface charge distribution from negative to positive which resulted in inhibition of protein binding to the cell membrane and subsequent loss of virulence of the virus. In case of the Vellore strain, the mutation G153W near the glycosylation site Asn154, resulted in a secondary structure conformational variation. This conformational change may in turn be responsible for affecting the glycosylation process.



Fig.3. Breeding habitats of JE vectors in Gorakhpur

JE Epidemic Investigation in Gorakhpur

During 2005 Gorakhpur faced a devastating JE epidemic outbreak affecting 6097 individuals with 1398 deaths. In intensity and magnitude, this epidemic surpassed all previous reported epidemics. A team from CRME visited Gorakhpur in November, 2005 to carry out ento-sero-epidemiological investigation during the course of the epidemic. Mosquitoes were collected after dusk with the help of aspirator from cattle sheds and pigsties and transported to the laboratory for identification and enumeration. Larval survey was conducted in different habitats like rice fields, irrigation canals, fallow fields, rice field pools, ponds (with water hyacinth), rain water pools, grass lands, cess pools, mud pools and paddy fields (Fig. 3).

A total of 14 different species of mosquitoes namely Cx. tritaeniorhynchus, Cx. vishnui, Cx. pseudovishnui, Cx. fuscocephala, Cx. gelidus, Cx. quinquefasciatus, Mansonia annulifera, Ma. indiana, Ma. uniformis, An. barbirostris, An. hyrcanus (gr) and An. peditaeniatus were collected. Cx. vishnui subgroups and Cx. gelidus, the primary vectors of JE, consisted 13% of the total mosquitoes collected. Wild-caught female mosquitoes were tested for JE virus by using antigen capture ELISA and insect bio-assay. All mosquito samples tested were found negative for JE virus.

Intravenous blood samples were collected from the patients clinically diagnosed as encephalitis and admitted in the district hospital, Gorakhpur. The age distribution of patients ranged from 8 months to 10 yr and majority of the patients (65.6%) were female children. All the specimens were refrigerated and transported to CRME laboratory on ice. The samples were tested for JEV-IgM antibodies by using MAC ELISA kits. All the 32 samples were found negative for JEV-IgM antibodies in both tests. The results were confirmed with MAC ELISA kits obtained from NIV, Pune.

DENGUE

Prevalence of Dengue in Jabalpur

The RMRC, Jabalpur conducted a study to assess the prevalence of dengue vectors in different seasons and their potential breeding habitats. In all, 6422 household were surveyed in different months and 25300 water holding containers were checked. Prevalence of *Aedes* species was not uniform in all the areas. Values for all the indices were significantly higher in Gwari Ghat area compared to other three areas and was lowest in SBI colony. Breteau index was higher than the threshold level in Gwari Ghat. *Aedes* infestation was recorded in all the seasons and in all the areas. Higher values were recorded in monsoon months followed by post monsoon months. (The trend was not uniform in all the areas (Fig. 4). Container Index (CI) was significantly less during summer season.



Fig.4. Season-wise Breteau, House and Container Index in Jabalpur

Study indicated that *Ae. aegypti* is present in all the seasons and in all parts of the city with peak prevalence during monsoon months. The specimens analyzed so far show that dengue is not an immediate threat. However, there is a need to be vigilant because of perennial prevalence of vector.

Dengue in Kolkata

Studies were conducted by NIV to determine the serotype of the dengue virus that caused a massive outbreak in Kolkata in September 2006. The ratio of males to females was almost one. The age group most affected was 18-24 yr. The samples collected were exclusively from the OPD and 58% of the cases were confirmed to be dengue by either MAC-ELISA or RT-PCR. Dengue 3 was detected in 12 clinical samples by multiplex RT-PCR. Two isolates were obtained which were confirmed to be DEN-3 and were found to be very similar to the Delhi 2003 virus.

Dengue and Dengue Haemorrhagic Fever (DHF) in Rajasthan

At DMRC, Jodhpur study was completed in five physiographic regions of Rajasthan – desert region

(Area I), hilly region (Area II), foot hills region (Area III), forest and river region (Area IV) and saline river region (Area V) in winter season. Data gathered from 20 villages and 5 towns, within 6581 houses (1612 urban and 4806 rural), involving human population of 37,525 inhabitants (8789 urban and 28,736 rural) were analyzed. Following observations emerged from the study :

- For developing a surveillance design for the status report of dengue vectors and viruses for a given area, regional level plans for each socio-ecological area are required which may involve separate rural and urban surveillance schemes. A generalized plan is not likely to be effective. In each of villages and towns, owing to socio-economic and ecological conditions, water storage habits of inhabitants differ and hence domestic vector surveillance has to be based on these criteria of villages/towns.

- For rural areas e-rains are best periods for adult surveillance and control operations thereof in desert, hilly and foot hills regions of Rajasthan whereas for forest and saline river ecosystems post rains are better months for adult surveillance.

- For urban areas reverse situation exists *i.e.*, in hilly and foot hills pre-rains is the better period for mosquito surveillance while for forest and saline river regions, post rains is the suitable period.

- Among all the types of containers examined, *Ae. aegypti* emerged as the dominant species and should be a target species for designing control strategy.

- In desert and hilly areas, pre-rains is the period of occurrence of disease whereas in forest, foot hills and saline river areas, post rain is the preferred time for disease appearance. This observation forms an important aspect for designing suitable disease prevention/management measures.

- Highest Adult House Index (AHI) of *Ae. aegypti* has been encountered during winter (17.4 %) in urban areas whereas seasonal difference in AHI was not observed in rural areas. However, sero-survey showed no active dengue cases during winters.

Acute Haemorrhagic Fever in Kalyan

An outbreak of acute hemorrhagic fever from Kalyan area was investigated in August 2005 with

clinical features of fever, bloody vomit and death in adults. Post mortem (PM) findings showed grossly haemorrhagic lungs, kidneys and necrotic liver. Sera and organs from dead patients, inoculated in suckling mice and cell culture did not yield any virus. Only one of 51 sera samples was positive for dengue.

Haematologically Important Binding Motifs in Dengue Type 2 Virus and Other Haemorrhagic Protein Families

Studies using sequence alignment and pattern search techniques at NIV revealed a CD36-related thrombospondin 1- binding motif in the dengue E protein at the C-terminus ectodomain region. Further, a Zinc-binding metalloprotease-like motif and a disintegrin-like motif reported in haemorrhagic snake venom toxins, was found to be present in the dengue E protein. Variants of these motifs were found in other flaviviruses. None of the motifs were found in the envelope protein of representative alphaviruses.

Disease Burden Study

Baseline data for designing a disease burden study was collected by NIV, Pune. Clinical profile indicated 25% DHF cases. The age/sex distribution indicated largest affected group to be 18-24 yr old males in Pune. Presence of multiple serotypes (DV-1, 2, 3) was established in Pune. Assessment of the cytokine levels in dengue cases revealed IFN- γ and IL-8 to be elevated in all dengue cases irrespective of the disease status while TNF- α and IL-6 were seen at increased levels in a few clinical categories. Passive surveillance in Maharashtra and other states revealed dengue IgM positivity in 488 of the 3984 serum samples.

Effect of Dengue Viruses on Hematopoietic Stem Cell Differentiation and Hemostatic Properties of Vascular Endothelial Cells

Donor platelets exposed to dengue 2 virus (Tr1751 strain) showed evidence of physiological activation and loss of collagen-induced inhibition. Further studies are ongoing to characterize this at a cellular and molecular level. *In vitro* human megakarocyte differentiation from hematopoietic stem (CD34+) cells were standardized for studying effect of dengue viruses.

COMMUNICABLE DISEASES

Vector Surveillance

Entomological investigations following outbreaks with suspected virus etiology were conducted in Muzaffarpur (Bihar), Ahmedabad (Gujarat), Bhandara and Nagpur (Maharashtra) and Bhubaneswar (Orissa). DEN virus antigens were detected only in *Ae. albopictus* collected by RMRC, Bhubaneswar. Field investigations were conducted in extensive field areas of six districts in AP following widespread epidemics. Profuse breeding of *Ae. aegypti* was noted in 20 affected and four unaffected villages. Only one village showed DEN antigen positivity

CHANDIPURA (CHP) VIRUS

Real Time PCR Assay

PCR assay was standardized employing primers and probes targeting the conserved regions of G gene. The real time PCR was found to be most sensitive.

Cloning and Expression of CHPV Gene

The entire G gene of CHPV was cloned and expressed using baculovirus expression system at NIV, Pune. Comparison of recombinant G protein (rGp)based ELISA for the detection of IgG-anti-CHPV antibodies with *invitro* neutralization assay employing 494 human and 251 pig sera collected from an endemic region documented 99.1% sensitivity and 90.7% specificity.

HLA Typing

Analysis of a total of 45 samples from Chandipura encephalitic paediatric cases revealed that the frequency of alleles, namely, HLA A2. HLA A3, HLA A26 and HLA A28 significantly increased in these children compared to healthy racially matched controls.

Susceptibility and Pathogenesis of CHP Virus in Animals

Age dependent susceptibility was studied in laboratory animals. Permanent sequelae developed mice were able to survive till their natural death. Ten day old rats were found suitable animal hosts/models for Chandipura virus by subcutoneous (SC) route. Strain of mice with yellow coat colour was found highly susceptible as compared to other stains of mice. This strain can be used to isolate the virus from the field samples. Adult homozygous athymic nude mice were found susceptible whereas their heterozygous siblings were found non-susceptible by SC route. Furthermore, early/young age heterozygotes (nu/+) were found more susceptible as compared to their homozygous (nu/nu) siblings.

Role of Viral and Host Factors in Pathogenicity

The role of virus in pathogenicity was studied in susceptible (15 day old), 50% susceptible (25 day old) and non-susceptible (60 day old) animals. Viremia and high virus titer in brain was noticed in susceptible animals, lower titers in 50% susceptible animals and undetectable level of virus titer in non-susceptible animals. It was found that IgG sero conversion is necessary to protect the animals from infection. Microarray was done to find out the mechanism involved in resistance. Analysis of first 50 upregulated genes indicated involvement of toll like receptor signaling and cytokine-cytokine receptor pathway. According to the results, virus binds to TLR4 receptor and nitric oxide induced by lipopolysaccharides inhibits the virus replication.

Ecological Studies

Ecological studies on CHP virus continued in Karimnagar and Warangal districts of AP. Blood meal analyses of sandflies showed differences in hosts preferred by each species *viz.*, *Ph. papatasi* fed predominantly on man, cow and fowls and *Ph. argentipes* on cows; The *Sergentomyia* spp were found to be negative for any of the blood meals tested. Studies to determine the reservoir for CHP viruses indicated 24.5% sero positivity of N antibody in 310 mammals trapped (*Mus* spp 49%, *Rattus rattus rufescens* 23.6%, *Suncus murinus-*29.5%).

HEPATITIS

Hepatitis **B**

Detection of Precore Mutants of Hepatitis B Virus by Ligase Chain Reaction in Patients of Chronic Liver Disease

Hepatitis B is one of the major and common causes of chronic hepatitis. Mutants of hepatitis B virus have important clinical and therapeutic implications. The most common pre c/c mutant is a point mutation from G - A at nucleotide 83 in the precore region of HBV genome. The most sensitive and specific method to detect these mutations is sequencing, which is expensive and time-consuming. One of the simple and reliable alternative methods is ligase chain reaction (LCR).

A study to evaluate the presence of HBV precore mutants by LCR in patients of chronic liver diseases has been completed at Maulana Azad Medical College, New Delhi. Results of the study revealed that precore mutant was responsible for more active liver disease as well as hepatocellular carcinoma (HCC). About 16% patients of Asian Indian origin were seen to suffer from mutant virus.

Role of Host Genetic Factors in HBV Infection in Family Contacts of HBV related Liver Disease Patients

Prevalence of chronic HBV infection in India is around 4.7%. HBsAg prevalence in close family contacts of patients with chronic liver disease is reported to be around 17-20%. A study was completed at G.B. Pant Hospital, New Delhi to determine the prevalence of HBV infection amongst the siblings and family contacts of index patient (first person in the family who presented with chronic HBV infection) and study the role of host genetic factors in relation to persistence and outcome of HBV infection. Results of the study suggest that family contacts of chronic HBV infected patients are at a much higher risk of acquiring the infection. HBsAg positivity is also observed to be much higher in such contacts. Genotypes A and D were found predominantly in Indian patients and their contacts. However, sequencing results revealed evidence of existence of recombinant genotypes in Indian patients. Besides, identical genotypes as well as surface gene mutations were found in patients and their contacts suggesting a horizontal intrafamilial mode of transmission.

Hepatitis E

Investigation of Epidemics

A total of 558 samples representing 17 epidemics of viral hepatitis from Maharashtra were screened at

NIV, Pune. Sixteen epidemics were attributed to HEV while one was caused by HAV.

Hepatitis E Vaccine

To develop candidate hepatitis E vaccine, DNA, DNA prime-protein-boost and DNA+corresponding protein+liposome-based approaches were attempted using the complete ORF-2 and a small portion within ORF-2 containing neutralizing epitopes (NE). For achieving high anti-HEV titres, gene gun-based immunization was superior for ORF2/NE-DNA vaccine. All approaches yielded significant anti-HEV and cellular response in mice. With the ORF2-liposome preparation, high titres of anti-HEV antibodies were observed on 12th day after first dose. The efficacy of different approaches/preparations was assessed in rhesus monkeys. The monkeys receiving 3 doses of DNA vaccine remained negative for anti-HEV antibodies. Excellent immune response was observed in monkeys receiving 2 doses of NE-DNA and one dose of NE protein and NE DNA+protein+liposome in 2 doses. The results demonstrated NE DNA and protein encapsulated in liposome to be an excellent candidate vaccine needing efficacy trials in humans.

Cytokines in Hepatitis E

ELISAs were carried out for quantitation of IL-4 and IL-12 cytokines in 57 acute-recovering hepatitis E patients including sequential samples collected from 16 patients, 14 fulminant hepatic failure in hepatitis E (FHFE) cases and healthy controls. IL-4 levels remained within normal limits in all samples. Higher IL-12 levels were recorded during the initial stage of self-recovering patients and in disease and after recovering from encephalopathy. Real-time PCR-based quantitation of plasma HEV RNA documented absence of the virus among fatal FHFE cases. Employing 15 sets of primers, full genomes were amplified and sequenced from two FHFE cases.

Multiplex Nested RT-PCR

For simultaneous detection of HAV, HEV and entero viruses, multiplex nested RT-PCR was standardized. A real time PCR for HEV viral load determination was standardized. The sensitivity of this assay is 10 copies of HEV type I RNA / reaction. Efficiency of membrane filter based virus concentration system was documented to be > 90%.

ROTAVIRUS

Rotavirus Surveillance

To estimate the proportion of rotavirus diarrhoea among children <5 yr, fecal specimens were collected from a total of 299 children suffering from acute diarrhoea. Thirty percent hospitalized children showed presence of group A rotavirus in their stools while none of the specimens from children visiting OPD was positive. Among ELISA positive samples, typing for VP7 gene indicated predominance of G1, G2 and G9 and typing for VP4 gene indicated higher prevalence of P[8] and P[4]. Adolescent and adult fecal samples were collected from 56 cases of acute gastroenteritis visiting OPD. ELISA/RNA PAGE positivity for rotavirus was detected in 7.14% specimens. Among these specimens G4 P[4], G9 P[4] P[8], G1 P[8] and G2G4 genotypes were detected.

Avian Rotavirus

In studies done at NIV, Pune 60% field chicken serum samples tested anti-rotavirus antibody positive indicating exposure of birds to avian rotavirus/similar agent circulating in Pune. Cultivation of avian rotavirus strain CH2 in embryonated eggs was carried out using yolk sac, amniotic, allantoic, allantoic + amniotic and chorioallantoic membrane routes for inoculation of virus. Presence of virus was visualized by immunoelectron microscopy while presence of viral RNA were detected by RT-PCR.

Preparation of Egg Yolk Antibodies against Human Rotaviruses

The birds vaccinated against human/poultry pathogens produce eggs having yolks with high level of antibody protein IgY. Three groups of SPF hens, each consisting of 7 birds were immunized at bi-weekly interval against human rotaviruses HRV1, HRV2 and HRV9 using 100µg dose. Sera collected were tested by ELISA to detect anti-rotavirus antibodies. All birds generated anti-rota antibodies. Western blot carried out using HRV9 showed presence of antibodies against major structural proteins (VP6/VP7/VP4) in birds sera.

MEASLES

Measles in Cuddalore in Tamil Nadu

During tsunami disaster, thousands of people were displaced causing major population movement in shortest time. On subsequent follow up, 101 cases of measles were detected in Cuddalore district. Mean age of affected individuals was 5.1 yr (range four months to 21 yr). A total of 39 % cases were above 5 yr old. RT-PCR and sequencing revealed measles genotype D8.

WHO Measles Genotyping Project

The project was initiated for genotype mapping of indigenous measles strains circulating in various parts of India and a voluntary participatory network of 16 centres in India was created as Measles Net India, Measles outbreaks from Satara (Maharashtra), Manipal (Karnataka), Patna (Bihar), Port Blair (Andaman & Nicobar) and (Chandigarh) and sporadic samples from Pune (Maharashtra) and Bijnor (Uttar Pradesh) were investigated. A total of 112 serum, 58 throat swab, 15 oral fluid and 35 urine samples were collected during this period. From these specimens, 22 sequences were detected and added to the NIV Indian measles sequence database. D7 was the new genotype detected for the first time in India.

Measles N gene Sequence from Brain of SSPE Patient

An 18-year-old adult male from North Karnataka presented at NIMHANS, Bangalore with weakness of right side of the body for 2 weeks, altered sensorium for one week and seizures for 3 days. NIV investigations detected serum IgM antibody against measles. Autopsied brain tissue sample was subjected to RT-PCR and sequencing. Results showed the presence of viral RNA in this tissue. Further sequencing of PCR positive product and phylogenetic analysis revealed the presence of measles genotype D7.

WHO Measles Aerosol Vaccine Trial

NIV was selected as the principal site for WHO-ICMR phase 1 vaccine trial on safety of an aerosol attenuated measles vaccine (open, non-controlled, sequential trial, by age group), for a period of two years.

NDIAN COUNCIL OF MEDICAL RESEARCH

NIV measles laboratory has been recognized as Central Measles Reference Laboratory for all three sites at Pune, Kolkata and Chennai. This laboratory participated in international efforts along with 6 global laboratories for standardization of procedures in measles vaccine trial.

INFLUENZA

Virological Surveillance

Influenza virus surveillance undertaken by NIV, Pune revealed that between April 2005 and March 06 virus strains, A (H1N1), A(H3N2) and type B similar to A/New Caledonia/20/99, A/Wyoming/3/03 and B/Sichuan/379/99 and B/Hong Kong/330/01 were circulating in Pune.

Avian Influenza in Navapur

The outbreak was investigated for bird flu in Navapur in February, 2005. NIV team played various roles and assisted in creating the isolation facility in rural hospital setting, training the staff in use of protective devices, established the bird flu OPD, monitored the suspected avian influenza patients admitted in isolation ward, established the quarantine procedures, initiated community surveillance, monitored culler's health, investigated the egret deaths, surveyed the water reservoir sites and collected migratory bird specimens for establishing the chain of transmission. Samples from suspected human avian influenza patients were screened by RT-PCR, real time PCR and virus isolation. H5N1 was not detected in any of the human samples tested.

Multicentre Influenza Surveillance

Analysis of 153 strains of influenza viruses isolated at the five regional centres in India indicated influenza virus circulation all through the year with different seasonality for each centre. Isolates were obtained from all age groups with maximum number of strains isolated from children of age 1-10 yr. Only one antigenic variant of A (H1N1), 5 of A(H3N2) and 5 of type B were circulating in Indian community. Sequence analysis of the HA1 gene indicated 95-99.79% homology. Study of M2 gene of 22 influenza A viruses from Pune indicated no substitution at any of the positions responsible for amantadine sensitivity.

Epitope Mapping

Studies using three groups of MAbs with varying immunofluorescence assay (IFA) pattern in ELISA additivity test delineated three non-overlapping distinct epitopes on N protein of influenza A(H3N2) virus. Year wise analysis of three epitopes on the N protein among the H1N1 and H3N2 strains isolated over a span of 28 yr in Pune indicated predominance of different epitopes in different years without any definite pattern.

Respiratory Syncytial Virus (RSV) Studies

Genetic analysis of nine HRSV strains isolated in 2002 and 2004 showed clustering in genotype GA5. Genotype specific substitutions could be identified in all the genotypes when compared to prototype strain A2.

CHIKUNGUNYA (CHIK) VIRUS

Outbreak Surveillance

A large-scale outbreak causing fever and arthralgia/arthritis in humans (>15 yr age) from 8 districts of AP was investigated. CHIK virus was demonstrated by PCR and IFA in the acute serum samples and IgM antibodies to CHIK virus confirmed that the outbreak was due to CHIK virus. Explosive Chikungunya outbreaks were confirmed for the first time in Karnataka in 15 districts upto March 2006. Specimens were collected and received from 1199 cases. CHIK diagnosis was made by virus isolation in 65.3% cases and by IgM presence in 33.7% cases.

Serology Studies

Samples from patients with arthralgia were received from different states and were tested simultaneously for dengue and CHIK IgM. Maharashtra (281/662), Karnataka (170/524)and AP (251/565) were found to be the affected states.

Vector Surveillance

Evidence of Chikungunya in vector mosquitoes was found in Solapur, Beed and Aurangabad districts of Maharashtra; parts of AP and Bidar and Bellary districts of Karnataka.CHIK virus was also isolated from *Ae. aegypti* pools.

POLIOVIRUS

During the period under report no wild poliovirus was isolated from any of the 1459 stool specimens from 729 acute flaccid paralysis (AFP) cases and 36 contacts of AFP cases. Virological results of AFP cases revealed polio vaccine virus (30), NPEV only (246) and negative (453). In contacts there were polio vaccine virus (6), NPEV only (15) and negative (15). Last wild poliovirus in Karnataka was detected in February 2004 and no wild virus has been isolated since then.

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

Increasing number of AIDS cases would require more questions to be addressed in terms of opportunistic infections, treatment of AIDS and preventing transmission. The Council's National AIDS Research Institute (NARI) at Pune continued epidemiological, clinical, immunological, virological and socio-behavioural studies on various aspects of HIV/AIDS.

Epidemiological Studies

Mapping, Size Estimation and Integrated Behavioural and Biological Assessment (IBBA) in High HIV Prevalence Settings in India

A study is being undertaken with the objectives to collect data in selected districts of the *Avahan* project states of Andhra Pradesh, Maharashtra, Tamil Nadu, Karnataka, Manipur and Nagaland and along the National Highways to address the following issues:

- 1. Major outcomes and impacts of the interventions funded by the Bill & Melinda Gates Foundation under the *Avahan* India AIDS Initiative by collecting behavioural and biological trend data in populations targeted by the interventions.
- 2. Estimating sizes of populations targeted by the project.
- 3. Modeling the impact of the intervention by a partner organization under *Avahan*.

The ICMR Institutes implementing the study are NARI, Pune, National Institute of Epidemiology (NIE), Chennai, National Institute of Nutrition (NIN), Hyderabad, RMRC, Dibrugarh, and National Institute of Medical Statistics (NIMS), New Delhi.

The mapping exercise is being carried out to assess the specific target groups-female sex workers (FSWs), men having sex with men (MSM), *Hijaras* and injecting drug users (IDUs) – for sampling frame development. The sampling frame is developed by considering each primary sampling unit. In majority of the places time location cluster sampling is being used and in some places the conventional cluster sampling is being adopted as per the need and rationale of the strategy. Respondent driven sampling is employed in select districts where the target population is hidden and difficult to reach. Data collection is under progress in various districts selected for the survey.

Evaluation of the Safety and Immunogenicity of an HIV Vaccine

The primary objective of the first phase I preventive HIV vaccine trial in India is to evaluate the safety and immunogenicity of increasing intramuscular doses of tgAAC09 and the secondary objective is to evaluate the impact of pre-existing immune response to AAV-2 on immunogenicity of tgAAC09. The screening process for the study was initiated in January 2005. Total 99 screening evaluations were performed on 80 potential volunteers. Forty subjects fulfilled the eligibility criteria for study participation. The enrolment was initiated in February 2005 and completed in January 2006. Thirty subjects have been enrolled in three dosage groups of tgAAC09.

The vaccine appears to be safe and well-tolerated at all dosage levels. The low and mid dose group volunteers have completed their study participation. The volunteers in the high dose group will complete the study follow up by January 2007.

Changes in Haemoglobin Level among AIDS Vaccine Trial Participants

The impact of repeated blood draws on haemoglobin levels among the HIV vaccine trial participants was assessed. The mean baseline haemoglobin level among 16 male and 14 female

volunteers was 14.9 and 12.8 gm% respectively. The average cumulative fall of haemoglobin was 0.14 increasing gradually to 1.28gm. The range of fall among males was 1.5 to 3.3 gm% and 1.2 to 2.6 gm% in female participants. However, this drop was of no clinical significance. Cumulative slope for haemoglobin drop was higher in males than females. Volunteers with higher baseline haemoglobin showed higher drop than those with lower values, irrespective of gender. Six of the 9 hematinic recipient women showed rise in haemoglobin levels. Repeated large blood draws did result in significant drop of haemoglobin in a majority of volunteers. Possible contributory factors like bleeding, nutritional deficiencies, concomitant drug use and parasitic infestations should be investigated.

Phase II Vaginal Microbicide Study using Praneem Polyherbal Formulation

The objective of the double blind randomized phase II study of Praneem (a polyherbal vaginal tablet) was to assess the long-term safety following six months of intra-vaginal use with each act of sex. Between July 2004 and August 2005, 142 women were screened and of them, 100 eligible participants were enrolled in the study. Participants were randomly allocated in equal proportion to the Praneem and placebo groups (50 in each group). The baseline characteristics of women enrolled in the two study groups were similar. The last follow up was completed in February 2006 and decoding in April 2006. Detailed analysis of the unblinded data is in progress.

Acceptability of PRO 2000 Vaginal Gel among HIV Un-infected Women

A study was conducted to assess the acceptability of PRO 2000 Gel among women during phase I safety clinical trial. Acceptability was assessed by quantitative and qualitative methods among 41 women. The overall acceptability of the gel was high, and majority of the participants (97.6%) liked the product. The colour, smell and consistency were liked by 97.5%, 29.3%, and 85.4% participants, respectively. About 66% and 4.9% did not express any favourable or unfavourable opinion about the smell and consistency, respectively. Few participants (9.8%) reported that they would prefer a fragrant product. Majority of women preferred colourless product as their clothes would not get stained because of the discharge and the product would be unnoticeable. Women commented that the male partners did not notice or feel the product if intercourse occurred one hour after the product use. Some participants reported diminished sexual pleasure to the male partners, which was attributed to the use of condoms, strange odour of product and excessive lubrication during sexual intercourse. Women felt that covert use would create unnecessary suspicion about their fidelity. They also expressed that the product should be available at an affordable cost.

Community Stakeholders' Perspective of Provision of Standard of Care (SOC) in HIV Prevention Trials

As part of preparedness and formative research for the HIV Prevention Trials Network (HPTN) vaginal microbicide trials, nine international sites including NARI, Pune conducted a qualitative study to collect information about facilities available to the treatment seekers, acceptance of the vaginal microbicides, research needs in this area and standard of care for the clinical trial participants and views about research actually needed in the country. Focus group discussions (FGDs) with 16 respondents and 6 potential women participants in microbicide trials gave following suggestions

- 1. Researcher should have necessary expertise to conduct research in an ethical manner.
- 2. Ensuring informed participation and involving community to decide the elements of SOC.
- 3. Improving locally available services through involvement of private or public sectors.
- 4. Enhancing the SOC to provide the best available care and
- 5. Employing holistic family-oriented approach for SOC.

Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy plus HIV Primary Care versus HIV Primary Care alone to Prevent the Sexual Transmission of HIV-1 in Sero-discordant Couples

This first international clinical trial using antiretroviral treatment for HIV prevention is a phase

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III, two-arm, randomized, controlled, multi-centre trial initiated by the HIV Prevention Trials Network (HPTN) supported by National Institutes of Health, USA. At NARI, Pune site, the HPTN 052 study began with a run-in period, by enrolling 10 HIV sero-discordant couples from July to September 2005. HIV sero-discordant couples with ART naive HIV-infected partners, CD4 cell count of 300 – 500 cells / mm³, both partners living together for a minimum of three months at enrollment, and planning to maintain their relationship for the duration of the study were enrolled.

HIV-infected index cases are assigned at random in a 1:1 ratio to either one of the two study arms, viz., ART upon enrollment plus HIV primary care (ART Arm) and HIV primary care without initiation of ART until the participant has two consecutive measurements of a CD4 cell count below 200 cells/mm³, or develops an AIDS-defining illness (delayed ART Arm). The primary objective of the HPTN 052 study is to compare rates of HIV infection among uninfected partners of HIV-infected index cases in the two study arms over a follow up period of 60 months.

Enrollment of 10 couples has been completed and all the couples are under followup. In all, 101 scheduled visits and 25 interim visits (participant initiated) have been completed. Retention of participants in the run-in phase of study is 100% and there have been no missed visits till date. Five index cases are on antiretroviral therapy (Arm 1). Currently, none of the index cases on the delayed arm (Arm 2) has qualified for ART initiation.

Of the 5 index cases randomized to the immediate ART treatment arm, four received Combivir (AZT + 3TC) and Efavirenz and one received Combivir and Atazanavir. All the five index cases showed good response to therapy with viral loads below detectable levels at the first quarterly visit and continue to remain virally suppressed till date.

Evaluation of Provider, Patient and Pharmacy Knowledge, Attitudes and Practices regarding HIV Care and Use of Antiretroviral Therapy

A total of 208 randomly selected public and private physicians participated in a survey by completing an interviewer-administered questionnaire aimed to assess their profile, and their practices related to HIV care with emphasis on antiretroviral treatment practices. Of these, 65 were randomly sampled from official hospital registration lists, and 11 from public hospitals with a response rate of 68.4% and 84.6% respectively. In addition, one randomly selected electoral ward from each of four geographical areas of Pune was mapped by trained study staff and 132 physicians were interviewed from these wards with an overall response rate of 90.4 %.

Of the 208 physicians surveyed, 97% completed the self-administered questionnaire. There were 19 questions (or items) in the questionnaire and these questions assessed skill sets for three different and important 'domains' of HIV care and management. These self-assessment scales show a good reliability and validity in assessment of physician skill sets. The scales can be used in larger surveys and will benefit identification of specific targets for advanced HIV training. They will also be useful for assessing the impact of clinical education initiatives.

Prevalence of HIV in Cutaneous Adverse Drug Reactions

Fifty seven persons presenting to the Dermatology OPD of Sassoon General Hospitals with adverse cutaneous reactions attributable to drug intake who did not know their HIV status were included as 'cases' in the study. The control group consisted of 75 age and gender matched patients with complaints other than drug rash and who did not have HIV related dermatoses.

Of the individuals presenting with drug rash, 8.8 % were HIV sero-positive, while only 1.3% of the control group were HIV positive. The sero-prevalence (8.8%) of HIV-1 in patients presenting with drug induced skin rash is much higher than the seroprevalence seen in the antenatal clinic attendees in the same hospital. When the presenting drug rash was Stevens Johnson Syndrome (SJS) or toxic epidermal necrolysis or was grade four drug rash (DAIDS/WHO grading criteria for adverse cutaneous drug reactions), or if the clinical presentation included oral, conjunctival or genital lesions there was a significant association with HIV sero-positivity.

While the association between presenting with a cutaneous drug reactions and testing positive for

HIV-1 is not statistically significant in this study, the high sero-prevalence and the odds ratio are suggestive of a significant association that definitely warrants a high index of suspicion in the clinical practitioner, resulting in targeted history taking and clinical examination and close follow up of patients presenting with adverse cutaneous reactions to drugs and HIV testing as deemed appropriate. A larger study including multiple public and private institutions will help validate the association seen in this pilot study.

Clinical Studies

Chemotherapy of Tuberculosis in HIV Infected Patients: Evaluation of Intermittent Short Course (RNTCP) Regimens

A total of 289 untreated pulmonary tuberculosis patients were enrolled in the study. Of these, 164 were HIV sero-negative and 125 were HIV sero-positive. The details of the treatment outcome are summarized in the Table-1. Of the 27 deaths observed during treatment, The instruments include standardized neuropsychological (NP) tests and self-report questionnaires.

The mean raw NP test scores for the HIV+ group were worse than those for the HIV- group on all measures, with medium effect sizes found on tests within most domains. Results indicate that (1) the NP battery chosen for this study was understood and accepted by both the HIV+ and HIV- Indian participants, and (2) the battery appears to be sensitive to the neurobehavioural effects of HIV and thus will be appropriate for bigger studies in future.

Data from this feasibility study suggest that the translated NP tests are sensitive to HIV-associated neurocognitive dysfunction, with similar associations between the NP measures and cognitive complaints and depression. These findings are in a relatively small sample, and need to be repeated within a larger cohort, using appropriate Indian-based norms.

Table 1.	Outcome	to	treatment
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	HIV positive (n = 125)		HIV negative (n = 164)		
	Soutum positive	Sputum negative	Sputum positive	Sputum negative	Total
Cured / Treatment completed	42	40	91	44	217
Defaulted	6	1	6	0	13
Expired during treatment	8	15	1	3	27
Treatment outcome awaited	3	2	1	15	21
Transfered out	2	5	0	0	7
Total	62	63	101	63	289

23 (85%) deaths were seen in the HIV sero-positive group. In the HIV sero-positive tuberculosis patients, 12.9% of the sputum AFB positive patients died while in the sputum AFB negative group, 23.8% of the patients died. The corresponding figures in the HIV sero-negative TB patients were 1% and 4.8% respectively. The difference in the mortality in the HIV sero-positive and HIV sero-negative TB patients was statistically significant.

Study of Neuro-cognitive Impairment in HIV Infected Individuals

To assess the neurocognitive impairment in HIV infected individuals, structured neurocognitive and neurological assessment methods developed at the University of California, San Diego (UCSD) were used.

Screening for Peripheral Neuropathy and Dementia in an HIV Infected Population using International HIV Dementia Scoring (IHDS)

Fifty HIV infected patients with CD4 count less than 200/mm³ and 50 controls were included in the study. The IHDS instrument consists of three tasks and each task was rated on a scale (0 to 4): (1) Assessment of memory registration; (2) Assessment of motor speed; and (3) psychomotor speed assessment. The total IHDS score was computed. The maximum possible score was 12 points.

Symptoms suggestive of peripheral neuropathy were more in cases and vibration extinction time was

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significantly less in HIV infected individuals than controls. Nearly 17 of 48 HIV (+) subjects had low scores on the IHDS screen (*i.e.*, < 10) and 7 of 48 HIV (-) subjects had IHDS scores of < 10. On analysis of the components of the IHDS, it was found that the differences between the HIV (+) and HIV (-) subjects were significant for both the memory recall and the psychomotor speed portions of the examination with psychomotor speed being the most distinguishing test. It was demonstrated that the IHDS can be used as a screening tool in the Indian population.

Pharmacokinetics of Generic Fixed-dose Combination of Nevirapine, Lamivudine and Stavudine in HIV-I Infected Adults

Generic fixed dose combinations (FDC) of regimens containing two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-NRTI (NNRTI) are widely regarded as crucial for scaling-up AIDS treatment in developing countries. Two triple drug combinations of nevirapine (NVP) and lamivudine (3TC) with either stavudine (d4T) or zidovudine (AZT) as the third drug are available as FDCs in the developing world. Since very limited data are available on the blood levels or pharmacokinetics of these drugs, a study was



Fig. 1. NACO ART centre : ART regimens among participants enrolled

undertaken with the aims to obtain information on the pharmacokinetic profiles of NVP, 3TC and d4T in HIV-infected patients on treatment with FDCs in India and to study the influence of immunological status, gender and body mass index (BMI) on the pharmacokinetics of these drugs.

Adequate levels of plasma concentrations of NVP, 3TC and d4t which were not influenced by the stage of immune suppression, gender and BMI, were observed in the study indicating that if patients take regular treatment, chances of failure due to inadequate drug levels are low. The results of the study suggest the need to explore pharmacogenetic differences that could impact drug levels in different populations.

National AIDS Control Organization Programme -NARI ART Link Centre

NARI has been identified as ART link centre. The centre aims to provide treatment for as many NARI research study participants as possible. The programme has initially been sanctioned for 500 participants. The centre began enrollment in December 2005. Total 136 participants were screened and 122 enrolled by end of March. Of the enrolled participants, 85 were males and 37 females. Participants who completed follow up in various studies carried out by NARI were enrolled in the ART centre. The treatment regimens for participants are shown in Fig.1. The treatment adherence was more than 95%.

Immunological Studies

HIV Genome Wide Cytotoxic T Lymphocyte (CTL) Response

In order to identify proteins that are preferentially targeted by immune response, genome wide search was made using overlapping peptides by IFN- γ ELISPOT assay. T cell IFN- γ response was measured in 31 (17 male/14 female, mean age 34 yr) HIV infected individuals at various stages of HIV disease (as identified by CD4 count ranges from 121 - 1382/cumm) using peptide matrix ELISPOT representing the entire HIV genome through 681 overlapping peptides. The peptides used were 15 amino acid (aa) long with 11 aa overlap.

Of the 31 patients 30 responded to at least one antigen. The magnitude of the response measured as spot forming units (SFUs / million cells) ranged from 140 to 1150 SFUs / million cells. Breadth of the response (number of antigens recognized) was considerably high (range: 20 to 100 peptides encompassing the whole viral genome). Twenty-one of the responders recognized peptides from multiple proteins. Gag was the most targeted protein eliciting response (mean SFU 555 / million cells) in 22 of 31 participants followed by Nef (18/31 responders, mean SFU 639 / million cells). Pol peptides were recognized by 24 individuals (mean SFUs of 446 / million cells). Env peptides were recognized by 17 of 31 patients (mean SFU 470 / million cells). Rev and Tat responses were weak in magnitude and seen in a small number of patients. When the breadth of the responses against individual antigens was assessed, Gag was the most targeted protein. The aa51 to aa250 in Gag, aa51 to aa150 in Nef, aa 480-aa520 and aa 550-aa 570 in Pol and aa 480- aa520 in Env antigens were the most targeted regions. There was no difference in recognition of antigenic regions recognized by the patients with low or high CD4 counts.

Response to CTL Peptides Conserved Across the HIV Subtypes

The CTL responses were determined in 19 HIV-1 infected individuals using matrix interferon- γ ELISPOT assay. Fifty-five peptides with >80% conservation across HIV-1 subtypes were identified from Los Alamos database and using the MotifScan software program. These included 26 epitopes from Gag, 10 from Pol, 6 from Env and 8, 3 and 2 peptides from Nef, Vpr and Vif, respectively.

In all, 80% of the 55 selected peptides were recognized by subtype-C infected persons. Fourteen (74%) participants responded to at least one or more HIV peptides, with majority (10/14) responding to one of the gag peptides (p17 and/or p24). Overall 50% of the responders recognized more than 8 peptides with one responding to as many as 15 peptides. The analysis of the frequently targeted peptides (both in number of



The figure above each bar indicates no. of patients recognizing the peptide/13 responder

Fig. 2. HIV-specific CTL response against conserved peptides in Indian patients estimated as SFU/million cells (Y axis) against no. of individual peptides (X axis) patients recognizing the peptides and the mean ELISPOT responses) showed that five p24, one gp41, three p17 and one Vif peptide were the most frequently targeted peptides followed by three Nef peptides. (Fig. 2).

Humoral and Cellular Immune Responses exhibited by Vaccinia HIV-1 C Gag Construct in BALB/c Mice Model

Groups of 10 mice each were injected subcutaneously with two doses of VGag viz: 1×10^6 and 1×10^7 PFU/mouse and control group mice were injected with saline and vector vaccinia (WR: 1×10^6 and 1×10^7 PFU/mouse). The immunization schedule included four doses at two weeks interval followed by a booster dose eight weeks after the fourth dose. The immunization and bleeding schedule is given in Fig. 3.



Fig. 3. Immunization schedule followed for mice immunization

Anti-HIV humoral response (anti-P24 antibody production) was estimated by ELISA. Detectable antibody response was seen against P24 in mice immunized with VGag 10^6 and 10^7 after 1st dose. The antibody levels increased with subsequent immunization in both the doses with response being higher to 10^7 PFU dose. (Fig. 4)



Fig. 4. HIV-1 C p24 antibody detection in mice immunized with VGag 10^6 and 10^7

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Generation of HIV Gag-specific T cell response was monitored by IFN- γ ELISPOT assay after 3rd, 4th and a booster dose using 49 HIV-1 C Gag overlapping peptides (NIH AIDS Research and Reference Reagent programme, Cat no: 3993). The response decreased after 4th and booster dose in both the groups of Vgag inoculated mice (30 & 2 SFU/million cells in Vgag10⁶, 22 & 14 SFU/million cells in Vgag10⁷ dose respectively.

Dominant HIV-1C Gag-specific T cell responses clustered within three regions of p24 correspond to the amino acids 140 to 210, 251-290, 321 to 361 and one

101 LDRIEEEQNKIQQKIQQKTQQAADGKVSQNYPIVQNLQGQMVHQKLSPR 150

151 TLNAWVKVIEEKAFSPEVIPMFTALSEGATPQDLNTMLNTVGGHQAAMQM 200

- 201 LKDTINEEAAEWDRLHPVHAGPIAPGQMREPRGSDIAGTTSTLQEQIAWM 250
- 251 TSNPPIPVGDIYKRWIILGLNKIVRMYSPVSILDIKQGPKEPFRDYVDRF 300

301 FKTLRAEQATQEVKNWMTDTLLVQNANPDCKTILKALGPGATLEEMMTAC 350 351 QGVGGPSHKARVL AEAMSQTNSVNILMQKSNFKGNKRMVKCFNCGKEGHI 400

401ARNCRAPRKKGCWKCGKEGHOMKDCTERQANFLGKIWPSHKGRPGNFLQN 450

Fig. 5. HIV-C Gag regions recognized by BALB/c mice (sequences in blue colour)

anti-retroviral treatment naive individuals from Pune, India. Twenty-one of the samples (19 samples with \geq 90% neutralization and two samples with 50 - 60% neutralization) were tested against panel of 12 primary HIV-1 subtype C isolates. The HIV-1 isolates were from three different states of India and were isolated at different time points (year 1999 to 2005) to ensure diversity among the isolates.

The cross-reactivity of neutralizing antibody response suggests likelihood of presence of shared neutralization determinants among Indian primary HIV-1 isolates. The finding may have important implication in HIV-1 vaccine development.

Neutralizing Antibody Responses in HIV-1 Subtype C Infected Recent Sero-converters

C2-V3 region of the env gene of HIV-I representative sequential samples of sero-converters demonstrating neutralization response within and after six months of infection (classified as early and late responders respectively) and those who did not show response was sequenced. The sequences were analyzed using DNASTAR software and subsequently alignment was done for V3 region using Clustal X software. The mean neutralization response demonstrated by three groups against the two isolates and the AA substitution

region of P7 corresponding to amino acids 389 to 430 of the Gag protein according to the HXB2 numbering system. The gag regions identified by BALB/c mice are shown in Fig.5.

Characterization of HIVspecific Neutralizing Antibody Response in Chronically Infected Individuals

Neutralizing antibody response to single heterologous primary HIV-1 subtype C isolate was assessed in plasma samples of 235 HIV-1 infected,

Table 2: Association of env V3 sequences from early, late responder non-responders with neutralization response	's and

Patient ID	PIP (months)	Log viral load	Mean neutralization	V3 sequences**
			response	
Early respon	der			CTRPNNNTRKSIRIGPGQTFYATGDIIGDIRQAHC 35
SC-6	3*	5.06	74	-V
	6	5.13	76	-V
SC-9	2*	3.99	85	TT
	8	3.7	86	STT
SC-20	3*	ND	69	SEN
	10	4.5	72	SN
Late respond	ler			CTRPNNNTRKSIRIGPGQTFYATGDIIGDIRQAHC 35
SC-25	6	4.23	21	
	12	ND	18	
	22*	3.68	70	
	28	3.83	87	
SC-26	27	4.54	6	ML
	38*	4.27	65	ML
	45	4.56	70	ML
SC-27	19	4.81	35	GY-
	25*	4.62	67	GY-
	32	4.80	86	GY-
Non responder (representative sequence)			?)	CTRPNNNTRKSIRIGPGQTFYATGDIIGDIRQAHC 35
SC-31-1	8	4.48	18	G
SC-31-2	13	5.21	15	G

* The time at which neutralization response emerged.

** The AAs marked in bold font are showing variation in seroconverter's sequences as compared to consensus from each group.

in the V3 region along with plasma viral load and post infection period is shown in Table 2.

Study of Human Anti-HLA Antibodies for Their Potential to Neutralize HIV-1

Study was carried out to understand whether the anti-HLA antibodies present in multiparous women can neutralize the HIV carrying of their partners' HLA markers. The experiment showed that HIV-1 incorporates HLA proteins, however, antibodies directed against these HLA molecules do not mediate HIV neutralizing activity. Since size of Env molecule is relatively much larger than HLA antibody complex, it may not cause steric hindrance for interaction of Env trimer with HS receptor on target cell.

CD4 Count Estimation and Experiences in the External Quality Proficiency Assessment for CD4 Count Estimation for Indian Laboratories

The external quality assessment scheme (EQAS) was initiated for some of the Indian laboratories as a pilot run in collaboration with Dr. Kovit Center of Excellence in Flowcytometry (COE) from Siriraj Hospital, Thailand. The stabilized whole blood samples received from COE were distributed to 12 Indian Laboratories and the results were obtained in the prescribed format. The results were sent to COE and after comparison with the other participating centres the results were received back at NARI and distributed to individual laboratories.

Twelve laboratories sent the results and the performance of majority of the laboratories was satisfactory except one. Four rounds were conducted in last year and the results of fourth round of testing are awaited. The exercise showed that the Indian laboratories' performance in EQAS was satisfactory, however there is a room for improvement especially for the non-communicating laboratories.

Distribution of HIV-1 Subtypes on the basis of *gag* Gene

The magnitude and complexity of the HIV-1 genetic diversity are one of the major challenges for vaccine development. Earlier reports from India identified the preponderance of subtype C and small proportion of subtype A and Thai B viruses (only among the IDUs in Manipur). Besides the envelope C2-V3 region, *gag* p24-p7 region has become important to study the genetic diversity of HIV-1 since the development of *gag* based heteroduplex mobility assay (*gag*-HMA) followed by sequencing and phylogenetic analysis. Based on envelope C2-V3/V5 region, subtype C viruses have been identified among the female sex workers in Kolkata. In this study undertaken at NICED, Kolkata, distribution of HIV-I subtypes on the basis of *gag* p24-p7 region has been reported.

The distribution and phylogenetic pattern of the HIV-1 type C *gag* p24-p7 sequences from Kolkata was studied compared to other Indian C strains from different regions. All the 51 sequences from Kolkata were analyzed with 44 sequences from western and northern India as available in the database. Clustal W multiple sequence alignment program was used and a phylogenetic tree was computed using the NJ method by MEGA version 2.1. The radial pattern of the tree was viewed for better observation (Fig.6). Two main clusters were formed. Majority (35 out of 44) of the Indian strains other than Kolkata formed the cluster – I



Fig. 6. Radial pattern of phylogenetic tree

while another group of sequences (cluster - II) comprised mostly the Kolkata strains (46 out of 51). Only five strains from Kolkata were lying within cluster - I while nine Indian strains resided within cluster - II with other Kolkata strains. The result showed the distribution pattern of the HIV-1 strains from the eastern part to be a little different from rest of the country.

The overall study revealed HIV-1 subtype C to be the most prevalent type in eastern part of India based on the gag p24-p7 region supporting earlier findings made on the subtyping of HIV-1 based on envelope C2-V3 region from this part of the country. A characteristic regional separation was also indicated by Kolkata strains when compared to the other Indian strains indicating that there might be a varying tendency persisting among the subtype C HIV-1 strains in eastern part of India.

AIDS Vaccine Clinical Trials in India

Adeno-associated Virus (AAV) based Vaccine

The AAV-based vaccine is promising as it is a non-pathogenic virus with a good safety profile. It is expected to produce good immunological response. The uptake of volunteers in the trial has been completed and follow up is going on. Safety data available from volunteers till now show that the vaccine is well tolerated and no study product related serious adverse event has been noted so far.

TBC-M4-Modified Vaccinia Ankara (MVA) based Vaccine

The MVA vaccine is the second vaccine candidate identified suitable for Phase I clinical trials in India. It is manufactured by Therion Biologics Corporation, Massachusetts, USA. An Indian scientist from the NICED, Kolkata was involved in designing this vaccine candidate. The Phase I trial of this candidate is ongoing at TRC, Chennai.

Molecular Virological Studies

Molecular Virology in the PEARLS Trials

Drug resistance mutations in HIV-1 pol gene were tested using commercially available kit for the participants of an ongoing ART clinical trial among HIV infected persons. Amplicon of 1.6 Kb for pol gene (Fig.7) was generated using this kit, which was further taken for sequence spanning 99 amino acids of protease and 335 amino acids of reverse transcriptase gene. Mutation pattern against antiretroviral therapy was categorized under (NRTIs), NNRTIs and protease inhibitors.



Sample No. 4 5 - Sample No. 5 6 - High Pos. Control Low Pos. Control 8 - Negative Control

Fig. 7. Amplification of pol gene by RT-PCR

HIV-1 Drug Resistance Mutations in PBMC Proviruses among ART Naïve and Treatment Experienced

Twenty-five ARV-naïve and 50-ARV treatment experienced chronically HIV-1 infected individuals were studied. The PBMC proviral DNA sequences of 75 HIV-1 infected individuals were analyzed. The ARV drug experienced had history of exposure to different ARV drugs, namely, nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs).

In ARV naïve patient PBMC specimens, no major drug resistance mutations in protease region were observed. Substitutions at subtype B minor drug resistance positions in protease region were observed in all drug naïve specimens. There were no drug resistance mutations in reverse transcriptase region. HIVDR mutations were observed in 52% treatmentexperienced patient specimens. The median duration of therapy was 1.9 yr and mean duration of ARV therapy was 2.36 yr. NRTI, NNRTI, and PI resistance mutations were observed in 42%, 38% and 8% treatment-experienced individuals respectively.

Genotypic and Phenotypic Chara-cterization of HIV-1 Subtype C Isolates

To delineate the characteristics of HIV-1 circulating in this region, genotypic and phenotypic characteri-zation of HIV-1 isolates obtained from HIV-1 seropositive individuals at various stages of infection was carried out.

Thirty-five HIV-1 isolates were subtype C and four were subtype A. Thirty-eight isolates were nonsyncytium inducing (NSI)/R5 tropic and one was

syncytium inducing (SI)/

X4/R5 tropic. The

sequence analysis of

V3

indicated that syncytium

induction and coreceptor

amino acids at positions

11 and or 25 of V3

region. Phylogenetic tree

analysis using MEGA

sequences formed two

different clusters while

sequences formed a

single cluster. Region

wise analysis of the two

demonstrated that 14

isolates from the state of

Maharashtra, two from

Gujarat and one from

Goa clustered together

and 11 isolates from Maharashtra and one

Goa

another cluster (Fig.8)

subtype

subtype

were

region

not

С

Α

clusters

formed

with

charged

HIV-1

usage

HIV-1

HIV-1

HIV-1

from

associated

positively

Fig. 8. Phylogenetic analysis of Indian HIV-1 isolates

Socio- Behavioural Studies

Psychosocial Stressors among HIV-infected Individuals with Reference to Partner Support Issues

This is an ongoing intervention study where the 'significant other' of the HIV positive patient is involved

to provide support to him/her. The study aims at assessing the level of anxiety and depression in HIV positive individuals, understanding various aspects associated with involvement of significant other/s in providing care and support to people living with HIV/AIDS (PLHAs) and develop novel approaches to provide psychosocial support to PLHAs at HIV testing and counseling facilities. The study has following three components: (1) field based: mental health needs questionnaire validation; (2) clinic based: (a) assessment of level of anxiety and depression in HIV positive individuals; (b) understanding the interpersonal communication



Fig. 9. Mental health needs questionnaire administration procedure

between the 'index partner' and the 'significant other and (3) intervention study. Fig.9 depicts the process involved in collection of data for development of the mental health needs assessment instrument.

Adolescent Reproductive and Sexual Health Education [ARSHE]: an Intervention Study

The aim of the study was to provide educational intervention in classrooms settings, supported by



Fig. 10. Students participating in end line survey

COMMUNICABLE DISEASES

exhibitions and visit to NARI. At Pune, six schools participated in the study (Fig.10). A total of 1080 questions were collected from students pertaining to various chapters of the intervention. Fig.11 depicts frequently asked questions on various chapters in the participatory schools.



Fig. 11. FAQs by students on different chapters at the various schools

HIV Infection in Injecting Drug Users of Manipur

HIV infection in India was largely considered to be heterosexual until a massive epidemic of HIV among injecting heroin users was reported in Manipur in 1990. There is a felt need of re-assessment of existing situation of intravenous drug users(IDUs) with current status of blood borne infections among them. A task force has been initiated to conduct research in basic, operational, behavioural and clinical areas in HIV/AIDS and to assist the State AIDS Control programme.

Studies done so far in Manipur have shown that most of IDUs belong to 21-25 yr age group and the prevalence of IDUs declined as the age advanced. Highest prevalence of HIV was found in 31-40 yr age group. About 17% of the IDUs were found to be unemployed and 34% were students. Heroin was most commonly used drug (55%) followed by spasmoproxyvon and other narcotic analgesics. TB was the most common opportunistic infection seen in patients suffering from AIDS. Clinical presentation and type and occurrence of opportunistic infections are quite different in Manipur from developed countries necessitating formulation of different set of guidelines for subjects of this state. This will help in better screening of patients, early detection and prompt treatment thus increasing the life span of such patients. In a country like India where latent TB infection is very high, INH prophylaxis should form an integral part of TB prevention in HIV patients.

REPRODUCTIVE HEALTH

Realizing the significance of good reproductive health in ensuring overall well being of an individual and the society, the Government of India, jointly with 149 other countries of the United Nations Organization, has decided to achieve the Millennium Development Goals (MDGs) by the year 2015. These goals are set to achieve: (i) eradication of extreme poverty and hunger; (ii) primary education for all; (iii) gender equality and women empowerment; (iv) reduced child mortality; (v) improved maternal health; (vi) reduced incidences of HIV/AIDS, malaria and other diseases; (vii) environmental sustainability; and (viii) a global partnership for development. Of these eight goals, three directly address to the issues related to reproductive health, reflecting the urgency on the part of governments to reduce the burden of reproductive ill health. Countries worldwide are striving hard towards reduction of infant and child mortality by two-thirds (goal 4); reduction of maternal mortality by three-fourth (goal 5); and to reverse the spread of HIV prevalence in 15-24 yr olds by 25% and infants infected with HIV by 50% (goal 6).

To ensure that the MDGs are achieved, the Council's National Institute for Research in Reproductive Health (NIRRH) at Mumbai has initiated several research programmes with special focus on reducing the burden of reproductive ill-health due to unmet need of contraception, unwanted and unsafe pregnancy termination, infertility and other reproductive disorders, increasing incidence of

reproductive tract infections (RTI) including sexually transmitted infections (STI) and HIV/AIDS, and geriatric health problems like osteoporosis in men/women. The research programmes are in accordance to the needs and perspectives of people taking into account the changing patterns of adolescent sexuality and fertility, increasing incidence of sexually transmitted infections including HIV/AIDS and concentration of reproductive ill-health among urban slum, rural and tribal areas. Research in the areas with a promise to improve the reproductive health has been initiated using newer technologies such as bioinformatics, system biology, structural genomics, proteomics and genomics.

The Council is also undertaking studies in the field of maternal and child health. Home based management of young infants at village level by trained health workers is being attempted in five states of the country. The Council has developed National Guidelines for Assisted Reproductive Technology Clinics in the country. National guidelines have also been developed for management of reproductive tract infections.

FERTILITY REGULATION BASIC RESEARCH Identification and Characterization of Sperm Antigens

(i) Using neonatal tolerization

Neonatal tolerization was used to raise antibody probes, which were used to delineate domain specific epididymal sperm proteins. Animals were tolerized at days 0 and 5 with rat testicular proteins and further immunized with either intact or soluble fractions of head (HI/HS) and flagellar domains (FI/FS) of rat caudal sperm. Western blot analysis using sera of tolerized immunized (TI) animals showed epididymis specific reactivity. The sera of animals in different groups identified proteins in the range of 27-200 kDa.



Fig. 1. Tissue specificity of sperm proteins

The sera were of the agglutinating type and the pattern of agglutination was either radial or comet shaped. A representative data of the immunohistochemical reactivity of TI sera with rat brain, heart, liver, kidney, spleen and thymus is shown in Fig. 1. No tissue apart from cauda epididymis showed any positive staining suggesting that the antigens recognized by all the sera were of epididymal origin.

(ii) Using antisperm antibodies

Using vasectomy induced autoimmunity approach, a sperm auto antigen, termed TSA70 was identified and immunochemically characterized. It was found to be a testicular auto antigen of ~70 kDa expressed post meiotically in stage specific pattern and is evolutionarily conserved across the species. The sequence of TSA70 showed homology with cenexin molecule. This is the first report showing the presence of cenexin on sperm.

(iii) Using proteomics approach

Proteomics was employed to identify differentially expressed sperm proteins acquired during epididymal maturation. The proteome profiles of rat testicular sperm were compared with caudal epididymal sperm as well as with proteins from different domains (head and flagellum) of caudal epididymal sperm. The profiles obtained were analyzed as many as 404 protein spots were resolved from testicular sperm and 495 from cauda epididymal sperm. Several spots were specific to epididymal sperm. Of these spots, two (AS1 and AS2) are being sequenced.

Role of a Novel Androgen Regulated HoxB2 Containing Gene Expressed in the Epididymis

A sperm specific protein designated HOXBESS was, identified by screening an epididymal cDNA library, using an agglutinating antibody raised against washed human sperm. The sequence of the positive clone showed homology with the conserved region of transcription factor Hox-B2. The epididymal specific expression of the 30kDa protein, (presence of a single 2.5kb transcript), its androgen dependency, conservation across the species and presence on the sperm surface were established. Acrosome reacted sperm of various species indicate a probable role for the protein in sperm-egg interaction and sperm maturation. The data indicated regionalized and cell

specific expression of HOXBESS that shares epitope identity with Hox-B2 transcription factor from embryo. Specific cytoplasmic localization, the difference in the size of the cognate epididymal protein from the HOX-B2 transcription factor expressed in the embryo and presence on the sperm suggests the role of HOXBESS as an effector molecule rather than a transcription factor.

Using the 5'RACE approach, the full length sequence of 1.657 kb was obtained from rat epididymis. The full length mRNA as well as its putative protein sequences was submitted to the NCBI GenBank and ascribed the accession nos. DQ399532 and ABD73307 respectively. Sequence analysis revealed homology to HOX-B2 transcription factor with an upstream extension of 560bp. Sequence analysis using bioinformatics tools showed a start site at 218bp and a stop site at 1135bp. Kozak sequence and poly⁺A tail were also identified. The deduced putative protein (31.5 kDa) with a precipitation index (pI) of 10.5 from an ORF of 917bp. A mitochondrial targeting peptide (1-30 A.A.) correlated with the immunolocalization of the protein on the midpiece of rat, monkey and human spermatozoa. A nuclear localization signal and the immunodominant region of 20 amino acids could also be identified. Potential transmembrane segments in the 305 aa sequence correlated with the integral membrane bound extra-cellular (secreted) form of the predicted protein location.

The protein exhibited differences in the amino and carboxyl termini from the conventional transcription factor, probably explaining the differences in their function. Sequence analysis of full length of the Hox-B2 containing sperm protein confirmed the earlier findings based on *in vivo* and *in vitro* observations. The observations further confirm that HOXBESS has a role to play in sperm function during fertilization.

Studies with 80kDa Human Sperm Antigen and Its Synthetic Peptides

The 80kDa human sperm antigen (HSA) has been reported to be a sperm specific protein responsible for inducing immunological infertility. Active immunization with purified antigen induced reversible infertility in male and female rats.

The immunohistochemical and immunofluorescent studies have suggested that 80kDa HSA is sperm specific antigen and its expression is developmentally regulated by testosterone. Synthetic peptides of this antigen immunobiologically mimic the native protein and immunogenic and active/passive immunization impaired fertility in rat, rabbit and marmoset. Thus, the use of 80kDa RSA and its synthetic peptides is suggested for development of an antifertility vaccine.

Modulation of c-kit Proto-Oncogene Function during Spermatogenesis in Mice

Infertility affects 5-7% of men, of these 30% are due to genetic factors, 10% due to 'Y' chromosome microdeletions and the remaining 90% are due to defects in autosomal genes. C-kit is one such autosomal gene. In certain cases, the infertility could be attributed to the functional defects of C-kit expression, since C-kit mutant mice are reported to be infertile. Study was conducted under an Indo-US programme to evaluate the role of C-kit during different stages of spermatogenesis at the molecular level using mice as an experimental animal.

During the year isolation of pure population of spermatogonial cells (SGCs) was done and they were used to study the role of c-kit in germ cell survival using serum-free short-term culture system. The results indicated that c-kit and its ligand, the stem cell factor (SCF) facilitate the survival of SGCs. Study of expression of c-kit during different stages of development revealed that it increased till day 60 following which no significant change was found suggesting maturation-associated expression. Method for the in vivo transplantation of SGCs into the seminiferous tubules via rete testis of busulfan-treated infertile mice has also been standardized. Sequence specific gene silencing in mice testis induced by electroporation-mediated transfer of short interference RNA (SiRNA) is being studied to evaluate the role of c-kit in SGC survival and differentiation.

Global mRNA Expression Studies on Apoptosis Related Genes in Human Endometrium during Menstrual Cycle

Deregulation of apoptosis in endometrium can result in aberrant proliferation and related diseases such as hyperplasia. Identification of key genes involved in endometrial apoptosis may help in elucidating prognostic markers for hyperplasia. Immunohistochemical localization of apoptosis regulating genes of the Bcl-2 family (such as Bcl-2 and Bax) in human endometrium during various phases of the menstrual cycle was undertaken earlier at NIRRH, Mumbai. To further elucidate the molecular pathway of apoptosis in endometrium, global expression of apoptosis related genes was investigated during the year by cDNA macroarray. Endometrial biopsies were collected from women volunteers at follicular (F), mid luteal (ML) and late luteal (LL) phases. Total RNA was extracted from the endometrial samples, cDNA was synthesized using specific primers and labeled with ³²P. Following hybridization with human apoptosis cDNA array on nylon membrane, the spots were visualized by phosphor imager. The array contained 205 genes involved in various apoptosis- regulating pathways. Increase in the intensity by 2-fold or more was considered to be significant. Exclusively 30 genes were upregulated in ML phases and 15 genes were upregulated in LL phases while 38 genes showed 2-fold rise in both ML and LL phases as compared to F phase. Preliminary analysis of the data revealed prominent role of the cell cycle regulating protein kinases and intracellular kinase network members in endometrial apoptosis. Further investigations are underway for validation of the results.

Dynamics of Early Folliculogenesis: Differential Gene Expression in Mouse Ovaries

The ovary contains a pool of primordial follicles containing oocytes arrested in meiosis and which are the source of developing follicles for the female. Transition of arrested primordial follicles to primary and secondary follicles is a crucial process in female fertility. Relatively few genes which control these events are known, thus identification of additional genes expressed during follicular development may reveal key players in this process. To investigate this RNA was extracted from ovaries of neonatal mice on days 2 and 4 and the gene expression profile was analysed by cDNA. The results revealed that 30% of genes were differentially expressed during transition of primordial to primary follicles. Amongst these genes, upregulation of cell cycle regulators, neurotransmitters and signal transduction elements was predominant. Genes responsible for growth, cell-cell communication and proliferation were also found to be upregulated. Further, to substantiate the gene expression results, the immunolocalisation of proteins such as GDF-9, (a differentiation marker), PCNA, (a marker for proliferation) and anti Mullerian hormone, (a growth regulator) were studied in the ovaries of neonatal mice. The results demonstrated that multiple gene cascades were involved during early folliculogenesis.

Mechanism of Action of Follicle Stimulating Hormone Binding Inhibitor (FSHBI) and its Synthetic Analogue Octapeptide (OP)

Gonadotropins FSH and LH play an important role in the proliferation and development of the follicles. Several autocrine/paracrine factors secreted by the ovary, directly or indirectly regulate the gonadotropin action. FSH binding inhibitor (FSHBI) purified and studied at NIRRH, is one such factor, which modulates FSH action by binding to its receptor. It is a ~ 4kDa protein and its N-terminal 8 amino acid sequence is an octapeptide (OP). Native FSHBI purified from human ovarian follicular fluid was shown to induce atresia in developing follicles. OP has also demonstrated a biological activity similar to native FSHBI. Study was conducted to elucidate the mechanism of action of FSHBI/OP in swiss mice. For this two pathways of apoptosis namely, the membrane receptor pathway and mitochondrial pathway were studied using flow cytometry and immunohistochemistry. Results indicated an overall increase in apoptotic population in atretic and FSHBI/OP treated groups as compared to the normal group. Interestingly, in the FSHBI/OP treated groups the membrane receptor pathway was dominant while in the atretic group it was mitochondrial pathway.

CLINICAL RESEARCH

Acceptability and Continuation Rates of 2 Monthly Injectable Contraceptive: Norethisterone Enanthate

At the initiative of Department of Family Welfare, the NIRRH, Mumbai is continuing a multicentric study on 2 monthly injectable contraceptive–norethisterone enanthate (Net-En) among women across the country.

Observations of the study based on 15,228 women months of use revealed that continuation rates at 12 and 18 months were 65.2 and 54% per 100 users respectively (Fig. 2). About 89% women said that the





Fig. 2. Cumulative continuation rate of Net-En injection

injectable contraceptive should be made available in the National Family Welfare Programme as it is convenient to take bimonthly injection instead of contraceptive pills. Over 79% of them recommended this method to their friends and relatives and 80.5% women were satisfied with the use of this method. During the reporting period, 409 women have completed 2 yr of injection use. The method was found to be very effective since there have been only three pregnancies reported so far. The major reason for discontinuation was migration and loss to follow up because of floating population.

Protocol amendment for bone mass density (BMD) and evaluation by DEXA among Net-En users was made. Some of the women's health groups raised issues about decrease in BMD among women who used 3 monthly injectable contraceptive, depo-provera. In view of this, NIRRH has initiated BMD evalution at 7 centres.

Clinical Trial with Intravasal Injectable Male Contraceptive

The RISUG (reversible inhibition of sperm under guidance), an intravasal injectable male contraceptive has been developed by the Council under GLP and GMP conditions and the same has been tested for its genotoxicity and mutagenicity. The data indicated that RISUG is safe in terms of genotoxicity, mutagenicity and carcinogenicity and is safe for clinical use. The Council plans to conduct extended Phase-III clinical trials with RISUG.

OPERATIONAL RESEARCH

Interventions in Urban Slums for Enhancing Participation of Men in Reproductive Health

Realizing the need for involving men in the family welfare program, the draft National Population Policy (2000) suggested a holistic approach and stressed on male involvement particularly in the context of prevailing gender inequality.

Operational research is being undertaken by NIRRH, Mumbai on the couples in urban slums to (1) identify program strategies (addressing only the men or couples together) for effective participation of men in programs aimed at improving reproductive health (safe motherhood, family planning/contraceptive use, RTI/STI and HIV/AIDS) of couples and (2) plan and evaluate interventions for enabling couples to gain correct knowledge about reproductive health issues concerning men and take appropriate actions to seek and avail reproductive health services.

So far, information has been collected from 1755 couples (both husbands and wives) from three health post areas (Mohili village, Bail Bazar and Asalfa village). About three-fifth of men were 19 to 39 yr old while 41% women were aged 17 to 29 yr. About 39% men were unskilled, while most (91.4%) of the women were housewives. Two-fifth of couples had three or more living children. Nearly one-fifth of husbands and one fourth of wives mentioned that they prefer to have more sons than daughters indicating gender bias. About one-fifth of wives reported that they had past history of abortion of which 12% had induced abortions. A little more than half (54%) of husbands and 47.8% wives reported that husbands accompanied wives for their antenatal check-ups.

A little more than two-fifths of husbands (43.4%) reported that their wives had undergone tubectomy and



Fig. 3. Current contraceptive use

10.1% husbands reported that they are using condom (Fig. 3). Only one person had undergone vasectomy. Regarding future intentions to use contraceptives, 30% husbands and 26.7% wives reported that they would not like to use contraceptive measures.

Regarding knowledge of reproductive health issues, 97.4% husbands and 96.4% wives were aware of HIV/AIDS, 74% husbands and 40% wives were aware of STDs and 43% husbands and 49% wives were aware of infertility.

The findings suggest that in order to enhance male responsibility in reproductive and sexual health matters (including safe motherhood, better contraceptive usage and health seeking behavior), the intervention strategies should address issues relating to gender equality and spousal communication.

INFERTILITY AND REPRODUCTIVE DISORDERS

FEMALE INFERTILITY

Studies on Polycystic Ovary Syndrome

Studies on Genetic Aspects of Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is an important endocrine disorder leading to infertility. A genetic susceptibility to the condition has now been well recognized. Evidence indicates that a small number of key genes may be contributing to predisposition to the syndrome, which in conjunction with environmental factors, may lead to its varied phenotypes. Study was carried out with the specific objective of determining the susceptibility loci for PCOS with particular emphasis on two of its important associated features *viz.*, hyperandrogenicity and obesity. Overall objective was to elucidate the associated genetic mutations and polymorphisms in Indian context in particular.

Probands for the study included women in reproductive age with oligoammenorrhea/chronic anovulation and hirsutism with or without obesity. Polycystic ovaries were confirmed through ultrasonography. A normal control group in

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MAJOR ICMR RESEARCH PROJECTS IN REPRODUCTIVE HEALTH

reproductive age and a grossly obese (BMI>35) control group were also included for comparison. The following candidate genes were analysed (i) CYP11A1 which encodes cytochrome P450 side chain cleavage enzyme, (ii) CYP17 which encodes the 17 α -hydroxylase enzyme and (iii) leptin, the obesity (OB) gene.

Coding sequences of CYP11A1 did not reveal any variants with regard to PCOS. Screening of the promoter region showed marked variations in frequency of the pentanucleotide (tttta)n repeat polymorphism in Indian women compared to that reported in the West. The 6 repeat allele which has been reported to be associated with raised androgen levels, was found to be predominant in Indian women, as against the 4 repeat allele which is predominant in Western population. Analysis of CYP17 showed significant association of PCOS with a T>C polymorphism in the promoter region. Leptin showed no variants in its coding region. In gross obesity, however, a novel variant was identified in exon 2 (accession number DQ054472). Screening of the non-coding exon 1 of the gene was also carried out in PCOS and control cases. A high prevalence of A>G polymorphism was found. Fig. 4 shows the heterozygous A>G polymorphism seen in a PCOS case. The study is being continued to determine the



Fig. 4. Heterozygous A>G polymorphism in leptin gene seen in a case of PCOS

association of polymorphism with PCOS and associated obesity.

Genes in Women with Premature Ovarian Failure

Study was undertaken with the aim to determine association of mutations/premutations in the FMR1, inhibin and FOXL2 genes in women with idiopathic premature ovarian failure (POF) and to identify the best candidate gene for determining predisposition to this condition. Seventy women aged <40 yr, with secondary amenorrhoea, elevated serum FSH levels (>40 mIU/ml) and normal karyotype and 30 regularly cycling fertile women were enrolled along with 25 family members of 19 index cases. Nine women with poor ovarian reserve (POR) were also recruited.

Screening of inhibin alpha gene by RFLP and SSCP analyses did not reveal any mutations. Inhibin beta A gene also did not reveal any mutations. Inhibin B levels were found to be significantly decreased in the POF patients as compared to controls. However, no significant differences were observed with respect to the POR group.

Having detected the C>T transition in the coding region of the FOXL2 gene, polyalanine tract of this gene was screened for mutations as expansion, deletion and single base pair substitutions however, no mutations were detected.

Sizing of CGG repeats in the FMR1 gene was done by PCR and PAGE. All patients and controls have been found to have CGG repeats in the normal range of 5-50. It was observed that 35-40 CGG repeats were most prevalent in Indian population. Study is being continued for screening of newer genes associated with ovarian function.

Assessment of Gene Mutations Associated with Congenital Adrenal Hyperplasia

Congenital adrenal hyperplasia (CAH) is an endocrine dysfunction characterized by deficiency of enzymes crucial for synthesis of steroid hormones by adrenals. More than 95% of the cases are known to be caused due to deficiency of the enzyme 21-hydroxylase. CYP21, the gene encoding 21- hydroxylase enzyme is located in close proximity to a pseudogene called CYP21P with approximately 98% homology. CYP21P is an inactive pseudogene whereas CYP21 encodes the active 21-hydroxylase enzyme. The CYP 21 gene shows a high degree of variability in copy number as well as substantial polymorphism at the DNA level. A total of 19 mutations and 29 polymorphisms have been identified in this gene in different populations. Data on Indian population is, however, sparse. Study has been undertaken with the specific objective to identify all the mutations and polymorphisms in the CYP21 gene in Indian cases with classical and non-classical CAH. A method based on PCR-sequencing is being set up



Fig. 5. PCR amplification of CYP21 gene into two fragments F1 and F2

– 1130bp

for the purpose. CYP21P has an 8bp deletion in exon 3 which differentiates it from the active CYP21. Taking advantage of this, allele specific primers have been designed for selective amplification of active gene CYP21. Fig. 5 shows the selective amplification of active CYP21 gene in two fragments of sizes 2.1 kb and 1.1 kb respectively. These amplified fragments are now being sequenced using primers designed to screen the entire gene including coding as well as non coding



Fig. 6. Partial sequence of promoter region of CYP21 gene

sequences. Fig. 6 shows the partial sequence of promoter region of the CYP21 gene.

Antigens involved in Ovarian Autoimmunity

In POF onset of amenorrhoea occurs in women <40 yr and is associated with hypergonadotropinism and hypoestrogenism. In a significant number of such idiopathic cases, POF is known to be associated with autoimmunity. Detection of specific autoantibodies

therefore remains the most practical clinical and research marker of autoimmune disease. With the development of a specific, simple, non-invasive and sensitive test, several POF patients were enrolled to screen for ovarian antibodies. Sera from 37 POF patients and 25 agematched controls were screened. Nine of the 37 samples were positive for ovarian antibodies. Most of the sera identified multiple antigens depicting the heterogeneity of the disease. By immunohistochemistry, it was observed that there was no uniformity in the targets of attack. The targets were either ooplasm of the oocyte, interstitial region of the corpus luteum or theca cells.

REPRODUCTIVE HEALTH

Expression of Endometrial Functional Markers in Fertile and Infertile Cases

Implantation involves a series of sequential events which culminate into the superimposition of an altered structural and molecular phenotype on the receptive endometrium. In view of this, it is highly pertinent to investigate the mechanism by which endometrium acquires an ability to accept the embryo and also the mechanism by which this receptivity is modulated in presence of an embryo. To elucidate the role of progesterone in endometrial acquisition of receptivity, comparative two-dimensional proteomics approach was employed to screen endometrial tissue proteomes of control and antiprogestin treated bonnet monkeys (*Macaca radiata*). Several proteins showing differential expression were identified in the endometrial maps of

control and treated animals. Uterine flushing from control and treated animals was also compared by 2D proteomics. Uterine flushings from antiprogestin treated animals showed abundance of some proteins in the MW range of 25-15 kDa and PI range of 4-7. 2D spots corresponding to these differentially expressed proteins have been cored and analysed.

Studies initiated with the objective to investigate endometrial alterations at structural and molecular level in response to embryonic stimuli during early pregnancy in bonnet monkeys were pursued further. Endometrial tissues were collected from pregnant and non-pregnant animals on days 6 and 9 post ovulation. Remarkable spatio-temporal alterations were observed in the endometrium at histological level with the advancement in pregnancy. Endometrial insulin like growth factor binding protein 1, prolactin,
cyclooxygenase-1 and -2 showed higher expression in pregnant animals as compared to non-pregnant animals demonstrating the role of pregnancy induced stimuli in modulating the endometrial profile.

Proteomic Approach for Assessment of Pathophysiology and Progression of Endometriosis

Studies were continued at NIRRH to understand the precise etiology and pathophysiology of



Fig. 7. Western blot showing endometrial antigens detected using sera from women with endometriosis P₁-P₅ Endometriosis patients, C1, C2 Control, NC Negative control (secondary only control)



Fig. 8. (A) 2D Western blot analysis using P2 serum; (B) 2D Western blot analysis using P1 serum

endometriosis using protemics approach. Using the sera from endometriosis patients, endometrial antigens of mol wt 30, 45, 88 and 220 kDa were detected by Western blot. To further characterize these identified antigens 2D Western blotting was carried out using the sera of patients, which had shown reactivity on 1D electrophoresis (Fig. 7 and 8). Immunohistochemistry revealed reactivity to glandular epithelium and stroma of human endometrium in secretory phase (Fig. 9). Studies are underway to ascertain the role of these antigens in the pathophysiology of endometriosis.



Fig. 9. Immunohistochemistry showing reactivity in glandular epithelium and stroma (P2 serum of human endometrium in secretory phase. (A) : P2 serum endometriosis serum; (B) Control serum; (C) Secondary only control.

MALE INFERTILITY

Genomic Study of Y Chrosome Microdeletion in Severe Oligoasthenozoospermic and Non-obstructive Azoospermic Males

Severe impairment of spermatogenesis due to genetic factors such as chromosomal abnormalities and microdeletions of the genes on the Y chromosome are increasingly seen to be some of the causes of male infertility. These factors could affect the embryo quality. Furthermore, assisted reproductive technologies (ART) such as intra cytoplasmic sperm injection (ICSI) is known to transmit these deletions to the male offspring. It thus emphasizes the need to screen infertile men who would be potential candidates for ICSI programme. A total of 650 infertile males (mean age 32 yr) have been screened and 54 new patients recruited, constituting a total of 180 subjects. Mean duration of trying time was 6 yr (2-11yr), 99% had primary infertility. Screening for microdeletions by 6 STS

primers was carried out. Additional 5 STS primers were used for AZFa, b and c regions and 100 subjects were screened with a total of 11 STS primers. Amongst the 180 subjects, 95 were azoospermic and 85 severe oligoasthenozoospermic.

Abnormal karyotype was seen in 4.4%. (mosaicism for Klinefelter's Syndrome in 7 and inversion of Y in 1) subjects. Microdeletions were seen in 3.48% men. No additional deletions were noted in 100 subjects where 5 more STS primers were used. Microdeletions in AZF, a and

b, were predominantly seen. Phenotype/genotype correlation was not observed although phenotype picture in the patients with microdeletions showed poor fertility prognosis with reference to testicular histology which showed Sertoli cell only in 5 cases and maturation arrest at spermatocyte level in one case; while, in 36% patients without deletions, testicular histology showed hypospermatogenesis which has a better fertility prognosis during ICSI. The study so far indicates a strong need for screening and counseling of couples undergoing ICSI in view of 7.8% genetic aberrations, which could be transmitted to the male progeny.

To understand the role of the gene and protein expression and its impact on spermatogenesis resulting in a particular infertile phenotype, the mRNA of the DAZ gene was studied. It showed a normal expression on the spermatogonia to the round spermatids in a normal testicular tissue, while a weak expression in the germ cells was observed in the subject who was azoospermic, but did not have a microdeletion indicating a low expression of the DAZ gene which could be the cause of decreased spermatogenesis (Fig. 10). Interesting leads with the RBM gene, one of the two frequently deleted loci seen in this study, have been observed. In-depth characterization of the this gene and protein has been undertaken. Standardisation of the Western blot for RBM in normal human testicular protein (which showed a size of approximately 43kDa) (Fig. 11) is in progress.

Immunolocalization was observed on the mid piece and post acrosomal region of the sperm of a fertile individual (Fig. 12). Expression of spermatogenic genes



Fig.10. (A) 2D Western blot analysis using P2 serum; (B) 2D Western blot analysis using P1 serum







Fig. 12. Immunofluorescence showing RBMY localization in normal human spermatozoa

and their proteins, the testicular growth factors and steroid hormones are interrelated in the complex cascade of spermatogenesis and any aberration in this interaction can lead to infertility.

Factors Modulating Spermatogenesis in Severe Oligoasthenozoospermia and Non Obstructive Azoospermia

Study was undertaken with the objectives to (i) understand the role of FSH and local secretory factors of Sertoli cells in spermatogenesis and to correlate these observations with testicular histology and (ii) to identify non-invasive markers of Sertoli cell secretory function in order to predict the potential of sperm retrievals during testicular sperm aspiration (TESA)/ICSI programmes for alleviating male infertility. Earlier observation revealed that FSH and testicular volume were not reliable indicators of spermatogenesis hence a better marker for sperm retrievals was explored. To evaluate whether serum inhibin B and FSH could be used together as indicators of spermatogenesis potentially and subsequently used as non invasive markers for sperm retrieval, 53 infertile men [(non obstructive azoospermia (29) and severe oligozoospermia (24)] and 10 proven fertile men (controls) were recruited. The result showed higher FSH values in azoospermic men with severe testiculopathy viz. Sertoli cell only/maturation arrest. Inhibin B was seen to be significantly lower in this group (Fig. 13) as



Fig. 13. Serum inhibin B levels in non-obstructive azoospermic and severe oligozoospermic men

compared to men with severe oligozoospermia indicating that the Sertoli cells as well as the germ cells were affected in subjects with high FSH and low inhibin secretion. Data so far suggest that when both these values are considered, the testicular pathology is more predictive and hence could be used as a non-invasive marker for sperm retrievals. The study is ongoing and more number of cases are being recruited.

Generation of Transgenic Mouse Model of Male Infertility to Study the Molecular Mechanism of Block of Spermatogenesis

Among the genes involved in spermatogenesis, c-kit appears to play a crucial role in gonadal differentiation and formation of spermatozoa. Development of c-kit transgenic infertile mice is ongoing at NIRRH under an Indo-US project. This will help to ascertain some of the causes of infertility in men.

Sequence specific primers were designed and PCR amplified 5' untranslated region of Rouse sarcoma virus LTR (RSV-LTR) using CMV-GFP plasmid as a template and an expected size of 157bp PCR product was obtained. The product was sequenced and the sequence confirmed with data base sequence. The amplified product was cloned in pMosblue vector at EcoRV site and transformed into E. coli competent cells. The presence of an insert was confirmed by colony PCR using vector specific primers. C-kit gene promoter was PCR amplified using gene specific primers and an expected size of 302bp PCR product was obtained. After sequence confirmation, the product was cloned in pMosblue vector. The presence of insert has been confirmed by both colony PCR and restriction digestion.

Spermiation Failure: A Potential Target for Contraception

Studies were carried out at NIRRH to deduce the role of estrogen in spermatogenesis. Estradiol treatment of adult male rats lead to failure of release of step 19 spermatids into the lumen in stage VIII and their retention in stages IX-XII. Effect of estradiol on cytoskeletal (F-actin, vimentin and β -tubulin) and junctional (N-cadherin and β -catenin) proteins in

REPRODUCTIVE HEALTH

seminiferous tubules in various stages of germ cell development is also being studied.

REPRODUCTIVE TRACT INFECTIONS/SEXUALLY TRANSMITTED INFECTIONS

Clinical Trial of Praneem

Abnormal vaginal discharge is the most commonly observed gynaecological condition for which women seek medical attention. There are multiple pathogens, which give rise to these complaints and clinical signs. A wide range of effective therapies have been tried and efficacy of some indigenous drugs is being evaluated. Praneem polyherbal tablet (PPT) developed as microbicide was tested during Phase II clinical trial for treatment of bacterial vaginosis, Candida and Trichomonas infections. A total of 141 women was included in the trial. Cure rates for bacterial vaginosis (BV), Candida and T. vaginalis (TV) were found to be 75.6%, 77.3% and 100% respectively. The data also indicated that the PPT treatment was more effective in presence of single pathogen (BV - 68.0%); Candida - 77.4%; TV - 100%) in comparison to cure rate in the presence of multiple pathogens [BV + Candida - 54.5%; BV + TV - 100.0%; Candida + TV - 50.0%]. Majority of the subjects (97.2%) reported symptomatic relief from the abnormal vaginal discharge. Phase III trials are planned in coming year.

Purification and Characterization of CD4 Independent 160kDa Sperm Receptor for HIV

Studies were carried out to understand the role of spermatozoa in transmission of HIV. The modality of HIV entry into spermatozoa on which conventional CD4 receptors are absent, is not yet clear. Attempts to understand the mechanism of HIV transmission resulted in identification of a CD4 independent 160kDa HIV receptor protein on the spermatozoa for the first time. Western blot analysis of sperm proteins demonstrated specific binding of gp120 as well as cell free HIV to 160kDa protein band. Further characterization demonstrated that 160kDa HIV binding protein is distinct from conventional CD4 receptors and binding of I¹²⁵gp120 to 160kDa protein can be displaced specifically by unlabelled gp120. Preliminary studies demonstrated the differential expression of this protein in sperm samples from individual donors and the samples devoid of this protein did not exhibit binding of gp120 HIV envelope glycoprotein to any protein in sperm extracts. Sequencing of the cDNA for 160kDa HIV receptor protein showed sequence homology with human mannose receptor. Efforts are on for development of modalities for the prevention of sexual transmission of HIV and to understand the mechanism of CD4 independent interaction of HIV.

DEVELOPMENT AND EVALUATION OF NEWER MICROBICIDES

Nisin: The Antimicrobial Peptide for the Control of Fertility and Sexually Transmitted Infections

Study to develop dual protective vaginal products having antimicrobial and spermicidal properties is ongoing at NIRRH. Antibacterial and spermicidal properties of nisin, a 34 amino acid peptide, have already been reported last year. During the year under report, to potentiate the anti-HIV activity, a cocktail of nisin with carrageenan was prepared using carbopol as a gelling agent. The study on effect of gel formulation on fertility in rabbits and on STI causing pathogens (*Chlamydia glabrata*, *C. parapsillosis*, *C. guillermondii*, *C. krusei*, *C.tropicalis*, *N.gonorrhoeae*, *Trichomonas vaginalis*, *E. coli* and *Staphylococcus aureus*) is in progress.

DEVELOPMENT OF NATIONAL GUIDELINES

National Guidelines for Management of Reproductive Tract Infections (including Sexually Transmitted Infections)

The Council is developing National Guidelines for Management of RTI/STIs for the purpose of incorporating in the Reproductive and Child Health Programme. The specific objectives are to (i) conduct a rapid review of management practices (operational, clinical, laboratory) on RTI/STIs at different levels of health system in India; (ii) share assessment findings with a group of experts and evolve operational as well as quality case management guidelines for RTI/STI services; and (iii) review the existing international guidelines for RTI/STIs and prepare operational and quality case management guidelines suitable for India's health facilities.

National Guidelines for Assisted Reproductive Technology (ART) Clinics

National Guidelines for Accreditation, Supervision and Regulation of ART Clinics in India, developed by the Council has been accepted by the Government after minor changes and these guidelines are in the process of translation into an act. As all ART clinics have the potential of sex selection, the Council has recommended that all the ART clinics be registered under PNDT act immediately and when ART act/bill will be developed and implemented all the ART clinics would be again registered under ART act for the purpose of accreditation, supervision and regulation of these clinics as this provision is not present in the existing PNDT act.

MATERNAL HEALTH

Management and Outcome of Previous Cesarean Section at Teaching Hospitals in India

Safety in childbirth for women with prior cesarean is a major public health concern. Repeat caesarean section and planned vaginal birth after caesarean section are both associated with benefits and harms and correct management represents one of the most significant and challenging issues in obstetric practice. Prospective data was recorded on management practices, associated complications and mortality for a period of 8 months in 2004-2005 on 15,664 consecutive cases of previous cesarean section reporting for delivery at 31 medical colleges/teaching hospitals.

A total of 1,55,863 deliveries were recorded, of which 28.1% were caesarean sections. The rate of repeat caesarean sections was 10.1%. The average age of the

women delivering by repeat caesarean section was 26.1 ± 3.9 yr. Of the total deliveries, 74.5% were second para, 42% were from rural areas and 89% were booked cases. Period of gestation was less than 37 weeks in 27.2% women. Vaginal delivery carried out in 25.8% women was successful in 62.3%. Overall, 16% women had successful vaginal birth after cesarean, 47% a repeat elective and the remaining 37% had an emergency cesarean section. Major indications for repeat cesarean section included dystocia (44.2%), previous 2 cesareans, fetal distress, doubtful scar integrity, nonprogress of labor, severe PIH/eclampsia and others. In majority of cases the surgical technique was conventional and only in 1.9% the Misgav- Ladach technique was used. Scar dehiscence and surgical complications were each observed in around 4% of cases. Out of 127 cases of uterine rupture, cesarean hysterectomy was performed in 38% women. Blood transfusion was given in 7.1% and post-operative complications were seen in 6%. Perinatal and maternal mortality was 26.4/1000 and 172/100,000 deliveries respectively.

Safety and Efficacy of Contraceptive Implant, Implanon

Implanon, a single rod contraceptive implant made by the Dutch manufacturer Organon provides contraceptive protection for maximum of 3 yr. It contains 68 mg of etonogestrel in a ethylene vinylacetate (EVA) copolymer core, surrounded by a EVA membrane. Etonogestrel (3 keto-desogestrel) is a synthetic progesterone derived from 19-nortestosterone and is biologically active metabolite of desogestrel. The efficacy and safety profile of desogestrel containing oral contraceptives is well established. A study was initiated at 17 centres in August 2004 to evaluate the efficacy, side effects, return of fertility following discontinuation and acceptability in terms of continuation rate of Implanon. The study also assessed users' perspective about the method and the relative choice of the method when offered through cafeteria approach. Implanon was offered within 5 days of the last menstrual period, concurrent with MTP and to those women who are lactating with age of the last child more than 6 months. Women (age group 20-38 yr) with proven fertility and having at least one living child were included in this trial. Till February 2006, 2550 women have been enrolled in the study and so far data on 2,355 women has been collected. Majority of Implanon acceptors were urban dwellers (69.3%), housewives (84.8%), literate (86.8%) and Hindu (78.2%) women. Net probabilities for discontinuation due to different reasons were computed by using life table technique. The discontinuation rate at the end of 12 months was 16.1%. The main reasons for discontinuation per 100 users are shown in Fig. 14. Less than 6 % of the acceptors gained



Fig. 14. Reasons for discontinuation of Implanon

more than 5 kg weight at 12 months of use of the device. Of these, only 3 women discontinued due to increase in weight of more than 5 kg. Six women experienced loss of 5 kg or more during the use of the implant. One case discontinued due to deep vein thrombosis. No method failure has been reported in this trial so far. No woman was lost to follow up. The cumulative continuation rates were 95.9, 91.8 and 83.9 per 100 users at 6, 9 and 12 months respectively. Eight hundred and thirteen women completed one year of use while 76 women have completed more than 18 months of use.

Assessment of Prevalence of Osteoporosis in Adult Population of India

The ICMR is carrying out a task force study at four centres–AIIMS, New Delhi, NIN, Hyderabad, SGPGIMS, Lucknow and NIRRH, Mumbai to establish REPRODUCTIVE HEALTH

peak bone mineral density (BMD) reference values for Indian men and women and to assess the prevalence of osteopenia and osteoporosis in Indian population. Preliminary analysis of data on 3642 subjects has shown that prevalence of osteopenia varied between 38.8-55.8% in males and 37.5-54.0% in females. Further, prevalence of osteoporosis was found to vary between 16.6-49.2% in males and 18.3-51.1% in females.

CHILD HEALTH

Home Based Management of Young Infants

The ICMR project on home based management of young infants (0-60 days) comprising care of infants at birth including resuscitation, care of normal and low birth weight babies, treatment of local infections, referral of sick infants and health education is ongoing in rural areas of five states in the country. The package of intervention is being delivered by appropriately trained village level workers - Shishu rakshaks (SR-a community chosen worker) in one arm and anganwadi workers(AWW) in second arm. Training is the most crucial activity in this project. A total of 278 SRs and 270 AWWs have been trained. Following completion of training in January 2005, independent evaluation of village level workers was carried out by Society for Education, Action and Research in Community Health (SEARCH) and ICMR for knowledge evaluation, assessment of skills, attitude and behaviour, hand washing, respiratory rate counting, weight recording, temperature measurement, detection and management of birth asphyxia and injection skill on dummies and interpersonal communication. Seventy percent SRs and 23% AWWs scored more than the cut off mark for delivery of intervention (Fig. 15). They were further provided reorientation training and reinforcement of skills during field practice. Of the SRs scoring >70%, 26 workers participated in piloting of intervention. They were provided further reorientation training and hands on practice. Fifty three probable cases of sepsis were successfully treated during piloting of intervention. Three deaths that occurred during piloting were unrelated to intervention. Results of piloting were reviewed by Data Safety Monitoring Board and Central Ethical Committee



Fig. 15. Proportion of SR/AWW with score 70 & above in final evaluation

of ICMR and were found to be satisfactory. The Committee recommended scaling up of intervention.

Effectiveness of Amoxycillin vs cotrimoxazole in the Treatment of Pneumonia in Children

Acute respiratory infection (ARI), mostly pneumonia, is one of the leading causes of death in younger children in developing countries. The Council carried out a multicentre study in 7 districts - Delhi, Nagpur, Trivandrum, Mumbai, Lucknow, Bhopal and Chandigarh at 14 rural primary health centres to study the effectiveness of 3 day amoxycillin vs 5 day cotrimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age. Data collection has been completed at all the centres in April, 2005. Final analysis of data is ongoing.

ADOLESCENT REPRODUCTIVE HEALTH Knowledge and Practices of Adolescent

Girls

Adolescents constitute one-fifths of India's population and yet their sexual health needs remain largely unaddressed in the national programme. The Council supported a community survey to study knowledge and practices of adolescent girls regarding reproductive health with special emphasis on hygiene during menstruation in 50 villages selected from 5 districts namely Kamrup, South-West Delhi, Mysore, Dhar and Barabanki. A total of 500 adolescent girls, 500 mothers of adolescent girls, 93 women opinion leaders and 150 women ICDS and health functionaries were interviewed using field tested research tools. It was observed that 93.6% girls were literate but only 49.2% went to school and 41% had no access to toilet facilities. The mean age of menarche was 12 yr. Most girls (70.6%) were not aware of menstruation till onset of menarche and had limited knowledge of physical changes during puberty. The main source of information was mother(37.6%), siblings(32.8%), and friends(27.6%) (Fig. 16). The onset of menarche caused fear (62.3%)and shock (43.9%) in them. Many mothers of adolescent girls considered menses as dirty and polluting (70.4%) but performed 'no ceremony' for menarche (56.8%). Common complaints of adolescent girls regarding menstruation included vaginal discharge, itching, smelling discharge and painful periods (Fig. 17). They



Fig. 16. Health seeking behaviour of adolescents with vaginal discharge



Fig. 17. Common complaints among adolescents

restricted movement of the girls within house (68%) and restrained them from consuming sour food. Nearly 57.6% girls and 74.1% mothers reused cloth after washing the menstrual discharge. It was found that knowledge of HIV/AIDS/RTIs/STIs was incomplete in all respondents (Table 1). Even though 85% girls, 69.6% mothers and 83.8% women opinion leaders had heard about HIV/AIDS, their knowledge about mode of transmission and prevention was limited. There is need of a multi-pronged strategy using all kinds of media to disseminate information on reproductive health of adolescent girls/women with special emphasis on hygiene during menstruation.

Table 1. Knowledge of HIV/AIDS among adolescentgirls (n=500) multiple response

Mode of transmission (%)	Prevention of HIV/AIDS (%)
Unprotected	Safe sex
sex 46.6	practices-37.8
Infected blood	Safe blood
transfusion	transfusion
(31.8)	(23.6)
Infected needle	Using sterilized
/syringes/	

Improving Service Utilization by Adolescents through Urban Health Posts in Mumbai

A project has been initiated with the aim to create an adolescent friendly environment at the Urban Health Posts as well as in the community and improve health service utilization by adolescents through networking within the existing health care infrastructure. A comprehensive adolescent health care program has been conceptualized in collaboration with Municipal Corporation of Mumbai service units to meet the multiple needs of adolescents, particularly for contraception and prevention of STIs. Study will be conducted in three phases-(i) preparatory phase of six months with situational analysis of the needs and perceptions of adolescents and identification of the partner institution with facilities to offer reproductive health services, (ii) intervention phase of two years for identification of adolescent related health issues and providing services and (iii) the third phase of six months for process, outcome measurement and preparation of the report.

The intervention phase of the project is ongoing. Following interventions have been done (i) Adolescent Friendly Centres were named as JAGRUTI, through a participatory approach. They were inaugurated in February, 2006 amidst a gathering of adolescents and local committee members and other stake holders. Information on (i) availability (ii) dissemination of services being provided at the centre was disseminated through pamphlets, posters and advertisement through cable TV. A number of non-health related activities were planned such as essay and drawing competitions to build rapport and attract the adolescents to the centre. (iii) meetings were held with parents, teachers and gatekeepers to build rapport and seek support in provision of sexual and reproductive health services to the adolescents.

The following output of interventions have been observed: (i) married adolescent women have started approaching the centre for family planning methods, pregnancy detection, complaints of vaginal discharge, menstrual complaints, infertility and other general health complaints, (ii) unmarried adolescent girls approached the centre for premarital counseling, menstrual complaints and queries on sexual and reproductive health, (iii) adolescent boys approached the centre mainly to procure condoms and also for information on a number of their sexual and reproductive health problems and (iv) older women also approached the centre for hypertension, arthritis or other general health complaints but to a lesser extent.

Evolving a Model for Improving Reproductive Health among Rural College Youth in Maharashtra

The ongoing study is based on developing and applying information, education, communication (IEC) and counseling intervention backed up by referral linkages with the district health services. The main objective of the study is to develop a replicable and sustainable model for provision of sexual and reproductive health services to college-based youth in Thane district. The ongoing study is of 30 months duration and will have an experimental design conducted in three phases. In order to assess the awareness and views about reproductive health as well as sexual behaviour of rural college youth, baseline data (qualitative and quantitative) have been collected. A self-administered, semi-structured questionnaire was used for survey, which included 1500 students (800 male and 700 female) in the age group 15-24 yr.

The following interventional activities were carried out during January to December 2005 in four experimental rural colleges. A total of 65 IEC and peer leader training programs were conducted throughout the year and 7795 students (4184 boys; 3611 girls) attended these programs. The subjects included were human physiology, conception, menstruation, masturbation, contraception, RTIs, STIs and HIV/ AIDS. Counselling centres were started in all the four experimental colleges in the month of July 2005. Trained counsellors made service provision available once a week for at least 5 h in each college. A total of 776 students (311 boys and 465 girls) attended these counselling centres in 5 months. IEC material (various books and pamphlets) collected from a number of organizations was made available at the college library for teachers and students for reference. A total of 1200

books, pamphlets on reproductive and sexual health of youth have been distributed among peer leaders, teachers and librarians. Orientation programs were conducted in colleges for all the teaching and nonteaching staff. A total of 20 male and female teachers from the colleges (average 5 teachers) took initiative on their own for further training.

Competitions such as essay writing, slogans, making poster and debates were organized in all experimental colleges. Students from NSS were provided with detailed information about 'peer educator' activity. Majority of the participants of the various competitions and NSS activity have opted for further detailed training as 'peer educators'. Students were also told about the 'peer educator' programme through regular IEC programmes in respective colleges. A total of 200 students (average 50 boys and girls from each college) were selected and provided with 'peer educator' training. Government health care providers (block level) have been oriented and reproductive health service provision was made available for students from experimental colleges at PHCs. Post survey in all colleges has been initiated in the month of December 2005.

NUTRITION

The National Institute of Nutrition (NIN), Food and Drug Toxicology Research Centre (FDTRC) and National Centre for Laboratory Animal Sciences at Hyderabad are engaged in studies on various aspects of nutrition *viz*. community studies, prevalence of nutrient deficiency disorders in tribal areas, clinical and basic studies in addition to food and drug toxicology studies. Periodical surveys by National Nutrition Monitoring Bureau (NNMB), development of low cost technologies for food fortification, transferring food fortification technologies to industries and government and to supply iodised salt and fortified foods to the community at an inexpensive cost through public distribution system are some of the efforts made by NIN in this direction.

COMMUNITY STUDIES

National Nutrition Monitoring Bureau

In view of the emerging problem of diet related chronic degenerative diseases, the NNMB carried out studies on the assessment of the prevalence of obesity and hypertension among adults in the rural communities of 8 states in addition to the ongoing routine diet and nutrition assessment surveys. As per WHO cut-off levels for waist circumference, about 1% men and 7% women had abdominal obesity. Similarly, about 25% men and 69% women were found obese as per WHO criterion of waist/hip ratio. About 27% men and women had hypertension. About 4% men and 3% women in rural Andhra Pradesh were found having hyperglycemia.

Preliminary analysis of the dietary survey revealed that the average daily intake of the cereals and millets was less (412 g) than the recommended level (460g). The intake of proteins in the form of pulses and protective foods such as green leafy vegetables, milk and milk products was grossly inadequate. The median intake of all the nutrients in general was lower than the RDIs and as regards the intake of micronutrients such as iron, vitamin A, riboflavin and folic acid, it was grossly deficient.

The overall prevalence of underweight (weight for age < median - 2SD of NCHS standards) of 1-5 yr

age group was 55%, which was similar among boys and girls. The prevalence of stunting and wasting was about 52% and 14% respectively. About 34 % adult men and 37% women had chronic energy deficiency (CED: BMI <18.5). The prevalence of overweight and obesity was 8% and 11% respectively. About 54% adult men and 72% non-pregnant non-lactating women were found to be anaemic.

Nutrition Surveys in Tsunami affected Areas

Surveys were carried out to assess the diet and nutritional status of the tsunami affected communities living in rehabilitation centres in Andaman and Nicobar Islands. The study revealed that the food and nutrient intake of the households/individuals was in general less than the recommended levels. The average intake of various nutrients except proteins was less than the RDA. The intake of micronutrients such as iron, vitamin A, free folic acid and riboflavin was grossly inadequate.

The prevalence of vitamin A deficiency signs such as conjunctival xerosis among preschool children was 2.7%. The prevalence of underweight among preschool children was about 48%, while that of stunting and wasting was about 37% and 16% respectively. About 17% adult males and 19% adult females showed varying grades of CED. The prevalence of various forms of undernutrition was relatively high among the settlers compared to local Nicobarese population.

Prevalence of Iodine Deficiency Disorders in Tribals of Madhya Pradesh

The RMRC, Jabalpur conducted a study to assess the prevalence of iodine deficiency disorders (IDD) in school children of Baigachak area of district Dindori in M.P. The prevalence of goiter was found to be 20%. More than 87% school children were found to have low urinary iodine which is the most reliable indicator of IDD. Iodine was low in females (91.62%) as compared to males (83.5%). The results indicate that though the prevalence of IDD has decreased in M.P., iodine deficiency is still a public health problem in the study area.

Nutrition Monitoring Survey in Jodhpur (Rajasthan)

Studies were conducted by DMRC, Jodhpur on a total of 28 villages from six tehsils covering 560 households. Socio-demographic and socio- economic information was recorded. All the members in the household were examined for nutritional deficiency signs, anthropometric measurements and dietary intake (24 h recall method) and history of nutritional morbidities in last 15 days was obtained. Dietary intakes of the individuals were recorded in alternate houses from each village. Protein calorie malnutrition (PCM) was higher in females compared to males. Undernutrition was very high in preschool children (81%) and was higher in SC and ST community (88 and 86%) compared to others (75%). Chronic energy deficiency in adults was observed to be higher in SC and ST community compared to others. Diet was grossly deficient in green leafy vegetables (GLV) followed by fats, pulses, legumes and other vegetables.

Nutritional Status and Morbidity in Pregnant and Lactating Women in Rajasthan

Data from 10 villages of Luni Panchayat Samiti of Jodhpur tehsil covering 792 women comprising 174 pregnant, 286 lactating and 332 non pregnant and non lactating women was collected. Initial trends revealed high prevalence of iodine deficiency disorder in pregnant and lactating women (65-71%). Consumption of normal iodized salt wss very low. Severe anemia (12.9 %) was more in pregnant women. IDD and iron deficiency anaemia (IDA) were more prevalent in OBC and SC. IDA was higher in pregnant and lactating women (86%) as compared to controls (76.5%). Severe anaemia was high in pregnant women (13%) in comparison to controls (2.8%). IDA was more in OBC and SC (47.5% and 28.7%), illiterates (61.3%) and low income group (37.3%). Diet of pregnant and lactating women was highly deficient in protein, calories and iron.

Nutritional Status of *Dongria Kondh* Tribe and Domb Scheduled Caste Populations of Orissa

Study has been carried out on nutritional status of *Dongria Kondh* primitive tribe and *Domb* scheduled caste populations of Orissa at RMRC, Bhubaneswar. The prevalence of underweight, stunting and wasting was 69%, 62%, and 38% respectively among *Dongria* while it was relatively lower among Domb children. The prevalence of chronic energy deficiency (CED-BMI <18.5kg/m²) was about 60% for both Dongria Kondh and Domb populations, while about 30% and 10% were having below normal and normal BMI. Less than one percent of these populations were overweight or obese. Prevalence of grade III CED was greater in Domb (17.6%) compared to Dongria (13%) populations .About 10% adults were normal in both the study groups. The proportion of household salt samples having less than the recommended levels of iodine (<15 ppm) was 51.2% in the Dongria Kondh in comparison to 18.9% in the *Dombs*. The prevalence of anaemia was 86.4% and 76.9% among Dongria Kondh and *Domb* populations respectively.

Intervention Study for Cholera, Intestinal Parasitism, Vitamin A deficiency and Scabies amongst Tribals of Orissa

A pilot study for cholera, intestinal parasitism, vitamin A deficiency and scabies amongst some primitive tribes of Orissa was undertaken by RMRC, Bhubaneswar in four identified primitive tribes *viz*. Bondo, Didayi, Kondha and Juanga residing in different geographical areas of Orissa. Findings revealed V. cholerae in 12.6%, E. coli in 40.5%, Salmonella spp. in 1% and Shigella spp. in 54% of the cases. A suitable intervention in the form of drugs, oral rehydration solution (ORS) and community awareness programme was undertaken. The rectal swab analysis showed a remarkable decline in V. cholerae. The prevalence of vitamin A deficiency in the form of Bitot's spot and night blindness among preschool (0-5 yr) and school going children (6-14 yr) reduced after intervention from 7.2% to 4.8% during follow up. A follow up examination of patients of scabies after appropriate intervention (both drug intervention and IEC) revealed that the disease has reduced from 20.3% to 9.5% in Bondo, 12.5% to 6.8% in Didayi, 14.8% to 8.6% in Juanga and 14.2% to 7.8% in Kandha population.

CLINICAL STUDIES

Effect of Supplementation of Micronutrients in Pregnant Women

A study was initiated to evaluate the effect of iron supplementation to pregnant women on haemoglobin

status and pregnancy outcomes. The data obtained from 600 pregnant women showed that the prevalence of anaemia was severe in early pregnancy (8% women) and late pregnancy (17.4% women).

Prevalence of intrauterine growth retardation (IUGR) and low birth weight is very high in India. A study was planned to measure body composition of newborn babies and relate it with maternal and cord blood trace element status. Two hundred newborns have been recruited and the study is in progress.

Clinical Trials of Protein/Zinc Supplementation to Full Term Infants

Several studies have demonstrated body fat to be high among children who were undernourished in young age and rehabilitated at later age. A study was initiated in the nutrition ward at Niloufer hospital to study the effect of varying degrees of protein supplementation in severely malnourished children on their recovery and body composition. Thirty-six children (mean age 28.1 months) were followed up for one month and the interim analysis of data was carried out. Mean calorie intake at home before admission was 842 cal / day which increased to 1540 cal / day at the time of discharge (30th day after admission). Mean weight of the children increased from 6.2 to 7.7 kg, by 30 days and body fat percentage also increased from 6.8% to 13.46%. In absolute terms, the total weight gain was 1433 gm in 30 days. The weight gain contributed by fat tissue was 41.2% and fat free mass contributed 843 gm. Mid arm circumference also increased significantly from 9.8 cm to 11.6 cm.

Undernutrition and stunting are major public health problems among preschool children in India. A study was undertaken to assess the effect of supplemental zinc (5mg/day) on the growth, body composition, respiratory and diarrhoeal morbidities in infants. In 475 children (males 18.7% and females 26.4%), of which 22% were low birth weight (LBW) babies, Zn supplementation was given after randomization. All the anthoropometric measurements were significantly low among LBW babies at all ages and significantly higher in boys at all ages as compared to NNMB data. Based on NCHS standards among infants with birth weights more than 2500 g (2 score classification), 10.2% and 19.6% were stunted at 12 and 18 months of age. Similarly, 35.1% and 45.5% were underweight at 12 and 18 months of age respectively.

Prevalence of Osteoporosis in Adult Population in India

Preliminary results of the study indicated that the peak bone mass of the young adults from high-income group was comparable to the Western standards. Bone densities in adults were related to the intake of calcium, body weights and socio-economic status. High prevalence of osteoporosis was observed in the lowincome groups. In addition, a study on pregnancy related changes in bone mass in women from low socioeconomic group was taken up to assess the extent to which bone mineral mobilization occurs in them. In addition, a study was initiated to assess the effect of overweight and obesity on the development of peak bone mass in 64 men and 36 women (age 20-35 yr) from high socioeconomic group. Their DEXA scans were generated at 3 sites viz., hip, spine, forearm and whole body. Studies are in progress.

BASIC STUDIES

Establishment of Screening Method for Micronutrient Bioavailability

A state of-the-art Caco-2 cell culture facility was established for the analysis of iron and zinc bioavailability under DBT's Crop-biofortification networking programme. The facility provides scientific and technical services for assessing bioavailability of micronutrientsm such as iron and zinc in staple foods.

Country Investment Plan/Food Fortification

The NIN has established a private-public partnership in food fortification of whole wheat flour with iron, folic acid and vitamin A and provided technical support in operationalizing Vijaya micronutrient fortified wheat flour, which is distributed through public distribution system (PDS) in two districts, *viz.* Ranga Reddy and Warangal on a pilot basis.

Double Fortified Salt (DFS)

Studies on the stability of iodine in DFS, which was developed as per the NIN's technology, showed the stability of iodine for more than 12 months with very little loss. The study also demonstrated that a modified method for iodine is essential for consistent and accurate estimation of iodine in DFS. Efforts are on to provide DFS through PDS at an affordable price in order

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MAJOR ICMR RESEARCH PROJECTS IN NUTRITION

NUTRITION

to make it easily accessible to the people belonging to low socioeconomic strata.

As part of research relevant to the community and also to meet the social obligation, the Institute provided low-cost technology know-how under technology transfer programme to an Industry of Andhra Pradesh Government for the production of quality iodized salt. As a result of technology transfer, quality iodized salt was made available for the public from June, 2006. through PDS in Andhra Pradesh @ Rs. 3.00 - 4.00 per kg.

DIETARY FATS

Role of Dietary n-3 PUFA or Trans Fatty Acids in Foetal Programming of Insulin Resistance in Rats

Nutritional deprivations/imbalances in utero alter physiology and metabolism of developing tissues/ organs postnatally and increase the risk of chronic adult diseases. Long chain polyunsaturated fatty acids (LC PUFA) are integral components of cell membranes and are important determinants of foetal growth and development. Docosahexaenoic acid is one of the abundant fatty acids present in brain, other neural tissues and the retina. Earlier studies indicated that increasing α -linolenic acid (18:3n-3, vegetable oil) or LCn-3 PUFA (fish oil) while keeping total PUFA constant in the diet, increased insulin sensitivity in target tissues of sucrose-induced insulin resistant rats. On the other hand, trans fatty acids (TFA) from Indian vanaspati decreased insulin sensitivity. Study was designed to evaluate the role of dietary fatty acids (TFA or 18:3n-3 or LCn-3 PUFA) in foetal programming of insulin resistance. The results showed that maternal n-3 PUFA or TFA did not alter insulin sensitivity in the offspring up to 100 days of postnatal life.

Effect of Sesame Lignans on Oxidative Stability of Edible Vegetable Oils

Tocopherols in oils are protective against oxidative deterioration during storage. However, to prevent thermo-oxidative degradation of oils due to deep-frying at high temperatures, addition of more efficient antioxidants is needed. Though, PFA (Prevention of Food Adulteration Act) approved antioxidants are added at permissible levels to edible oils and food products, at higher concentrations these synthetic antioxidants are toxic. In view of this there is a need to identify novel, natural components of foods with radical scavenging and antioxidant activity.

Lignans of sesame (Sesame indicum) seeds were isolated and tested for their effects on thermal / storage (at 180°C or 60 days at room temperature), stability of edible (soyabean-SBO, sunflower-SFO, rice bran-RBO and palmolein-POL) oils. The study included i) determining total free radical scavenging activity (RSA) using 2,'2', diphenyl picryl hydrazine (DPPH) ii) total free tocol content iii) lignan profile iv) PUFA composition. The order of the RSA of oils before heating was as follows: RBO=SBO>SFO>PO. Addition of 1.2-% lignans to SBO or POL increased percent retention of total tocols at the end of 120 min of heating. Heating of oils (at 180-200°C) increased sesamol and decreased sesamolin, while sesamin was relatively resistant to heat. These results suggest that sesame ligans may have potential applications as natural antioxidants for the thermal stabilization of edible vegetable oils.

Effect of Maternal Dietary Trace Element Restriction on Body Adiposity and Insulin Resistance in the Offspring

Studies on maternal magnesium restriction in WNIN rats showed an irreversible increase in the body fat % in the offspring by three months of age and also induced insulin resistance at 6 months. While the increased body adiposity, decreased lean body mass, fat free mass and reduced insulin response to glucose challenge persisted till 18 months of age in magnesium restricted offspring, insulin resistance observed in them at 6 months of age did not persist at later time points.

Although glucose tolerance and insulin sensitivity / resistance were comparable among the offspring of different groups at all the time points studied, pups born to Zn restricted mothers rehabilitated from birth or weaning had higher body adiposity (in males) and decreased insulin secretion (in females) compared to controls. However, changes seen at 3 - 6 months of age were transient in nature and no differences were observed among different groups of offspring at later time points. Adiposity changes were seen only in the males, whereas changes in insulin secretion were apparent in females born to Zn restricted mothers.

Feeding chromium-restricted diet for 3 months did not affect the body weight gain, glucose tolerance, insulin resistance and lipid profile parameters in WNIN female rats. Cr restriction *per se* had no adverse effect on the reproductive performance of the rats even when continued through pregnancy or supplemented from conception. The studies are in progress.

DEGENERATIVE DISEASES MOLECULAR BIOLOGY

Dietary and lifestyle changes result in an unprecedented rise in obesity and insulin resistance. Using rat model, the role of dietary saturated fatty acids and trans fatty acids in inducing insulin resistance was demonstrated. Clustering of type II diabetes in certain families and analysis of ethnic populations indicate a strong genetic background of the disease albeit indirectly. The etiology of type 2 diabetes (T2DM) is multifactorial and studies indicated a major role of the genetic factors. Study was initiated to assess the role of polymorphism within PPARy, ADRB 3, resistin and adiponectin genes in developing T2DM in Indian population.

PHYSIOLOGICALLY ACTIVE NON-NUTRIENTS IN FOODS

Phenolic Content and Anti-oxidant Activity of Plant Foods :Vegetables and Fruits (including Dry Fruits)

Plant derived anti-oxidants such as flavonoids and related phenolics are considered powerful anti-oxidants. There is inverse relationship between fruit and vegetable intake and risk of degenerative diseases. Efforts are on to generate a database on the commonly consumed anti-oxidant plant foods of India and the contribution of the phenolic content to their anti-oxidant activity (AOA). The total phenolic content and AOA of some commonly consumed green leafy vegetables and fruits (including dry fruits) was determined.

Among green leafy vegetables, *Raphanus sativus* (raddish greens) and spinach had the highest and lowest amounts of phenolics respectively. Diphenyl picryl hydrazyl (DPPH) scavenging activity was the highest in fenugreek and the least in *gori methi* leaves. Mint

had the highest and *Moringa oleifera* lowest reducing power, while iron chelating activity was the highest in *Basella rubra* and the least in mint.

Among fresh fruits, black grapes had the highest and watermelon the lowest phenolic content while tomato had the highest reducing power and iron chelating ability. Red guava had the highest DPPH radical scavenging activity while lemon, fig and passion fruit had the least DPPH chelating ability and reducing power.

Among the dry fruits studied, walnuts had the highest anti-oxidant activity while cashew nuts, almonds and piyal seeds had the lowest activity.

Development of Recipes Rich in Anti-oxidant Activity and Their Acute Effects

Seventeen AOA rich recipes (salads) based on green gram and bengal gram sprouts were developed. Addition of some vegetables decreased the AOA of the recipe while some of them did not affect it. It was found that addition of lemon juice, pepper and salt did not decrease the AOA of legume sprouts and the AOA of these salad recipes was higher than that of sprouted legumes. All the recipes were accepted reasonably well by human volunteers.

The consumption of these salad recipes had acute effects in apparently healthy adult, male human volunteers. Although they did not affect the oxidative stress (plasma thio barbituric acid - TBAR) in the subjects, they prevented the time dependent deterioration of the antioxidant activity (ferric reducing antioxidant power : FRAP) of their blood plasma on consumption of white bread. Also, they appeared to protect the plasma against exogenously induced oxidation *in vitro* with copper sulphate.

STUDIES ON STEM CELLS

Nestin Positive cells/Pancreatic Progenitors

The islets isolated from adult mice were cultured for 48 h and subsequently overlaid onto matrigel to study the proliferation of nestin positive cells (NPC). The serum free medium consisted of combination of epidermal and fibroblast growth factors to promote the differentiation of progenitors. The results showed an appreciable number of immunospecific NPC (20-30%)

NUTRITION

within a week of culture as compared to the direct seeding the islets on to the matrigel (5-10%). The confluency of the cultures was of greater magnitude by 2 weeks (50%).

Immunolocalization of NPC

NPC were studied in different age groups of mice (3 d, 1 wk, 2 wk 4 wk old and adult). To understand the localization profile of the NPC between exocrine *vs* endocrine fraction of the pancreatic tissue. NPC positive cells were present both in exocrine and endocrine fractions of the tissue. However, immunolocalization was more diffused in the lower age groups such as 3 d and 1 wk as compared to 6 wk. Distinct presence in both exocrine and endocrine tissue of the 6 wk adult mice was observed suggesting that pancreatic exocrine fraction can also be explored as the source of insulin secreting cells.

CATARACT AND RETINAL DEGENERATION

Expression of α-Crystallins under **Pathological Conditions**

Studies have been initiated to understand the expression of small heat shock protein, α -crystallins, under various pathological conditions such as diabetes, cancer and nutritional deficiencies. Elevated expression of α -crystallin in various diabetic tissues was reported for the first time.

Role of Functional Foods and Nutraceuticals in Degenerative Conditions

Aldose reductase inhibitors (ARIs), antiglycating agents and antioxidants may ameliorate the eye complications in diabetes. Preliminary screening and *ex vivo* lens organ culture studies suggest that tannoids of *amla* have significant aldose reductase inhibitory potential. A few dietary agents are found to be effective in preventing protein glycation *in vitro*. Studies are in progress to understand the mechanism of inhibition and to understand their effect in animal models.

FOOD AND DRUG TOXICOLOGY

FOOD SAFETY

The Government of India has initiated projects to create awareness on food safety and strengthen food

safety monitoring system in India. The Ministry of Health and Family Welfare has identified NIN as the nodal centre to conduct a country survey.

A project on utilization of detoxified moldy sorghum using lactobacillus is in progress. A DST sponsored project on genotoxicological effects of pesticides in agricultural workers in Guntur district is being carried out to assess the toxic effect in occupationally exposed farmers.

Fluorosis is one of the major public health problem. Animal models to demonstrate the mitigating effects of divalent cations (magnesium, calcium) in fluoride-induced toxicity have been developed.

Detoxification of mycotoxins by lactic acid bacteria isolated from fermented *Sorghum* and *Cassia tora* was initiated based on earlier findings of reduction in mycotoxins by natural fermentation of mouldy sorghum with *Cassia tora* seeds.

DRUG TOXICOLOGY

Non-nutrients in diet play an important role in prevention and management of chronic diseases. The antimutagenic properties of commonly consumed spices/ condiments like turmeric, garlic and mustard have been demonstrated in animal and human studies. The results suggest their possible use as chemopreventers.

Ginger is widely consumed and known to possess anti-inflammatory properties. Experiments *in vivo* and *in vitro* showed antigenotoxic properties of the garlic.

Toxicity due to environmental lead exposure was investigated in pregnant women and children. Socioeconomic and nutritional status was correlated with lead toxicity.

OTHER STUDIES

Studies on Mutant Obese Rats

A DNA primer sequence OBP specific for GR-Ob strain was obtained last year. However, expression studies using the cloned PCR product did not show any difference between the parental WNIN and the GR-Ob mutant rat indicating that the cloned region was not unique to GR-Ob strain. With respect to microsatellite markers, a new set of 33 markers was attempted and out of these 17 markers showed amplification. Among the 17 markers, four showed inter and intra strain variations.

Studies on Growth Parameters in Various Strains of Rats

Studies on baseline data of six different rat strains maintained at the Centre showed differences between them in terms of growth rate, total as well as percentage of body fat, lean body mass, day and night time activities and clinical chemistry parameters like glucose, triglyceride and total cholesterol. Growth rate was maximum in Sprague Dawley rats, which also showed higher total body fat, sodium and potassium. Among the strains body weight was lowest for Fischer 344N. The WNIN strain maintained for the last 84 yr in the NIN and at NCLAS has the highest percentage of body fat, lowest night time activity, increased resting time and increased plasma triglyceride. Both systolic and diastolic blood pressures were more in males than in females. In male rats, CFY strain had highest blood pressure followed by WNIN, WKY, F-344, Holtzman and Sprague Dawley in that order. However, in females the order was Holtzman, F-344, WNIN, CFY, WKY and SD. Heart rate was highest in WNIN rats followed by CFY, WKY, Holtzman, SD and F-344 rats.

Isolation, Characterization and Maintenance of Primary Cultures of Pancreatic Islet Cells from NIN Wistar Mutant Obese Rats

WNIN Ob/Ob mutant obese rats showed euglycemic and Gr/Ob obese rats showed hyperglycemic response after intraperitoneal glucose injection. WNIN Ob/Ob mutant obese (Ob/Ob, Gr/Ob) and lean rats demonstrated immunolocalisation of insulin using DAB-HRP conjugate. The ultrastructure of islets isolated from three phenotypes has been characterized by scanning and transmission electron microscopy.

NUTRITION EDUCATION

Development of Communication Strategies to Improve Nutrition and Health related Knowledge of NSS Volunteers

Nutrition education is an important tool to bring awareness about good nutrition practices among the public. In the present education system students are exposed to nutrition related information to some extent as part of their curriculum, mostly only up to high school level. Apart from the curriculum, mass media and interpersonal communication are the other sources available for the students to obtain information on heath and nutrition. The National Service Scheme (NSS) is one of the major programmes run by the Ministry of Human Resource Development, to train and encourage the college going youth to take up some community welfare program. The NSS student volunteers spend about 120 h per year to carry out various social service activities in community level. It is important to impart nutrition information among the NSS volunteers. Hence, NSS volunteers (degree level) were selected as respondents.

One set of colour folders was developed on different nutritional themes such as energy, protein, vitamins and minerals, fat, nutrition during adolescent age, nutrition during pregnancy, and obesity. The folders were used in the first intervention while for the second intervention a CD with a folksong was developed on the nutritional themes, which are already identified. It is proposed to educate the women of reproductive age group (18-45 yr) about the importance of micronutrients like iron, vitamin A, and iodine. In addition, a colour flipchart was developed.

Food Consumption Pattern of NSS Volunteers

Analysis of the data indicated that 50.3% of the NSS volunteers reported regular intake of meals and 20% of them reported to have the habit of consuming snacks between the meals. As regards the cereal intake 75% of them were consuming more than 1 cereal and remaining 25% of them were consuming only rice as the staple diet. Regarding the intake of pulses, 33% of them were not consuming pulses daily. Most of them belong to agricultural family. Only 50% of them consumed milk and milk products daily.

The daily intake of fruits, vegetables and green leafy vegetables (GLV) was minimum. Only 9% of the NSS volunteers reported consumption of GLV daily while another 9% volunteers did not consume them. About 54% of them consumed GLV weekly twice. Similarly 49% consumed fruits twice a week and 21% never had fruit. Regarding the processed food intake the results indicated that 20% of them consumed processed food weekly twice and 40% of them consumed aerated cool drinks once a week.

Nutrition Knowledge Improvement Levels of NSS Volunteers

The knowledge levels were significantly different among the students of rural, urban and district headquarters. Significant improvement in nutrition knowledge levels was seen before and after intervention in all the three areas. A subgroup analysis of the data (district head quarters) indicates that increment in nutrition knowledge scores was significantly different between experimental and control group. Better nutrition education and suitable communication materials will improve the nutrition knowledge and food consumption practices of NSS volunteers of degree colleges. Since the NSS volunteers are involved in community education programmes, educating the students may help to educate the community on health and nutrition aspects.

Nutrition Knowledge and Impact of Nutrition Education on Adolescent Girls

Maternal nutrition plays an important role in the development of foetus and the outcome of pregnancy. Poor nutritional status and lack of awareness of the nutrition during pregnancy and lactation among the low body weight expectant mothers in urban slums result in delivering low birth weight babies and other complications during delivery.

Analysis of baseline data revealed that 68% of adolescent girls were not aware of the physical and physiological changes that take place during the adolescent phase. With regard to the knowledge levels of breast feeding practices and complementary feeding, 81% girls expressed lack of awareness of the health benefits of mother's milk/colostrum while 77% mentioned lack of awareness about the food groups and balanced diet. With regard to the importance of micronutrients during the adolescent stage and pregnancy, 96% girls mentioned lack of awareness of the health benefits of vitamin A, 71% were unaware of the causes and consequences of anaemia, 92% had no knowledge of importance of iodine and iodine deficiency disorders and 74% were not aware of the causes of goitre.

Regarding the family life education, 95% adolescent girls indicated lack of awareness about the importance of nutritious diet and nutrients for women before marriage and 71% girls indicated that they were not explained about the various aspects of sex. As regards the exposure of these adolescent girls to information, education and communication (IEC) strategies to educate on the above themes, about 85% of the girls expressed that they were not given proper exposure to the educational outreach activities using different IEC methods by any organization. Based on the analysis of the data, 8 communication materials are being developed in order to use them for intervention.

Study of Nutritional Factors responsible for Positive Deviance in Child Nutrition in a Rural Setting

The positive deviance (PD) approach is a strategy that identifies factors which enable some children to thrive in harsh environments. PD refers to the ability of some caretakers to encounter successful practices that enable them to raise well-nourished children in communities where there is poverty and malnutrition. It is an extremely practical approach, which may be applied to any field of child development. Studying what positive deviant families are doing, makes it possible for the community members to know that local solutions exist (certain foods, methods of feeding, health practices) and would convince them to search for these solutions in their own communities. In Bangladesh, a study had shown that family dietary habits, hygiene and psychosocial interaction had far greater impact on child nutrition than income. The positive deviance methods of enquiry have been tried in different countries like Bangladesh, Bolivia, Vietnam, Nepal and Bhutan.

In India there have not been extensive studies on the nutritional factors contributing to positive deviance among children. Hence, an investigation was initiated to identify the nutritional factors responsible for positive deviance. As part of the study, household survey for collection of data on the determinants (exclusive breast feeding, caregiving and health seeking behaviour of positive deviance from the mothers of children who were identified as positive (70 children) and negative (70 children) was undertaken from villages around Ibrahimpatnam rural ICDS Centres.

NUTRITION

ENVIRONMENTAL AND OCCUPATIONAL HEALTH

Exposure to industrial chemicals and environmental pollutants results in serious health hazards among the factory workers and general public. The National Institute of Occupational Health (NIOH) at Ahmedabad and its two regional centres located at Kolkata and Bangalore are studying the health problems of workers engaged in various industries as well as effect of pollution on local populations.

Occupational Health Hazards among Salt Workers in Remote Salt Sites in Rann of Kutch

A total of 2104 subjects including 1549 salt workers (majority with over 10 yr exposure) working

at different salt sites in the little Rann of Kutch and 555 control subjects from the nearby villages were studied. The work related general symptoms and skin and eye symptoms were significantly higher among the salt workers. Overall, the production workers had higher prevalence of these symptoms / morbidities than the non-production workers. The mean systolic and diastolic blood pressure among different categories was comparable. A significant increase in urinary sodium excretion and serum pH was observed in salt production workers.

Intervention study showed significant decrease in pre and post shift systolic blood pressure and post shift diastolic blood pressure following use of personal



protective equipments There (PPE). was decreased excretion of sodium and potassium per milimole of creatinine in the urine. Intervention measures such as gumboots and goggles were acceptable to the salt workers and they felt more comfortable with PPE while working with salt (Fig.1).

Postural Load in Computer Work -Time-frequency Representation of Surface Myoelectric Signals of Back Muscles

Survey of nearly 500 professional computer operators, in computer-based tasks, such as, telecommunication, call centres

Fig. 1. A) workers are working without protective devices. B) Skin lesions in feet and hands

and banks elucidated multiple stressors (e.g., material interfaces, job characteristics, pointing devices, chairdesk complex, working conditions and environment, work time schedules). The material interfaces and workplace factors caused musculoskeletal problems among the operators, with moderate to severe pain and discomfort in body parts. In order to examine the mechanistic aspects of postural load in computer work, the longitudinal study elucidated loading characteristics on spinal and para-spinal muscles and tissues. A special test rig was designed to simulate experimental set up for assessment of postural load in different categories



Fig. 2. Subject in experimental set up

of tasks, such as text processing, graphics manipulation and data entry. (Fig.2). The long-term experimentation (21 experimental condition x 3 task varieties x 15 volunteers x 8 muscles) included systematic recording of surface myoelectric signals (EMG) from the lower and upper back muscles. The muscle activities analyzed with respect to timing and amplitude characteristics, as well as frequency contents (spectral density) were analyzed. The continuing activity of a muscle resulted in decrease in median frequency of the power spectra of the signal, which was attributed to reduction in the propagation velocity of depolarization along the muscle fibres and fatigue of the muscle. For chair height of 18 inch and keyboard heights 24 to 30 inches, the median frequencies of the upper trapezius fibres stayed at higher level with the increasing keyboard height in different types of computer tasks. The median frequencies of the right and left erector spine indicated the load sharing of the muscles. The decrease in the median frequency in case of graphics application at 21-inch chair height was a distinctive fatiguing trend, in comparison to other computer tasks. Studies will further refine and optimize the numerical methods of analysis for characterizing the activity pattern and assessing the state of the muscle during prolonged activity.

Health Risk Assessment and Development of Intervention Programme in Slate Pencil Workers of Mandsaur

Study was carried out for finding the prevalence of silicosis and other dust related morbidities among slate pencil workers and the community residing in the vicinity. Of the 514 subjects (25-55 yr) included in the study, 194 were occupationally exposed to silica, 159 were residing in the vicinity of the state pencil units and 161 were living 5 kms away (unexposed group). Mean duration of exposure was 18 yr for males and 20 yr for females. Among occupationally exposed group 21% subjects had silicosis, 2% had silico-tuberculosis and 10% had tuberculosis while 43% subjects showed normal chest radiographs. Similarly, among the paraoccupationally exposed group 13% subjects had silicosis, 6% had silico-tuberculosis and 8% showed features of tuberculosis while 73% subjects had normal X-ray. Among the unexposed group 3% subjects showed nodular opacities on chest X-ray, 2% had features of tuberculosis along with nodular opacities and 12% showed symptoms of tuberculosis while 84% had normal X-ray.

The ambient air monitoring in the vicinity of slate pencil cutting units revealed dust concentration to be around 284.74 while in control village it was 138.07. Similarly, the silica concentration was high in slate pencil factory area compared to control area. The results indicated inadequacy of the local exhaust system in protecting the health of the slate pencil workers. It also highlighted that the use of local exhaust system without proper air cleaning device results in silicosis and silicotuberculosis in the community living around such factories.

Poison Information Centre

An episode of mass organophosphate (OP)poisoning in a remote village of Ahmedabad, characterized by abdominal pain, vomiting, diarrhoea, excessive secretions and respiratory distress was investigated in 15 persons who developed signs and symptoms of OP poisoning.

Role of Environmental Chemicals in Human Reproduction

Study was carried out to assess the effect of exposure to toxic metals on semen quality and reproductive hormone status in 212 subjects. High levels of lead and cadmium were detected in blood and seminal plasma of subjects indicating that these metals persist in the environment. A negative correlation was observed between seminal plasma lead levels and sperm count and seminal plasma lead levels and sperm DNA integrity. Lead was observed to be toxic at 30µg/dl. Higher serum copper levels were found in asthenozoospermic and teratozoospermic subjects indicating toxic effect of copper on male reproductive function. Subjects with occupational exposure to toxic agents were found to have a higher risk of developing subfertility The study suggested that occupational and environmental exposure to lead and copper can lead to deterioration of semen quality.

Assessment of Air Pollution due to Adulteration of Petroleum Fuels

A study was undertaken for estimation of different types of air pollutants emitted at source level from different types of vehicles due to adulteration of petroleum fuels with kerosene and other solvents. The result of the pilot study showed that with increase in percentage of kerosene in petrol the concentration of SPM increased while reverse trend was observed for common volatile organic compounds (VOCs) like benzene, toluene, xylene and ethyl benzene (Fig. 3).



Fig. 3. VOCs concentration in different composition of petrol with kerosene

Environmental Health Study in Jodhpur

The levels of air, water and soil pollution were measured and a population based cross sectional health survey was carried out in Jodhpur city by DMRC, Jodhpur. High to critical level of air pollution was observed in all seasons at traffic intersections/ commercial sites, more so in winter. These traffic intersections were surrounded by residential settlements and population living neareby is likely to be exposed to these critical levels of air pollution. Majority (71.3%) of households were exposed to medium level of vehicular traffic pollution followed by low (17.6%) and high (11.1%) vehicular pollution. Prevalence of asthma/ COPD was 4.4% in households exposed to high vehicular pollution, 3.2% in those exposed to medium and 2.6% in those exposed to low vehicular pollution. Similarly, 25.5% of the population felt indoor smoke problems in which prevalence of respiratory diseases was 8.1%, as compared to 6.2% in those not having indoor smoke pollution. Prevalence of tuberculosis was 1.5% in former group of households while it was 0.5% in later group About 8.6% of the population had industrial air pollution in their surroundings (3.6% from mines and 5.6% from other industries). At industrial sites, the values of RSPM and SPM were within limits prescribed for industrial areas, but these also affected nearby residential areas. In the 8.6% population, which had the industrial air pollution in their surroundings, prevalence of respiratory diseases was 9.9% as compared to 6.4% in remaining population. The levels of SPM at industrial sites were higher in winters. The cases of hypertension, asthma, acute lower respiratory tract infections and cancers showed an increasing temporal trend, which might in part be due to built up of gaseous and particulate pollutants.

Among city residents 25.5% of the population felt indoor smoke problems. Maximum prevalence of respiratory diseases was present in the population dependent on biomass for fuel. It was only 6.1% among LPG users. The other causes of these diseases could be the different habits of individuals as 3.1% were smokers, 3.0 % used oral tobacco (*zarda*) and 5.9% consumed *gutka*, though 88.0% of population was not addicted to such habits.

Health Risk Assessment of Rural and Urban Population Due to Indoor/ Ambient Air Pollution

A pilot study was undertaken at the selected petrol pumps of Ahmedabad city to know the effect of benzene exposure in 37 petro fillers. Information about work conditions, smoking habits, alcohol consumption and socio-economic status was collected by pre-designed questionnaire. Air sampling and confirmation and estimation of benzene released in the environment during the process of petrol filling was done. A questionnaire survey along with medical examination of petrol fillters was undertaken to assess the morbidity pattern of such workers. Burning / watering of eyes, cough, headache, fatigue, irritation of throat and skin were the common complaints of workers while icterus and pallor was observed in some workers. These results suggest the presence of benzene, toluene, and xylene in the environment during the process of petrol filling. Presence of trans trans- muconic acid in blood of petrofillers reflected presence of benzene exposure.

Assessment of Persistent Organic Pollutants–PCDDs and PCDFs in Biological Media

Polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzo furans (PCDFs) represent a class of organic environmental pollutants containing carbon, hydrogen, oxygen and chlorine that exhibit potential risks for human health. Study was undertaken in Ahmedabad, Vadodara and Surat cities for residue analysis of dioxin and furans in animal foods and biological samples. The findings of the study show contamination of the environment with residues of dioxin and furan. In the entire sample matrix the concentration of dioxins was greater than that of furans. The total estimated quantity of dioxin in egg samples was 7.49, 9.32 and 13.35 while in chickens it was 7.05, 9.38 and 7.67 in Ahmedabad, Vadodara and Surat respectively. Dioxins were significantly at higher levels in primiparas than in multiparas. A decreasing trend was visible in residue levels of the dioxin in subjects who had their second delivery as compared to those with first delivery. From the correlation regression analysis, positive correlation of dioxin with the age of the subject was seen. The dioxin residues negatively correlated with weight, height and skin fold thickness. The residues significantly correlated with the milk fat.

National Environmental Health Profile and Comparative Health Risk Assessment

The NIOH is participating in a national project funded by Ministry of Environment and Forest and WHO to find out the environmental health profile and comparative health risk assessment in nine important urban cities of the country. The results in Ahmedabad city revealed that the pollutant levels were high in Naroda industrial area compared to residential and commercial area. At all the places the level of sub particulate matter (SPM) was elevated. Higher morbidity from cardiorespiratory diseases was noted. Gasto-enteritis problems were also high. SPM, benzene and other volatile organic compounds were quite high in Kolkata also where major health problems reported by people were respiratory and gastro-intestinal complaints.

Renal Tubular Dysfunction and Oxidative Stress among Electroplating Workers

Study to assess the renal tubular dysfunction and oxidative stress in workers exposed to chromium during chromium plating process was continued at Regional Occupational Health Centre (ROHC), Kolkata in 50 chromium plating workers and 50 office workers (controls). Results of the study indicated that urine chromium level was significanlty increased in chromium exposed workers as compared to controls. However, in both the groups the urine chromium levels were lower than biological exposure indices of $30 \ \mu\text{g/g}$ of creatinine. The levels of total urinary N-acetyl-B-D-glucosaminidase and isoenzymes A and B among chromium-exposed workers were significantly higher when compared to the control group.

Assessment of Health Status of Workers Exposed to Storage Grain Dust

Study was continued in 107 load handling, ancillary, quality control and depot administrative workers (of which 29.35% were SC and 70.65% general caste) to assess their health status. The symptomatic changes, joint pain and back pain were high in all categories of workers. All workers had lower total leucocytes count and higher blood IgE and eosinophil count during follow up study. Different categories of workers in storage grain handling had higher lung volumes during initial study in comparison to follow up study. In both the studies non-smokers had higher values compared to smokers. Only in ancillary and depot administration workers some of the flow rates were higher in smokers compared to non-smokers. Respiratory impairment increased in some categories of workers in the follow up study compared to the initial study. In general caste workers in the initial study, it was 12.98% and in the follow up study it was 27.27% and in the scheduled caste workers, it was 6.25% in the initial study and 18.75% in the follow up study respectively. Mild obstructive types of impairments were found in both categories of subjects in the follow up study.

Clinico-epidemiological Study of Arsenic Exposed Population in West Bengal

A project was conducted with the objective to measure the arsenic content of water and other biological samples to confirm the level of arsenic exposure. Arsenic in drinking water collected from different sources like tubewells and ponds of nine villages of Katlamari Gram Panchayat was measured. It was found that out of the total, 79% showed levels >150µg/l whereas 24% had values between 50-150µg/l.

NON-COMMUNICABLE DISEASES

In India, non-communicable diseases (NCDs) are estimated to account for 53% of all deaths and 44% of disability-adjusted life years (DALYs).

Based on current trends, it has been projected that these conditions would rise from 3.78 million in 1990 (40.4% of all deaths) to 7.63 million in 2020 (66.7% of all deaths). There has been a two fold rise in prevalence of coronary heart disease in rural (3-4%) and a six fold rise in urban (8-10%) areas over the past four decades. A recent report of WHO has estimated that India would have to forego about US\$ 250 million in the national income over the next 10 years in tackling these diseases.

During the year the Council continued studies on cancer, cardiovascular diseases, diabetes, mental health, neurosciences and non-communicable disease surveillance etc. Studies in cancer are being carried out mainly at Council's Institute of Cytology and Preventive Oncology (ICPO) based at NOIDA.

ONCOLOGY

National Cancer Registry Programme and Cancer Atlas project provided data on cancer occurrence as well as cancer care patterns. The preparatory activities for screening for common cancers in three districts of Himachal Pradesh have been completed. Understanding the pathogenesis of oral cancers was addressed through different task force studies. A brainstorming meeting suggested the future areas of research on oral cancers. population figures (denominator) for calculation of incidence rates, based on the 5-yr age group figures from the 2001 census, have been calculated for all the registry areas. It is proposed to initiate a Centre for Disease Informatics and Research, which would help in developing a database on cancers, cardiovascular diseases, stroke and diabetes.

CERVICAL CANCER

Polymorphism of Tumour Necrosis Factor a Gene in Cervical Cancer

The host immune responses may be one of the most important factors in the natural history and persistence of human papillomavirus (HPV) infection. The ICPO has initiated a study on polymorphism in immunomodulatory genes especially in tumour necrosis factor α (TNF α), a cytokine with potent immunomodulatory function in cervical cancer. One hundred and thirty cervical cancer tissue biopsy samples showed 10 SNPs (single nucleotide polymorphism) in the promoter region of TNF α gene. Analysis of these loci revealed that -308 locus is more polymorphic than -238 but larger sample size is needed for further analysis.

Expression of Targeted Ribozyme against HPV 16 E6 and E7 Genes in **Cervical Cancer**

knock-down E6 & E7 genes of HPV to de-regulate

The study was designed to develop a strategy to

NATIONAL CANCER REGISTRY PROGRAMME

The National Cancer Registry Programme (NCRP) was initiated in 1981-82, with the objectives of collection of authentic data on cancer occurrence, undertaking epidemiological studies, and developing human resource in cancer epidemiology and registration. The data have already been analysed and given in last year's report. During the year, population based cancer registries in north-eastern India tried to finalize the data for the years 2003 and 2004. The



Fig. 1. (a) Structural folding of native E6 Ribozyme appended with HPV-E6 RNA RNA of HPV16 (only one of the suboptimal structure is represented). Probable targets are selected comparing many sub-optimal structures



and binding of ribozyme to its correct sequence



M E6 E6 E7 E7 E6-E7 M



(b) Cloning of target E6 and E7 genes in pGEM T vector - Amplified PCR product of E6 and E7 and E6-E7 togather is represented in 2% Agarose gel showing 480 base pair product of E6-E7. Lane 1,8-PhiX Marker Hae III digest, Lane 2,3-E6, Lane 4,5-E7 and Lane 6,7-E6-E7 together



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(c) Sequencing of library of E6-E7 clones for the correct orientation respective to T7 promoter

the cell cycle and cell proliferation using catalytic RNA (ribozyme), which possesses high specificity in its targeting capability. Designing of ribozyme and cloning of E6 and E7 target genes have been done using Zuker's RNA Folding software program. The catalytic RNA has also been cloned in eukaryotic expression (pol II) vector. (Fig.1 a,b,c) Construction of pol III-based expression cassette which produces high copy number transcripts of ribozyme for stable transfectants is underway.

Biological Behaviour of HPV Infection in Uterine Cervix

A project is being pursued to study the prevalence of HPV infection among Indian women in reproductive age group, the epidemiological risk factors associated with acquisition of HPV infection, rate of progression/ regression/persistence of HPV infection and risk factors related to persistent HPV infection. During the year under report, a total of 6796 women were screened cytologically through Pap smear. Cervical scrapes for HPV were collected in 389 women and HPV testing by PCR was carried out in 272 women.

Transcriptional Control of HPV Oncogene

The pioneering research on Curcumin, a new anticancer agent derived from turmeric has been found to control HPV in cervical cancer. DBT-funded indepth molecular studies have demonstrated Curcumin's ability to suppress HPV transcription and constitutive AP-1 activity in cervical cancer cells. The results will be utilized in designing an effective and safe therapeutic protocol for treatment and prevention of HPV infection and cervical cancer.

Molecular Genetic Basis of Cervical Cancer

With the aim of identifying genes with a differential pattern

of expression between cervical carcinomas and normal cervix, GeneChip Human Genome Focus arrays were used which analyzed the expression level of $\sim 8,500$



Fig. 2. (a) Scatter plot showing up-regulated (orange) and downregulated genes (green) in cervical cancer tissues with respect to normal cervix



Fig. 2. (b) Probe array image of cervical cancer sample

transcripts and variants including 8,400 well characterized human genes. A pilot study was conducted on three HPV positive samples from patients with invasive cervical carcinoma and one sample (used as control) from a subject undergoing hysterectomy for non-neoplastic condition for microarray study. (Fig.2 a and b) Further analysis in a larger group of cervical cancer patients in different clinical stages will be done for confirmation and elucidation of specific marker genes.

Molecular Markers for Detection and Progression of Cervical Cancer

The DBT-funded study was initiated to analyze the expression of selective markers, which have been shown in isolated studies to be relevant in HPV mediated carcinogenesis. It included apoptosis related proteins: transcription factors NF-kB and AP-1 cell cycle regulator p53 and cyclinD1. Out of 121 cervical



Fig. 3. Localization of NF-kB proteins in the different histological stages of cervix (yellow arrow - cytoplasmic stain, red arrow - nuclear stain)

tissue specimens of different grades (64 invasive cancers, 31 high grade and low grade lesions and 26 control tissues) 66 were positive for HPV16 and 2 for HPV18. Immunohistochemical analysis of these samples showed that proteins of the NF-kB family– p65 and p50, AP-1 family member c-fos and c-jun and p53 were over-expressed in cervical cancer (Fig. 3).

Development of HPV Diagnostics for Early Detection of Cervical Cancer

User friendly, cost effective and dry collection of cervical scrape / biopsy imprint specimens as "Paper Smears" have been developed by ICPO and submitted for US patent. This technique coupled with a single tube multiplex PCR procedure is being developed using HPV L1 consensus as well as HPV type-specific primers for diagnosis of high risk (HPV16/18) and other HPV infections in DNA isolated from cervical scrapes.

Genetic Polymorphism in E6 And E7 Genes of HPV Type 16 and 18 in Cervical Cancer

Study is ongoing to determine the HPV variants specific to Indian population. HPV 16 was detected in 34 out of 74 biopsy specimens of cervical carcinomas collected from patients attending the Gynaecology clinics. More samples of HPV are being acquired for sequencing of their E6, E7 and LCR regions.

Development of DNA-based Prophylactic Vaccines against High Risk HPV Type 16 / 18

Analysis of India-specific HPV 16 variants is in progress at ICPO while *in vitro* studies have been



Fig. 4. (a) Sall digestion of CRPV-pLAII plasmid releasing the expected size fragments of 8,0 kb CRPV genome and the vector backbone of 3.5 kb. Lane 1:-1 Hind III digest marker; Lane 2: - CRPV-pLAII digested with Sall; Lane 3: - CRPVpLAII undigested



Fig. 4. (b) Amplification of the complete L1 ORF of CRPV.

initiated with cottontail rabbit papillomavirus (CRPV) strain to establish the animal model. The CRPVpLAII plasmid having full length the cottontail rabbit papillomavirus genome has been received (Fig.4 a and b). The full-length sequence

of CRPV L1 has now been confirmed by sequencing and its cloning into expression vectors is in progress.

HPV Vaccine Trial

Two successful HPV virus-like particle (VLP) vaccines have been developed and are in phase III clinical trials. Since Indian initiatives to develop HPV vaccines are in infancy, India is going to initiate clinical trial of these vaccines shortly. A memorandum of understanding (MOU) has been signed between Merck and ICMR for clinical trial of Gardasil (Merck vaccine) against HPV 16 and 18 in India. ICPO has been given the responsibility to develop a protocol and to coordinate the HPV vaccine programme in India.

Role of Genetic Polymorphism of GSTM1 and GSTT1 in Cancer Development

GST is a family of enzymes involved in xenobiotic detoxification and protection against carcinogens, mutagens and genotoxic compounds. Study was performed to determine the association of



Fig. 5. GSTM1 and GSTT1 null polymorphism in various cancers

polymorphisms of GSTM1 and GSTT1 gene loci in development of cervical and other cancers. Case control studies were conducted in cervical, oesophageal, oral, liver, chronic myeloid leukaemia and breast cancer patients and it was found that one or the other GST gene is associated with susceptibility to these cancers (Fig. 5).

BREAST CANCER

Multidisciplinary Study

Study demonstrated involvement of Her-2/neu oncogene amplification and overexpression in significant proportion of breast cancer patients. Sporadic and familial breast cancer cases revealed only a few novel mutations in breast cancer susceptibility genes, BRCA1 and BRCA2 and in p53 tumour suppressor gene. Preliminary studies revealed high binding activity of AP-1 and NF-kB in malignant cases. It also showed selectively high expression of c-fos and down-regulation of fra-1. The p50 expression was high in cancer cases while p65 was found to be very low.

Study of BRCA1 and BRCA2 Gene Expression in Human Breast Cancer Cells

The ICPO identified novel germline mutations in breast cancer susceptibility genes BRCA1, BRCA2 and p53 in breast cancer patients from India which was reported last year. Hypermethylation of the BRCA1 promoter region has been strongly correlated with lack of estrogen and progesterone receptor expression. To see the status of methylation within the BRCA1 promoter region in a large spectrum of sporadic as well as familial



Fig. 6. Methylation analysis of the BRCA1 promoter region in tumour samples in sporadic breast cancer. Lane 1- Methylated control of BRCA1; Lane 2- Negative control; Lane 3 and Lane 9 shows hypermethylated BRCA1 promoter.

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breast cancer, 50 tumour biopsies from sporadic breast cancer and 10 normal blood samples were analyzed. Only 15 cases (30%) showed hypermethylation of the BRCA1 gene. (Fig.6) Further study is in progress.

ORAL CANCER

Study is ongoing for understanding the role of drug metabolizing enzymes in causation of oral cancers in a cohort of 2,031 individuals with precancerous lesions. Samples of blood and biopsy/ oral scrape were collected from all cases and controls for analysis of CYP1A1, GSTM1 and GSTT1 gene polymorphisms. Patients of pre-cancerous and cancerous lesions are being treated as per existing hospital practice.

Another study is ongoing to identify the common chromosomal changes specific to oral cancers in India at primary tumour site and metastatic lymph node using comparative genomic hybridization and related molecular cytogenetic techniques. The comparative genomic hybridization profile in 131 tumour samples showed that the most frequently observed chromosomal alterations were on 1p, 3q, 5p, 7q, 7p, 8q, 9q, 11q, 12p, 20q, 20p, 14q, 17p and 19p chromosomes and losses/ under presentations were on 3p, 8p, 18q, 11q, 9p, 4q and 5q chromosomes.

The project on oral cancer immunology focuses on analyzing T cell receptor repertoire (TCR, V β , V γ and V δ as well as immunophenotypes $\alpha\beta$ & $\gamma\delta$) and clonality in lymphocytes (by heteroduplex analysis) present in peripheral blood, tumour compartment and lymph nodes of patients suffering from cancer of buccal mucosa. Studies demonstrated a decreased CD3 ζ chain expression, which translates into inefficient T cell signaling resulting in partial or complete loss of T cell function. A possible role of TNF- α was demonstrated. Patients reporting with recurrence of the disease exhibited low CD3- ζ chain expression at diagnosis. Comparative study before and after treatment showed increase in CD3- ζ chain expression after surgery or radiotherapy.

OESOPHAGEAL CANCER

Oesophageal Cancer in North East Region

Study is ongoing to investigate the role of genetic factors and tobacco smoking in the etiology of

oesophageal cancer in North-East population. The ICPO received 43 blood samples and 59 tissue biopsies and has analyzed p53 and GST μ (GSTM) mutation and polymorphism in oesophageal pre-cancer and cancer cases by PCR-SSCP and direct DNA sequencing. Mutation in p53 gene in exon 5 and 7 was checked. Out of 18 cases, mutation was detected in exon 5 in two cases (11.1%) and in exon 7 in one case (7.6%).

COMMON CANCERS

Screening for cancers of cervix, breast and oral cavity has been initiated in three districts of Himachal Pradesh. Screening would be carried out by the paramedical workers of the State health services. Facilities have been set up at district level for diagnosis and management of cancers and precancers. The required referral chain would be created. The preparatory work for the project has been accomplished including development of manuals and conduct of baseline KAP survey. Subsequent to training of physicians and paramedical workers, the target age group (persons above 30 yr of age) would be screened for cancers of cervix, breast and oral cavity.

ATLAS OF CANCER IN INDIA

The project on development of an atlas of cancer in India was initiated with financial support from the World Health Organization during the years 2001 and 2002. Subsequent support is being provided by the ICMR. The minimum crude incidence rates (all sites) in either sex have been calculated. The data shows that some of the districts in the country have higher cancer incidence rates than the established population based cancer registries. A special effort has been made to cover the north-eastern states under the project. The data for the years 2003 and 2004 is being analysed.

CARDIOVASCULAR DISEASES

A study on community control of rheumatic fever/ rheumatic heart disease (RF/RHD) under Jai Vigyan Mission Mode Project is ongoing. Under the epidemiology component, the cross sectional survey in about 8026 school children (age group 5-14 yr) revealed the prevalence of group A Streptococcus

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(GAS) in sore throat as 8.8 % and 2.5 % respectively in northern and southern parts of India. The registry component of the project showed RF/RHD prevalence of 0.36 to 1.43 per thousand in the age group 5-14 yr. Also community based registries are ongoing at Chandigarh, Vellore, Cochin and Indore for developing module for estimating prevalence of RHD in community and management of this disease. The lower prevalence of RF/RHD reported by the registries at Chandigarh, Vellore and Cochin in this project couldn't be extrapolated to all parts of the country as different states are in different stages of epidemiological transition. Satellite registries under the module are being initiated at Jammu, Shimla, Dibrugarh and Mumbai. One satellite registry in a tribal area in Kerala (Wayanad) has been started in March 2006. The emm typing of GAS strains revealed a high heterogeneity in the strains circulating in the community. This raises challenges to the multivalent vaccine approach based on N terminal region of M protein. Newer approaches including the use of conserved C terminal sequence of M protein are being investigated.

Another study to determine normative blood pressure (BP) in children and adolescents has been initiated under Jai Vigyan Mission Mode Project on control of RF/ RHD. Blood pressure, height and weight were measured in 50,000 school children aged 5 to 14 yr at Chandigarh, Vellore, Kochi, Indore and Wayanad. Kochi centre collected data on a stratified random sample of approximately 18,662 school children in various age groups. It was observed that diastolic hypertension predominates in school children. Further, the systolic or diastolic hypertension was significantly higher in girls than in boys. Overweight and obesity showed a definite relationship with hypertension in both boys and girls across all age groups. Further, a rising trend in obesity and overweight in children was noticed in a short period from 2003 to 2005.

A multicentric project to determine salt sensitivity and candidate gene polymorphisms in essential hypertension in tribal population of Mizoram, tea garden communities of Assam and indigenous Assamese population was initiated in March 2005 with the objectives to determine the prevalence of salt sensitive blood pressure in hypertensive and normotensive subjects. A pilot study in normotensives and hypertensives from tea garden population in Dibrugarh and Mizoram showed higher prevalence of salt resistant subjects. However, study on larger sample size will be undertaken.

A task force project on relation of candidate gene variants regulating triglyceride metabolism to serial changes in childhood body mass index and coronary artery disease risk factors in young adulthood was initiated in September 2005. The multicentric project aims to determine the frequency of polymorphisms in APOA-V gene, hepatic lipase and PPAR- γ in subjects of Delhi cohort and their relation to changes in body mass index (at different stages of growth). The project also proposes to study the association between above mentioned gene variants and development of risk factors for coronary artery disease (LDL sub fractions, triglycerides, cholesterol, insulin and impaired glucose tolerance) in adults.

DIABETES

An Advanced Centre for Genomics in Type 2 Diabetes Mellitus at Madras Diabetes Research Foundation, Chennai has been initiated. The Centre aims to undertake both research and training. For research component, two proposals on study of genes related to maturity onset diabetes of the young (MODY) and early onset diabetes and study of genes implicated in ion channel dysfunction in diabetes have been initiated. The aim is to determine the prevalence of MODY in different regions of India and screen the known gene variants in unrelated diabetic subjects and normal glucose tolerant subjects so as to find the association with the disease. Training will be imparted to students, educators, health professionals and research scientists from 3rd year onwards.

Preliminary studies on the effect of camel milk in type 1 diabetes in population of north-west Rajasthan (Raica community) indicated its important role in glycemic control, lipid profile and quality of life. On the behest of Ministry of Health and Family Welfare, the task force on camel milk and diabetes, was constituted and two projects *viz*. effect of camel milk on glucose metabolism in adults and hypoglycemic/insulin like activity of camel milk using an animal model have been initiated with collaboration of NIN, Hyderabad and SP Medical College, Bikaner.

The document "Guidelines for Management of Type 2 Diabetes" was brought out by the Council in March, 2005. These Guidelines have been widely circulated to the medical colleges and practicing doctors and are placed on the Council's website.

ASTHMA

ICMR funded study for evaluation of the role of α -tocopherol and oxidant-antioxidant balance in the treatment of bronchial asthma was completed at the V.P. Chest Institute, Delhi. The study showed that both the treatments, inhaled beclomethasone dipropionate (group A) and inhaled beclomethasone dipropionate supplemented with α -tocopherol (group B) resulted in significant improvement in symptoms, decreased the occurrence of nocturnal exacerbations, increased the percentage of asymptomatic days and reduced the requirement for rescue salbutamol. Supplementation of standard therapy with inhaled corticosteroids using dietary sources or α -tocopherol as a therapeutic agent has the potential to reduce the requirement of inhaled corticosteroids and long term treatment may reduce the severity of disease.

MENTAL HEALTH

The mental health problems and behavioural disorders are under-reported and get less attention due to stigma attached to them. At national level, mental health policy has been the focus of public health during the last two decades. The national level programme of integrating mental health with primary health care is one such example. Various studies were undertaken during this period which covered various aspects of mental health.

Urban Mental Health Problems and Service Needs

The migration of populations from rural to urban areas and growth of urban areas has tremendous implications for mental health of the people living in these areas. The growth of urban areas affects the economic, environmental and social structure, which leads to general and mental health problems. At international level, efforts are being made to improve overall situation in urban areas. WHO's Healthy Cities project, a long-term international development project, has become a major public health movement.

The task force study on urban mental health problems and service needs was planned with above situation in mind. Study is being carried out at Delhi, Chennai and Lucknow with the objectives to assess epidemiology and health service research of the common mental disorders (including syndromal and sub-syndromal) and stress related problems, development of a feasible mental health service delivery module for common mental disorders and stress related problems through primary health care providers and to develop an intervention module for victims of domestic violence.

At Delhi centre, a total of 1283 households were visited by the research team in Delhi. At Lucknow centre, field areas were selected from three socioeconomic strata. Data collection related to common mental disorders has been initiated. Sample is being taken from lower socio-economic strata. Data at Chennai centre was collected from three areas of different socio-economic groups. General health questionnaire (GHQ) positivity at Delhi was 36.3% while Chennai and Lucknow centres showed a GHQ positivity of 35.6% and 22.8% respectively with an average of 32% GHQ positive subjects across the three sites. The syndromal cases among the GHQ positive subjects were in the range of 10-20%.

Symptom profile of sub-syndromal mental health problems (SMHPs) as shown by the data collected for this component include depression, anxiety, pain/ somatisation and *dhat*, harmful use of psychoactive substances, mixed symptoms and possible physical comorbidity.

Mental Health Service Needs and Service Delivery Models in the Disaster (Earthquakes) Affected Population in Gujarat

Gujarat faced devastating earthquake on the morning of 26th January, 2001. The ICMR initiated a

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task force study on mental health service needs and service delivery models in the disaster (earthquakes) affected population in Gujarat. The pilot study highlighted the definitive need to focus on emotional and psychological needs of the disaster affected populations. The overall goal of main study was to study the mental health service needs and various service delivery models in the earthquake affected population of Gujarat. The objectives of the main study were to estimate the prevalence and pattern of mental health morbidity, individual and community factors associated with mental health morbidity, perception of affected people about mental health services, service need and assessment of service delivery models for their usefulness and acceptance in the affected communities. The psychiatric morbidity profile of the affected population included depressive disorder, anxiety and somatoform disorder. The qualitative research methods highlighted that counseling, drug treatment, crisis intervention, group activities, spiritual activities and yoga were common services provided. These services were provided by general relief providers, counselors from corporation and government team, NGO workers, religious groups, community organizations and psychiatrists. NGOs played an important part in provision of mental health services. Only 10-15% of the affected population utilized these services. There were inconsistencies in counseling sessions.

Mental Health Needs Assessment and Service Delivery Models in Tsunami Affected Population of Coastal Tamil Nadu

Coastal areas of Tamil Nadu were rocked by a devastating tsunami on the morning of 26th December 2004. The worst affected area was Nagapattinam, which saw the maximum devastation. To assess the situation, the ICMR initiated a task force study on mental health needs assessment and service delivery models in tsunami affected population of coastal Tamil Nadu. The pilot study was carried out with the objectives to (1) assess mental health problems and service needs of the disaster affected population of Chennai, Nagapattinam, Cuddalore, and Kanyakumari, (2) assess mental health service delivery models in the tsunami

affected communities, (3) assess the need of imparting necessary skills and training to the primary care providers and peripheral field workers, (4) assess the difference in service load (secondary data is to be collected on the profile *i.e.* the nature of the disorder and the total number of patients before and after the disaster) and (5) identify the different levels (according to severity) of affected groups in the tsunami hit area and their needs. Study was undertaken by the Institute of Mental Health at Chennai through four field based collaborating centres at Chennai, Nagapattinam, Cuddalore, and Kanyakumari in the tsunami affected areas. The team at Institute of Human Behaviour and Allied Sciences (IHBAS), Delhi provided overall coordination. The results of the pilot study showed two third positivity of psychological disturbances on GHQ. Psychiatric morbidity ranged from 8-52% in GHQ positive subjects. There was no significant psychiatric morbidity among populations from exposed areas and purposely selected severely affected areas. It has been found that post traumatic stress disorder (PTSD) rates were much lower as compared to that reported in Western literature. There were wide range of emotional, behavioural and psychological problems among the affected populations. Another finding of the study was that there was significant increase in alcohol consumption among the affected communities.

Suicide Behaviour

Suicide is a major preventable public health problem. The pilot study on suicide behaviour indicated wide acceptability of the instruments without any negative effect in the community. The objectives of the task force include study of prevalence of suicidal ideation and suicidal attempt in the community, correlates of suicidal ideation only and protective and risk factors contributing to suicidal attempt. The main study has calculated the prevalence of suicide ideators/ attemptors in a representative sample of different socioeconomic strata of Delhi. The detailed in-depth follow up has been planned in another population on the identified ideators and attemptors. Field work and data collection (base line) for analytic component has been completed. A total of 1100 respondents (550 men and 550 women) were screened for prevalence component from 11 colonies of different socio-economic strata in Delhi. Out of this 21.4% subjects were found positive for stage-II instrument, 11.1% fulfilled the criteria for ideators. Females had higher ideation rates (15.5%) as compared to males (6.7%) (Fig. 7). The ideation rates



Fig. 7. Suicide ideation rates

were higher in less educated, unskilled workers and lower in people from low socio-economic status and women. The severity gradation was high in adolescents, young men and single (unmarried/widowed/divorced) persons. Study of duration of ideation showed that 30% were in recent category (less than one month), 46% in short-term (six months) while 24% in long-term (more than six months) category. Steps have been taken to initiate second centre in southern India (Vellore).

CAUSES OF DEATH BY VERBAL AUTOPSY

The task force project on verbal autopsy was initiated in Jan 2001 as pilot project and subsequently in January 2003 as a main study. The study instruments were developed, tested and validated in the pilot phase. In the main phase the study was expanded to cover five states representing different geographical regions of the country. Two rounds of six monthly surveys were conducted to collect data on deaths that occurred six months back in Assam, Bihar, Maharashtra, Rajasthan, and Tamil Nadu. These surveys were conducted by RMRC, Dibrugarh, IRMS, Delhi, NIE, Chennai and NIRRH, Mumbai. The data collection and report generation for all the centres is over. Data on over 10,000 deaths have been collected from all the centres. Results revealed that 75% of the deaths were adult deaths. In Bihar and Rajasthan maximum number of deaths was observed from infectious and parasitic diseases. On the other hand, diseases of the circulatory system were reported as the major cause of death (25-27%) in Tamil Nadu, Dibrugarh and Maharashtra. Cancer is another cause of major mortality in these states closely followed by pulmonary tuberculosis. Accidents, injury and poisoning have also been reported in these centres. The data from all the centres is being compiled.

NEUROSCIENCES

Risk of Malformations in Children of Women with Epilepsy

A task force project has been undertaken with the objectives of assessing the risk of congenital malformations in children of women with epilepsy (WWE). The secondary objectives include study of (a) course of epilepsy during pregnancy, (b) effect of epilepsy in pregnancy, (c) impact of duration and type of epilepsy and type of anti-epileptic drugs on malformations in children of women with epilepsy. The study plan includes folic acid administration at enrolment, ultrasonography (USG) at 16-18 weeks or at first visit, fetal echo at 24 weeks and antiepileptic drug (AED) level every trimester. The USG (brain, spine and abdomen) of children and echo of fetus were carried out when indicated. So far 463 women with epilepsy and 428 controlled subjects have been recruited.

The results revealed the incidence of major malformations to be 2.39% in WWE and 1.21% in control group. Seizure frequency during pregnancy increased in 19.06 patients, decreased in 21.46% and remained unchanged in 59.48% patients. Preliminary data suggest that epilepsy itself is an independent risk factor for malformations (3.23%). Polytherapy was found to be associated with higher percentage of malformations (6.52%). Seizure frequency did not influence outcome while presence of generalised tonic clonic seizures (GTCS) was associated with higher poor outcome. Periconceptional folic acid intake protected the child from malformations. AED levels did not correlate with outcome.

Neurocysticercosis

The task force project undertaken with the aim to quantify the contribution of neurocysticercosis to the etiology of seizure disorder in the community was continued. The study found the seroprevalence of cysticercosis in the community to be about 12.5%. Seroprevalence in patients with active epilepsy or recent onset seizures was found to be 51.6%. On CT scan, this group was found to have positivity for neurocysticercosis in 27.7% cases. This indicates that cysticercosis might be the cause of active epilepsy/ recent onset seizures even in those persons in whom the CT scan does not reveal any neurocysticercosis lesions due to lesion resolution.

Homocysteine and Stroke

A community based study on homocysteine and a case control study on risk factors of ischaemic stroke and haemorrhagic stroke was carried out. The mean homocysteine levels in community were found to be $18.45\pm8.3 \text{ }\mu \text{ol/l}$. About 55% people had higher homocysteinemia. Mean homocysteine levels in vegetarians were much higher than in the non-vegetarians.

The case control study showed that high homocysteine was a risk factor for hemorrhagic stroke, but not for ischaemic stroke. Fasting blood sugar >126, cholesterol level >250 and triglycerides >150 were the risk factors for haemorrhagic stroke as well as ischaemic stroke.

As regards hypertension, odds ratio of ischaemic stroke was found to be 4.07 and for haemorrhagic stroke odds were 17.49 times more in persons with hypertension as compared to those who had normal blood pressure. Low folic acid level was risk factor for both types of stroke. In addition, vitamin B 12 level, vegetarian diet and abnormal carotid thickening were also found to be significant in ischaemic stroke.

N O N - C O M M U N I C A B L E DISEASE SURVEILLANCE

Recognizing the global concern in the rising premature morbidity and mortality due to NCDs (cardiovascular diseases, diabetes, obesity, cancers, chronic lung diseases *etc.*), and observing this disturbing trend in developing countries, including India, the Council conducted a 6 site study (at Ballabgarh, Chennai, Delhi, Dibrugarh, Nagpur and Trivandrum) in 2003-2004 to collect data on selected risk factors (alcohol, tobacco, fruits and vegetables, physical activity, weight, height, blood pressure and waist circumference) for NCDs.

As a follow up of this study, a multi-site study on the biochemical risk factors for NCDs was planned and coordinated at the same sites and populations in 2005-2006. The study participants included 7874 men and women aged 15-64 yr who had participated in the steps 1 and 2 of study in the urban, rural and slum/peri-urban populations. The biochemical risk factors selected were fasting sugar, total and HDL cholesterol and triglycerides. The overall mean fasting blood sugar levels in men were 5.65mmol/l (urban), 5.15mmol/l (rural), and 5.47 mmol/l (slum), while in women they were 5.53 mmol/l (urban), 5.23 mmol/l (rural) and 5.53 mmol/l (slum) respectively. There were 43.7% men and 39.7% women at all centres and populations with total and HDL cholesterol ratio of 4.5. Trivandrum had the highest proportion of men and women with the abnormal ratio (57.2% and 48.8% respectively) while the least was at Dibrugarh (men, 30.6% and women, 31.4%). Overall, there were 4.1% men and 2.7% women with dyslipidemia in all populations.

BASIC MEDICAL SCIENCES

As in the previous years the major activities of the Council in basic medical sciences have been carried out in the fields of biochemistry, cellular and molecular biology, genomics, haematology, genetics, immunology, pharmacology, toxicology and traditional medicine. Intramural research in the fields of pathology and haematology is being carried out at Institute of Pathology (IOP), New Delhi and Institute of Immunohaematology (IIH), Mumbai respectively.

PATHOLOGY TUMOUR BIOLOGY

Breast Cancer

Study of Candidate Genes Associated with Breast Cancer Susceptibility

Study is aimed to identify low penentrance genes associated with breast cancer risk in north Indian population. Polymorphisms/mutations in low



FIg. 1. Ethidium bromide-stained gel showing (a) *Taq1* digested PCR product of VDR gene. Lane 1 contains m.w. marker (100-bp ladder). Lanes 2,7 and 8 show intact amplicon of 391 bp. Lanes 3,4 and 6 show amplicons of 391, 350 and 41 bp, representIng heterozygous pattern (b) *Apa1* digested PCR product showing amplicons of 196, 135 and 61 bp. Lanes 1, 2, 3, 4, 7, 8, 9 show intact amplicon. Lanes 5 & 6 represents heterozygous pattern.



FIg. 2. Genetic alterations in GSTM1 and GSTT1 in breast cancer patients. Presence of 480 bp PCR product shows presence of wild typ GSTM1 gene, 215 bp PCR product shows presence of wild type GSTT1 gene. β-Globin gene was used as internal control which was detected by the presence of 267 bp PCR product. Lanes 2,3,4,5,6,7 & 8 show GSTT1 null mutation and lanes 2,3 & 5 show GSTM1 null mutation

penetrance genes, CYP17, VDR and GST were analyzed in breast cancer patients and in controls. Screening for A2 polymorphism in CYP17 gene increased incidence of heterozygous and homozygous carrier of A2 polymorphism in early onset breast cancer cases which is responsible for extra site for estrogen synthesis and higher circulating estrogen levels.

Studies have also been initiated to investigate the role of low penetrance VDR gene polymorphism(s) for giving susceptibility to familial and sporadic breast cancer. It was investigated whether 3' UTR (Taq I, Apa I) polymorphisms in the VDR gene have any association with altered breast cancer risk in north Indian population.

A series of 204 breast cancer patients along with 200 controls were screened for Apa I (intron 8) and TaqI (exon 9) polymorphisms in VDR (Fig. 1) gene. Patients included 105 early onset, 65 late onset and 34 familial cases. No statistically significant association was found between polymorphic VDR genotype with

breast cancer risk. Further, Poly A repeat in VDR gene will be studied to find the genetic linkage with ApaI/TaqI cluster in the 3'UTR region which is important for regulation of mRNA stability.

Besides this GSTs were also studied in the same population. GSTM1 genotype was analyzed in 80 breast cancer patients and 17 controls. Null genotype was observed in 27% patients (13.7% early onset and 12.5% late onset type) while 73% showed wild type alleles. Among controls null genotype was observed in 29% and wild type allele in 71% individuals. Cases and controls were also analyzed for GSTT1 genotype. Null genotype was found in 37% patients and wild type in 63% cases. GSTT1 null genotype was

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observed in 29% and wild type allele in 71% control individuals in 35% early onset and 40% late onset patients (Fig.2).

Study of Molecular Characteristics of Familial and Early Breast Cancer

Studies on molecular characterization of early onset and familial cancer have shown decreased expression of estrogen receptors (ER) in early onset and familial cases and increased expression of cyclin D in familial cases. Study was undertaken to characterize molecular changes in oncogenes, tumour suppressor genes, apoptotic genes and DNA mismatch repair genes of early onset breast cancer with or without family history and mutations in BRCA 1 /2 genes.

The cytokeratin (CK 5,6,7 and 14) profile was studied in 57 cases of breast cancer to evaluate the cellular origin, (*viz.* basal or luminal cells) and for functional classification of breast cancer. Immunohistochemical profile of CK5/6 and CK7 was studied in paraffin embedded sections. The basal cytokeratin CK5/6 was expressed in 26.3% and luminal cytokeratin CK7 in 8.69% cases (Fig.3). CK14, studied in 30 cases was seen to be expressed in 20% cases. Correlation of these cytokeratins with molecular profile of breast cancer cells in different groups is being studied.

Fig. 3. Cytokeratin 7 expression in a case of infiltrating ductal carcinoma

Androgen receptor (AR) positivity was observed in 40% carcinoma breast patients (Fig.4). ER immunostaining was seen in 35% cases while 44% cases were positive for progesterone receptor (PR)

duct carcinoma of breast expression. Immunostaining for EGFR was positive in

FIg. 4. Androgen receptor nuclear immunopositivity in infiltrating

40% cases while TGF-beta receptor showed positive in 40% cases while TGF-beta receptor showed positivity in 32% cases. Statistically significant higher positivity for ER, PR and TGF-beta receptors was observed in cases positive for AR. EGFR positivity also showed a higher trend in AR positive cases but was not statistically significant. Of the total 30 familial cases of breast cancer, ER and PR expression was seen in 33.3% and 56.6% respectively. AR positivity was found in 50% while EGFR was expressed in 46.6% of familial breast cancer patients. TGF-beta receptor positivity was seen in 33.3% cases.

Urogenital Malignancies

Study of the Host Immune Response in Patients with Superficial Transitional Cell Carcinoma

The study evaluated the cytokine (Th1 and Th2) balance in peripheral blood mononuclear cells (PBMCs) of transitional cell carcinoma (TCC) patients in order to assess the immunological factors influencing the anti-neoplastic activity of intravesical combination BCG/IFN $\alpha 2\beta$ in patients. Study was done to measure the dynamics of systemic Th1 and Th2 cytokine responses in patients who had not received any therapy prior to transurethral resection of bladder tumour (TURBT) (pre-therapy) and the immune responses in the same group of patients were compared following TURBT and intravesical combination therapy (post-therapy) using flow cytometry.

Forty-one patients with histologically confirmed superficial TCC treated by TURBT followed by




intravesical combination immunotherapy formed the study group. Patients were followed up every third month for duration of 6 months to 3 years (median follow up of 22.5 months). The circulating levels of Th1 and Th2 cytokines were determined in the sera of normal healthy subjects (20) and superficial TCC patients prior to therapy (41, pre-therapy) and following combination BCG/IFN $\alpha 2\beta$ intravesical therapy (37, post-therapy). The mean levels of Th1 cytokines, IL-2 and TNF α were significantly reduced whereas significantly enhanced levels of Th2 cytokines like IL-4, IL-6 and IL-10 were observed in pre-therapy patients as compared to healthy volunteers (Fig.5). The mean levels of IFN γ , IL-2 and TNF α increased whereas the Th2 cytokines, IL-4 and IL-10 were concomitantly reduced in patients following combination treatment as compared to patients prior to intravesical treatment (Fig.6).



FIg. 5. Th1/Th2 cytokines in normal and pretherapy patients



FIg. 6. Expression of Th1/Th2 cytokines in TCC patients prior to and following intravesicle combination immunotherapy

The expression of p53, $p21^{waf1}$ and growth factor receptors such as VEGFR and TGF β R was

studied in 32 cases of superficial TCC to evaluate the relevance of transforming proteins in the progression of superficial bladder cancer. Expression of p53 was seen in 68.75% cases, and that of VEGFR in 46.87%. Loss of p21^{waf1} was observed in 32.75% cases and TGFBR in 56.25% cases. The study showed that while p53 and VEGFR expression was increasing with increasing grade of tumour (Fig.7), TGF β R decreased with increasing grade of tumour (Fig.8). The study also showed that the biomarker profile of p53+/VEGFR+/p21+/ TGF β R – was a predictor of recurrence, progression and decreased survival.



 Fig. 7. VEGFR expression in a case of TCC bladder on cell spots
 Fig. 8. TGFβR expression in TCC bladder

Hematopoietic-Lymphoid Malignancies Prognosis and Response to Chemotherapy in Acute

Leukaemia Patients

Earlier studies revealed that pattern of in vitro sensitivity of leukaemic cells to chemotherapeutic drugs vincristin, daunorubicin, methotrexate, cytosine arabinoside and L-asparaginase can be correlated with clinical response of the patients. During the year expression of genes commonly involved in drug resistance was studied by real-time RT- PCR (TaqMan probe assay) to see if gene expression could be indicator of drug sensitivity pattern in individual patient samples. The mean mRNA expression level of the selected genes (MDR, DHFR, GST-pi, p53) was calculated for each case. Of the 12 samples analyzed for the relative expression of genes DHFR, GST, MDR and p53, 6 samples were of acute myeloid leukaemia (AML), 5 of acute lymphoblastic leukaemia (ALL) (3 of B-ALL, 2 of T-ALL) and 1 of biphenotypic leukaemia.

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Preliminary results showed mean GST-pi expression significantly upregulated in AML and T-ALL, mean MDR expression significantly upregulated in AML and downregulated in B-ALL, T-ALL and biphenotypic leukaemia, mean DHFR expression significantly upregulated in T-ALL as well as in AML and B-ALL and mean p53 expression significantly upregulated in AML and T-ALL (Fig.9). More samples are being analyzed to see if chemosensitivity can be correlated with expression pattern of these selected genes.



Fig. 9. Gene expression profile of GST-pi, MDR, DHFR, and p53 in leukemic samples

Expression of Cell Cycle Regulators in Acute and Chronic Myeloid Disorders

Chronic myeloproliferative disorders remain stable for years and often transform to an accelerated phase of blast crisis. Study was done to understand the significance of expression of cell cycle regulators (p53, p21 and MDM2) and proliferative and apoptotic markers (PCNA and CPP32) in bone marrow specimens of 40 patients [15 with AML, 15 with chronic myeloid leukaemia (CML) and 10 with myelodysplastic syndrome (MDS)]. p53 expression was found in 28%, p21 in 25% and MDM2 in 23% samples. p53 expression was higher in AML while p21 and MDM2 expression was higher in CML. PCNA and CPP expression was highest in MDS. Twenty per cent samples showed overexpression of P21 and MDM-2 in the absence of p53 expression indicating that p53 independent pathway may be involved in cell cycle regulation in these samples. MDM-2 expression was highest in CML with blast crisis and was significantly associated with low/ absent apoptosis suggesting that MDM2 overexpression

may be related to a higher grade of myeloid proliferative diseases and its progression to acute leukaemia.

PATHOLOGY OF INFECTIOUS DISEASES

Genital Chlamydiasis

Development of Diagnostic Assay for *C. trachomatis*

During the year under report, determination of sensitivity and specificity of developed antichlamydial monoclonal antibody clones was done in addition to their characterization by Western blot. Sensitivity of clones was determined by monoclonal antibody titers against C. trachomatis antigen by immunofloursence assay. Further the reactivity of three developed antichlamydial clones (Dl0.4, H.5.6 & B2.2) was evaluated in 200 endocervical specimens by enzyme immunoassay (EIA) and compared with cell culture. The positivity for clones in EIA was 45%, 43% and 35% respectively when compared with cell culture method which was 46%. The maximum positivity was detected with species specific clone (D10.4) which can react with any serovar/ serovars of C. trachomatis followed by clone (H.5.6) D serovar specific, thereby indicating a high prevalence of serovar D of C. trachomatis in female genital tract.

Cytokine Gene Expression Profile in Endocervical Lavages in *C. trachomatis* Infected Women

Cell mediated immune responses play a major role in clearance and resolution of chlamydial infection. Further, chlamydial infection at mucosal sites provides sustained antigenic stimuli for host immune responses with the induction of cytokine production. Cytokine production profiles of PBMC and lavage cells in response to stimulation with *C. trachomatis* antigen and PHA were compared in patients positive for *C. trachomatis* infection and in controls. Levels of IFN γ and IL-10 were found to be higher in cervical lavage cells of positive cases when compared with controls which suggests a mixed type of immune response and a probable establishment of conditions within the host cell milieu for long term persistence of *C. trachomatis*.

Role of Chlamydial Heat Shock Proteins (cHSP) in Pathogenesis of Genital Tract Infection in Women

cHSPs are known to be immunopathogenic proteins due to their structure homology with host HSP proteins, which contribute to persistence of Chlamydia inside the host cell. Responses to cHSP60, have been associated with sequelae of upper genital tract disease in infected women. Study was done for cloning and expression of chsp60 gene in order to elucidate its pathogenic role and further development of diagnostic kit for detection of Chlamydia infection by serological diagnosis of chlamydial heat shock proteins 60 and 10 (cHSP60 & cHSP10) by ELISA using specific peptides. cHSP60 and cHSP10 showed strong positivity in C. trachomatis positive patients compared to negative patients or patients positive for other sexually transmitted pathogens. The sensitivity and specificity of cHSP60 in comparison to DFA was 76.9% and 89.3% respectively.

Inclusion Protein and Their Contribution towards Chlamydial Pathogens

During developmental cycle, the intracellular bacterial pathogen *C. trachomatis* remains confined within a vacuole known as an inclusion. It is thought that pathogen-derived products are transported through this membrane, where they combine with host cell factors necessary for bacterial development. Despite the complete genomic sequencing of *C. trachomatis*, the identity and function of most *Chlamydia* gene products that interface with the host cell remain a mystery. At a molecular level the inclusion membrane (Inc) defines the critical inferface between *Chlamydia* and the host cell.

100bp L



549 bp

Fig. 10. Agarose gel electrophoresis for amplified product of Inc gene showing 549 bp band.

Therefore, study was done for cloning and expression of Inc gene which may be responsible either for the protective/pathogenic function or in the development of *C. trachomatis*. For this study, primers were designed for inclusion gene and PCR was standardized. Optimum condition for amplification of inclusion gene was achieved and a PCR product of 549bp was obtained (Fig.10). Further cloning and protein expression is in progress.

Role of Iron in Pathogenesis of *C. trachamatis* Infection

deprivation synergistically Iron helps C. trachomatis to decrease levels of reactive oxygen species (ROS) in late stage of development thereby helping chlamydiae to persist. To study the role of iron in persistence of chlamydial infection, levels of ROS in vitro in culture system in different conditions were evaluated. It was found that during Chlamydia infection, there was decrease in ROS levels (75 to 35) which further decreased on addition of iron chelator (dichlorofluorescein, DCF) (Fig.11). In addition, studies were targeted on the transferrin receptor mediated iron uptake, which may lead to ROS generation resulting in host apoptic cell death. Higher expression of Bcl 2 (anti-apoptotic protein) was detected in Chlamydia infected cells.



Fig.11. Level of reactive oxygen species (ROS) as probed through dichloroflourescein (DCF) in different conditions at 48 hpi of *C. trachomatis* and visualized by confocal microscopy a) Culture of McCoy cells alone b) McCoy cell culture –ve for *C. trachomatis* where DCF was added c) McCoy cell culture infected with *C. trachomatis* + DCF added d) culture CT infected but DCF negative

Immune Responses to *C. trachomatis* Infection in Spontaneous Aborters

Study was undertaken to find the precise immunological mechanism whereby infection with C. trachomatis adversely affects early stage pregnancy in women leading to miscarriage. Spontaneous aborters (SA) in the Ist/IInd trimesters of pregnancy were enrolled alongwith their male partners and samples of non-macerated aborted endometrial curettage tissue (ECT) and blood were collected. After ruling out infection with other pathogens in SA and presence of male factors in their partners, SA were divided into group I, i.e. those with no past history of spontaneous abortion and group II, *i.e.* those with past history of ≥ 1 spontaneous abortion. The prevalence of chlamydia in group I was 16.6% and 10.7% by IHC and PCR respectively in ECT while in group II it was 12.5% by IHC/PCR. Cytokine expression in ECT is being studied in CTR infected SA.

Leishmaniasis

Discovery of Virulence-related Genes in *Leishmania* using Microarray

Genomic microarray based analysis was carried out using various stages of the parasite during transformation from promastigote to amastigote stage. To understand the process of differentiation of Leishmania, global variation in gene expression in promastigotes, an intermediate stage of differentiation (PA24) and axenic amastigotes in culture was assessed using a L. donovani genomic microarray with 4224 clones in triplicate. During intermediate stage of differentiation 24h after shifting the promastigotes into amastigotes (PA24), there were 68 (~1.5%) clones with \geq 1.7 fold higher expression in comparison with promastigotes, whereas in terminally differentiated amastigotes there were 239 (~5.65%) such clones. Of particular interest were certain genes that exhibited a transient increase or decrease in expression at the PA24 stage. Kinases showed a transient increase and surface molecules PSA and amino acid permeases showed a brief decrease at the PA24 stage. Also, the proportion of differentially expressed genes that represent surface molecules was greater in Am/Pro microarrays than in PA24/Pro microarrays. The microarray results have been validated using Northern blots or RT-PCR. The results provide important leads about the genes involved in the early differentiation process of *L. donovani* that may contribute to virulence.

Evaluation of Localized Immune Response in PKDL Patients

Localized responses in KA and PKDL were studied using semi-quantitative RT-PCR. Intralesional cytokine gene expression was analyzed in 28 PKDL and 14 KA patients. Data revealed mixed Th1 and Th2 responses, as reflected by elevated IFN- γ , TNF- α , TGF- β , interleukin (IL)–10, IL-6 and IL-4 with minimal expression of IFN- γ R1 message in PKDL lesions compared to normal skin tissue. In comparison with KA, message for IFN- γ , TNF- α and IL-6 were found significantly elevated in PKDL lesions, implying an important role of these cytokines in PKDL pathogenesis.

Identification and Characterization of *L. tropica* Isolated from Indian Patients of Cutaneous Leishmaniasis

Study was carried out for molecular and immunological characterization of L. tropica species causing cutaneous leishmaniasis (CL) in Bikaner, Rajasthan. Clinico-epidemiological analysis of 98 cases suggested that the preponderance of infection is higher in males than in females with highest prevalence in the age group of 5 to 30 yr and variability in lesion types and number. Comprehensive molecular and immunological studies were carried out for identification and characterization of species in 32 cases. Culture was positive in 43.75% cases and direct microscopy in 59.3% cases. To affirm if the clinical isolates belonged to L. tropica species, isolates were subjected to nested ITS-1 PCR-RFLP analysis. Result yielded typical band patterns of L. tropica in DNA from both culture and clinical samples. That isolates belonged to L. tropica was confirmed by IFA using species-specific monoclonal antibodies. Comparative analysis showed that kDNA minicircle PCR primers were 84.37% sensitive for detecting the parasite directly in clinical samples. The present study is the first



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comprehensive molecular and immunological investigation of CL caused by *L. tropica* in India which carries immense importance from epidemiological and treatment point of view.

Other Studies

Use of Placental Tissue in Human Environmental Bio-monitoring of Pollutants

During the year under report, approximately 4000 pregnant women attending Safdarjung Hospital OPD were screened for possible exposure to pollutants. A total of 150 women who reported exposure to agricultural chemicals during pregnancy and 100 placental samples collected from them at the time of delivery were selected. Pesticide residues (synthetic pyrethrins) and pollutants (like cycloheptatrienylium bromide and naphthalene) were detected from placental extracts.

BIOCHEMISTRY

Studies on the effect of chronic ethanol feeding on transport of folate and expression of its transporter in rat intestine were done at PGIMER, Chandigarh. Folate deficiency is the most common sign of chronic alcoholism. Intestinal malabsorption of the folate is a contributing factor of alcohol induced folate deficiency in male Wistar rats fed 1g/kg body weight ethanol orally for 12 weeks. Chronic ethanol feeding was found to decrease the binding as well as transport of folic acid by altering various kinetic characteristics of the processes at both the intestinal and renal brush border membrane level. Decreased uptake of folate across the intestinal epithelium was associated with reduced expression of mRNA of folate carrier. Moreover, transport was reduced all across the crypt villus axis after chronic ethanol feeding. Using various activators and inhibitors of different signaling pathways it was observed that folate transport is regulated by cAMP dependent protein kinase A.

A study on antioxidant vitamin supplements as palliative treatment of bone disorders was done at Dr. D.Y.Patil Medical College, Pune. A group of 198 patients suffering from skeletal disorders like osteoporosis, renal osteodystrophy, bone malignancy and fractures underwent baseline assessment of biochemical markers *viz*. [osteoblastic markers: serum alkaline phosphatase (ALP), free Ca++ and inorganic phosphorus (Pi); osteoclastic markers: serum tartarate resistant acid phosphates (TrACP) and malon dialdehyde (MDA) and the antioxidant markers: serum superoxide dismutase (SOD) and erythrocyte reduced glutathione (GSH)]. The test group was then divided into 3 groups-group A (Evinal 400mg), B (Celin 500mg) and C (Evinal + Celin) for antioxidant supplementation for a period of 90 days. There was significant improvement in levels of serum MDA, serum TrACP, serum ALP, SOD and GSH. The response improved with duration of supplementation. Results revealed that antioxidant vitamin E and C individually or conjointly improve the bone status in various skeletal pathologies and hence may serve as cost effective, palliative supplements in addition to curative treatment.

IMMUNOLOGY

A study on antigen-dependent lymphocyte activation thresholds in adaptive immunity aimed at examining the effects of antigen-induced structural changes in antigen receptors on biochemical control of lymphocyte activation was done at International Centre for Genetic Engineering and Biotechnology and National Institute of Immunology, New Delhi. Studies revealed for the first time the relationship between signal amplitude and its duration during signal transduction. Study on B cells demonstrated that amplitude of the initial pulse of the signal dictates how far and how fast it will travel through the downstream networks. Further, the amplitude of the initial pulse was shown to be dependent upon an amplification system that was controlled through a feed back loop between cyplasmic calcium ions and reactive oxygen.

GENOMICS AND MOLECULAR MEDICINE

Studies to understand the mechanism of transcription termination in mycobacteria were done at IISc, Bangalore. Intrinsic transcription termination signals provide an extremely economical mechanism for the termination process since they can function in the absence of proteins. So far the process of termination has been mainly studied in *E. coli* and confined to *E. coli* paradigm. A versatile algorithm

(GeSTer) for genome-wide analysis of transcription termination signals has been developed. The new algorithm is applicable for the analysis of potential terminators from all sequenced bacterial genomes. In addition to the classical E. coli (or text book) type terminators, the algorithm identifies several new kinds of structures as putative terminators. By in vitro and in vivo experiments, these novel structures were shown to function as effective terminators in mycobacteria. The different kinds of terminators are concentrated within the first 50 nucleotides downstream of coding sequences in most bacterial genomes indicating that they serve the same purpose. The algorithm is fastest and most accurate for identifying the terminators and other secondary structure motifs involved in regulation of gene expression. In addition, it would serve as an invaluable tool in predicting the organization of genes, operons and for the development of expression systems.

Study for molecular diagnosis of common opportunistic infections in cancer was completed at Kidwai Memorial Institute of Oncology, Bangalore. Frequency and type of opportunistic infections (invasive fungal infections (IFI), *T.gondii, P jirovecii* and cytomegalovirus infections) in various types of malignancies were determined using PCR. The cause of fever due to the above mentioned pathogens was investigated by molecular and conventional means in a total of 200 episodes of fever (182 with haematological malignancies and 18 with solid tumours; 132 with febrile neutropenia and 68 with fever but with normal counts). Fever could be ascribed to IFI in 16% cases *T.gondii* in 13.5%, *P jirovecii* in 11% and CMV in 5.5% cases.

Molecular genetic analysis of some forms of inherited childhood blindness and genetic counselling of affected families was done at L V Prasad Eye Institute, Hyderabad. The study involved molecular genetic characterization of 3 ocular diseases affecting children– retinoblastoma, primary congenital glaucoma (PCG) and anterior segment dysgenesis. Retinoblastoma is a childhood intraocular malignancy resulting from mutation of both alleles of the R81 gene. Standardization and screening of 50 retinoblastoma patients for mutations was carried out by SSCP. Mutations detected included a few novel as well as recurrent mutations. Majority of mutations result in premature termination of protein. PCG is a form of glaucoma manifesting at birth. This study revealed mutation of CYP181 causing PCG in Indian populations. The R368H mutation was found to be the most prevalent CYP181 mutation. In addition, it was found that the myocilin gene is a cause of PCG in some families. Anterior segment dysgenesis is a group of disorders arising from developmental anomalies in the anterior segment of the eye. The PAX6 gene for aniridia and the FOXC1 gene for Axenfeld Reiger anomaly were studied and found to have novel mutations in the patients tested. Overall, the results of the study provide data on these disorders in Indian patient populations for the first time and can be useful in devising screening/genetic counseling strategies for patients.

HUMAN GENETICS

A study was conducted at Indian Statistical Institute, Kolkata on the effect of Alu insertion/deletion polymorphism at the DCPI locus on blood pressure and lipid levels among individuals belonging to defined haplogroups from two tribal populations-Toto and Bhutia of India. Toto are exclusively rural while Bhutias live in both rural and urban habitats and their dietary habits and lifestyles have also changed in recent decades. About 283 samples from Totos and 455 from Bhutia were obtained. The individuals were also genotyped with respect to insertion/deletion polymorphism at the DCP1 (ACE) locus to estimate the impact of this polymorphism on blood pressure. All Toto individuals (30) were homozygous for In/Ins at the DCP1 locus. In Bhutia out of 75 individuals about 34% were homozygous for Ins/ Ins, 51% were heterozygous (Ins/Del) and 14% were all homozygous for Del/Del. The study revealed that metabolic syndrome can be a major health problem even in traditional ethnic groups.

PHYSIOLOGY

Study to investigate neuro-chemical regulation of REM sleep and cellular changes after REM sleep deprivation was completed at Jawaharlal Nehru University (JNU), New Delhi. The study investigated a) the involvement of gamma amino butyric acid (GABA) in the laterodorsal tegmentum and pedunculo-pontine tegmentum(PPT) area in the brain (where the REM-ON neurons are located) in REM sleep regulation; b) changes in membrane lipid peroxidation after REM sleep

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deprivation; c) whether REM sleep deprivation dephosphorylates Na-K ATPase for increasing its activity. The results reveal that GABA in PPT modulates REM sleep. Synaptosomal membrane lipid peroxidation was decreased after REM sleep depriviation, which was mediated by increased norepinephrine (NE) and the action was mediated through the α 1 adreneceptors. The results also suggest that calcium plays a role in REM sleep deprivation induced decreased lipid peroxidation. There was a significant decrease in phosphorylated form of synaptosomal Na-K ATPase after REM sleep deprivation, which was again mediated by NE acting through the α 1 adrenoceptor. REM sleep deprivation also increased the transcription of $\alpha 3$, $\beta 1$ and $\beta 3$ subunits. The study showed that after REM sleep deprivation there was an increase in the level of phosphatidylethanolamine, however, it was not mediated by NE.

PHARMACOLOGY

Design and development of new class of antitubercular agents was carried out at Central Drug Research Institute (CDRI), Lucknow with the cell wall of the bacterium as target and based on well known inhibitors. A number of compounds have been synthesized belonging to different prototypes viz. glycosylated amino acid, hydroxamates, ureides, alcohols and glycoconjugates; glycosylated cyclopropyl phenyl methanones; glycosylated ureas and C-nucleosides; thiazidine thiones and glycosyl enamines. All the synthesized compounds have been evaluated for antitubercular activity in vitro and the selected potent compounds have also been evaluated in vivo. Glycosyl amino alcohols and thiazidine thiones have emerged as new class of antituberculars active in MDR strains and in vivo also offer new leads for further optimization.

Studies on the antileishmanial properties of novel naphthaquinonoid derivatives and their therapeutic applications were conducted at Jadavpur University, Kolkata to develop diospyrin, a plant derived lead compound into an effective chemotherapeutic agent. Synthesis, characterization and biological evaluation of novel derivatives (aminoanalogues of diospyrin) was achieved. Data indicated variable inhibitory efficacy of the compounds against parasite cells in a dose-dependent manner, the ethanolamine derivative showing the most marked enhancement in activity as compared to its precursors (*viz*. diospyrin and its diethylether derivative). Evaluation of antileishmanial activity of new derivatives in the infective *L.donovani* strain maintained *in vivo* through serial passages in hamsters showed that the diospyrin derivative achieved nearly 56% inhibition as compared to ~70% inhibition by the standard drug. Combination therapy with diospyrin derivative along with IFN- γ on days 14, 16, 18, 20 and 22 post infection in mice showed 44% inhibition, however, 74% inhibition was noted in the infected animals.

TRADITIONAL MEDICINE

At the Centre for Advanced Research on Drug Development from Selected Natural Products at CDRI, Lucknow clinical trials were undertaken on Picroliv and further studies were conducted on *Centella asiatica* and *Terminalia chebula*.

Studies on C.asiatica showed angiogenesis in mice, wound healing activity at different doses in chorio-allantoic membrane model and normal wound healing in guinea pig. It also showed anti-oxidant activity which may have added to the effect. A mixture of C. asiatica and curcuminoids also showed wound healing activity in cutaneous punch wound and diabetic wound in rat. Extract and active principles isolated from it showed enhanced learning and memory functions. Fingerprinting and regulatory pharmacological and pharmacokinetic studies were undertaken. Shelf-life and accelerated stability studies of the alcoholic extract and asiaticoside indicated stability for more than 2 yr. Besides studies on the mechanism of action, systemic toxicity and bioavailability studies are ongoing. Terminalia chebula showed good anti-stress and antioxidant activity.

At the Advanced Centre for Research in Clinical Pharmacology of Traditional Medicine at TN Medical College, Mumbai, and BYL Nair Charitable Hospital, Mumbai studies were undertaken to understand mechanism of action of *Pterocarpus marsupium* as an antidiabetie agent. It has been found to modulate angiogenesis and exert immunomodulatory effect. It protected pancreatic β cells from the damage induced by streptozotocin (STZ) in rat insulinoma cell lines (RINmf) which appears to be a consequence of antioxidant effects. It also restored insulin secretion from STZ damaged pancreatic β -cells although insulinmimetic actions could not be demonstrated. A novel formulation (ACTM 001) has been found effective in preventing recurrence of diarrhoea in children with malnourishment. ACTM 001 significantly reduced the number of diarrhoeal episodes over a period of 75 days. Further experimental and *in vitro* studies indicated that the three constituent plants prevented bacterial translocation to the mesenteric lymph nodes from the intestine and one of them exerted anti-bacterial effect *in vitro*. A novel herbal formulation from Neem oil (ACTM 002) helped in de-sloughing and hastened wound healing.

A flexible dose multicentric trial was undertaken during 2002-2004 to investigate the blood glucose control in type 2 diabetes with *Vijaysar* (*P. marsupium*) in patients already on an allopathic mono-therapy and to determine adverse effects of this plant. The study was carried out in four centres attached to teaching medical institutions in India representing different segments of the population. Of the 503 patients considered for analysis, 196 completed 20 wk. of treatment. Analysis by the mixed effects model confirmed the anti-diabetic property of *Vijaysar*. Subgroup analysis indicated the need for change of regimen as early by week two of *Vijaysar* treatment for some of the uncontrolled allopathic mono - therapy patients.

Studies on manufacturing, standardisation and quality control of formulations of traditional remedies/ natural products at Regional Research Laboratory, were continued. Raw materials for Jammu manufacturing the formulations were collected and standardization and quality control were carried out before dispatching them to Central Biostatistical Monitoring Unit (CBMU) for distribution. Studies were also carried out to reduce the fraction of P. marsupium (Vijaysar) without changing the profile. The residue on reconstitution continued to have same activity. Chemical markers were identified, four showed hypoglycemic and two hyperglycemic activity. VS - 5 fraction showed additional antibacterial and anti-tuberculosis activity. Further studies are being done for validation.

Survey of Medicinal Plants of Western Ghats

The RMRC, Belgaum has been designated by the Council as the Coordinating unit of multicentric project on survey of medicinal plants of Western Ghats. During the year information for 500 medicinal plants used by local traditional practitioners from the Western Ghats has been collected, along with 497 herbarium sheets of 332 plant species and 514 photographs of 318 plants species. Database development is in progress. The database will provide detailed information on botanical name, synonyms, local names, description of the plant parts used by the tradititional practitioners, medicinal uses, formulation, chemical composition, pharmacology/toxicology and clinical trials *etc.*

HAEMATOLOGY HAEMOGLOBINOPATHIES

Isolation of Foetal Cells from Maternal Blood for Non-invasive Prenatal Diagnosis of Thalassaemia

Study was undertaken to evaluate the feasibility of development of a non-invasive technology using maternal blood prenatal diagnosis in foetus. So far efforts have not been 100% successful. However in 90% of cases it is now possible to pick up foetal nucleated red cells using a combination of monoclonal antibodies. A well designed nested PCR is able to detect the β thal mutations in the foetal cells.

Development and Validation of ELISA for HbA2– A Novel Screening Method for β -Thalassaemia Carriers

An ELISA has been developed successfully at Genetic Research Centre, Mumbai. The test has great utility in control of β -thalassaemia. It is simple, accurate, inexpensive and precise and suitable for transforming into a user friendly kit.

Molecular Characterization of $\alpha\beta$ Thalassaemia and Persistence of Foetal Haemoglobin

Study is ongoing at IIH to understand the basic biology of expression of foetal haemoglobin gene in the adult. Several molecular variants of hereditary persistence of foetal haemoglobin (HPFH) with varying amount of deletion of HbF gene were detected. Studies are ongoing to find out point mutations which lead to HPFH.

BLEEDING DISORDERS

Thrombohaemorrhagic Balance in Haemophilia – Implications for Alternative Therapeutic Approach

Coinheritance of thrombophilia genes as a possible ameliorating factor in severe haemophilia was investigated at IIH, Mumbai. Till date 58 haemophilia patients (< 1% deficient factor) have been evaluated, 29 of whom had milder presentation. Around 60% patients with milder presentation had one or more positive thrombophilia markers whereas only 12% clinically severe phenotypes had thrombophilia markers. Studies are ongoing to analyze which of the markers have overwhelming importance in reducing the severity of the disease. In 40% mildly affected patients, thrombophilia markers tested were not exhaustive.

Thromboelastographic Characterisation of Severe Haemophilia

Global assessment of coagulation system was done by thromboelastography (TEG) of whole blood. Advantage of using the whole blood is that the cellular contribution of coagulation can also be detected. TEG was done in more than 60 haemophilia patients with deficient factor level of < 1%. (Severe by definition). Following patterns were observed: Hypercoagulable (normal), normal with increased fibrinolysis, long latent period followed by split suggesting factor deficiency and no split at all suggesting severe factor deficiency (split was seen in all these patients on addition of antifibrinolytics to the blood). These four patterns have broad clinical correlation. Pattern 1 was clinically mild and has more often co-inherited thrombophilia markers. Pattern 2 and 4 should theoretically improve on antifibrinolytics.

Genetic Aspects of Essential Hypertension in North East India

Three groups of adult people (>500) from North-East were studied to investigate whether any genetic polymorphism of important genes is linked to hypertension in tea garden workers: i) Tea garden workers with very high prevalence of hypertension (60%), ii) Mizo population with low (<5%) prevalence and iii) native Assamese population with intermediate prevalence (5-15%) of hypertension. Seven genetic polymorphisms-ACE, AGTR1, CYPIIB2, IC-WT, SF, E-NOS and I-NOS were tested. It was found that ACE D/D gene was strongly linked to hypertension and was also linked in different families. The finding suggested that in many of these patients ACE inhibitors may not be the right choice of first line drugs for hypertension.

Detection of Factor IX Mutation and DNA Sequencing

More than 100 affected families were tested for mutation of factor IX gene. In 90% Gujarati population with moderately severe haemophilia B, a founder mutation Gly60Ser involving epidermal growth factor domain was found (Fig.12). A mismatch PCR technique has been developed to detect the mutation quickly for quick prenatal diagnosis in these patients. Sequencing



Fig. 12. Mismatch PCR showing Glygoser (GI0430A) mutation in factor IX gene

needs to be done in all these patients to detect the mutation. In 12 cases in whom sequencing could be done, seven different mutations were found.

HAEMOGLOBINOPATHIES/BLOOD DISORDERS AMONG TRIBALS/ OTHER GROUPS

Jai Vigyan Mission Project on Community Control of Thalassaemia

The Council has recently completed a multicentric project on community control of thalassaemia with

centres in 6 states of the country viz. Punjab, Assam, Gujarat, Maharashtra, Karnataka and West Bengal in which 59,667 cases have been screened. All the centres achieved the target of screening 5000 students. Colleges were selected from different areas of the cities and students from at least 15-30 colleges were screened at different centres. The overall prevalence of betathalassemia trait was 2.6% and ranged from 1.6% in Dibrugarh to 3.4% in Ludhiana. The prevalence of Hb E trait was 25.2% in Dibrugarh and 4.1% in Kolkata while occasional cases of Hb E trait were seen in the other 4 centres. A total of 261 students in Dibrugarh were homozygous for Hb E while 74 students in Dibrugarh (1-5%) had Hb E thalassemia. Students with Hb S trait were seen mainly in Vadodara (2.5%) and Mumbai (0.5%) while Hb D trait was more common in Ludhiana (1.2%). In Bangalore, 6 students had betathalassemia and 6 sickle cell disease. Few students with thalassemia trait and HPFH trait were encountered at most of the centres with an overall prevalence of 0.1%. There were 33 students who had other structural hemoglobin variants like Hb Q, Hb J and same uncharacterized variants.

There were 73 different caste groups from various regions of the country representing the ethnic diversity in the country. However, in 29 of these castes the total of students were less than 50. Hence the prevalence of different hemoglobinopathies in these groups could be an accurate estimate. Among others, a higher prevalence of thalassemia trait was seen in Vellalas (9.3%), Sindhis (8.6%), Aroras (7.5%) and Lohanas (6.3%). The prevalence of Hb S trait was 15.6% in the scheduled tribes. The prevalence of Hb D trait varied from 2.0 to 4.8% in the Aroras, Prajapatis and Sikhs. The higher prevalence of Hb E trait (94.4% and 38.8%), Hb E disease (8.5% and 11.0%) and Hb E thalassemia (20.7% and 4.8%) were seen in the Chandra Seniya Kayastha Prabhu and Chettiar casters. The other caste groups showing a higher prevalence of Hb E trait were Baidya (9.4%), Billiva (22.2%), Shetty (23.8%) and Chimba (5.2%).

There was a representation of students originating from all the states and Union Territories of India. There were some students from neighboring countries like

Bangladesh (1552), Pakistan (221), Nepal (25), Maldives (10) and Bhutan (4). In most of the states of India, the prevalence of beta-thalassemia trait varied from 1-3%. It was >3% in Andhra Pradesh (3.3%), Haryana (5.4%), Madhya Pradesh (3.8%), Rajasthan (3.1%) and West Bengal (3.9%). The prevalence in students originated from Pakistan was 8.4%. Occasional students with HbS trait were found in many states while the highest prevalence was 3.0% in Gujarat. The prevalence of Hb D trait was >1.0% in Jharkhand (1.7%), Manipur (1.8%), Punjab (1.2%) and the immigrants from Pakistan (2.4%). Hb E trait was most common in the north eastern states of Assam (27.1%), Arunachal Pradesh (18.2%), Meghalaya (10.3%) and Tripura (16.0%). Hb E trait was also seen in students originating from Chandigarh (910.0%), Lakshadweep (14.7%), West Bengal (4.4%) and immigrants from Bangladesh (4.0%). However, Hb E was also seen in several other states in lower frequencies.

The overall prevalence of beta thalassemia trait in antenatal women was found to be 3.0% ranging from 1.3% in Dibrugarh to 4.2% in Kolkata. These women belonged to 72 different caste groups representing genetic diversity. Higher prevalence of beta thalassemia trait was seen in Aroras (9.38%), Sindhis (8.5%), Mandals (7.85%), Pilais (6.25%), Lohanas (6.67%), Jains (4.48%), Kayasthas (4.65%), Khatris (4.6%) and Baidyas (4.35%).

Intervention Programme for Nutritional Anaemia and Haemoglobinopathies amongst Primitive Tribal Populations in India

A multicentric project on intervention for nutritional anaemia and haemoglobinopathies was completed in 16248 individuals from primitive tribes of Maharashtra, Gujarat, Orissa and Tamil Nadu. Sickle cell trait was found in 1.2-22% of the population. Worm infestation and iron deficiency status was also investigated in them and 22-70% of the population was found to been iron deficient. Iron replacement and anthelminthic treatment lead to substantial rise in haemoglobin in these tribal populations. Areas where sickle cell genes are common, nutritional co-morbidities are also prevalent.

Incidence and Molecular Characterization of G-6-PD Deficiency in North-East India

Up to March 2005, a total of 1696 subjects (748 males and 948 females) in the age group of 4 to 70 yr from Dibrugarh, Sivasagar, Jorhat and Kamrup districts of Assam were screened for G6PD deficiency of which 3% were found G-6-PD deficient. The deficiency in males was 5.5% and in females 1.2%. During April 2005-March 2006, another 996 blood samples belonging to 37 ethnic groups of Assam were screened. The overall deficiency of G-6-PD was found to be 2.1% (male 3.2%, female 1.5%). The ABO blood group pattern among the population was also studied. The most predominant blood group among the study subjects was O (37.3%), followed by B (31.9%), A (22.6%) and AB (8.2%). Negative Rh factor was observed among 1.5% subjects. Further study is in progress.

Haemoglobinopathies in SC/ST Population in Madhya Pradesh

The RMRC, Jabalpur conducted a study to estimate the prevalence of various haemoglobinopathies in SC and ST populations of Nimar in M.P. Sickle haemoglobin is most common haemoglobinopathy in both tribal and scheduled caste groups ranging from moderate (13%) to high (27%) prevalence (overall prevalence 18%) (Fig. 13). The



Fig. 13. Prevalence of haemoglobinopathies and G-6-PD deficiency in Nimar

lowest prevalence was obseved in Balai SC group (13.4%) and the highest was in Barela tribe (27.2%). The overall prevalence of β -thalassaemia trait in the five population groups under study was 1.6% which varied from 1 to 2.3%.

Sickle Cell Disease among SC/ST Population of Madhya Pradesh

Sickle cell disease is common in scheduled castes (SC), scheduled tribes (ST) and other backward castes (OBC) of Jabalpur area. Intervention *i.e.* supplementation with folic acid and quick administration of anti-pyretic/anti-inflammatory drugs (as and when needed) along with health education, reduced the severity of the disease considerably. There was reduction in clinical severity of the disease in most of the patients (81%) after intervention.

A study was conducted by RMRC, Jabalpur to know the morbidity profile of sickle cell disease in a total of 350 patients. About 50% of them belonged to SC (Jharia, Mehra, Deharia, etc.) community, 9% to ST and another 20% to OBCs (Kurmi, Lodhi, Yadav, Sahu). Among the main clinical complications for which patients sought medical intervention were painful crisis of bone and joints with fever (85%) and abdominal pain/splenic pain (30%). Splenomegaly was the most common clinical sign reported in 66% of the patients of all age groups (Fig. 14).



INDEX: FJ- Fever+ Joint pain, **FJS**- Fever+Joint pain+ Splenomegaly, **FAp**- Fever+Abdominal Pain, **FApS**- Fever+ Abdominal pain+Splenomegaly, **HS**-Hepetomegaly+ Splenomegaly

Fig. 14. Combination of clinical signs and symptoms in sickle cell disease patients

SUPPORTING FACILITIES

Two institutes of ICMR, the National Institute of Epidemiology (NIE) located at Chennai and Institute for Research in Medical Statistics [renamed as National Institute of Medical Statistics (NIMS) in November 2005], New Delhi provided consultancy and statistical support to scientists of the Council's head quarters, its institutes and other non-ICMR institutions. The NIE is conducting a field-epidemiology training programme. Besides, both the institutes are participating in various multicentric trials.

International collaboration in biomedical research between India and other countries and with international agencies, is ongoing. The Council also arranges exchange visits of biomedical scientists to and from Indian foreign laboratories. The Council also coordinates the WHO Biennium programme of fellowships to Indian scientists.

The Council has undertaken to protect new knowledge generated in the field of biomedical sciences by establishing an Intellectual Property Rights (IPR) Unit. The Unit is engaged in organizing programmes for IP awareness, protection and dissemination among the scientific community.

NATIONAL INSTITUTE OF EPIDEMIOLOGY (NIE), CHENNAI

Indian Ocean Tsunami

On 26 December 2004, a tsunami secondary to the major Indonesian earthquake had struck the coast of Tamil Nadu. The NIE conducted a community-based survey in tsunami-affected coastal fishing village with the major objective of estimating the prevalence of posttraumatic stress disorder (PTSD) and identifying the risk factors for PTSD. Activities were also continued on mental health following tsunami. A longitudinal study of mental and social health outcomes is planned in collaboration with University of Southern California, USA.

Field Epidemiology Training Programme (FETP)

The NIE has been conducting a two-year field epidemiology training programme (FETP) since 2001. A total of 45 scholars from 14 states were admitted for the course till January 2006 and 15 scholars have graduated. The scholars represent different states in the country namely Andhra Pradesh, Orissa, West Bengal, Bihar, Madhya Pradesh, Tamil Nadu, Himachal Pradesh, Maharashtra, Uttaranchal, Mizoram and Andaman and Nicobar islands.

FETP scholars investigated several outbreaks during the year 2005-2006. Some of the important outbreaks include one of hepatitis in Mehragaon village, (Uttaranchal), of measles in Hussendih, Purulia district (West Bengal), diarrhoea in an expatriate community in New Delhi, of chickenpox in Binjha village (Jabalpur), outbreak of acute febrile illness in a local club in Patna (Bihar), hepatitis E outbreak in Hyderabad (A.P.) and Chikungunya outbreak in A.P.

Clinical Trial with Vijaysar (*Pterocarpus marsupium*) for Type 2 Diabetes Mellitus

The NIE continued a multicentric trial to study the blood glucose control in type 2 diabetes with *Vijaysar* in patients already on an allopathic monotherapy and to determine adverse effects of this plant remedy. Results revealed that *Vijaysar* is safe at 6g daily dosage for treatment of type 2 diabetes. No side effect was attributable to it nor were there any signs of overt hypoglycemia. Out of 503 patients considered for analysis, 196 completed 20 weeks of treatment and 179 of them had their blood glucose controlled.

Multicentric Feasibility Study of Intradermal Administration of Tissue Culture Anti Rabies Vaccine

Multi-site intradermal administration of small doses of cell culture and purified embryonated rabies

SUPPORTING FACILITIES

vaccines protects humans bitten by proven rabid animals. Intradermal administration is an effective way of decreasing the cost of these vaccines in developing countries. Several countries have been successfully using these vaccines intradermally for the control of human rabies. The ICMR undertook a multicentric study to assess the feasibility of clinical trial of intradermal administration of these vaccines. Four indigenous vaccines (Abhayrab PVRV, Coonoor PVRV, Rabipur PCECV and Vaxirab PDEV) were administered intradermally. French PVRV (Aventis) was given intramuscularly. A sample size of 10 was selected for each of the vaccine arm in the three participating centres. The findings of the study indicated that all the vaccines given intradermally were safe. Three vaccines i.e. Abhayrab PVRV, Coonoor PVRV and Rabipur PCECV produced immune response above the protective level in almost all the volunteers by day 14 and the immune response was sustained till 90 days of follow up. The response to Vaxirab PDEV, however, was low as compared to other vaccines (Fig. 1). The findings of the feasibility survey in selected districts



Fig.1. Geometric mean antibody titres (GMT) to different cell culture and purified embryonated rabies vaccines

indicated that most of district hospitals had the required skill and necessary facilities for intradermal administration of rabies vaccines. Based on the results of the present study, three vaccines *i.e.* Abhayrab PVRV, Coonoor PVRV and Rabipur PCECV have been recommended for intradermal administration in India.

Leprosy Vaccine Trial

The NIE is the international co-ordinating centre for the multicentric trial to assess the efficacy and effectiveness of 6-month multi-bacillary MDT (uniform MDT) for all types of leprosy patients through general health services. Trial is being conducted at 5 centres in India and one centre in China. Till April, 2006, 2504 patients have been enrolled. Interim analysis was completed and a report has been prepared.

Mapping, Size Estimation and Integrated Behavioural and Biological Assessment in High HIV Prevalence Settings in India

Study is continuing with the aim to gather data for impact monitoring and evaluation of Avahan India AIDS Initiative funded by the Bill and Melinda Gates Foundation in 71 districts of six states and five national highway sites. The proposed mapping, size estimation and integrated behavioural and biological assessment will provide some of the key data needed to assess major outcomes and impacts of the interventions. The specific objectives of the study include collection of data in selected districts of the Avahan project states of Andhra Pradesh, Maharashtra, Tamil Nadu, Karnataka, Manipur and Nagaland and along the national highways. The NIE has been identified as the implementing agency for Tamil Nadu where the activities have been divided into 2 phases. In the I phase identification of research agency, recruitment of project staff, orientation and training of study team and launch of programme at Madurai, Salem and Dharmapuri have been done.

Prevalence and Distribution of Cardiovascular Risk Factors in an Urban Industrial Population in South India

A study was done by NIE to determine the prevalence of cardiovascular risk factors in 1163 subjects in an industrial unit in Chennai. The results indicated high prevalence of behavioural risk factors– tobacco use-(39%), central obesity (63%), hypertension (31%) and diabetes (15%) among them. Effective risk factor intervention programme is being developed for this population to favourably modify the risk factors and decrease the cardiovascular disease risk in the future.

NATIONAL INSTITUTE OF MEDICAL STATISTICS (NIMS), NEW DELHI

Components of Under-five Mortality Trends, Current Stagnation and Future Forecasting Levels

The investigation aimed to study the changes in each of the components of under-five mortality during the period 1978–2002, to analyze the factors associated with the apparent stagnation of child mortality rate in India and to develop projection scenarios of the infant mortality rate (IMR) and under 5 mortality rate (U5MR) by states by the year 2016. The study examined the impact of utilization of antenatal and natal services on neonatal mortality. It has also looked into the levels of IMR and U5MR among socially and economically disadvantaged groups. Besides, the study attempted to examine the reasons for slowing down of the rate of decline in child mortality in recent years by analyzing the prevalence of high-risk births among advantaged/ disadvantaged groups and relating the same to differentials in the utilization of health care services.

A rapid decline observed in IMR and under-five mortality during 1980-90 was followed by a period of stagnation from 1993 as it was hovering around 72 per thousand live births. The stagnation during this period may indicate that the programmes addressing reduction in child mortality were not effective in reducing the IMR as a large proportion of infants were dying in neonatal stage. Thus, the programmes such as RCH programme, immunization programme and ICDS were not really oriented towards capturing infants dying during the neonatal stage. The other reason of stagnation in IMR could be the lack of access to health and other types of services to disadvantaged/vulnerable groups.

The IMR and child mortality projected up to 2016 shows that India might not be able to achieve the set target of IMR as 30 by 2010 without making concerted efforts to improve the content and quality of RCH services and concentrating on community mobilization strategies. In addition, economic and social reforms should be commensurate with the programme interventions bringing about appreciable reduction in IMR and child mortality in the near future.

Assessment of the Impact of Food Fortification on Child Health in Madhya Pradesh

The World Food Programme entrusted the project to NIMS with the objectives to study the impact of fortified food among children (age 6-59 months) in Sanchi and Vidisha districts of Madhya Pradesh and to undertake end line evaluation of the impact of supplementation. It was observed that there is considerable improvement in the prevalence of anaemia in both the blocks. As regards the level of vitamin A deficiency, the decline is significantly higher in the intervention block as compared to the control block. The percentage of severely malnourished children also reduced significantly in both the blocks from base line to end line.

HIV Estimation and Analytical Study of HIV Sentinel Surveillance Data

The NIMS is carrying out study to review the HIV estimation methodology, to validate the assumptions and provide estimate of HIV burden in the country every year based on HIV sentinel surveillance (HSS) data and carry out in-depth analysis of HSS data. Review of estimation methodology and validation of assumptions used in estimation was carried out in 2003. Every year it is reviewed and deliberated among experts after which consensus is obtained to finalize the estimate of HIV burden in the country. In 2004 it was estimated that 5.08 adults in the age group 15-49 yr were infected with HIV. In addition, there were 56,787 infected children born to infected mothers. The estimated number of persons with HIV infection in 2005 was 5.206 million. Number of HIV infections in urban and rural areas by sex during 2003 - 05 is given in Fig. 2. Fig. 3 depicts the estimated number of HIV infections in India during 2003-05. Since, inception of the sentinel surveillance in India, the number of sentinel sites has been increasing. In 2005, the total number of sentinel sites stands at 704. The population considered from all the risk groups included only the age group 15-49 yr. so that HIV estimate derived is for the adult population prone to be exposed by high-risk behaviour and/or exposed to bridge population. However, the number of newborn children with HIV was also estimated using information on infected mothers.



Fig. 2. Number of HIV Infections in 15-49 yr age group for 2003-05 by residence and sex



Estimated HIV infected persons (in million)

Fig. 3. HIV Estimates in India

Study of Level of Job Satisfaction among the Scientists of ICMR Institutes

The study was undertaken by NIMS to examine the level of job satisfaction of scientists from various ICMR institutes. In order to sustain high quality research and the growth of the organization, it is important to ensure that the scientists and the other supporting staff are satisfied with working environment including facilities available to carry out their work and recognition of their efforts. The study intends to apprise the management about the contextual work environment of the scientific staff spread across the country. The response rate was around 85%. The survey work related to the study has been completed and data is being analyzed. SUPPORTING FACILITIES

As part of modernization of ICMR libraries, the Council is undertaking electronic dissemination of information for optimal utilization of the resources available. Subscription for full text electronic database ProQuest (contains about 550+ full text medical journals) has been renewed for six ICMR libraries. JCCC (J-Gate Custom Content for Consortia) has been renewed to promote resource sharing among all libraries of ICMR institutes. To promote usage of JCCC@ICMR, regional training programmes were organized at NIN, Hyderabad (Southern Region Institutes), RMRC, Bhubaneswar (Eastern), NIV, Pune (Western) and NIMS, New Delhi (Northern). The updated print version of Union Catalogue of Journals in ICMR Libraries is ready for distribution among all medical libraries and medical research institutes in India.

INTERNATIONAL COLLABORATION

ICMR co-ordinates international The collaboration in biomedical research between India and other countries such as Bulgaria, France, Germany, USA, Cuba, Canada, China, Iran, Myanmar, Mozambique etc and national and international agencies such as WHO, Ministry of Science and Technology etc. During the year a total of 73 exchange visits of scientists to and from India were arranged under international collaborative projects / programmes. An MOU for South-South collaboration has been signed between the MRC (South Africa), FIOCRUZ (Brazil) and ICMR to work together on health issues of mutual importance. During the year five meetings of Health Ministry's Screening Committee (HMSC) were organized wherein 73 projects for international collaboration / assistance were approved by the Indian side.

To achieve the objective of building up a highly skilled pool of biomedical researchers the ICMR has taken up a new initiative and ICMR International Fellowships have been awarded to six young and three senior Indian biomedical scientists, who have successfully undertaken visits to foreign laboratories. Under the International Fellowship Programme for visit of scientists belonging to developing countries to India for training / exposure to the latest advancements of knowledge in the area of work, one scientist has visited an ICMR institute for training.

INTELLECTUAL PROPERTY RIGHTS

The Council is taking steps for promoting a culture of identifying and protecting new knowledge that could lead to intellectul property (IP) generation for commercialization. For this, primary focus is on increasing IP awareness, generation, identification, protection, dissemination, regulation, valuation and mobilization. To fulfil these objectives, the Council has continued its ongoing activities and taken some new initiatives.

A total of 8 patents including 5 national phase applications of Patent Cooperation Treaty (PCT) have been filed at Indian Patent Office as well as in Europe, Japan, Brazil, Singapore and USA. One patent application from VCRC, Pondicherry titled "A process for the preparation of mosquito larvicidal formulation from *Bacillus thruringiensis var. israelensis*" has been granted while one design registration application titled "New Model of Cycle Rickshaw" from ROHC (Eastern), Kolkata filed in June 2005 has been approved. Redesigned new model of cycle rickshaw is ready for technology transfer to Kolkata based company, Luna Tyre Pvt Ltd and negotiation is going on to enter into MOU. Another ICMR invention related to double fortified salt developed at NIN, Hyderabad is at advanced stage of negotiations for transferring to Hyderabad based industry- Tata Salt Pvt. Ltd.

TRAINING PROGRAMMES

Various institutes of ICMR continued to organize training programmes and workshops in areas of current interest of scientists. Besides this, consultancy and referral services were provided in all scientific disciplines.

ICMR PERMANENT INSTITUTES / CENTRES

- National JALMA Institute for Leprosy and Other Mycobacterial Diseases Dr. Miyazaki Marg Taj Ganj Agra 282001
- National Institute of Occupational Health Meghani Nagar Ahmedabad 380016
- National Institute of Epidemiology 1, Sathyamurthi Road, Chetput Chennai 600031
- Tuberculosis Research Centre Mayor V.R.Ramanathan Road (Spurtank Road), Chetput Chennai 600031
- National Institute of Malaria Research 22, Sham Nath Marg Delhi 110054
- Food and Drug Toxicology Research Centre National Institute of Nutrition Jamai Osmania Hyderabad 500007
- National Centre for Laboratory Animal Science National Institute of Nutrition Jamai Osmania Hyderabad 500007
- National Institute of Nutrition Jamai Osmania Hyderabad 500007
- 9. National Institute of Cholera and Enteric Diseases
 P-33, CIT Road Scheme XM
 P.O. Box 177 Beliaghata
 Kolkata 700010
- Centre for Research in Medical Entomology 4, Sarojini Street Chinna Chokkikulam Post Box No. 11 Madurai 625002

- Enterovirus Research Centre Haffkine Institute Campus Acharya Donde Marg Parel Mumbai 400012
- ICMR Genetic Research Centre National Institute for Research in Reproductive Health Campus Jehangir Merwanji Street Parel Mumbai 400012
- National Institute for Research in Reproductive Health Jehangir Merwanji Street Parel Mumbai 400012
- Institute of Immunohaematology 13th Floor, New Multistoreyed Building K.E.M. Hospital Campus Parel Mumbai 400012
- National Institute of Medical Statistics ICMR Head Quarters Campus Ansari Nagar New Delhi 110029
- Institute of Cytology and Preventive Oncology I-7, Sector – 39 NOIDA 201301
- Institute of Pathology Safdarjang Hospital Campus New Delhi 110029
- Rajendra Memorial Research Institute of Medical Sciences Agam Kuan Patna 800007
- Vector Control Research Centre Medical Complex Indira Nagar Pondicherry 605006
- National AIDS Research Institute Plot No. 73, Block G, P.B.No.1895 Bhosari Industrial Estate Pune 411026
- 21. National Institute of Virology 20-A, Dr.Ambedkar Road P.B. No.11 Pune 411001

REGIONAL MEDICAL RESEARCH CENTRES

- Regional Medical Research Centre Nandankanan Road
 P.O. Chandrasekharpur Bhubaneswar 751016
- Regional Medical Research Centre N.E.Region, East-Chowkidinghee Post Box No. 105 Dibrugarh 786001
- Regional Medical Research Centre for Tribals Medical College Campus Nagpur Road P.O.Garha Jabalpur 482003
- Desert Medicine Research Centre P.O.Box No. 122 New Pali Road Jodhpur 342005
- Regional Medical Research Centre Post Bag No.13 Port Blair 744101
- Regional Medical Research Centre National Highway No.4 Belgaum 590010

ICMR CENTRES FOR ADVANCED RESEARCH

1.	National Informatics Centre A-Block, CGO Complex Lodi Road New Delhi 110003
2.	Advanced Research Centre for Cellular and Molecular Reproduction Indian Institute of Science Sir C.V. Raman Avenue Bangalore 560012
3.	Centre for Advanced Research on Clinical Pharmacology Seth G.S. Medical College and K.E.M. Municipal Hospital Acharya Donde Marg Parel Mumbai 400012
4.	Centre for Advanced Research on Aging and Brain University of Hyderabad Hyderabad 500046
5.	Centre for Advanced Study in Molecular Medical Microbiology Indian Institute of Science Sir C.V. Raman Avenue Bangalore 560012
6.	Advanced Centre for Liver Diseases G.B. Pant Hospital New Delhi 110002
7.	ICMR Advanced Centre for Research in Nutrition Nutrition Foundation of India C-13, Qutab Institutional Area New Delhi 110016
8.	Centre of Advanced Research on Liver Diseases All India Institute of Medical Sciences Ansari Nagar New Delhi 110029
9.	Centre of Advanced Research in Medical Mycology Postgraduate Institute of Medical Education and Research Chandigarh 160012

SEMINARS/SYMPOSIA/WORKSHOPS/CONFERENCES

The following ICMR aided seminars/symposia/workshops/conferences were held during 2005-06

TITLE	DATE	ORGANISERS
I National Conference of AIDS Society of India Asicon-2005	April 2-4, 2005	Unison Medicare and Research Centre Mumbai
Workshop on Counselling in HIV	April 2-3, 2005	Armed Forces Medical College and Command Hospital Southern Command Pune
I Annual Congress of Indian Association of Medical Microbiologists	April 3-4, 2005	Institute of Medical Sciences Banaras Hindu University Varanasi
National Symposium on Influenza: Epidemiology and Control	April 4, 2005	Vallabhbhai Patel Chest Institute University of Delhi Delhi
Symposium on Quality in Radiological Imaging and Radiation Safety of Patients and Staff	April 16, 2005	All India Institute of Medical Sciences New Delhi
CME on Reproductive and Child Health	April 16-17,2005	Armed Forces Medical College and Command Hospital Southern Command Pune
International Conference on Microbial Diversity-2005	April 16-18, 2005	University of Delhi South Campus New Delhi
Workshop on Cancer Gall bladder	April 23-24, 2005	Banaras Hindu University Varanasi
National Conference on Solid and Hazardous Waste Management: Problems and Solutions	April 28-29, 2005	International Development Centre B-138 Nav Aakar Building Bhikaji Cama Place New Delhi
Workshop on Total Hip Replacement	May 8, 2005	Medical College and Hospital Kozhikode

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Scientific Seminar/Workshop of Technical Staff of ICMR	May 8-10, 2005	Federation of All India ICMR Employees Pune
Symposium Workshop on Protocol in Laboratory Diagnosis of Inherited Disorders	May 14, 2005	Madurai Medical College and Government Rajaji Hospitals Madurai
Workshop on Statistics for Medical Journal Editors	June 3-4, 2005	Seth G.S. Medical College and K.E.M.Municipal Hospital Parel Mumbai
Workshop on Advancd Techniques in Microbiology and Biotechnology	June 9-11, 2005	Selvamm Arts and Science College Nammakkal
CME on Obesity- The Global Epidemic of The Century	June 20, 2005	Rural Medical College of Pravara Medical Trust Ahmednagar
International Workshop on High Altitude: Health Related Issues and High Altitude Medicine	July 13-14, 2005	High Altitude Medical Research Centre Leh
International Conference on Nanomaterials: Nano-2005	July 13-15, 2005	Mepco Schlenk Engineering College Virudhunagar
II National Workshop on Basic Techniques in Molecular Biology, Bioinformatics and Pharmacogenomics	July 27-Aug 3, 2005	Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry
Conference on Environmental Pollution and Management- Future Challenges	July 29-30, 2005	J.S.S.Medical College Mysore
National Hands-on-Workshop on Molecular Biology in the New Millennium	August 5-19, 2005	Armed Forces Medical College and Command Hospital Southern Command Pune
International Conference on Biosciences, Biotechnology and Biodiversity Analysis	August 8-10, 2005	Modern College Of Arts, Science and Commerce Pune
56th Conference of Indian Association of Pathologists and Microbiologists (Kerala Chapter) and 3rd National CME in Pathology	August 13-15, 2005	Medical College and SAT Hospital for Women & Children Thiruvananthapuram

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VII National Workshop on Science and Technology of Sensors based on Nanomaterials	August 18-31, 2005	Jai Narain Vyas University Jodhpur
Conference of Association of Physiologists and Pharmacologists of India, Chandigarh Chapter	August 20, 2005	Government Medical College and Hospital Chandigarh
Worksop on Essential Medicines: Adverse Drug and Therapeutic Drug Monitoring	August 22-23, 2005	K.G's Medical University Lucknow
Workshop on Paediatric Practice - Basics and Beyond	August 27-28, 2005	Armed Forces Medical College and Command Hospital Southern Command Pune
Workshop on Concepts and Trends in Obstetrics, Gynaecology and Infertility Hyderabad	September 3, 2005	Deccan College of Medical Sciences and Owaisi Hospital and Research Centre
National Level Short Term Training Programme on Experimental Parasitology, Molecular Biology and Immunodiagnostics	September 5-25, 2005	University of Kashmir Srinagar
National Symposium on Inborn Metabolic Disorders and Regional Conference of Association of Clinical Biochemists of India	September 8-10, 2005	Association of Clinical Biochemists of India Kochi
National Conference on Frontiers in Environmental Sciences and Engineering	September 15-17, 2005	Bharathiar University Coimbatore
National E.N.T. Update-2005	September 17-18, 2005	Armed Forces Medical College and Command Hospital Southern Command Pune
International Symposium on Stem Cells: Premises and Promises for Research Therapeutics	September 18-21, 2005	National Institute for Research in Reproductive Health Parel Mumbai
International Meeting on National Consultation on Drug Resistance - Malaria, T.B. and HIV/AIDS	September 19-21, 2005	Seth G.S.Medical College and K.E.M.Municipal Hospital Parel Mumbai

International Symposium on Electronics in Cancer	September 25 - October 1, 2005	Maulana Azad Medical College and Associated Hospitals New Delhi
International Workshop and Symposium on Inborn Errors of Metabolism	September 28 - October 2, 2005	Sir Gangaram Hospital New Delhi
Seminar on Clinical Research- Practice and Prospects	September 30 - October 1, 2005	Jadavpur University Kolkata
International Symposium on Ocular Leprosy Kolkata	October 1-2, 2005	Indian Alumni Group of International Centre for Eye Health
Seminar and Workshop on Labour Appraisal and Management Practices	October 1-2, 2005	Armed Forces Medical College and Command Hospital Southern Command Pune
IV Biennial Conference of Indian Association for Medical Informatics	October 1-2, 2005	Sri Guru Ram Das Institute of Medical Sciences and Research Amritsar
XVII National Symposium on Chronobiology	October 1-3, 2005	Banaras Hindu University Varanasi
International Symposium on Scientific Approaches to Quality, Safety and Efficacy Assessement of Botanical Products	October 3-6, 2005	Regional Research Laboratory New Delhi
VIII Conference of International Biometric Society	October 4-7, 2005	University of Agricultural Sciences Gandhi Krishi Vignan Kendra Campus Bangalore
Symposium on Excitement of Science and Platinum Jubilee Celebrations of The National Academy of Sciences	October 6-7, 2005	National Academy of Science Allahabad
Workshop on Association of Physiologists and Pharmacologists of India (Gujrat Chapter)	October 7-9, 2005	Association of Physiologists and Pharmacologists of India Surat
Workshop on Practical Pediatric Oncology	October 8-9, 2005	Moti Lal Nehru Medical College Allahabad
National Symposium on Advances in Magnetic Resonance and its Applications	October 8-11, 2005	Regional Research Laboratory Jammu Tawi

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National Symposium on Bio- Diversity : Current Status and Perspects	October 17-18, 2005	Pt.Ravishankar Shukla University Raipur
Conference of Indian Association of Medical Microbiologists	October 19-23, 2005	Sri Ramchandra Medical College and Research Institute (Deemed University) Chennai
National Seminar on Emerging Trends in Plant Taxonomy	October 20-22, 2005	Nagpur University M.G.Marg Nagpur
An Interactive Workshop on Building and Managing Clinical Trial Capacity in India: Challenges in Ethics, Equity and Efficiency	October 21-22, 2005	Indian Council of Medical Research New Delhi
Indo-US Emergency Medicine Summit- 2005	October 21-23, 2005	All India Institute of Medical Sciences New Delhi
Seminar on STD/HIV Infections and Allied Topics and Wokshop on Live Demonstration on HIV cases at School of Tropical Medicine	October 21-23, 2005	Indian Association for Study of Sexually Transmitted Diseases and AIDS Kolkata
Conference on Emerging Health Challenges	October 22-24, 2005	International Medical Science Academy Jaipur
National Workshop on Bioinformatics	October 22-24, 2005	Sri Venkateswara University Tirupati
National Symposium on Plant Science Research in India : Challenges and Prospects	October 24-25, 2005	Botanical Survey of India Dehradun
Workshop on Water Quality Monitoring	October 27, 2005	National Institute of Cholera and Enteric Diseases Kolkata
National Conference on Ageing and Dying Relevance of Indian Perspective to End-of-Life Care	November 4-6, 2005	Indian Institute of Technology Kharagpur
International Conference of Malaria	November 4-6, 2005	National Institute of Malaria Research Delhi

27th Annual Conference of Association of Obstetricians and Gynaecologists	November 5-6, 2005	University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
Workshop on VII Postgraduate Course in Endocrine Surgery	November 6-9, 2005	Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
Medical Development Congress: Drugs and Pharmaceuticals in relation to Infectious Diseases as its Central Theme	November 8-9, 2005	Indian Council of Medical Research New Delhi
Conference on Challenges faced by Nurses/Midwives in Prevention and Control of HIV/AIDS in India	November 10-12, 2005	Nursing Research Society of India Jammu
12th Annual Conference of Vascular Society of India	November 10-13, 2005	Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram
Workshop on Water Quality Monitoring	November 11, 2005	National Institute of Cholera and Enteric Diseases Kolkata
XIV National Conference of the Indian Association of Oral and Maxillofacial Pathologists	November 11-13, 2005	Indian Association of Oral and Maxillofacial Pathologists Agra
National Workshop on Development of Guidelines for Effective Home Based Care and Treatment of Children suffering from Severe Undernutrition	November 11-13, 2005	All India Institute of Medical Sciences New Delhi
71st Annual Meeting of Indian Academy of Sciences	November 11-13, 2005	Bharathidasan University 4, Bharathidasan Road Tiruchirapalli
Conference on Hypertension, CAD and Atherosclerosis	November 12-13, 2005	University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
24 Biennial Conference of the Indian Association of Leprologists	November 12-14, 2005	Indian Association of Leprologists Agra

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Conference and Workshop on Global Clinical Trials in India: Prospects and Challenges	November 14-16, 2005	Federation of Indian Chamber of Commerce and Industry New Delhi
International Conference on Toxicology, Environmental and Occupational Health	November 14-17, 2005	Industrial Toxicology Research Centre Lucknow
Symposium on Molecular Mechanism of Disease and Drug Action	November 16-18, 2005	Saha Institute of Nuclear Physics Kolkata
XXXVII Annual Meeting of the Nutrition Society of India	November 17-19, 2005	National Institute of Nutrition Hyderabad
Workshop on Water Quality Monitoring	November 18, 2005	National Institute of Cholera and Enteric Diseases Kolkata
National Symposium on Plant Biotechnology -New Frontiers	November 18-20, 2005	Central Institute of Medicinal and Aromatic Plants Lucknow
17th National Congress of Parasitology	November 19-21, 2005	Regional Medical Research Centre Dibrugarh
TWOWS 3rd General Assembly and International Conference on Women's Impact on Science and Technology in New Millennium	November 21-25, 2005	Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore
CME on Special Types of Breast Cancer with Clinical Implication and Recent Advances in the Diagnosis of HIV Infection	November 23, 2005	Aligarh Muslim University Aligarh
21 st Annual Convention of Indian Society for the study of Animal Reproduction and National Symposium on Recent Trends in Animal Reproduction	November 23-25, 2005	Indian Society for the Study of Animal Reproduction Jammu
National Symposium on Developmental Dynamics	November 23-25, 2005	University of Kalyani Kalyani
XX Carbohydrate Conference	November 24-26, 2005	Lucknow University

National Conference on Path to Health- Biotechnology Revolutions in India	November 24-26, 2005	Centre for Biotechnology Anna University Chennai
32nd Annual Conference of Indian Immunology Society	November 24-27, 2005	Postgraduate Institute of Medical Education and Research Chandigarh
Guha Research Conference - 2005	November 24-28, 2005	University of Pune Goa
Workshop on Research Methodology	November 25-26, 2005	P.S.G.Institute of Medical Sciences and Research Coimbatore
Workshop on Anatomical Basis of Clinical Procedures	November 25-26, 2005	Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai
International Symposium on Medicinal Plants and Herbal Products in Biomedicine and their Efficacy in the Present Era	November 25-27, 2005	University of Calcutta Kolkata
I National Bioethics Conference of the Indian Journal of Medical Ethics	November 25-27, 2005	Indian Journal of Medical Ethics Mumbai
Conference on Perinatology: Current Dilemmas and Future Perspectives	November 26-27, 2005	Command Hospital Southern Command Pune
Conference on Advances in Pharmaceutical Research and Technology - Drug Discovery, Development and Delivery	November 26-29, 2005	BY Patel Pharmaceutical Education and Research Development Centre Ahmedabad
IV International Congress on Women, Work and Health-2005	November 27-30, 2005	The Society for Working Life New Delhi
Symposium on Simple Analytical Procedures in Clinical and Forensic Toxicology	November 28, 2005	Amrita Institute of Medical Sciences and Research Centre Kochi
54th Annual Conference of Indian Asoociation of Pathologists and Microbiologists	November 28 - December 3, 2005	Indian Association of Pathologists and Microbiologists Indore
National Seminar on Emerging Trends and New Vistas in Chemistry	November 29-30, 2005	University of Calicut Kozhikode

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Symposium on Nutrition and Development Transition	November 29 - December 1, 2005	Nutrition Foundation of India New Delhi
17 Annual Conference of the Physiological Society of India	December 1-3, 2005	M.R.Medical College Gulbarga
International Conference cum Workshop on Frontiers in Molecular Endocrinology	December 1-10, 2005	University of Hyderabad Hyderabad
XXI International tRNA Workshop	December 2-7, 2005	Indian Institute of Science Bangalore
National Conference of Infertility	December 3-4, 2005	Indian Fertility Society New Delhi
XVI National Congress of Veterinary Parasitology and National Symposium on Integrated Animal Parasite Management	December 6-8, 2005	College of Veterinary Science and Animal Husbandry Durg
International Workshop on Neurochemical Techniques	December 6-15, 2005	Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai
Workshop on Water Quality Monitoring	December 8, 2005	National Institute of Cholera and Enteric Diseases Kolkata
46th Annual Conference of Association of Microbiologists of India	December 8-10, 2005	Osmania University Hyderabad
Symposium on Emerging Trends in NeuroSciences	December 11-14, 2005	National Institute of Mental Health and Neurosciences Bangalore
51 Annual Conference of the Association of Physiologists and Pharmacologists of India	December 11-15, 2005	Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry
International Conference cum Workshop on Frontiers in Molecular Endocrinology	December 12-15, 2005	University of Hyderabad Hyderabad
EMBO Workshop on Upstream and Downstream of Hox Genes	December 14-17, 2005	Centre for Cellular and Molecular Biology Hyderabad

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Medicine Update-2005	December 15-17, 2005	Maulana Azad Medical College and Associated Hospitals New Delhi
35th Annual Conference of Indian Academy of Cytologists	December 15-18, 2005	Shri M.P.Shah Medical College Jamnagar
International Symposium on Advances in Research on Neuro- Degenerative Diseases	December 16-17, 2005	Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai
Workshop on Functional Endoscopic Sinus Surgery and Septorhinoplasty Surgical Procedure	December 16-18, 2005	Max Balaji Hospital Delhi
15th International Conference on Frontiers in Yoga Research and its Application	December 16-19, 2005	Vivekananda Kendra Yoga Anusandhan Samsthan Bangalore
National Seminar on Biomedical Laboratory Science	December 17-19, 2005	Vidyasagar University Midnapore
International Symposium on Translation Research : Apoptosis and Cancer	December 18-21, 2005	All India Institute of Medical Sciences Thiruvananthapuram
Regional Workshop on Recent Trends in Techniques of Medical Laboratory and Biotechnology	December 19-30, 2005	Loyola College Chennai
Workshop on Water Quality Monitoring	December 22, 2005	National Institute of Cholera and Enteric Diseases Kolkata
III Conference of the Biotechnology Society of India	December 22-25, 2005	Manesar
National Commemorative Conference on Tsunami	December 26-29, 2005	Madurai Kamaraj University Madurai
XXIX Indian Social Science Congress	December 26-30, 2005	Indian Social Science Congress Lucknow
38th Annual Conference of Indian Pharmacological Society	December 28-30, 2005	Indian Pharmacological Society Chennai
CME cum International Symposium on Pediatric Malignancies	December 29-31, 2005	All India Institute of Medical Sciences New Delhi

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National Conference on Recent Trends in Estimation and Optimization - Theory and Applications	January 1-2, 2006	Institute of Science Nagpur
93rd Session of the Indian Science Congress	January 3-7, 2006	Indian Science Congress Association Hyderabad
V National Level Biological Congress on Biotechnology : A Global Perspective	January 6-7, 2006	Muthayammal College of Arts and Science Nammakkal
National Symposium on Molecules, Interactions and Design: A Biophysical Perspective	January 7-10, 2006	West Bengal University of Animals and Fishery Sciences Kolkata
International Symposium on Frontiers in Genetics and Biotechnology - Retrospect and Prospect	January 8-10, 2006	Osmania University Hyderabad
III South East Asia and Western Pacific Bi-Regional Tephinet Scientific Conference	January 9-12, 2006	National Institute of Epidemiology Chennai
National Conference on Immunology in Health and Disease	January 11-12, 2006	Institute of Life Sciences Kanpur
International Conference on Antioxidants, Oxidative Stress and Inflammation in Chronic Diseases	January 12-13, 2006	Dr. Ambedkar College Nagpur
Silver Jubilee Symposium on Ethnobotany in the New Millennium	January 12-14, 2006	National Botanical Research Institute Lucknow
46th Annual Conference of Indian Society of Haematology and Transfusion Medicine	January 14-16, 2006	Regional Institute of Medical Sciences Imphal
Workshop on Nutrition, Environmental Health and Development	January 16-21, 2006	Regional Occupational Health Centre(Eastern) Kolkata
VI National Conference of Indian Society for Human and Animal Mycologists and Workshop on Mycology	January 17-18, 2006	The Nizam's Institute of Medical Sciences Hyderabad

XXIX All India Cell Biology Conference and Symposium on Gene to Genome : Environmental and Chemical Interaction	January 18-20, 2006	Industrial Toxicology Research Centre Lucknow
International Symposium on Recent Trends in Macromolecular Structure and Function	January 18-20, 2006	University of Madras Chennai
Workshop on Gene Expression Analysis	January 19-28, 2006	Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences University of Madras Chennai
National Symposium on Recent Trends in Malarial Studies	January 20-21, 2006	Abasaheb Garware College Pune
National Seminar on Challenges and Opportunities posed by Biotechnology	January 20-21, 2006	PES College of Pharmacy Bangalore
4th National Conference of Indian Association of Applied Microbiologists	January 20-21, 2006	M.G.R. College Hosur
23rd Annual National Conference of Indian Society for Medical Statistics	January 20-22, 2006	Jawaharlal Nehru Medical College Belgaum
International Conference on Ethnopharmacology and Alternative Medicine	January 20-22, 2006	Amala Cancer Hospital and Research Centre Thrissur
National Conference of Indian Association of Public Health and Preventive and Social Medicine	January 21-24, 2006	S.V.Institute of Medical Sciences Tirupati
International Conference on Application of Radiotracers in Chemical, Environmental and Biological Sciences	January 23-27, 2006	Saha Institute of Nuclear Physics Kolkata
XI International CME on Surgical Pathology and Cytology	January 26-28, 2006	Kolkata Asoociation of Practicing Pathologists Kolkata
Bi-Annual Conference of Orthotics and Prosthetics Society of India	January 26-29, 2006	National Institute for the Orthopaedically Handicapped Kolkata
Seminar On Sports Psychology : Expanding Horizon	January 27-29, 2006	Jai Narain Vyas University Jodhpur

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Oral Cancer Conference-2006	January 27-29, 2006	Regional Cancer Centre Thiruvananthapuram
III National Teachers Science Conference- 2005	January 27-30, 2006	Karnataka Rajya Vijnana Parishat Manasgangotri
National Conference on Bio- Diversity	January 30-31, 2006	Loyola College Chennai
International Conference on Biodiversity of Insects : Challenging issues on Management and Conservation	January 30 - February 3, 2006	Bharathiar University Coimbatore
IAP-RCPCH-PGI Course on Evidence Based Medicine Chandigarh	January 30 - February 1, 2006	Postgraduate Institute of Medical Education and Research
International CME - Progress in Pathology - An International Update	February 1-3, 2006	St.John Medical College and Hospitals Bangalore
XX Annual State Conference of Association of Maharashtra Obstetrics and Gynaecological Societies	February 3-5, 2006	Rural Medical College of Pravara Medical Trust Ahmednagar
Workshop on Health Problems and Health Care System among Indian Tribes with special emphasis on Tribes of Eastern Ghats	February 6-8, 2006	Andhra University Visakhapatnam
National Conference on Luminescence and its Applications	February 7-9, 2006	Amravati University Amravati
Symposium on Emerging Trends in Biochemistry	February 9-10, 2006	Panjab University Chandigarh
Asia Regional Conference on Aging with Health and Dignity	February 9-11, 2006	Bangalore University Bangalore
National Seminar on Scientific Validation and Technical Evaluation of Ancient Medical Systems	February 10-11, 2006	Indian Institute of Technology New Delhi
International Workshop and Symposium on Epispadias and Ex Strophy Bladder	February 10-12, 2006	K.G's Medical University Lucknow

XXII All India Congress of Indian Society of Perinatology and Reproductive Biology	February 10-12, 2006	Indian Society of Perinatology and Reproductive Biology Ahmedabad
National Conference on Radio- Map to Disease Free India: Sharing Resposibilities	February 11-13, 2006	National JALMA Institute for Leprosy and other Mycobacterial Diseases Agra
CME on Oral Precancer and Cancers : Challenges Ahead	February 12, 2006	Moti Lal Nehru Medical College Allahabad
Seminar on Health Status of Tribal Women and Children	February 13-14, 2006	University of Pondicherry Pondicherry
17th National Symposium on Materials Research Society of India	February 13-15, 2006	Lucknow University Lucknow
Naional Workshop and Symposium on Animal Experimentation and Animal Ethics	February 13-16, 2006	Mahatma Gandhi Institute of Medical Sciences Sevagram
National Workshop on Immunology and Immunoinformatics	February 14-15, 2006	Sri Ramachandra Medical College and Research Institute Chennai
Symposium on Therapeutic and Diagnostic Products for Reproductive Health: Recent Trends and Future Prospects	February 14-16, 2006	Indian Institute of Technology Roorkee
National Symposium on Biological and Clinical Relevance of Placenta	February 15, 2006	Vardhman Mahavir Medical College and Safdarjung Hospital New Delhi
Silver Jubilee Symposium on Molecular Profiling and Cancer Management and 25th Annual Convention of International Association of Cancer Research	February 15-18, 2006	Advanced Centre for Treatment Research and Education in Cancer Tata Memorial Centre Navi Mumbai
14 National Symposium on Ultrasonics	February 16-18, 2006	Ultrasonics Society of India New Delhi
XXVII Annual Conference of the Indian Academy of Forensic Medicine	February 16-19, 2006	North Bengal Medical College Darjeeling
National Symposium on Biotechnology - Trends and Perspectives	February 17-18, 2006	Sri Krishnadevaraya University Anantapur

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International Conference on Bio-Terrorism and Public Safety	February 17-18, 2006	Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai
Seminar on Treatment of Heart Failure in Particular Heart Transplantation	February 17-19, 2006	National Network for Organ Sharing Chennai
National Conference and Work- Shop of Indian Society of Prenatal Diagnosis and Therapy	February 17-20, 2006	All India Institute of Medical Sciences New Delhi
XXXV National Seminar on Crystallography	February 22-24, 2006	National Physical Laboratory New Delhi
International Congress on Gamete Biology: Emerging Frontiers in Fertility and Contraceptive Development	February 22-25, 2006	National Institute of Immunology New Delhi
10th Convention of Association for Promotion of DNA Fingerprinting and other DNA Technologies	February 23-24, 2006	Centre for Cellular and Molecular Biology Hyderabad
XXXI Annual Conference of Environmental Mutagen Society of India	February 23-25, 2006	National Institute of Nutrition Hyderabad
National Seminar on Recent Trends in Molecular Biology	February 24-25, 2006	College of Life Sciences Cancer Hospital and Research Institute Gwalior
World Conference on Expanding Paradigms: Science, Consciousness and Spirituality	February 24-25, 2006	All India Institute of Medical Sciences New Delhi
14th Annual Conference of Indian Association for the Study of the Liver	February 24-26, 2006	Government Medical College and Hospital Nagpur
International Symposium on Human Genetics and Public Health and XXI Annual Conference of Indian Society of Human Genetics	February 24-27, 2006	Jawaharlal Nehru University New Delhi
Symposium on Recent Trends in Streptococcal Diseases	February 25, 2006	Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai
Workshop on Pediatric Otolaryngology and 12th Annual Conference of Association of Paediatric Otolaryngologists of India	February 25-26, 2006	Lady Hardinge Medical College and Associated Hospitals New Delhi
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VIII FIMS/IIS Advanced Immunology Course - Focus on Clinical Immunology	March 1-5, 2006	All India Institute of Medical Sciences New Delhi
Conference on Emergencies in Pediatric Practice and Peadiatric HIV Infection and AIDS	March 4-5, 2006	Command Hospital Central Command Lucknow
III Annual Conference of Indian Thyroid Society and International Symposium on Recent Advances in Management of Thyroid Disorders	March 4-5, 2006	Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
Endosurg-2006 International Minimal Access Surgery Conference and Live Workshop	March 10-12, 2006	All India Institute of Medical Sciences New Delhi
CME on Lead Exposure in Children and Women in India: Sources, Evaluation and Prevention	March 12, 2006	St.John's Medical College and Hospitals Bangalore
National Symposium on Emerging Zoonoses: with special reference to bird flu	March 16-17, 2006	Sher-e-Kashmir University of Agriculture Sciences & Technology Jammu
National Conference on Information Technology : Setting Trends in Modern Era	March 18-20, 2006	N.C.College of Engineering Panipat
National Symposium on New Frontiers in Fermentation and Food Biotechnology	March 21-22, 2006	Punjabi University Patiala
V Annual Congress and International Update of Indian Society of Cleft Lip, Palate and Craniofacial Anomalies	March 23-26, 2006	Indian Society of Cleft Lip, Palate and Craniofacial Anomalies Guwahati
CME Programme in Surgical Gastroenterology	March 24-26, 2006	Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
International Conference on Opportunistic Pathogens in AIDS	March 27-29, 2006	All India Institute of Medical Sciences New Delhi

TRAINING PROGRAMMES CONDUCTED BY ICMR INSTITUTES DURING 2005-2006

Leprosy

At the National Institute of Epidemiology, Chennai :

♦ Workshop on Surveillance for Leprosy at Chennai (September 20, 2005).

Diarroheal Diseases

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

- Indo-US Workshop on Diarrhoeal Protozoan Parasites-New Challenges in the Era of HIV/ AIDS (October 3 - 5, 2005).
- ✤ JICA-NICED Domestic Training Programme (October 17-29, 2005).
- 3rd Country JICA-NICED Training Programme (November 21 December 4, 2005).
- Indo-US Workshop on Water Quality Monitoring Jointly organized with IIIH &PH, Kolkata (February 21 -22, 2006).

Japanese Encephalitis

At the Centre for Research in Medical Entomology, Madurai :

 Training-cum-Workshop on Surveillance and Control of JE with emphasis on Implementation of Vaccination Programme in India (January 23 – 25, 2006).

Dengue

At the Centre for Research in Medical Entomology, Madurai :

 Training-cum-Workshop on Dengue Surveillance, Control and Management in India (March 22 – 24, 2006).

Avian Influenza

At the National Institute of Epidemiology, Chennai :

♦ Workshop in the Context of Avian Influenza at Chennai (January 14 – 16, 2006).

Vector Control

At the Vector Control Research Centre, Pondicherry :

 Hands - on -Training on Application of Molecular Biology in Vector Borne Disease Control (May - July, 2005).

Reproductive Health

At the National Institute for Research in Reproductive Health, Mumbai :

- Training Course on Gynaecological Cytology and Colposcopy for WHO- In Country Fellows (December 27, 2005– January 7, 2006).
- Training Course on Molecular Diagnosis of Sexually Transmitted Infections (March 6 24, 2006).

Nutrition

At the National Institute of Nutrition, Hyderabad :

 Training of Trainers (ToT) from Regional Centres under the World Bank, MOHFW assisted "Capacity Building Project for Food Safety" (June 21-22, 2005).

- Training Programme for Food Inspectors (June 27- July 1, 2005).
- XXXIV Annual Training Course on Endocrinological Techniques and their Applications (August 16 – September 23, 2005).
- XXXXIII Post-Graduate Certificate Course in Nutrition (January 2- March 15, 2006).
- ✤ 38th Laboratory Animal Technicians Training Course (June 15 July 30, 2005).
- 26th Laboratory Animal Supervisors' Training Course (September 1- November 30, 2005).

Occupational Health

At the National Institute of Occupational Health, Ahmedabad :

- Workshop on Practical Methods for Silica Dust Control under Indo- US Collaborative Project (January 18-19, 2006).
- Training programme on Health Aspects of Chemical Accidents [January 24 - 25, 2006 (at Vapi) and March 29 - 30, 2006 (at Kolkata)]

Laboratory Techniques

At the National Institute for Research in Reproductive Health, Mumbai :

 Training Course on Safe Laboratory Practices with respect to Handling of Radioactive Materials and Radioimmunoassay and Related Technique (November 26, 2005).

At the National Institute of Nutrition, Hyderabad :

 XXXIV Annual Training Course on Endocrinological Techniques and their Applications (August 16 –September 23, 2005).

At the Regional Medical Research Centre, Bhubaneswar :

Workshop on Diagnosis of Infectious Diseases by using Molecular Tools (December, 26, 2005).

Research Methodology

National Institute of Epidemiology, Chennai :

 Training Programme on Research Methodology and Controlled Clinical Trials for the Post-Graduate Siddha Scholars at National Institute of Siddha, Tambaram Sanatorium, Chennai (May 9-20, 2005).

ICMR Headquarters

 Indo – US Workshops on Research Methodology for Undergraduate students and Young Faculty at Delhi and Mumbai (March 21-25 and November 14 -18, 2005 respectively).

Biomedical Communication

Workshop on Biomedical Communication at Nizam's Institute of Medical Sciences, Hyderabad (September 5 – 6, 2005).

RESEARCH SCHEMES FUNDED DURING 2005-2006

Epidemiology and Communicable Diseases

SI. No.	Title of the Project	Investigator/Institute	Grant Released During the year (Rs. in lakhs)
1.	Screening for drug resistant <i>M.leprae</i> using mouse foot pad in replace cases of MB leprosya multicentric study	Dr. U.D. Gupta National JALMA Institute for Leprosy and other Mycobacterial Diseases Agra	3.45
2.	Field programme for the epidemiological studies in leprosy at Ghatampur	Dr. Kiran Katoch National JALMA Institute for Leprosy and Other Mycobacterial Diseases Agra	23.76
3.	Diagnosis and molecular epidemiology of tuberculosis in the North-East	Dr. V.M.Katoch National JALMA Institute for Leprosy and Other Mycobacterial Diseases Agra	_
4.	Study of viability of <i>Mycobacterium leprae</i> in clinical samples and possibility of its presence in the environment using nucleic acid amplification techniques	Dr. V.M.Katoch National JALMA Institute for Leprosy and other Mycobacterial Diseases Agra	3.15
5.	Molecular epidemiology of tuberculosis in slum areas of Agra	Dr. B.M.Agrawal S.N.Medical College and Hospital Agra	3.74
6.	Recognition of the non structural protein NS3 of Japanese encephalitis virus by antiviral cytotoxic T lymphocytes raised by intracerebral immunization	Dr. R.Manjunath Indian Institute of Science Bangalore	6.08
7.	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	1.58

8.	Evaluation of ovarian function in female patients with multibacillary leprosy	Dr. Neena Khanna National Tuberculosis Institute Bangalore	4.31
9.	Purification and characterization of a new toxin produced by candidate cholera vaccine strains	Dr Durg Vijai Singh Institute of Life Sciences Bhubaneswar	1.57
10.	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	2.21
11.	Epidemiology of viral hepatitis in tribal population of Orissa, M.P, Chhattisgarh and Jharkhand	Dr. S.K.Kar Regional Medical Research Centre Bhubaneswar	10.45
12.	Enteral feeding with omega-3- polyunsaturated fatty acids and its effect on course of experimental pneumonia by <i>Streptococcus pneumoniae</i>	Dr. Sanjay Chibber Panjab University Chandigarh	2.30
13.	Phage therapy of <i>Klebsiella</i> <i>pneumoniae</i> induced experimental pneumonia and septicemia	Dr. Sanjay Chibber Panjab University Chandigarh	-
14.	Virulence of <i>P. aeruginosa</i> in relation to catheter- associated urinary tract infections	Dr. Kusum Harjai Panjab University Chandigarh	_
15.	Effect of outer membrane proteins from <i>Salmonella typhi</i> grown under different stress conditions on macrophages	Dr. Praveen Rishi Panjab University Chandigarh	0.08
16.	Genotypic analysis of pol gene for drug - resistance associated mutations in antiretroviral - naive patients with HIV infection	Dr. S.K.Arora Postgraduate Institute of Medical Education and Research Chandigarh	2.63
17.	Screening for drug resistant <i>M.leprae</i> using mouse foot pad in replace cases of MB leprosy - a multicentric study	Dr. Bhushan Kumar Postgraduate Institute of Medical Education and Research Chandigarh	2.63

18.	Development of fluorescent labeled polyclonal antibody reagents for specific identification of <i>Aspergillus</i> <i>Candida</i> and <i>Cryptococcus</i> in paraffin embedded tissue sections	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	1.59
19.	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	2.05
20.	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	2.87
21.	Identification and characterization of a toxin from enteroaggregative <i>Escherichia coli</i>	Dr. Sujata Ghosh Postgraduate Institute of Medical Education and Research Chandigarh	4.62
22.	Study on the cellular responses by a non - CT novel toxin of <i>Vibrio cholerae</i> w07	Dr. Sujata Ghosh Postgraduate Institute of Medical Education and Research Chandigarh	3.10
23.	Role of parasite and host factors in the pathogenesis of trichomoniasis	Dr. Nancy Malla Postgraduate Institute of Medical Education and Research Chandigarh	-
24.	Molecular epidemiological typing of <i>Streptococcus</i> <i>pneumoniae</i> strains	Dr. Praveen Kumar Postgraduate Institute of Medical Education and Research Chandigarh	5.12
25.	Screening of pregnant women and their neonates for group B streptococcus colonization	Dr. Praveen Kumar Postgraduate Institute of Medical Education and Research Chandigarh	1.73
26.	Identification of novel mutation pattern in the ParC and GyrA genes of ciprofloxacin resistant clinical isolates of <i>Neisseria</i> gonorrhoeae	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	4.22

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INDIAN COUNCIL OF MEDICAL RESEARCH

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27.	Immunity to group B streptococci : evaluation of susceptibility to opsonophagocytosis by human immune sera and expression of inhibitor of opsonophagocytosis by Indian isolates	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	3.40
28.	Evaluation of protective immune mechanisms against HIV in exposed yet unifected individuals	Dr. Ajay Wanchu Postgraduate Institute of Medical Education and Research Chandigarh	4.39
29.	Effect of antiretroviral therapy on cytokine and chemokine profile in peripheral blood and genital secretions of women with HIV infection	Dr. Ajay Wanchu Postgraduate Institute of Medical Education and Research Chandigarh	4.89
30.	Multi-site monitoring of human influenza in India - Phase I	Dr. Nalini Ramamurthy King Institute of Preventive Medicine Chennai	3.68
31.	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	6.60
32.	Multicentric feasibility study on the use of intradermal administration of tissue culture antirabies vaccines in India (Coordinating Centre)	Dr. M.D.Gupte National Institute of Epidemiology Chennai	_
33.	Multicentric feasibility study on the use of intradermal administration of tissue culture antirabies vaccines in India	Dr. Sambandham Shantha Stanley Medical College and Associated Hospitals Chennai	_
34.	Human leucocyte antigen (HLA) and non-HLA gene polymorhism studies in HIV and HIV-TB patients	Dr. P.Selvaraj Tuberculosis Research Centre Chennai	3.25

35.	Chemotherapy of tuberculosis in HIV-infected patients : an evaluation of intermittent short course (RNTCP) regimens	Dr. Soumya Swaminathan Tuberculosis Research Centre Chennai	_
36.	Polymerase chain reaction (PCR) for detection of Mycobacterium genus specific genome, <i>M.fortuitum</i> and <i>M.</i> <i>chelonae</i> genomes in vetreous aspirate membranes and blood of Eales' disease patients	Dr. H.N.Madhavan Vision Research Foundation Chennai	6.01
37.	Standardasation & application of polymerase chain reaction (PCR) as a rapid diagnostic test for the detection of <i>Toxoplasma gondii</i> genome in the blood and intraocular fluids of clinically suspected <i>Toxoplasma</i> chorioretinitis patient	Dr. K.Lily Therese Vision Research Foundation Chennai	6.51
38.	Multicentric feasibility study on the use of intradermal administration of tissue antirabies vaccines in India	Dr. Jeeva Kalai Selvan Pasteur Institute Conoor (Nilgiris)	_
39.	Multicentric feasibility study on the use of intradermal administraion of tissue culture antirabies vaccines in India	Dr. Ashok Kumar Rawat Municipal Corporation of Delhi Delhi	-
40.	Analysis of isoniazid and rifampicin resistance mutations in the clinical isolates of <i>M.tuberculosis</i> by sequencing and dot-blot hybridization	Dr. Mridula Bose Vallabhbhai Patel Chest Institute University of Delhi Delhi	1.39
41.	Mycobacterial-epithelial interaction in innate immune response to tubreculosis and its role in transcriptional regulation of inducible nitric oxide synthase (INOS)	Dr. Mridula Bose Vallabhbhai Patel Chest Institute University of Delhi Delhi	2.49
42.	<i>In vitro</i> biointeractions between Candida species, <i>Aspergillus fumigatus</i> and some other human pathogenic fungi	Dr. H.S.Randhawa Vallabhbhai Patel Chest Institute University of Delhi Delhi	1.05

43.	Molecular characteriastion of respiratory isolates of <i>Moraxella catarrhalis</i>	Dr. S.S.Thukral Vallabhbhai Patel Chest Institute University of Delhi Delhi	3.38
44.	Prevalence of <i>M.pneumoniae</i> infection in patients of acute exacerbation of chronic obstructive pulmonary disease	Dr. Mandira Varma Basil Vallabhbhai Patel Chest Institute University Of Delhi Delhi	1.70
45.	Impact of malaria on pregnant women and pregnancy outcome	Dr. Abdul Mabood Khan Regional Medical Research Centre Dibrugarh	3.75
46.	Epidemiology and immune response against Japanese encephalitis virus strains at molecular level in north- eastern region of India	Dr. Siraj Ahmed Khan Regional Medical Research Centre Dibrugarh	13.70
47.	Prevalence of West Nile virus activity in Assam vector incrimination and epidemiology	Dr. Siraj Ahmed Khan Regional Medical Research Centre Dibrugarh	11.85
48.	Studies on HIV/AIDS and drug abuse in Dimapur, Nagaland	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	_
49.	Studies on HIV/AIDS and drug abuse in Aizwal, Mizoram	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	_
50.	Studies on HIV/AIDS and drug abuse in Eastern and north eastern part of India - Coordination Unit	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	_
51.	Diagnosis and molecular epidemiology of tuberculosis in the North-East	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	3.96
52.	Multi-site monitoring of human influenza in India - Phase I	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	3.43
53.	Sibling species profiling of the forest malaria vector Anopheles virus complex in north east India	Dr. Anil Prakash Regional Medical Research Centre Dibrugarh	7.00

54.	Transmission dynamics of bancroftian filariasis : factors affecting the vector efficiency of <i>Culex</i> quinquefasciatus	Dr. G.B.K.S.Prasad Jiwaji University Gwalior	-
55.	Study of viability of <i>Mycobacterium leprae in</i> clinical samples and possibility of its presence in the environment using nucleic acid amplification techniques	Dr. S.K.Suneetha Blue Peter Research Centre & D.L.R.C. (Lepra India) Hyderabad	3.37
56.	Study of viability of <i>Mycobacterium leprae</i> in clinical samples and possibility of its presence in the environment using nucleic acid amplification techniques	Dr. A.S.Niyaz Ahmed Centre for DNA Fingerprinting and Diagnostics Hyderabad	5.10
57.	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C	Dr. Md.Afjaz Habeeb Deccan College of Medical Sciences & Allied Hospitals Hyderabad	3.32
58.	Application of heuristic engine : novel forecasting software tool to predict the outbreak of JE in Andhra Pradesh	Dr. U.Suryanarayana Murty Indian Institute of Chemical Technology Hyderabad	-
59.	Multicentric feasibility study on the use of intradermal administration of tissue culture antirabies vaccines in India	Dr. G.Sampath Institute of Preventive Medicine Hyderabad	-
60.	A monitoring and analysis of anti-HIV active early pregnancy associated protein-1 and 2 in pregnant women	Dr. A.K.Kondapi University of Hyderabad Hyderabad	5.28
61.	Epidemiology of viral hepatitis in tribal population of Orissa, M.P., Chhattisgarh, Jharkhand	Dr. Anup R. Anvikar Regional Medical Research Centre for Tribals Jabalpur	8.54

62.	Concomitant infection of intestinal parasites with filariasis	Dr. Dasarathi Das Regional Medical Research Centre for Tribals Jabalpur	0.32
63.	Screening for drug resistant <i>M.leprae</i> using mouse foot pad in relapse cases of MB leprosy	Dr. Gigi J.Ebenezer Schieffelin Leprosy Research and Training Centre Karigiri	3.33
64.	An approach to immunotherapy against visceral leishmaniasis	Dr. Subrata Majumdar Bose Institute (New Campus) Kolkata	1.80
65.	Screening for drug resistant <i>M.leprae</i> using mouse foot pad in replace cases of MB leprosy	Dr. Gitanjali Saha Greater Calcutta Leprosy Treatment and Health Education Kolkata	0.86
66.	Therapeutic efficacy of positively charged liposomes against <i>Leishmania donovani</i>	Dr. Nahid Ali Indian Institute of Chemical Biology Kolkata	2.41
67.	Statistics in genetic medicine: developing methods for quantitative trait locus mapping and estimating genotype - environment interactions	Dr. Saurabh Ghosh Indian Statistical Institute Kolkata	1.00
68.	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 and SS.K.M. Hospital Kolkata	3.29
69.	Epidemiology of viral hepatitis in tribal population of Orissa, M.P., Chattisgarh and Jharkhand	Dr. Abhijit Chowdhury Institute of Postgraduate Medical Education and Research and SS.K.M. Hospital Kolkata	10.68
70.	Insight into pathogenic mechanisms in antituberculosis drug (ATD) induced hepatotoxicity	Dr. A.K. Santra Institute of Postgraduate Medical Education and Research Kolkata	2.37

71.	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	6.69
72.	Phase IV trial of miltefosixe in the treatment of visceral leishmaniasis (kala azar)	Dr. S.K.Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	_
73.	Multi-site monitoring of human influenza in India - Phase I	Dr. S.K.Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	3.64
74.	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	1.37
75.	Multicentric feasibility study on the use of intradermal administration of tissue culture antirabies vaccines in India	Dr. S.S.Dutta Pasteur Institute Kolkata	_
76.	Studies on molecular mechanism of macrophage response during experimental murine staphylococcal infection and its implication in 'septic shock'	Dr. Biswadev Bishayi University College of Science and Technology University of Calcutta Kolkata	1.28
77.	Gender bias in intra-household food consumption: dietary intakes and patterns	Dr. A.K.Nigam Institute of Applied Statistics and Development Studies Lucknow	6.00
78.	Assessment of determinants of intra venous device associated nosocomial infections in pediatric wards	Dr. Amita Jain K.G's Medical University Lucknow	7.50
79.	Treatment of Japanese encephalitis - a double blind placebo controlled clinical trial	Dr. Rashmi Kumar K.G's Medical University Lucknow	2.21

80.	Role of bacteria in the pathogenesis of juvenile idiopathic arthritis	Dr. Amita Aggarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	_
81.	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	2.75
82.	Molecular characterization of ethambutol resistant <i>Mycobacterium tuberculosis</i> - implication in molecular diagnosis	Dr. T.N.Dhole Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	5.84
83.	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	1.07
84.	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	0.78
85.	Role of antiganglioside antibodies and IgG Fc-receptor (FCYR) polymorphisms in development of <i>Campylobacter</i> related Guillain-Barre syndrome	Dr. K.N.Prasad Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	_
86.	Host parasite relationship : a study on host immunity to survival of <i>Mycobacterium tuberculosis</i> isolates	Dr. R.M.Pitchappan Centre for Advanced Research in Health and Behaviour Madurai	8.01
87.	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	21.99
88.	Quantitation of pathogenic Vibrio spp in seafoods using molecular methods	Dr. I.Karunasagar College of Fisheries Mangalore	2.65

89.	Shiga toxigenic <i>Escherichia</i> <i>coli</i> (STEC) in foods of animal origin and clinical samples	Dr. B.Dhanashree Kasturba Medical College and Hospital Mangalore	0.94
90.	Study of viability of <i>Mycobacterium leprae</i> in clinical samples and possibility of its presence in the environment using nucleic acid amplification techniques	Dr. R.S.Jadhav Stanley Browne Laboratories Miraj	10.95
91.	Acute-phase proteins during <i>Mycobacterium smegmatis</i> infection in mice : induction kinetics and their role (s) in immunoregulation and host defense	Dr. P.P.Singh National Institute of Pharmaceutical Education and Research Mohali	_
92.	Acute-phase reactants during <i>Mycobacterium tuberculosis</i> (h37rv) infection in mice : induction kinetics and their role(s) in immunoregulation and host-defense	Dr. P.P.Singh National Institute of Pharmaceutical Education and Mohali	1.33
93.	Screening fot drug resistant <i>M.leprae</i> using mouse foot pad in relapse cases of MB leprosy	Dr. R.Ganapati Bombay Leprosy Project Mumbai	2.06
94.	Malaria - a study on prevalence of malaria and chloroquine resistance in rural area	Dr. G.S.Vijay Kumar J.S.S.Medical College Mysore	2.06
95.	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	0.75
96.	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	3.29

97.	Etiological significance of microscopic colitis in chronic diarrhoea in children and its pathogenesis	Dr. Shinjini Bhatnagar All India Institute of Medical Sciences New Delhi	9.66
98.	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	7.61
99.	Multi-site monitoring of human influenza in India - Phase I	Dr. Shobha Broor All India Institute of Medical Sciences New Delhi	4.11
100.	Cloning and expression of <i>Mycoplasma pneumoniae</i> p1 gene and its fragments to study their role in cytoadherence	Dr. Rama Chaudhry All India Institute of Medical Sciences New Delhi	3.34
101.	Aerobic and anaerobic bacteriological profile of diabetic foot ulcers with special reference to methicillin resistant <i>Staphylococcus aureus</i>	Dr. Benu Dhawan All India Institute of Medical Sciences New Delhi	2.52
102.	Multilevel epidemiological analysis to assess the role of community level effects on public health/family-welfare	Dr. S.N.Dwivedi All India Institute of Medical Sciences New Delhi	1.29
103.	Study of carbapenemase production, amongst nosocomial isolates of gram-negative bacteria in a tertiary care hospital	Dr. Arti Kapil All India Institute of Medical Sciences New Delhi	3.34
104.	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	1.85
105.	Molecular analysis of cytokine gene polymorhism in leprosy	Dr. N.K.Mehra All India Institute of Medical Sciences New Delhi	1.28

106.	Detection, identification and molecular characterization of intestinal coccidia and microsporidia in patients with chronic diarrhoea and malabsorption syndromes	Dr. B.R.Mirdha All India Institute of Medical Sciences New Delhi	0.84
107.	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	_
108.	Standardisation of antifungal susceptibility testing for filamentous fungi and characterisation of drug sensitive and drug resistant fungal isolates in myoctic keratitis	Dr. Niranjan Nayak All India Institute of Medical Sciences New Delhi	3.11
109.	Comparison of diagnostic efficacy of histochemistry with histology and urease based tests before and after eradication therapy for <i>H.pylori</i> in peptic ulcer disease	Dr. M.P.Sharma All India Institute of Medical Sciences New Delhi	0.78
110.	Rapid and accurate diagnosis of tuberculosis using a novel set of primers directly from clinical samples	Dr. Sarman Singh All India Institute of Medical Sciences New Delhi	4.83
111.	Evaluation of cytokine proflie and th1/th2 shift in HIV infected Indian patients	Dr. Madhu Vajpayee All India Institute of Medical Sciences New Delhi	4.19
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	1.75
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 Kusht Nivaran Sangh New Delhi	_

114.	Detection analysis of food - borne parasites using molecular approaches	Dr. Jaishree Paul Jawaharlal Nehru University New Delhi	_
115.	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	_
116.	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	3.51
117.	Prospective study of hepatitis C virus in north - eastern India	Dr. Premashis Kar Maulana Azad Medical College and Associated Hospitals New Delhi	0.24
118.	Statistical modeling HIV/AIDS epidemic	Dr. Arvind Pandey National Institute of Medical Statistics New Delhi	_
119.	Development of probiotic strains of lactobacilli of desirable characteristics for reproductive health	Dr. G.P.Talwar Talwar Research Foundation New Delhi	2.08
120.	Targeted delivery of polypeptide toxin to tumour cells using long circulatory sterically stabilised liposomes as a carrier	Dr. P.C.Ghosh University of Delhi South Campus New Delhi	_
121.	Studies on the role of virs gene in the pathogenesis of <i>Mycobacterium tuberculosis</i>	Dr. Anil K.Tyagi University of Delhi South Campus New Delhi	4.02
122.	Multicentric feasibility study on the use of intradermal administration of tissue culture antirabies vaccines in India	Dr. Saudan Singh Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	_

123.	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis - C	Dr. Anurag Tandon Metro Multispeciality Hospital NOIDA	2.26
124.	Operational feasibility and impact of co-administration of albendazole and DEC in controlling lymphatic filariasis	Dr. S.P.Pani Vector Control Research Centre Pondicherry	6.20
125.	Further strengthening of the National Leptospirosis Reference Centre	Dr. S.C.Sehgal Regional Medical Research Centre Port Blair	_
126.	Surveillance for drug resistance to anti-TB drug in HIV seronegative tuberculosis patients in Pune	Dr. A.R.Risbud National AIDS Research Institute Pune	_
127.	Chemotherapy of tuberculosis in HIV-infected patients : an evaluation of intermittent short course (RNTCP) regimens	Dr S.P.Tripathy National AIDS Research Institute Pune	3.48
128.	Molecular markers for identification of some important mosquito vectors in India and their genetic variabilities in different geographical populations	Dr. Yogesh S.Shouche National Centre for Cell Sciences Pune	3.43
129.	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	5.77
130.	Epidemiology of viral hepatitis in tribal population of Orissa, M.P., Chattisgarh and Jharkhand	Dr. Vidya A.Arankalle National Institute of Virology Pune	10.87
131.	Multi-site monitoring of human influenza in India - Phase I	Dr. A.C.Mishra National Institute of Virology Pune	3.66

132.	Identification and characterization of candidate antigens of malaria vector <i>Anopheles stephensi</i> for vector directed transmission blocking/ anti mosquito immunity	Dr. S.K.Gakhar Maharshi Dayanand University Rohtak	_
133.	A multiplex PCR approach for the simultaneous and rapid detection of important opportunistic viral infections in renal and bone marrow transplant recipients	Dr. George T.John Christian Medical College and Hospital Vellore	3.10
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	5.82
135.	Molecular surveillance for neonatal rotavirus disease and strains	Dr. Gagandeep Kang Christian Medical College and Hospital Vellore	2.15
136.	Establishing laboratory based surveillance network to monitor anti - microbial resistance	Dr. M.K.Lalitha Christian Medical College and Hospital Vellore	_

Reproductive Health and Nutrition

137.	Effect of community based peer counselling on infant feeding practices and infant growth in rural Uttar Pradesh:a positive deviance study	Dr. Deoki Nandan S.N.Medical College and Hospital Agra	5.39
138.	A study of psychological and service dynamics of illegal abortion in rural areas of India	Dr. Deoki Nandan S.N.Medical College and Hospital Agra	3.93
139.	Social and cultural aspects of women suffering from pulmonary tuberculosis: issues for social and national programme	Dr. B.S.Bhavsar B.J.Medical College Ahmedabad	0.46

140.	Gender issues affecting health of women working in unorganised sectors	Dr. Anjali Nag National Institute of Occupational Health Ahmedabad	0.57
141.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. Binod C. Agrawal Taleem Research Foundation Ahmedabad	_
142.	Human Reproduction Research Centre	Dr. Gauri Ganguli Moti Lal Nehru Medical College Allahabad	11.08
143.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Gauri Ganguli Moti Lal Nehru Medical College Allahabad	_
144.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - implanon	Dr. Gauri Ganguli Moti Lal Nehru Medical College Allahabad	_
145.	National Nutrition Monitoring Bureau	Dr. M.B.Rudrappa Directorate of Health and Family Welfare Services Bangalore	10.00
146.	Genomics of male infertility	Dr. Arun Kumar Indian Institute of Science Bangalore	2.93
147.	Genomics of male infertility	Dr. T.C.Anand Kumar Inter Academy Bio-Medical Science Forum Bangalore	2.00
148.	Genomics of male infertility	Dr. K.M.Prasanna Kumar M.S.Ramaiah Medical College and Teaching Hospital Bangalore	0.51
149.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. Prabha S.Chandra National Institute of Mental Health and Neurosciences Bangalore	1.04
150.	Human Reproduction Research Centre	Dr. B.S.Kodkany Jawaharlal Nehru Medical College Belgaum	7.20

151.	A study of factors affecting acceptability of microbicides among different population groups in India	Dr. B.S.Kodkany Jawaharlal Nehru Medical College Belgaum	2.01
152.	Effectiveness of 3 day amoxycillin versus 5 day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: - a multicentric open labeled trial	Dr. Rashmi Diwedi Gandhi Medical College and Associated Hospitals Bhopal	_
153.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. Uday Jain Mahila Chetna Manch Bhopal	_
154.	A study of roles and capacities of panchayati raj institutions to manage the grass root health system	Dr. J.Vaseer Samarthan Bhopal	1.77
155.	National Nutrition Monitoring Bureau	Dr. S.K.Kar Regional Medical Research Centre Bhubaneswar	10.00
156.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. S.K.Kar Regional Medical Research Centre Bhubaneswar	2.23
157.	Evaluation of oxidative damage, mitochondrial oxidant generation and antioxidant defenses in testis of rat during critical stages of maturation and their modulation by thyroid hormone (T3)	Dr. G.B.N.Chainy Utkal University Bhubaneswar	2.60
158.	Gender issues affecting health of women working in unorganised sectors	Dr. S.S.Rath Utkal University Bhubaneswar	1.28
159.	A study of psychological and service dynamics of illegal abortion in rural areas of India	Dr. S.S.Rath Utkal University Bhubaneswar	3.93

160.	Human Reproduction Research Centre	Dr. Vijay Shree Mahasani S.P.Medical College and Associated Group of Hospitals Bikaner	10.53
161.	Assessment of antioxidant status in pregnancy induced hypertension	Dr. Gurjit Kaur Government Medical College and Hospital Chandigarh	1.93
162.	Influence of oxidative stress on cyclin dependent kinase and heat shock proteins in meiotic mouse spermatocytes	Dr. M.P.Bansal Panjab University Chandigarh	2.66
163.	Evaluation of effectiveness of zinc in restoring the altered thyroid and liver functions following lithium treatment	Dr. D.K.Dhawan Panjab University Chandigarh	_
164.	Effect of metformin and weight reduction on insulin like growth factor 1, insulin sensitivity and clinical, biochemical and endocrinal parameters in obese infertile women with PCOS	Dr. Lakhbir Kaur Dhaliwal Postgraduate Institute of Medical Education and Research Chandigarh	2.12
165.	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	3.49
166.	Human Reproduction Research Centre	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	6.08
167.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	-
168.	Effect of levonorgestrel on G-protein mediated signal transduction on platelet function in female rabbits	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	1.45

169.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - implanon	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	-
170.	Effectiveness of 3 day amoxycillin versus 5 day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: - a multicentric open labeled trial	Dr. Sunit C.Singhi Postgraduate Institute of Medical Education and Research Chandigarh	1.37
171.	Effect of vitamin E supplementation on soluble p-selectin levels in pre-eclampsia	Dr. Sujata Wangkheimayum Postgraduate Institute of Medical Education and Research Chandigarh	1.30
172.	National Nutrition Monitoring Bureau	Dr. V.Vasanthi Directorate of Public Health and Preventive Medicine Chennai	10.00
173.	Human Reproduction Research Centre	Dr. P.M.Shanthamani Government Kasturba Gandhi Hospital for Women & Children Chennai	10.37
174.	Human Reproduction Research Centre	Dr. V.Madhini Government Kilpauk Medical College and Hospital Chennai	9.94
175.	Human Reproduction Research Centre	Dr. S.Devambigai Government R.S.R.M. Hospital Chennai	10.88
176.	Human Reproduction Research Centre - Regional Centre for Clinical Research	Dr. V.Madhini Institute of Obstetrics and Gynaecology and Government Hospital for Women & Children Chennai	10.86
177.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - implanon	Dr. A.Sundaravalli Institute of Obstetrics and Gynaecology and Government Hospital for Women & Children Chennai	_

178.	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	3.85
179.	A study of the pathologic changes in the enteric nervous system in children with chronic constipation	Dr. Priya Ramachandran The Child Trust Hospital and Medical Research Foundation Chennai	0.50
180.	Care and needs of people living with HIV/AIDS (PLWHA): a diagnostic study in the context of long term care	Dr D. Jayalakshmi University of Madras Chennai	1.80
181.	Human Reproduction Research Centre	Dr. Sabita Patnaik S.C.B.Medical College Cuttack	8.82
182.	Home based management of young infants	Dr. Saraswati Swain The National Institute of Applied Human Research and Development Cuttack	7.00
183.	Human Reproduction Research Centre	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	11.9
184.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	_
185.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	-
186.	A study of roles and capacities of panchayati raj institutions to manage the grass root health system	Dr. N.C.Hazarika Regional Medical Research Centre Dibrugarh	1.77
187.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	-

188.	A study of psychological and service dynamics of illegal abortion in rural areas of India	Dr. Lalitha Kabilan The Gandhigram Institute of Rural Health & Family Dindigul	3.93
189.	National Nutrition Monitoring Bureau	Dr. W.R.Hegan Directorate of Health, Medical Services and Medical Education Gandhinagar	10.00
190.	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. M.C.Das Gauhati Medical College and Hospital Guwahati	18.43
191.	A study of psychological and service dynamics of illegal abortion in rural areas of India	Dr. M.C.Das Gauhati Medical College and Hospital Guwahati	3.93
192.	A study of factors affecting acceptability of microbicides among different population groups in India	Dr. M.Prakashma Academy for Nursing Studies Hyderabad	2.01
193.	Genetic and molecular studies in diabetic nephropathy	Dr. Q.Hasan Bhagvan Mahavir Hospital Medical Research Centre Hyderabad	3.10
194.	Evaluation of role of environmental hazards in the etiology of female reproductive failure	Dr. Roya Rozati Bhagvan Mahavir Hospital Medical Research Centre Hyderabad	2.62
195.	Detection of lead toxicity, functional consequences and prevention	Dr. B.Dinesh Kumar National Institute of Nutrition Hyderabad	_
196.	Bioavailability of iron and zinc in representative Indian and US diets	Dr. K.Madhavan Nair National Institute of Nutrition Hyderabad	6.65
197.	Assessment of the prevalence of osteoporosis in the adult population of India	Dr. Veena Shatrugna National Institute of Nutrition Hyderabad	19.58
198.	Central Reference Laboratory of the National Nutrition Monitoring Bureau	Dr. B.Sivakumar National Institute of Nutrition Hyderabad	10.00

199.	National Nutrition Monitoring Bureau	Dr. B.Sivakumar National Institute of Nutrition Hyderabad	10.00
200.	The effectiveness of an integrated feeding and care intervention among 3-15 month old infants in Andhra Pradesh, India	Dr. Shahnaz Vazir National Institute of Nutrition Hyderabad	_
201.	Genetic and molecular factors in the aetiology of endometriosis	Dr. Vijaya Lakshmi Kodati Vasavi Medical and Research Centre Hyderabad	1.55
202.	Care and needs of people living with HIV/AIDS (PLWHA): a diagnostic study in the context of long term care	Dr. M C Arun Manipur University Imphal	2.42
203.	A study of factors affecting acceptability of microbicides among different population groups in India	Dr. T.G.Singh Regional Institute of Medical Sciences Imphal	2.01
204.	National Nutrition Monitoring Bureau	Dr. Tapas Chakma Regional Medical Research Centre for Tribals Jabalpur	10.00
205.	A study of reproductive and sexual health education of adolescents	Dr. R.S.Goel Indian Institute of Health Management Research Jaipur	2.15
206.	A study of cardiovascular disease related lifestyles and their behavioural determinants among different population groups in India	Dr. S.D.Gupta Indian Institute of Health Management Research Jaipur	1.51
207.	Rethinking on post-partum care : a strategic review	Dr. N.Ravichandran Indian Institute of Health Management Research Jaipur	2.00
208.	Human Reproduction Research Centre	Dr. Adarsh Bhargava S.M.S.Medical College and Hospital Jaipur	12.46

209.	Studying the utilization of emergency contraceptive services through paramedics in India	Dr. Adarsh Bhargava S.M.S.Medical College and Hospital Jaipur	2.66
210.	A study of psychological and service dynamics of illegal abortion in rural areas of India	Dr. Adarsh Bhargava S.M.S.Medical College and Hospital Jaipur	3.93
211.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - implanon	Dr. Anju Taly S.M.S.Medical College and Hospital Jaipur	-
212.	Aetiology of abnormal sperm function in infertile cases	Dr. N.K.Lohiya University of Rajasthan Jaipur	4.00
213.	Human Reproduction Research Centre	Dr. Sadhna Sharma Government Medical College and S.M.G.S.Hospital Jammu	12.28
214.	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	_
215.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. Sadhna Sharma Government Medical College and S.M.G.S.Hospital Jammu	_
216.	Human Reproduction Research Centre	Dr. Kiran Pandey G.S.V.M.Medical College Kanpur	11.00
217.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. I.J.K.Soni G.S.V.M.Medical College Kanpur	_
218.	A study of roles and capacities of Panchayati Raj institutions to manage the grass root health system	Dr. K.Pappu Child in Need Institute Kolkata	1.77
219.	A study of cardiovascular disease related lifestyles and their behavioural determinants among different population groups in India	Dr. Ranjit Basu Indian Institute of Bio-Behavioural Sciences Kolkata	1.51

220.	Human Reproduction Research Centre - Regional Centre for Clinical Research	Dr. Samir Roy Institute of Postgraduate Medical Education and Research and SS.K.M. Hospital Kolkata	13.08
221.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. B.K.Saumondal Institute of Postgraduate Medical Education and Research and SS.K.M. Hospital Kolkata	_
222.	Human Reproduction Research Centre	Dr. P.S.Chakraborty Medical College and Eden Hospital Kolkata	12.87
223.	Social and cultural aspect of women suffering from pulmonary tuberculosis: issues for social and national programme	Dr. S.K.Ray Medical College and Eden Hospital Kolkata	0.41
224.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Mamtaz Sanghamitra Medical College and Eden Hospital Kolkata	_
225.	Human Reproduction Research Centre	Dr. Joydev Mukherjee R.G.Kar Medical College and Hospital Kolkata	10.98
226.	National Nutrition Monitoring Bureau	Dr. A.Roy Chowdhury Regional Occupational Health Centre(Eastern) Kolkata	10.00
227.	Impact of daily zinc supplementation to infants born with low birth weigth on mortality and severe disease requiring hospitalization	Dr. Dilip Mahalanabis Society for Applied Studies Kolkata	9.30
228.	Prediction of ovulation in women and evaluation of saliva and urine	Dr. A.K.Bhattacharya University College of Science Kolkata	4.45
229.	A study of reproductive and sexual health education of adolescents	Dr. Sibnath Deb University College of Science and Technology Kolkata	3.64

230.	Effectiveness of 3 day amoxycillin versus 5 day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: - a multicentric open labeled trial	Dr. Shally Awasthi K.G's Medical University Lucknow	3.01
231.	Effectiveness of 3 day amoxycillin versus 5 day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: - a multicentric open labeled trial - co-ordinating unit	Dr. Shally Awasthi K.G's Medical University Lucknow	2.85
232.	Human Reproduction Research Centre	Dr. Vinita Das K.G's Medical University Lucknow	6.32
233.	Home based management of young infants	Dr. Vinita Das K.G's Medical University Lucknow	7.00
234.	Modulation of stress associated biochemical changes in infertile male seminal plasma by Indian herbal preparations	Dr. Abbas Ali Mahdi K.G's Medical University Lucknow	1.24
235.	Screening for prevalence of breast pain and nodularity	Dr. Sandeep Kumar K.G's Medical University Lucknow	3.56
236.	A study of factors affecting acceptability of microbicides among different population groups in India	Dr. V.K.Srivastava K.G's Medical University Lucknow	2.01
237.	Single stage treatment of spina bifida with hydrocephalus based on a prediction rule derived from cranial ultrasound	Dr. A.K.Wakhlu K.G's Medical University Lucknow	1.76
238.	A study of reproductive and sexual health education of adolescents	Dr. S.P.Pandey Pt.G.B.Pant Institute of Studies in Rural Development Lucknow	2.15

239.	Assessment of the prevalence of osteoporosis in the adult population of India	Dr. Eesh Bhatia Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	12.67
240.	Gender issues affecting health of women working in unorganised sectors	Dr. B.Nalani Madurai Kamaraj University Madurai	1.18
241.	Human Reproduction Research Centre	Dr. S.Gowrie Madurai Medical College and Government Rajaji Hospitals Madurai	12.94
242.	Sperm DNA damage in male infertility and its influence on reproductive outcome	Dr. Satish Kumar Adiga Kasturba Medical College and Hospital Manipal	1.70
243.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Rukma Idnani L.L.R.M.Medical College Meerut	_
244.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. Rukma Idnani L.L.R.M.Medical College Meerut	_
245.	Human Reproduction Research Centre	Dr. Usha Sharma L.L.R.M.Medical College Meerut	9.93
246.	Studying the utilization of emergency contraceptive services through paramedics in India	Dr. Usha Sharma L.L.R.M.Medical College Meerut	2.66
247.	Human Reproduction Research Centre	Dr. Rekha G.Dever Grant Medical College and Sir J.J.Group of Hospitals Mumbai	6.99
248.	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	_
249.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. Rekha G.Dever Grant Medical College and Sir J.J.Group of Hospitals Mumbai	_

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250.	Effectiveness of 3 day amoxycillin versus 5 day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: - a multicentric open labeled trial	Dr. Madhuri Kulkarni Lokmanya Tilak Municipal Medical College and L.T.M.G. Hospital Mumbai	1.50
251.	A study of psychological and service dynamics of illegal abortion in rural areas of India	Sh. Donta Balaiah National Institute for Research in Reproductive Health Mumbai	3.93
252.	Assessment of the prevalence of osteoporosis in the adult population of India	Dr. Rashmi S.Shah National Institute for Research in Reproductive Health Mumbai	15.04
253.	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. Vinita Salvi Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai	7.00
254.	Studying the utilization of emergency contraceptive services through paramedics in India	Dr. Vinita Salvi Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai	2.80
255.	Care and needs of people living with HIV/AIDS (PLWHA) : a diagnostic study in the context of long term care	Dr. Vinita Salvi Seth G.S.Medical College and K.E.M.Municipal Hospital Mumbai	0.87
256.	A study of cardiovascular disease related lifestyles and their behavioural determinants among different population groups in India	Dr. Manisha Sen University of Bombay Viddyanagri Campus Mumbai	1.51
257.	Effectiveness of 3 day amoxycillin versus 5 day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: - a multicentric open labeled trial	Dr. A.K.Niswade Government Medical College and Superspeciality Hospital Nagpur	1.50
258.	National Nutrition Monitoring Bureau	Dr. D.J.Dhande Public Health Institute Building Nagpur	10.00

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259	Serum nitric oxide levels as early marker in pregnancy induced hypertension	Dr. Chitra Sinha M.G.M.Medical College and Hospital Navi Mumbai	1.89
260	Assessment of the prevalence of osteoporosis in the adult population of India	Dr. A.C.Ammini All India Institute of Medical Sciences New Delhi	15.18
261	Demographic and clinical profile of young diabetics in a tertiary care hospital in north India	Dr. A.C.Ammini All India Institute of Medical Sciences New Delhi	2.66
262	Congenital CMV infection in offspring of immune mothers	Dr. Lalit Dar All India Institute of Medical Sciences New Delhi	6.81
263	National Neonatal Perinatal Database	Dr. A.K.Deorari All India Institute of Medical Sciences New Delhi	_
264	Effect of (ALA 8,13,18)- magainin II amide on human trophoblast cells <i>in vitro</i>	Dr. Debabrata Ghosh All India Institute of Medical Sciences New Delhi	6.01
265.	Diabetes mellitus and vulvovaginal candidiasis : prevalence of infection and its rationale management	Dr. Ravinder Goswami All India Institute of Medical Sciences New Delhi	3.34
266	High dose and low dose azithromycin in cystic fibrosis: an intervention study to evaluate effect on disease parameters	Dr. S.K.Kabra All India Institute of Medical Sciences New Delhi	2.73
267	Effectiveness of 3 day amoxycillin versus 5 day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: - a multicentric open labeled trial	Dr. S.K.Kabra All India Institute of Medical Sciences New Delhi	0.78
268	Resolution of Bitot's spots after administration of mega-dose of vitamin A in a cohort of children in 1-5 years of age with Bitot's spot	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	2.99

269.	Diagnosis of genital tuberculosis in infertile women and the effect of anti tubercular therapy	Dr. Alka Kriplani All India Institute of Medical Sciences New Delhi	2.39
270.	Genomics of male infertility	Dr. Kiran Kucheria All India Institute of Medical Sciences New Delhi	2.04
271.	Association between low birth weight and autoimmune markers of diabetes in a young Delhi cohort	Dr. R.Lakshmy All India Institute of Medical Sciences New Delhi	7.26
272.	Immunogenetic and humoral profile of diabetes mellitus in Asian Indians	Dr. N.K.Mehra All India Institute of Medical Sciences New Delhi	6.40
273.	Human Reproduction Research Centre	Dr. Suneeta Mittal All India Institute of Medical Sciences New Delhi	11.45
274.	To evaluate the correlation between levels of cytokines (II-6,II-8,II-10) in seminal plasma in different groups of infertile men and correlation with sperm morphology, functions and bacterial infection in semen	Dr. D.Nageswara Rao All India Institute of Medical Sciences New Delhi	2.09
275.	A randomized controlled trial on the efficacy of yogic intervention in premenstrual syndrome	Dr. Ratna Sharma All India Institute of Medical Sciences New Delhi	3.86
276.	Social and cultural aspect of women suffering from pulmonary tuberculosis: issues for social and national programme	Dr. B.B.Riwari Dr.Ram Manohar Lohia Hospital New Delhi	_
277.	A study of reproductive and sexual health education of adolescents - Co-ordinating centre	Dr. Azad S.Kundu Indian Council of Medical Research New Delhi	-
278.	A study of factors affecting acceptability of microbicides among different population groups in India	Dr. Azad S.Kundu Indian Council of Medical Research New Delhi	3.40

279.	A study of cardiovascular disease related lifestyles and their behavioural determinants among different population groups in India-Co-ordinating Unit	Dr. Azad S.Kundu Indian Council of Medical Research New Delhi	3.75
280.	A study of factors affecting acceptability of microbicides among different population groups in India - coordinating Unit	Dr. Azad S.Kundu Indian Council of Medical Research New Delhi	1.00
281.	A study of psychological and service dynamics of illegal abortion in rural areas of India-Co-ordinating Unit	Dr. Azad S.Kundu Indian Council of Medical Research New Delhi	3.20
282.	Central Co-ordinating Unit for Contraception Research	Dr. Rakesh Mittal Indian Council of Medical Research New Delhi	18.00
283.	Home based management of young infants - Co-ordinating Unit	Dr. Rakesh Mittal Indian Council of Medical Research New Delhi	_
284.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant Implanon - Co-ordinating Unit	Dr. Rakesh Mittal Indian Council of Medical Research New Delhi	-
285.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Sh. N.C.Saxena Indian Council of Medical Research New Delhi	_
286.	Metabolic and molecular changes in diabetic rat tissues : their control and reversal by antidiabetic compounds	Dr. Najma Zaheer Baquer Jawaharlal Nehru University New Delhi	2.02
287.	Effect of microwaves on reproductive patterns in male rats	Dr. Jitendra Behari Jawaharlal Nehru University New Delhi	3.40
288.	Urogynaecological complaints in postmenopausal women with particular reference to stress incontinence (evaluation and management)	Dr. S.S.Trivedi Lady Hardinge Medical College and Associated Hospitals New Delhi	_

289.	Hepatitis C virus infection during pregnancy and its effect on the course and outcome of pregnancy	Dr. Ashok Kumar Maulana Azad Medical College and Associated Hospitals New Delhi	4.60
290.	Care and needs of people living with HIV/AIDS (PLWHA) : a diagnostic study in the context of long term care	Dr. Richa Dewan Maulana Azad Medical College and Associated Hospitals New Delhi	0.40
291.	Evaluation of clinical, ultrasonographic and laboratory predictors of preterm labour	Dr. Rewa Tripathi Maulana Azad Medical College and Associated Hospitals New Delhi	6.34
292.	Genomics of male infertility	Dr. Satish K.Gupta National Institute of Immunology New Delhi	1.98
293.	Recombinant human zona pellucida glycoprotein binding characteristics to spermatozoa and subsequent biochemical changes	Dr. Satish K.Gupta National Institute of Immunology New Delhi	2.31
294.	Proteomic studies of spermatogenically inactive (postnatal) and active (adult) sertoli cell secretory products to determine factors responsible for the regulation of spermatogenesis	Dr. S.S.Majumdar National Institute of Immunology New Delhi	3.03
295.	Estimation of spread of HIV/AIDS	Dr. M.Kapilashrami National Institute of Health and Family Welfare New Delhi	_
296.	Gender issues affecting health of women working in unorganised sectors	Dr. A.M.Khan National Institute Of Health and Family Welfare New Delhi	0.45
297.	National Nutrition Monitoring Bureau	Dr. Arvind Pandey National Institute of Medical Statistics New Delhi	10.00
298.	Spatial dimensions of reproductive health status and services : an analysis of RCH/RHS/RFHS	Dr. Arvind Pandey National Institute of Medical Statistics New Delhi	_

299.	PHC facility survey of demographically weak districts	Dr. R.J.Yadav National Institute of Medical Statistics New Delhi	4.00
300.	Knowledge and practices of adolescent girls regarding hygiene during menstruation	Dr. Dinesh Paul National Institute of Public Co-Operation and Child New Delhi	1.83
301.	A study of reproductive and sexual health education of adolescents	Dr. Shashi Prateek Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	2.95
302.	Role of multistage postnatal counseling of primipara in reproductive child health	Dr Shashi Prateek Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	2.07
303.	Human Reproduction Research Centre	Dr. Sudha Salhan Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	11.02
304.	Study of health consequences of domestic violence with special reference to reproductve health	Dr. Prabha Ramalingaswami Vulimiri Ramlingaswami Foundation New Delhi	_
305.	Development of recombinant protein, insulin like polypeptide-p from <i>Momordica</i> <i>charantia</i> and docking and dynamics study with insulin receptors	Dr. Shubhangi Khedkar SIES-Indian Institute of Environment Management New Mumbai	2.19
306.	Human Reproduction Research Centre	Dr. Prasad Neurencar Goa Medical College Panaji	6.00
307.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. Prasad Neurencar Goa Medical College Panaji	_
308.	Home based management of young infants	Dr. Sushma Pandey Patna Medical College and Hospital Patna	7.00
309.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. Sushma Pandey Patna Medical College and Hospital Patna	_
310.	Human Reproduction Research Centre	Dr. Sheela Sharma Patna Medical College and Hospital Patna	11.78
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311.	Stimulatory effects of antioxidants in pollutant - induced male sterlity of mammal	Dr. Akhileshwari Nath Patna University Patna	7.87
312.	Human Reproduction Research Centre	Dr. Syed Habeebullah Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	8.26
313.	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	_
314.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. Syed Habeebullah Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	_
315.	Reproductive and child health care problems among the six primitive tribes of Tamil Nadu	Dr. T.Subramanyam Naidu University of Pondicherry Pondicherry	4.89
316.	Growth during early infancy and its relation with risk factor for adult diseases	Dr. Shobha S.Rao Agharkar Research Institute Pune	0.36
317.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. K.Barucha B.J.Medical College and Sasoon General Hospital Pune	_
318.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - implanon	Dr. K.Barucha B.J.Medical College and Sasoon General Hospital Pune	_
319.	Human Reproduction Research Centre	Dr. P.R.Naphade B.J.Medical College and Sasoon General Hospital Pune	6.00
320.	Human Reproduction Research Centre	Dr. K.Coyaji King Edward Memorial Hospital Research Centre Pune	5.98

321.	A study of reproductive and sexual health education of adolescents	Dr. Seema Sahay National AIDS Research Institute Pune	1.64
322.	Social and cultural aspects of women suffering from pulmonary tuberculosis: issues for social and national programme	Dr. Aarti Nagarkar University of Pune Pune	_
323.	A study of roles and capacities of Panchayati Raj institutions to manage the grass root health system	Dr. S.S.Chahar Maharshi Dayanand University Rohtak	1.77
324.	A study of psychological and service dynamics of illegal abortion in rural areas of India	Dr. J.S.Malik Pandit Bhagwat Dayal Sharma Postgraduate Institute of Medical Sciences Rohtak	3.93
325.	Home based management of young infants	Dr. B.S.Garg Mahatma Gandhi Institute of Medical Sciences Sevagram	15.77
326.	A study of roles and capacities of Panchayati Raj institutions to manage the grass root health system	Dr. U.S.Mishra Centre for Developments Studies Thiruvananthapuram	1.77
327.	Impact of dietary counselling and food supplementation on the lipid profile status of population in Thiruvananthapuram	Dr. S.Chellammal Kerala Agricultural University Thiruvananthapuram	_
328.	A study of reproductive and sexual health education of adolescents	Dr. M.K.C.Nair Medical College and SAT Hospital for Women & Children Thiruvananthapuram	2.59
329.	Effectiveness of 3 day amoxycillin versus 5 day co-trimoxazole in the treatment of non-severe pneumonia in children aged 2-59 months of age: - a multicentric open labeled	Dr. K.Rajamohan Medical College and SAT Hospital for Women & Children Thiruvananthapuram	1.50

trial

330.	Social and cultural aspect of women suffering from pulmonary tuberculosis: issues for social and national programme	Dr. Rama Devi Medical College and SAT Hospital for Women & Children Thiruvananthapuram	0.40
331.	Human Reproduction Research Centre	Dr. Sheela T. Shenoy Medical College and SAT Hospital for Women & Children Thiruvananthapuram	14.48
332.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. P.B.Sulekha Devi Medical College and SAT Hospital for Women & Children Thiruvananthapuram	_
333.	Phase III multicentric clinical trial with subdermal single - rod contraceptive implant - Implanon	Dr. P.B.Sulekha Devi Medical College and SAT Hospital for Women & Children Thiruvananthapuram	_
334.	National Nutrition Monitoring Bureau	Mrs. Rasheeda Bai State Nutrition Bureau Nutrition Research Centre Thiruvananthapuram	10.00
335.	Home base management of young infants	Dr. S.D.Iyenger Action Research and Training for Health Udaipur	7.00
336.	Study of plasma homocysteine levels in Indian mothers and its correlation to low birth weight in neonates	Dr. Kalpana Mahadik R.D.Gardi Medical College Ujjain	2.02
337.	A study of reproductive health problem among men and women in urban slums with speical reference to sexually transmitted infections	Dr. N.P.Das M.S.University of Baroda Vadodara	3.90
338.	Obesity in school going children	Dr. Uma Mahadevan Iyer M.S.University of Baroda Vadodara	_
339.	Human Reproduction Research Centre	Dr. S.L.Pagi Sir Sayajirao Gaikwad Medical College and Hospital Vadodara	12.48
340.	Poverty, under-nutrition and fertility nexus in rural eastern Uttar Pradesh	Dr. R.C.Yadav Banaras Hindu University Varanasi	0.87

341.	A study of cardiovascular disease related lifestyles and their behavioural determinants among different population groups in India	Dr. V.Jacob Jose Christian Medical College and Hospital Vellore	1.51	
	Non-C	Communicable Diseases		
342.	Mental health service needs and service delivery models in the disaster affected	Dr. A.P.S.Chouhan Hospital for Mental Health Ahmedabad	4.06	

	population, Ahmedabad centre		
343.	Cholinesterase and paraoxonase patterns in organophosphate (OP) poisoning	Sh. Ashwin B.Patel National Institute of Occupational Health Ahmedabad	_
344.	Assessment of feasibility of dust control devices for small silica flour milling units in India	Dr. Habibullah N.Saiyed National Institute of Occupational Health Ahmedabad	8.00
345.	Cancer in north east India: understanding the role of pesticides	Dr. Habibullah N.Saiyed National Institute of Occupational Health Ahmedabad	12.21
346.	Cancer in North-East India: understanding the role of tobacco	Dr. Habibullah N.Saiyed National Institute of Occupational Health Ahmedabad	6.43
347.	Rural Cancer Registry	Dr. D.V.Bala The Gujarat Cancer and Research Institute Ahmedabad	8.69
348.	Population Based Cancer Registry	Dr. Eric Zomawig Civil Hospital Aizwal	8.69
349.	Cancer in North East India: understanding the role of pesticides	Dr. Eric Zomawig Civil Hospital Aizwal	1.04
350.	Cancer in North-East India: understanding the role of tobacco	Dr. Eric Zomawig Civil Hospital Aizwal	2.45

351.	National Cancer Registry: Coordinating Unit (Technical Wing)	Dr. A.Nandakumar Kidwai Memorial Institute of Oncology Bangalore	_
352.	National Cancer Registry - Hospital Based	Dr. P.S.Prabhakaran Kidwai Memorial Institute of Oncology Bangalore	1.55
353.	National Cancer Registry - Population Based	Dr. P.S.Prabhakaran Kidwai Memorial Institute of Oncology Bangalore	11.08
354.	A study of serum her-2/neu expression in cancer breast	Smt. P.Girija Ramaswamy Kidwai Memorial Institute of Oncology Bangalore	1.63
355.	Cancer in North East India: understanding the role of pesticides	Dr. A.Nandakumar National Cancer Registry Programme (ICMR) Bangalore	1.00
356.	Cancer in North-East India: understanding the role of tobacco	Dr. A.Nandakumar National Cancer Registry Programme (ICMR) Bangalore	1.40
357.	A prospective serial correlative study of neurocysticercosis by clinical and imaging methods	Dr. A.Nalini National Institute of Mental Health and Neurosciences Bangalore	7.70
358.	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	_
359.	Evaluation of beta - amyloid as a diagnostic marker for Alzheimer's disease	Dr. Sarada Subramanian National Institute of Mental Health and Neurosciences Bangalore	1.75
360.	Prevalence and significance of transfusion transmitted virus (TTV) in various forms of liver diseases	Dr. M.Irshad National Tuberculosis Institute Bangalore	4.00

361.	Prospective evaluation of simplified ACHE and NADPH diaphorase histochemistry in the diagnosis of Hirschsprung's disease and allied disorders	Dr. Usha Kini St.John's Academy of Health Sciences Bangalore	0.68
362.	Mental health service needs and service delivery models in the disaster affected population in Gujrat,Bhuj centre	Dr. M.P.Tilwani Hospital for Mental Health Bhuj	_
363.	Effect of camel milk on glucose metabolism in adults with normal glucose tolerance in <i>raica</i> community: a cross over study	Dr. R.P.Agrawal S.P.Medical College and Associated Group of Hospitals Bikaner	7.82
364.	Study of dietary habits and thrombogenic risk factors in premature coronary artery disease in the North-West part	Dr. Raja Babu Panwar S.P.Medical College and Associated Group of Hospitals Bikaner	6.07
365.	Modulation of endotoxin mediated hepatotoxicity by natural antioxidants	Dr. Praveen Rishi Panjab University Chandigarh	_
366.	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	_
367.	Telomere status and microsatellite instability in Indian patients with hepatocellular carcinoma	Dr. Yogesh K.Chawla Postgraduate Institute of Medical Education and Research Chandigarh	2.48
368.	Virological, serological tumour markers and serum pro and anti-angiogenic factors in the spectrum of chronic liver diseases and hepatocellular carcinoma	Dr. Yogesh K.Chawla Postgraduate Institute of Medical Education and Research Chandigarh	3.62
369.	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	4.64

370.	Study of the expression of matrix metalloproteinases and mechanism of extracellular matrix remodelling in Takayasu's arteritis disease	Dr. Veena Dhawan Postgraduate Institute of Medical Education and Research Chandigarh	6.14
371.	Nonalchoholic fatty liver disease insulin resistance and metabolic syndrome : is there an etiologic association	Dr. R.K.Dhiman Postgraduate Institute of Medical Education and Research Chandigarh	1.04
372.	Immunohistochemical and ultrastructural study of articular cartilage of osteoarthritic knee joint	Dr. Madhur Gupta Postgraduate Institute of Medical Education and Research Chandigarh	2.15
373.	Detection of argpyrimidine levels in lenses of patients with age-related cataract, and correlation with genetic polymorphism of the alpha - crystalline gene in these patients	Dr. Jagat Ram Postgraduate Institute of Medical Education and Research Chandigarh	3.16
374.	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	6.24
375.	Effects of non - ionic polymers or surfactant additives on stress induced apoptosis in type II pneumocytes	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	_
376.	Genetic mapping of non syndromic congenital hearing loss with reference to connexin 26 mutations	Dr. Naresh K.Panda Postgraduate Institute of Medical Education and Research Chandigarh	1.00
377.	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	2.67

378.	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	0.93
379.	Angiogenesis in human astrocytic tumours and its relationship to major angiogenic growth factors	Dr. B.D.Radotra Postgraduate Institute of Medical Education and Research Chandigarh	1.51
380.	Jai Vigyan mission mode project on RF/RHD (registry protocol)	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	9.95
381.	Molecular genetic analysis of malignant round cell tumours with special reference to their diagnostic application	Dr. A.Rajwanshi Postgraduate Institute of Medical Education and Research Chandigarh	2.20
382.	To study the effect of predominant methanogenic flora on the outcome of lactose hydrogen breath test in healthy north Indians and patients with IBS	Dr. Satyavati Rana Postgraduate Institute of Medical Education and Research Chandigarh	2.54
383.	Atherosclerosis and apoptosis: effect of different forms of HDL on scavenger receptor mediated apoptosis of differentiated monocytes	Dr. Savita Kumari Postgraduate Institute of Medical Education and Research Chandigarh	5.00
384.	Telomerase in human gall bladder carcinogenesis	Dr. J.D.Wig Postgraduate Institute of Medical Education and Research Chandigarh	1.45
385.	Development of blood repellant and anti microbial surgical gowns	Dr. M.Madhusoothanan A.C.College of Technology Chennai	_
386.	National Cancer Registry - Hospital Based	Dr. V.Shanta Cancer Institute (W.I.A.) Chennai	0.76
387.	National Cancer Registry - Population Based	Dr. V.Shanta Cancer Institute (W.I.A.) Chennai	4.18

388.	Urban mental health problems and their service needs	Dr. S.Nambi Institute of Mental Health Chennai	5.18
389.	A low-cost and sensitve mass screening tool for furtre osteoporotic fracture risk in women and men	Dr. K.Jagadeesan K.J.Hospital Research & Postgraduate Centre Chennai	5.18
390.	Causes of death by verbal autopsy - a pilot study	Dr. M.D.Gupte National Institute of Epidemiology Chennai	5.99
391.	Role of tetraspanin proteins, p53 family proteins, rac 1-tiam 1 signal transduction, cadherin, catenins and proteases and its inhibitors in retinoblastoma and correlation with aggression	Dr. S.Krishnakumar Vision Research Foundation Chennai	2.45
392.	Study of ezrin, EGFR, IGF-1R, HGF,c-met c-fos and c-jun expression in uveal melanoma correlating known clinico- pathological parameters and with proliferation marker MIB-1	Dr. S.Krishnakumar Vision Research Foundation Chennai	3.82
393.	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	_
394.	Prevalence of rubella virus associated congenital cataract: detecton of the virus in the lens aspirates	Dr. H.N.Madhavan Vision Research Foundation Chennai	_
395.	Role of metalloporphyrins in therapeutics of cardiovascular complications during hypoxic stress	Dr. Ramesh Chandra Dr.B.R.Ambedkar Centre for Biomedical Research University of Delhi Delhi	_

396.	Genomic studies of asthma in Indian population	Dr. Balaram Ghosh Institute of Genomics and Integrative Biology Delhi	11.45
397.	Quantitative assessment of exposure to indoor fungi in relation to sensitization in childhood asthma in Delhi	Dr. A.B.Singh Institute of Genomics and Integrative Biology Delhi	-
398.	Urban mental health problems and their service needs	Dr. N.G.Desai Institute of Human Behaviour and Allied Sciences Delhi	8.41
399.	Mental health service needs and service delivery models in the disaster affected population in Gujrat	Dr. N.G.Desai Institute of Human Behaviour and Allied Sciences Delhi	_
400.	Predictors of physical function among the old	Dr. N.K.Chadha University of Delhi Delhi	_
401.	Determinants of the functional status of the older Indian	Dr. N.K.Chadha University of Delhi Delhi	3.31
402.	To study the mechanism of exertional breathlessness (<i>i.e.</i> development of practical applications arising from advances in visceral mechanisms <i>i.e.</i> J.receptors, chemoreceptors etc.	Dr. Ashima Anand Vallabhbhai Patel Chest Institute University of Delhi Delhi	_
403.	National Cancer Registry - Hospital Based	Dr. F.U.Ahmed Assam Medical College and Hospital Dibrugarh	2.82
404.	Population Based Cancer Registry	Dr. Nandita Chowdhury Assam Medical College and Hospital Dibrugarh	2.82
405.	Cancer in North-East India understanding the role of pesticides	Dr. Nandita Chowdhury Assam Medical College and Hospital Dibrugarh	1.04
406.	Cancer in North-East India understanding the role of tobacco	Dr. Nandita Chowdhury Assam Medical College and Hospital Dibrugarh	1.04

407.	A study on treatment seeking behaviour and reporting pattern of patients to health service centres espicially with fever symptom	Sh. Himanshu Kumar Chaturvedi Regional Medical Research Centre Dibrugarh	-
408.	Epidemiological evaluation of the impact of insecticide treated mosquito nets on occurrence of Japanese encephalitis cases in two selected endemic PHC areas of Assam, India	Dr. Prafulla Dutta Regional Medical Research Centre Dibrugarh	4.50
409.	Malaria control in a forest fringe village of Assam : a pilot study	Dr. Prafulla Dutta Regional Medical Research Centre Dibrugarh	2.82
410.	Study on coronary heart disease and hypertension in Mizoram tribal health sub- plan scheme	Dr. N.C.Hazarika Regional Medical Research Centre Dibrugarh	6.77
411.	Population Based Cancer Registry	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	12.21
412.	Comprehensive study of carcinoma oesophagus in North- East India - multidisciplinary approach	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	_
413.	Cancer in North-East India: understanding the role of pesticides	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	15.26
414.	Cancer in North-East India: understanding the role of tobacco	Dr. J.Mahanta Regional Medical Research Centre Dibrugarh	_
415.	Population Based Cancer Registry	Dr. Yogesh Verma Sir Thutob Namgyal Memorial Hospital Gangtok	_
416.	Cancer in North-East India: understanding the role of pesticides	Dr. Yogesh Verma Sir Thutob Namgyal Memorial Hospital Gangtok	1.04
417.	Cancer in North-East India: understanding the role of tobacco	Dr. Yogesh Verma Sir Thutob Namgyal Memorial Hospital Gangtok	_

418.	Population Based Cancer Registry	Dr. Jagannath Sharma Dr. B. Borooah Cancer Institute Guwahati	_
419.	Cancer in North-East India: understanding the role of pesticides	Dr. Jagannath Sharma Dr. B. Borooah Cancer Institute Guwahati	1.04
420.	Cancer in North-East India: understanding the role of tobacco	Dr. Jagannath Sharma Dr. B. Borooah Cancer Institute Guwahati	2.45
421.	Homocysteine and stroke	Dr. N.C.Borah Institute of Neurological Sciences Guwahati	8.69
422.	Relation of candidate gene variants regulating triglyceride metabolism to serial changes in childhood body mass index and coronary artery disease risk factors in young adulthood	Dr. G.R.Chandak Centre for Cellular and Molecular Biology Hyderabad	1.10
423.	Characterisation of novel genes expressed during curcumin induced differentiation of mouse embryonal carcinoma cells	Dr. Usha K.Srinivas Centre for Cellular and Molecular Biology Hyderabad	2.94
424.	Epidemiology of road traffic accidents (RTA) in Hyderabad - Deccan, Andhra Pradesh, India	Dr. Prasanta Mahapatra Institute of Health Systems Hyderabad	2.98
425.	Role of human papilloma virus, proliferative markers, and p53 in the genesis and prognosis of ocular surface squamous neoplasia	Dr. Geeta K.V. L.V.Prasad Eye Institute Hyderabad	3.69
426.	Effect of camel milk on glucose metabolism in adults with tolerance and type 2 diabetes in <i>raica</i> community : a cross over study	Dr. Ahmad Ibrahim National Institute of Nutrition Hyderabad	5.58
427.	Hypoglycemic/insulin like activity in camel milk : identification, isolation and characterization of the active principle	Dr. M.Raghunath National Institute of Nutrition Hyderabad	5.13

428.	Prevalence of asymptomatic carotid artery stenosis in individuals more than 40 years attending a tertiary care centre in South India	Dr. Subhash Kaul The Nizam's Institute of Medical Sciences Hyderabad	1.19
429.	Role of <i>Chlamydia pneumoniae</i> in various sub-gropus of ischemic stroke	Dr. Subhash Kaul The Nizam's Institute of Medical Sciences Hyderabad	0.99
430.	Population Based Cancer Registry	Dr. Y.M.Singh Regional Institute of Medical Sciences Imphal	0.99
431.	Cancer in North-East India: understanding the role of pesticides	Dr. Y.M.Singh Regional Institute of Medical Sciences Imphal	1.04
432.	Cancer in North-East India: understanding the role of tobacco	Dr. Y.M.Singh Regional Institute of Medical Sciences Imphal	_
433.	Jai Vigyan mission project on RF/RHD (Registry Component)	Dr. Anil Bharani M.G.M.Medical College and M.Y.Hospital Indore	8.66
434.	Prevention of disability among pre - school children	Dr. M.K.Mathur S.M.S.Medical College and Hospital Jaipur	-
435.	Study of factors promoting active ageing in a rural community	Dr. Gift Norman Schieffelin Leprosy Research and Training Centre Karigiri	1.36
436.	Cardiovascular disease surveillance among adivasi population of Wayanad district	Dr. K.K.Haridas Amrita Institute of Medical Sciences and Research Centre Kochi	6.00
437.	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	22.27

438.	Establishment of Jai Vigyan mission mode project on RF/ RHD in the district of Wayanad (Satellite Centre)	Dr. R.Krishan Kumar Amrita Institute of Medical Sciences and Research Centre Kochi	_
439.	Creation and evaluation of a clinical strategy to screen for congenital heart disease in newborn	Dr. R. Krishna Kumar Amrita Institute of Medical Sciences and Research Centre Kochi	6.26
440.	Comparative cost-analysis of health expenditure between tobacco smoker families in the city of Calcutta	Dr. S.P.Mukhopadhyay All India Institute of Hygiene and Public Health Kolkata	_
441.	Epidemiology of major neurological disorders - a random sample survey in the city of Calcutta	Dr. Shyamal K.Das Bangur Institute of Neurology Kolkata	4.44
442.	Multi-centered clinical trials of bio-active integrated orbital implant on human subjects	Dr. D.Basu Central Glass and Ceramic Research Institute Kolkata	_
443.	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	1.94
444.	Study of the mechanism of action of noval resistance modifying agents (RMAS) overcoimg multi drug resistance (MDR) in cancer	Dr. Soumitra K.Choudhuri Chittaranjan National Cancer Institute Kolkata	3.51
445.	Evaluation of purified glutaminase as a potential inhibitor of tumoural angiogenesis	Dr. Putul Maity Chittaranjan National Cancer Institute Kolkata	_
446.	Molecular mechanism of cardiac hypertrophy : identification of differentially expressed genes by cDNA microarray in hypertrophied rat heart	Dr. Arun Bandyopadhyay Indian Institute of Chemical Biology Kolkata	2.02
447.	Kit formulation of thiolate complexes of technetium - 99 m using S - Thiomethyl as a novel protecting group for SH - containing ligands	Dr. Mita Chatterjee Debnath Indian Institute of Chemical Biology Kolkata	_

448.	Experimental evaluation of snake venom as an anticancer agent	Dr. Aparna Gomes Indian Institute of Chemical Biology Kolkata	2.02
449.	Development of new radiopharmaceuticals for nuclear brain imaging : pharmacokinetics and mechanism of action	Dr. Mridula Misra Indian Institute of Chemical Biology Kolkata	6.93
450.	<i>In vitro</i> effects of leishmanial lipid(s) on immunological responses of peripheral blood mononuclear cells and/or synovial fluid cells of rheumatoid arthritis patients	Dr. Krishna Das Saha Indian Institute of Chemical Biology Kolkata	2.17
451.	Effect of omeprazole on regulation of matrix metalloproteinases and remodelling of extracellular matrix in gastrodupdenal ulcar	Dr. Snehasikta Swarnakar Indian Institute of Chemical Biology Kolkata	0.93
452.	Genetic epidemiology of cardiovascular disease : search for genes and estimation of genotype- environment interactions in a homogenous ethnic group	Dr. P.P.Majumder Indian Statistical Institute Kolkata	_
453.	Studies on the spectrum and mechanism of liver disease in chronic arsenic toxicity	Dr. Abhijit Chowdhury Institute of Postgraduate Medical Education and Research and SS.K.M. Hospital Kolkata	10.00
454.	Prevalence of <i>H.pylori</i> and CAG A antibody status in patients with gastric carcinoma and healthy controls : possible mechanism of carcinogenesis involving cytokine response and apoptosis	Dr. Uday Chand Ghoshal Institute of Postgraduate Medical Education and Research and SS.K.M. Hospital Kolkata	_
455.	Fingerprints of polycyclic aromatic hydrocarbon (PAH) responsive cytochrome p450 genes as a biomarker of lung and oral cancer	Dr. Devendra Parmar Industrial Toxicology Research Centre Lucknow	2.86

456.	Genetic and environmental interactions in Parkinson's disease	Dr. Devendra Parmar Industrial Toxicology Research Centre Lucknow	2.00
457.	Fingerprints of blood cytochrome p450 biomarker of exposure and effect	Dr. Devendra Parmar Industrial Toxicology Research Centre Lucknow	8.31
458.	Proteomics based approaches for the development of peripheral protein biomarker(s) and assessment of contribution of selected environmental chemicals in the onset of Parkinson's disease	Dr. Mahendra Pratap Singh Industrial Toxicology Research Centre Lucknow	1.19
459.	To study the epidemiology of rheumatic diseases in rural and urban population of Lucknow (North India)	Dr. S.K.Das K.G's Medical University Lucknow	11.01
460.	Assessment of <i>agnor</i> technique as tumour marker in cervical carcinogenesis	Dr. Vinita Das K.G's Medical University Lucknow	0.58
461.	MR correlates of post- traumatic epilepsy	Dr. Mazhar Husain K.G's Medical University Lucknow	4.31
462.	Diagnostic value of nuclear magnetic resonance (proton NMR) and its implications on aetio-pathogenesis in human breast tissue	Dr. Sandeep Kumar K.G's Medical University Lucknow	4.51
463.	Prevention of disability among pre - school children	Dr. J.V.Singh K.G's Medical University Lucknow	0.07
464.	Role of cycloxygenase- 2 expression in the treatment of cancer cervix	Dr. Kirti Srivastava K.G's Medical University Lucknow	6.71
465.	Urban mental health problems and their service needs	Dr. S.C.Tiwari K.G's Medical University Lucknow	4.89

466.	Titration of BCG doses by measuring urine cytokines and leucocytes in Indian patients with transitional cell carcinoma of urinary bladder in order to decrease BCG related complications without affecting its efficacy	Dr. Anant Kumar Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	3.00
467.	Molecular approaches for early detection of gall bladder cancer	Dr. G.Choudhuri Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	11.89
468.	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	0.80
469.	A study of risk factors in stroke with reference to vitamin B12 and homocysteine	Dr. U.K.Misra Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	4.40
470.	Genetic polymorphisms and gall stone disease	Dr. Balraj Mittal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	3.79
471.	Relationship between genetic variations and risk of esophageal and gastric cancers in Kashmir	Dr. Balraj Mittal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	2.90
472.	Studies on the genetics of inherited aniridia in Indian population	Dr. P.Sundaresan Arvind Eye Hospital and Postgraduate Institute of Ophthalmology Madurai	_
473.	Genetic and structural analysis of myocilin protein involved in juvenile onset primary open angle glaucoma	Dr. P.Sundaresan Arvind Eye Hospital and Postgraduate Institute of Ophthalmology Madurai	_
474.	Involvement of transcription factor gene pax6 in various congenital ocular anomalies in Indian population	Dr. P.Sundaresan Arvind Eye Hospital and Postgraduate Institute of Ophthalmology Madurai	1.27
475.	Investigations on hydroxyapatite coatings of Ti and Ti - 6a1 - 4v for dental implants	Dr. V.Surendra Shetty College of Dental Surgery Manipal	_

476.	Comparative evaluation of <i>triphala</i> and chlorhexidine as a mouthwash : a controlled clinical trial	Dr. Shobha Tandon College of Dental Surgery Manipal	0.11
477.	Development of laser spectroscopy techniques for early detection and follow up therapy in breast malignancy	Dr. Jacob Kurien Kasturba Medical College and Hospital Manipal	1.92
478.	Effect of long term endosulfan exposure on male fertility	Dr. N.Pratap Kumar Kasturba Medical College and Hospital Manipal	_
479.	Anticancer and radiosensitizing effect of plumbagin and its structural analogues : a preclinical study	Dr. B.S.Satish Rao Kasturba Medical College and Hospital Manipal	2.22
480.	Evaluation of the DNA damage in the cultured peripheral blood lymphocytes of head and neck and esophagus carcinomas and the predictor of response to radiotherapy	Dr. M.S.Vidyasagar Kasturba Medical College and Hospital Manipal	1.83
481.	Phase III trial to assess effectiveness of hyperthermia with radiation in the treatment of advanced head and neck cancer	Dr. N.G.Huilgol Dr.Balabhai Nanavati Hospital & Medical Research Centre Mumbai	_
482.	National Cancer registry - Population Based	Dr. M.R.Kamat Indian Cancer Society Mumbai	7.37
483.	Causes of death by verbal autopsy	Dr. C.P.Puri National Institute for Research in Reproductive Health Mumbai	0.23
484.	Assessment impact of hormones on dissemination of breast cancer cells in general circulation due to tumour handling during surgery	Dr. R.A.Badwe Tata Memorial Hospital Mumbai	0.92
485.	National Cancer Registry - Hospital Based	Dr. K.A.Dinshaw Tata Memorial Hospital Mumbai	1.78

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486.	National Cancer Registry Rural Cancer Registry	Dr. K.A.Dinshaw Tata Memorial Hospital Mumbai	_
487.	Invitro 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	_
488.	Radioprotective effect of <i>Ocimum sanctum (Tulasi)</i> in patients undergoing hemi body irradiation : a double blind randomised trial	Dr. Rajiv Sarin Tata Memorial Hospital Mumbai	_
489.	Differential diagnosis of sttuttering and normal non-fluency	Dr. S.R.Savithri All India Institute of Speech and Hearing Mysore	2.41
490.	Hypertension in children - a longitudinal study on changes in blood pressure over a period of time	Dr. D.Narayanappa J.S.S.Medical College Mysore	3.64
491.	Analysis of the T cell receptor repertoire (vbeta, vgamma and vdelta) and immune dysfunction in patients with oral cancer	Dr. Shubhade V.Chiplunkar Advanced Centre for Treatment, Research & Education in Cancer Navi Mumbai	6.40
492.	Molecular cytogenetic studies in oral cancer	Dr. Manoj B.Mahimkar Advanced Centre for Treatment, Research & Education in Cancer Navi Mumbai	0.35
493.	Evaluation of mechanism(s) of turmeric / curcumin - mediated chemoprevention	Dr. G.B.Maru Advanced Centre for Treatment, Research & Education in Cancer Navi Mumbai	1.69
494.	Therapeutic angiogenesis in rabbit hind limb ischemia model using plasmid DNA carrying human hepatocyte growth factor (HGF)	Dr. Rita Mulherkar Advanced Centre for Treatment, Research & Education In Cancer Navi Mumbai	3.14

495.	Evaluation of chemopreventive effects of polyphenolic components from Indian grapes	Dr. Asha G.Ramchandani Advanced Centre for Treatment, Research & Education in Cancer Navi Mumbai	0.97
496.	Studies on the molecular mechanism of tamoxifen - induced apoptosis of astrocutoma cells	Dr. Neelam V.Shirsat Advanced Centre for Treatment, Research & Education in Cancer Navi Mumbai	1.72
497.	Oxidative stress among griatric population	Dr. V.A.Kulkarni M.G.M.Medical College and Hospital Navi Mumbai	4.14
498.	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	0.99
499.	To evaluate radiolabeling and efficay of radiolabelled beta-cyclodextrin for infection imagung	Dr. G.P.Bandopadhyaya All India Institute of Medical Sciences New Delhi	1.98
500.	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	5.35
501.	Prevalence of restless legs syndrome in the Indian community in the adult population : an epidemiological study	Dr. Manvir Bhatia All India Institute of Medical Sciences New Delhi	_
502.	Assosciation of <i>Chlamydia</i> infection with cervical intraepithelial neoplasia	Dr. Neerja Bhatla All India Institute of Medical Sciences New Delhi	4.55
503.	Elucidation of the molecular mechanism of hypertension : role of genetic variants of nitric oxide synthase, free radical homeostasis and cell adhesion molecules and their interplay in the disease	Dr. Nibhriti Das All India Institute of Medical Sciences New Delhi	-

504.	Role of intratympanic dexamethasone therapy in sudden sensorineural hearing loss (SSNHL)	Dr. R.C.Deka All India Institute of Medical Sciences New Delhi	0.99
505.	Amphotericin B nasal lavage and coritcosteroid nasal combination therapy in allergic fungal sinsutits	Dr. R.C.Deka All India Institute of Medical Sciences New Delhi	1.02
506.	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	_
507.	Determinants of the functional status of the older Indian	Dr. A.B. Dey All India Institute of Medical Sciences New Delhi	3.91
508.	Role of genetic factors in tropical pancreatitis	Dr. P.K.Garg All India Institute of Medical Sciences New Delhi	1.67
509.	Development of rapid diagnostic test for detection of autoantibodis in myasthenia gravis by plate and dot-blot elisa	Dr. M.Irshad All India Institute of Medical Sciences New Delhi	3.44
510.	Recovery and stability of routine chemistry analytes and enzymes from serum/whole blood spotted on filter paper	Dr. B.L.Jailkhani All India Institute of Medical Sciences New Delhi	1.91
511.	Role of free radical scavenger and the effect of antioxidants on their levels in patients with ankylosing spondylitis - to investigate the possible role of antioxidants as thera- peutic agents in ankylosing spondylitis	Dr. Arvind Jayaswal All India Institute of Medical Sciences New Delhi	_
512.	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	_

513.	Childhood Hodgkin's disease : role of Epstein - Barr virus (EBV) association, cellular proliferation and apoptosis parameters in relation with the treatment outcome	Dr. S.K.Kabra All India Institute of Medical Sciences New Delhi	3.10
514.	Emerging biochemical markers of mycardial injury following coronary artery bypass grafting (CABG) with or without cardiopulmonary bypass (CPB)	Dr. Shailaja C.Kale All India Institute of Medical Sciences New Delhi	1.51
515.	Epidemiolgy of gall bladder cancer with special reference to nutritional risk factors	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	1.05
516.	Prevalence of obesity and associated diseases amongst well to do adolescent children in the national capital territory of Delhi	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	7.15
517.	Comparison of plasma homocystein levels in patients with mitral stenosis with and without left atrial thrombus	Dr. G.Karthikeyan All India Institute of Medical Sciences New Delhi	1.15
518.	Relation of candidate gene variants regulating triglyceride metabolism to serial changes in childhood body mass index and coronary artery disease risk factors in young adulthood	Dr. R.Lakshmy All India Institute of Medical Sciences New Delhi	15.3
519.	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	2.08
520.	Risk factors of substance use and abuse in offspring of substance abuse patients	Dr. Manju Mehta All India Institute of Medical Sciences New Delhi	_
521.	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	2.00

522.	Incidence of micronuclei in differentiated thyroid cancer patients treated with low dose of I - 131 for remnant ablation	Dr. G.S.Pant All India Institute of Medical Sciences New Delhi	0.61
523.	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	2.00
524.	Relationship between genetic polymorphism in drug metabolising enzymes, cyp1a1 and gstm1 and risk of developing oral precancer and cancer among consumers of tobacco and chewing products	Dr. Ranju Ralhan All India Institute of Medical Sciences New Delhi	43.00
525.	Myopathic disorders: a comparative clincopathological and <i>in</i> <i>vitro</i> proton magnetic resonance spectroscopy (MRS) study on muscle biopsies	Dr. Chitra Sarkar All India Institute of Medical Sciences New Delhi	4.21
526.	Haemostatic and molecular defects predisposing to acute nonembolic stroke in children and young Indians	Dr. Renu Saxena All India Institute of Medical Sciences New Delhi	4.21
527.	Evaluation of waveform characteristics and visual acuity infantile nystagmus and the changes induced by its management	Dr. Pradeep Sharma All India Institute of Medical Sciences New Delhi	-
528.	Ultrasound biomicroscopic study in primary angle closure glaucoma families	Dr. Ramanjit Sihota All India Institute of Medical Sciences New Delhi	_
529.	Circulating and myocardial cytokines and circulating brain natriuretic peptide in diated cardiomyopathy	Dr. K.K.Talwar All India Institute of Medical Sciences New Delhi	2.63
530.	Amniotic membrane transplantation in acute ocular burns : randomised controlled clinical trial	Dr. Radhika Tandon All India Institute of Medical Sciences New Delhi	1.11

531.	National Cancer Registry- Population Based	Dr. Kusum Verma All India Institute of Medical Sciences New Delhi	3.75
532.	Impact of nutritional strategies and multiple antioxidant therapy on progression and management of Parkinson's disease	Sh. S.Vivekanandhan All India Institute of Medical Sciences New Delhi	_
533.	Molecular study on mitochondral dysfunction in Parkinson's disease	Sh. S.Vivekanandhan All India Institute of Medical Sciences New Delhi	4.67
534.	National Cancer Registry- Coordinating Unit(operational wing)	Dr. Bela Shah Indian Council of Medical Research New Delhi	_
535.	Development of sentinel health monitoring centres in India	Dr. Bela Shah Indian Council of Medical Research New Delhi	_
536.	Jai Vigyan mission mode project on control of RF/RHD (Co-ordinating Unit)	Dr. Bela Shah Indian Council of Medical Research New Delhi	_
537.	Development of artificial bone material	Dr. A.R.Ray Indian Institute of Technology New Delhi	_
538.	Pathophysiological, biomechanical and metallurgical study of orthopaedic implants	Dr. R.K.Saxena Indian Institute of Technology New Delhi	_
539.	Comprehensive study of carcinoma oesophagus in North- East India - multidisciplinary approach	Dr. Sunita Saxena Institute of Pathology New Delhi	9.31
540.	Cancer in North-East India: understanding the role of pesticides	Dr. Sunita Saxena Institute of Pathology New Delhi	10.48
541.	Cancer in North-East India: understanding the role of tobacco	Dr. Sunita Saxena Institute of Pathology New Delhi	13.16

542.	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	3.70
543.	Investigation into androgen - independent activation of androgen receptor in prostate cancer	Dr. Rakesh Kumar Tyagi Jawaharlal Nehru University New Delhi	1.72
544.	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	_
545.	Perdictors of advancde fibrosis in non alchoholic steato-hepatitis (NASH) and comparison of the efficacy of metformin versus rosiglitazone in the treatment of NASH	Dr. Vineeta Vijay Batra Maulana Azad Medical College and Associated Hospitals New Delhi	2.26
546.	Prospective study of n - acetyltransferase 2 (NAT2) gene and cytochrome p - 4502e1 gene as susceptible risk factors for antituberculosis drug - induced hepatitis	Dr. Premashis Kar Maulana Azad Medical College and Associated Hospitals New Delhi	6.33
547.	Relation of candidate gene variants regulating triglyceride metabolism to serial changes in childhood body mass index and coronary artery disease risk factors in young adulthood	Dr. H.P.S.Sachdeva Maulana Azad Medical College and Associated Hospitals New Delhi	_
548.	Correlation between periodontitis and serum lipid levels : a clinical evaluation	Dr. Mahesh Verma Maulana Azad Medical College and Associated Hospitals New Delhi	2.42
549.	Role of IGF - 1 and TNF alpha in progress and treatment of neurodegenerative diseases	Dr. Kakoli Ghoshal National Institute of Immunology New Delhi	_

550.	Causes of death by verbal autopsy - a pilot study	Dr. Arvind Pandey National Institute of Medical Statistics New Delhi	1.64
551.	Causes of death by verbal autopsy - Coordinating Unit	Dr. Arvind Pandey National Institute of Medical Statistics New Delhi	1.64
552.	Comparison of arthroscopically assisted anterior cruciate ligament reconstructions using bone graft and semitendinosus graft for the management of symptomatic anterior cruciate ligament de- ficient knees: clinical study	Dr. Deepak Choudhary Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	5.07
553.	Prevention of disability among pre - school children	Dr. H.C.Goyal Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	-
554.	Risk of malformations in children of women with epilepsy - prospective, controlled study	Dr. D.C.Jain Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	8.06
555.	Flow cytometric assays to evaluate prognosis and patient's response to chemotherapy in acute leukaemia	Dr. Sumita Saluja Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	4.32
556.	Clinical and radiological assessment of patients of severe arthritis of hip joint by hybrid total hip arthroplasty and comparative analysis of results with cemented THR and cementless THR arthroplasty	Dr. Awadesh Kumar Singh Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	_
557.	Cancer in North-East India: understanding the role of pesticides	Dr. B.C.Das Institute of Cytology and Preventive Oncology NOIDA	4.48
558.	Cancer in North-East India: understanding the role of tobacco	Dr. B.C.Das Institute of Cytology and Preventive Oncology NOIDA	7.89

559.	Comprehensive study of carcinoma oesophagus in North East India - multidisciplinary approach	Dr. Ashok Sehgal Institute of Cytology and Preventive Oncology Noida	_
560.	Non-invasive glucometer	Dr. Gourish M.Naik Goa University Panaji	_
561.	Mental health service needs and service delivery models in the disaster affected population, Rajkot centre	Dr. M.J.Somani Government Medical College Rajkot	_
562.	Control of cancer - a district level operational research project	Dr. H.L.Kapoor Indira Gandhi Medical College Shimla	_
563.	Population Based Cancer Registry	Dr. Sekhar Chakravarty Silchar Medical College Silchar	_
564.	Cancer in North-East India: understanding the role of pesticides	Dr. Sekhar Chakravarty Silchar Medical College Silchar	1.04
565.	cancer in North-East India: understanding the role of tobacco	Dr. Sekhar Chakravarty Silchar Medical College Silchar	2.59
566.	Effects of phytoestrogens (genistein and amodin) on cell growth in BRCA 1 blocked ovarian cancer cells	Dr. P.C.Priya Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram	1.22
567.	Evaluation of T-cell mediated signal transduction of oral cancer patients in relation to immune response	Dr. Prabha Balaram Regional Cancer Centre Thiruvananthapuram	1.48
568.	National Cancer Registry - Hospital Based	Dr. M.Krishnan Nair Regional Cancer Centre Thiruvananthapuram	3.09
569.	Cyclo-oxygenases-2 inhibition for enhancement of survial in high grade astrocytoma: a pilot phase 2 study	Dr. Beela Sarah Mathew Regional Cancer Centre Thiruvananthapuram	1.43

570.	Trivandrum quality of life study : study on quality of life in breast cancer patients undergoing treatment with curative intent	Dr. Manoj Pandey Regional Cancer Centre Thiruvananthapuram	3.03
571.	Folate receptor, heterogenous ribonucleoprotein, human papillomavirus and epithelial tumour progression	Dr. M.Radhakrishna Pillai Regional Cancer Centre Thiruvananthapuram	1.25
572.	Angiotensin II in the pathogenesis of myocardial lesions in magnesium deficiency	Dr. K.Shivakumar Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram	2.00
573.	Registry of pregnancy in women with epilepsy	Dr. Sanjeev V.Thomas Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram	_
574.	Antitumour activity of isoquinoline alkaloid berberine and its mechanism of action	Dr. Ramadasan Kuttan Amala Cancer Hospital and Research Centre Thrissur	_
575.	Anticonvulsant drug induced alterations in calcium and vitamin-D metabolism	Dr. Bindu Menon S.V.Institute of Medical Sciences Tirupati	2.60
576.	Evaluation of intraoperative somatosensory evoked potentials (SSEPS) and motor evoked potentials (MEPS) changes in patients undergoing spinal cord surgery	Dr. K.Srinivasa Babu Christian Medical College and Hospital Vellore	2.38
577.	Jai Vigyan mission mode project on RF/RHD (registry protocol)	Dr. Vinohar Balraj Christian Medical College and Hospital Vellore	9.64
578.	Jai Vigyan mission mode project on community control of RF/RHD in India (epidemiology of GABHS)	Dr. K.N.Brahmadathan Christian Medical College and Hospital Vellore	5.23
579.	Studies on mucosal alterations in response to surgical manipulation of the small intestine	Dr. Molly Jacob Christian Medical College and Hospital Vellore	1.86

580.	Conformational studies of <i>Taenia solium</i> metacestode proteins diagnostic for neurocysticercosis : Is there a role for unfolding to improve antigenicity	Dr. Anna Oommen Christian Medical College and Hospital Vellore	1.40
581.	Characterization of impaired butyrate oxidation by colonic epithelial cells in inflammatory bowel disease	Dr. B.S.Ramakrishna Christian Medical College and Hospital Vellore	_
582.	Psycho-social consequences of elder abuse and neglect : a study of the implications of elder abuse to mental well being among rural elderly of north coastal Andhra Pradesh	Dr. B.Devi Prasad Andhra University Visakhapatnam	1.42
	В	asic Medical Sciences	
583.	Leprosy genomics : the genomic diversity of leprosy bacillus and expression of its genes in human host	Dr. V.M.Katoch National JALMA Institute for Leprosy and other Mycobacterial Diseases Agra	_
584.	Studies on the effect of the anticancer platinum compounds cisplatin and carboplatin on the rat intestinal brush border membrane	Dr. Riaz Mahmood Aligarh Muslim University Aligarh	0.89
585.	Studies on experimentally produced antibodies against peroxynitrite modified - histones	Dr. Khurshid Alam Jawaharlal Nehru Medical College Aligarh	1.43
586.	A study on the regulation of insulin action by fenugreek seeds (<i>Trigonella foenum</i> <i>graecum</i>) in an animal model of insulin resistance	Dr. C.V.Anuradha Annamalai University Annamalai Nagar	2.04
587.	Evaluation of the antidiabetic and beneficial effect of <i>Cassia auriculata</i> l.(tanner's cassia) in experimental diabetes	Dr. L.Pari Annamalai University Annamalai Nagar	3.07

588.	Proposal for support for an ICMR programme of advanced research and training in human molecular cytogenetics	Dr. H.Sharat Chandra Centre for Human Genetics Bangalore	12.32
589.	Functional genomics of the proteins interacting with the bacterial cell division protein FTSZ in the proliferating and dormant <i>Mycobacterium tuberculosis</i> h37rv	Dr. P.Ajit Kumar Indian Institute of Science Bangalore	_
590.	Gene-expression profiling of normal and malignant human retina and eyelids	Dr. Arun Kumar Indian Institute of Science Bangalore	2.84
591.	Metabolic engineering of terpenoid indole alkaloid biosynthetic pathway for enhanced production of anticancer drugs, vincristine and vinblastine in <i>Catharanthus roseus</i>	Dr. C.Jayabaskaran Indian Institute of Science Bangalore	3.75
592.	Expression profiling of genes regulated by TGF beta using gene microarray approach	Dr. P.Kondaiah Indian Institute of Science Bangalore	8.08
593.	Functional and structural genomics of reca intein of <i>Mycobacterium tuberculosis</i> and <i>M.leprae</i>	Dr. K.Muniyappa Indian Institute of Science Bangalore	-
594.	DNA topoisomerase 1 from mycobacteria : studies on <i>in</i> <i>vivo</i> role and development of peptide inhibitors	Dr. V.Nagaraja Indian Institute of Science Bangalore	6.33
595.	Immunogenomics and pathogenomics of <i>M.tuberculosis</i> and <i>M.bovis</i> (BCG)	Dr. R.Nayak Indian Institute of Science Bangalore	-
596.	DNA repair and susceptibility to cancer	Dr. M.R.S.Rao Indian Institute of Science Bangalore	_

597.	Elucidation of the mechanism of reaction catalyzed by serine hydroxymethyl- transferase by solving the 3D structures and develop/ design structure-based drugs against cancer	Dr. H.S.Savithri Indian Institute of Science Bangalore	2.25
598.	A functional genomics approach to understand the mechanism of slow growth pehnotype in Mycobacteria	Dr. Umesh Varshney Indian Institute of Science Bangalore	17.61
599.	Molecular genetic basis of hot water epilepsy	Dr. Anuranjan Anand Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	7.29
600.	Functional genomics of human transcriptional cofactors and histone deacetylases - a special reference to cancer	Dr. T.K.Kundu Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	2.39
601.	Purification of anti-malarial compounds from Indian herbs and elucidation of their mode of action in <i>Plasmodium</i> <i>falciparum</i>	Dr. Namita Surolia Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	2.00
602.	A molecular genetic study of special sub-groups of psychoses	Dr. Sanjeev Jain National Institute of Mental Health and Neurosciences Bangalore	4.29
603.	Establishment of Central Molecular Genetic Laboratory for psychiatry and neurology at NIMHANS, Bangalore	Dr. Sanjeev Jain National Institute of Mental Health and Neurosciences Bangalore	13.84
604.	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	_
605.	Puerperal cerebral venous thrombosis: a genetic approach to etiology	Dr. D.Nagaraja National Institute of Mental Health and Neurosciences Bangalore	_

606.	Degenerative ataxias : search for novel genes involved in hereditary ataxia in the Indian population	Dr. Pramod Kumar Pal National Institute of Mental Health and Neurosciences Bangalore	2.14
607.	Handigodu diseases - Phase II	Dr. K.Taranath Shetty National Institute of Mental Health And Neurosciences Bangalore	_
608.	Pharmacological characterisation of serotonin transporters in rat brain- effect of antidepressants	Dr. M.N.Subhash National Institute of Mental Health and Neurosciences Bangalore	3.84
609.	Molecular genetics of neuro-muscular disorders	Dr. Anisya Vasanth National Institute of Mental Health and Neurosciences Bangalore	1.63
610.	A survey of the medicinal plants of Western Ghats - Co-Ordinating Centre	Dr. S.D.Kholkute Regional Medical Research Centre Belgaum	5.17
611.	Detection and identification of fungal pathogens in blood using molecular probes	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	_
612.	Characterization of virulent genes of enteroaggregative <i>E.coli</i> to correlate their role in disease progression	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	3.41
613.	Characterization of outer membrane protein p4 from non-typeable <i>H.influenzae</i> in order to check the protective efficacy	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	4.47
614.	High density lipoproteins and atherosclerosis : functional characterization of nf-kb in differentiated monocytes in the presence of different forms of high density lipoproteins	Dr. Sujata Ghosh Postgraduate Institute of Medical Education and Research Chandigarh	5.11
615.	Alternative mechanistic aspect of chronic organophosphate neurotoxicity	Dr. Kiran Deep Gill Postgraduate Institute of Medical Education and Research Chandigarh	4.60

616.	Examination of structural aspects of the intermolecular interactions among crystallins in the lens	Dr. Manni Luthra Guptasarma Postgraduate Institute of Medical Education and Research Chandigarh	2.86
617.	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	3.87
618.	Immunohistochemical, ultrastructural and molecular analysis of viral infections of renal allografts	Dr. Kusum Joshi Postgraduate Institute of Medical Education and Research Chandigarh	2.58
619.	Studies on the regulation of folic acid transport in rat intestine	Dr. Jyotdeep Kaur Postgraduate Institute of Medical Education and Research Chandigarh	3.36
620.	Role of phospholipases A2 and NADPH oxidase in apoptotic and inflammatory gene expression induced by cigarette smoke condensate, a complete carcinogen in lung epithelial cells	Dr. K.L.Khanduja Postgraduate Institute of Medical Education and Research Chandigarh	1.41
621.	Pharmacogenetics of cytochrome p-450 2c19 and 2d6 in North Indians	Dr. K.K.Kohli Postgraduate Institute of Medical Education and Research Chandigarh	3.06
622.	Biomechanical properties of the bone allografts with various bone preservation technique	Dr. O.N.Nagi Postgraduate Institute of Medical Education and Research Chandigarh	1.30
623.	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	-
624.	Genetic characterization of the spiral and coccoid forms of <i>H.pylori</i> and mutational analysis of the urease gene	Dr. Pallab Ray Postgraduate Institute of Medical Education and Research Chandigarh	_

625.	Facial reconstruction of skulls	Dr. Daisy Sahni Postgraduate Institute of Medical Education and Research Chandigarh	1.46
626.	Detection of mutations in the btk gene in patients with x-linked agammaglobulinemia (XLA) and determination of carrier status in phenotypically normal female relatives	Dr. Biman Saikia Postgraduate Institute of Medical Education and Research Chandigarh	0.55
627.	Alginate nanoparticles as carriers of antitubercular drugs: pharmacokinetics and therapeutic potential against experimental tuberculosis	Dr. Sadhna Sharma Postgraduate Institute of Medical Education and Research Chandigarh	1.12
628.	Protective efficacy of <i>M.tuberculosis</i> complex specific protein antigens against experimental tuberculosis	Dr. Indu Verma Postgraduate Institute of Medical Education and Research Chandigarh	3.79
629.	Immunotherapeutic potential of 30 kDa secretory protein of <i>Mycobacterium tuberculosis</i> in mouse model	Dr. Indu Verma Postgraduate Institute of Medical Education and Research Chandigarh	3.12
630.	Immunoprophylactic studies in filariasis using recombinant parasitic enzymes : transglutaminase and thioredoxin peroxidase	Dr. Perumal Kaliraj Centre for Biotechnology Chennai	7.45
631.	A study on the efficacy of alcohol oxidase loaded erythrocytes in combating methanol toxicity	Dr. R.Sheela Devi Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences University of Madras Chennai	5.88
632.	Neuroimmunomodulation by archi cerebellum	Dr. R.Sheela Devi Dr.A.L.Mudaliar P.G.Institute of Basic Medical Sciences University of Madras Chennai	0.78
633.	A survey of the medicinal plants of Western Ghats	Dr. S.Ignacimuthu Entomology Research Institute Chennai	_

634.	Antimycobacterial activity of Solanum trilobatum, Adhatoda Vasica and Garcinia Pictoria	Dr. S.Ignacimuthu Entomology Research Institute Chennai	5.78
635.	Central Biostatistical Monitoring Unit for Traditional Medicine Research	Dr. M.D.Gupte National Institute of Epidemiology Chennai	7.66
636.	Clinical Pharmacology Unit	Dr. V.Kumaraswami Tuberculosis Research Centre Chennai	_
637.	A study of the biology and the growth characteristics of human corneal limbal stem cell	Dr. S.Krishnakumar Vision Research Foundation Chennai	6.42
638.	Analysis of polymorphism and expression profile of genes of mammalian cell entry (MCE) operons in clinical isolates of <i>M.tuberculosis</i>	Dr. Vani Brahmachari Dr.B.R.Ambedkar Centre for Biomedical Research University of Delhi Delhi	5.99
639.	Identification and characterization of antidiabetic compounds from <i>Annona squamosa</i> and <i>Ocimum</i> <i>sanctum</i>	Dr. Ramesh Chandra Dr.B.R.Ambedkar Centre for Biomedical Research University of Delhi Delhi	4.75
640.	Cloning and functional characterisation of eto-binding protein in normal and acute myeloid leukemia	Dr. Daman Saluja Dr.B.R.Ambedkar Centre for Biomedical Research University of Delhi Delhi	3.56
641.	Genetic diversity of <i>Plasmodium falciparum</i> and <i>P.vivax</i> in india using molecular markers	Dr. Hema Joshi National Institute of Malaria Research Delhi	1.63
642.	Molecular characterization of <i>Anopheles fluviatilis</i> complex: development of species specific diagnostic markers and microsatellite markers	Dr. Sarala K.Subbarao National Institute of Malaria Research Delhi	_
643.	Effect of anti-diabetic compound isolated from <i>E.jambolana</i> (fruit-pulp) on diabetic complications in experimental animals	Dr. Suman Bala Sharma University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	4.06

644.	Biochemical studies on the mechanism of action of hypoglycemic compound(s) from central part of stem of <i>Musa</i> <i>sapientum</i> (banana)	Dr. Rimi Shukla University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	0.79
645.	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 University of Delhi Delhi	3.56
646.	Bronchial reactivity in diabetic guinea pigs	Dr. Mohammad Fahim Vallabhbhai Patel Chest Institute University of Delhi Delhi	0.57
647.	Responsiveness of airway rapidly adapting receptors to cigarette smoke inhalation in normal and sensitized rabbits	Dr. Krishnan Ravi Vallabhbhai Patel Chest Institute University of Delhi Delhi	8.44
648.	Investigation of antihepatotoxic activity of certain traditionally used plant species of Assam	Dr. J.C.Gogoi Assam Medical College and Hospital Dibrugarh	-
649.	Genetic analysis of pancreatitis in Indian population	Dr. G.R.Chandak Centre for Cellular and Molecular Biology Hyderabad	_
650.	Handigodu disease - Phase II	Dr. G.R.Chandak Centre for Cellular and Molecular Biology Hyderabad	_
651.	Gene expression profiling of skeletal muscle stem cells using DNA microarrays	Dr. Jyotsna Dhawan Centre for Cellular and Molecular Biology Hyderabad	_
652.	Search for mutations in alpha- crystallin from cataract patients	Dr. Ch.Mohan Rao Centre for Cellular and Molecular Biology Hyderabad	_
653.	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	_
654.	Genetic diversity in primitive Indian tribes	Dr. Lalji Singh Centre for Cellular and Molecular Biology Hyderabad	2.59
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655.	Role of p53 homolog p73 in transcriptional regulation of human caspase genes induced by anti-cancer drugs	Dr. Ghanshyam Swarup Centre for Cellular and Molecular Biology Hyderabad	5.64
656.	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 <i>M.tuberculosis</i>	Dr. Sangita Mukhopadhyay Centre for DNA Fingerprinting and Diagnostics Hyderabad	3.18
657.	Isolation and characterization of human hepatic progenitors for the treatment of liver diseases	Dr. C.M.Habibullah Deccan College of Medical Sciences & Allied Hospitals Hyderabad	13.21
658.	PPAR mediated regulation of glucose metabolism and coronary heart diseases: understanding the mechanism of action	Dr. Nasreen Z.Ehtesham National Institute of Nutrition Hyderabad	4.52
659.	Centre for Advanced Research for Pre-clinical Toxicology	Dr. B.Sivakumar National Institute of Nutrition Hyderabad	7.67
660.	Studies on glutathione mediated heme degradation and its relevance in conditions of thalassemia and sickle cell anaemia	Dr. Ch.V.Ramana Devi University College of Science Hyderabad	0.61
661.	Screening of plants of North- East India for anticancer activities : isolation, characterization and evaluation	Dr. Thounaojam Bhagirath Manipur University Imphal	9.24
662.	Preclinical investigations on the molecular mechanism of testicular/post-testicular contraceptive effects of the seed products of <i>Carica papaya</i>	Dr. N.K.Lohiya University of Rajasthan Jaipur	1.90

663.	X-ray crystallographic analysis of some medicinally important alkaloids with an emphasis on the role of weak interactions	Dr. Rajnikant University of Jammu Jammu Tawi	0.51
664.	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	2.37
665.	Protein phosphorylation in <i>M.leprae</i> and <i>M.tuberculosis</i> - its role in metabolism and pathogenesis	Dr. Lavanya M. Suneetha Schieffelin Leprosy Research and Training Centre Karigiri	-
666.	Cloning and characterization of a fungal protease inhibitor from the hemolymph of tasar silkworm <i>Antheraea mylitta</i>	Dr. A.K.Ghosh Indian Institute of Technology Kharagpur	5.64
667.	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	0.20
668.	Adrenergic, gabaergic and serotonergic gene expression, their interaction on insulin secretion and pancreatic beta-cell proliferation	Dr. C.S.Paulose Cochin University of Science and Technology Kochi	2.22
669.	Antigens and immune response in tuberculous infections	Dr. Parul Chakrabarti Bose Institute (Main Campus) Kolkata	7.45
670.	A search for an immuno adjuvant from <i>neem</i> (<i>Azadirachta</i> <i>indica</i>): studies on the modulation of immunogenecity of carcinoembryonic antigen (CEA) and tumour protection in a murine model	Dr. R.N.Baral Chittaranjan National Cancer Institute Kolkata	3.07

671.	Synthesis of organo selenocyanate compounds and evaluation of their lipid peroxidation inhibitory activity	Dr. Sudin Bhattacharya Chittaranjan National Cancer Institute Kolkata	1.14
672.	Cytotoxicity and genotoxicity of arsenic compounds and their modulation by natural factors	Dr. Madhumita Roy Chittaranjan National Cancer Institute Kolkata	0.66
673.	Studies on neuropharmacologi- cal profile of some Indian medicinal plants, with special emphasis on anxiety and stress	Dr. Dipankar Bhattacharyya Dr.B.C.Roy Postgraduate Institute of Basic Medical Sciences Kolkata	1.55
674.	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	2.92
675.	Potential plant as antileishmanial drug	Dr. Sharmila Chattopadhyay Indian Institute of Chemical Biology Kolkata	2.2
676.	Molecular mechanisms of virulence loss associated with laboratory maintenance of the enteric pathogen <i>Vibrio cholerae</i>	Dr. Rukhsana Chowdhury Indian Institute of Chemical Biology Kolkata	_
677.	Targeting of vesicular flavonoid to liver in combating hepatic fibrosis caused by chronic arsenic ingestion	Dr. Nirmalendu Das Indian Institute of Chemical Biology Kolkata	0.94
678.	Molecular and immunological investigation of O-acetylated sialoglycoconjugates in childhood acute lymphoblastic leukaemia (ALL) and their biological significance	Dr. Chitra Mandal Indian Institute of Chemical Biology Kolkata	_
679.	Role of sialoglycoconjugates in host-parasite interactions in visceral leishmaniasis	Dr. Chitra Mandal Indian Institute of Chemical Biology Kolkata	4.43

680.	Investigation on the antineoplastic efficacy of some metel-complexes in experimental animal models	Dr. K.K.Mukherjea Jadavpur University Kolkata	2.97
681.	Rotavirus genomics	Dr. T.N.Naik National Institute of Cholera and Enteric Diseases Kolkata	9.22
682.	Amniotic membrane transplantation in ocular surface disorder	Dr. Himadri Datta Regional Institute of Ophthalmology Kolkata	2.67
683.	Role of <i>Moringa oleifera</i> root extract in the management of epilepsy - a biochemical and electrophysiological study	Dr. Debjani Guha University College of Medicine Kolkata	3.81
684.	Isolation, purification and characterization of antibacterial activity against <i>Vibrio cholerae</i> from medicinal plants	Dr. P.K.Bag University College of Science Kolkata	3.62
685.	Inventorisation of medicinal plants in <i>Ayodha</i> hills, Purulia district, W.B., documentation and analysis of indigenous knowledge system on their use by ethnic communities located near Ayodha hills	Dr. Dulal Chandra Pal World Wide Fund for Nature- India (WWF-India) Kolkata	1.29
686.	Handigodu diseases - Phase II	Dr. S.S.Agarwal Central Drug Research Institute Lucknow	_
687.	Search for the cell wall and membrane protein(s) of <i>Candida</i> <i>albicans</i> to be used as target molecule	Dr. P.K.Shukla Central Drug Research Institute Lucknow	2.17
688.	Development of new chemotherapeutic agents and drug combinations for the multi-drug resistant/severe malaria treatment	Dr. Renu Tripathi Central Drug Research Institute Lucknow	1.38
689.	Chemopreventive effects of black tea and its constituents	Dr. Yogeshwer Shukla Industrial Toxicology Research Centre Lucknow	1.47

690.	Metabolic, hormonal and genetic relationship in obese Indians	Dr. Neena Srivastava K.G's.Medical University Lucknow	1.36
691.	Isolation, characterisation and biolgical screening of <i>Fumaria indica</i> on the cell cycle of hepatocellular carcinoma in experimental animals	Dr. Ch.V.Rao National Botanical Research Institute Lucknow	1.03
692.	Angiotensin converting enzyme (ACE) gene polymorphism and receptor gene mutations in diabetic nephropathy and essential hypertensives	Dr. Sarita Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.00
693.	Molecular epidemiology of human and animal hepatitis E viruses (HEV) in India	Dr. Rakesh Aggarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	_
694.	Role of alpha, beta and gamma delta T - cells in Takayasu's arteritis	Dr. Soniya Nityanand Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	2.01
695.	Identification of graft- facilitating cells in human bone marrow and G-CSF mobilized peripheral blood stem cell harvests	Dr. Soniya Nityanand Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	3.24
696.	Expression of <i>M leprae</i> virulence genes in hetrologous hosts and analysis of the mechanism of virulence of selected genes	Dr. K.Dharmalingam Madurai Kamaraj University Madurai	9.50
697.	Evaluation of the effect of to potecan in combination with radiation in cultured human fibroblasts	Dr. G.C.Jagetia Kasturba Medical College and Hospital Manipal	_
698.	Comprehensive evaluation of structural and functional changes in the hip in Handigodu syndrome	Dr. Benjamin Joseph Kasturba Medical College and Hospital Manipal	0.34
699.	DNA methylation regulated genes in oral cancer	Dr. K.Satyamoorthy Manipal Academy of Higher Education Manipal	7.00

700.	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	3.96
701.	Novel systems for improved delivery of antidiabetic drugs	Dr. M.S.Nagarsenker Bombay College of Pharmacy Mumbai	0.22
702.	Cognitive and learning effects of <i>Butea frondosa</i> , <i>Eclipta alba</i> and <i>Nardostachys</i> <i>jatamansi</i>	Dr. Sushma A.Mengi C.U.Shah College of Pharmacy S.N.D.T.Women's University Mumbai	7.08
703.	Jai Vigyan mission project on community control of thalassaemia syndromes - awareness,screening,genetic counselling and prevention	Dr. Kanjaksha Ghosh Institute of Immunohaematology Mumbai	4.08
704.	Incidence and molecular characterization of G6PD deficiency in North-East India	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	9.07
705.	Setting up of an umbilical cord blood stem cell bank at Institute of Immunohaematology	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	_
706.	Study of some genetic aspects of essential hypertension in North-East Region	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	20.93
707.	Model to predict <i>in vivo</i> milk/plasma ratios of therapeutic drugs	Dr. Anurupa Maitra National Institute for Research in Reproductive Health Mumbai	-
708.	Endometrial maps of receptive and non-receptive uterus in primates	Dr. Geetanjali Sachdeva National Institute for Research in Reproductive Health Mumbai	-
709.	Role of neuron-glial interactions during post- embryonic development in Drosophila	Dr. Veronica Rodrigues Tata Institute of Fundamental Research Mumbai	2.10
710.	Comparison of efficacy of metformin and spironolactone in the management of polycystic ovarian syndrome	Dr. A.C.Ammini All India Institute of Medical Sciences New Delhi	0.55

711.	Ophthalmic drug formulations using polymeric nanoparticles as carriers	Dr. N.R.Biswas All India Institute of Medical Sciences New Delhi	4.30
712.	Hypoxia and CPG island methylation of selected loci in tumor cell genome : modulation of methylation and subsequent effects on cell proliferation and chemotherapeutic response	Dr. Parthaprasad Chattopadhyay All India Institute of Medical Sciences New Delhi	8.53
713.	Detection of apoptosis in human periodontal ligament during orthodontic tooth movement	Dr. Ritu Duggal All India Institute of Medical Sciences New Delhi	1.44
714.	Molecular basis of disregulation of interferon- gamma generation and function in tuberculosis patients	Dr. H.Krishna Prasad All India Institute of Medical Sciences New Delhi	10.61
715.	Expansion of adult human bone marrow and cord blood stem cells for reconstituting marrow and for reprogramming into hepatocytes	Dr. Lalit Kumar All India Institute of Medical Sciences New Delhi	3.97
716.	Genetic polymorphism of cholesterol ester transfer protein in hyperlipidemic patients: a case control study	Dr. Kalpana Luthra All India Institute of Medical Sciences New Delhi	3.55
717.	Differential cell response of goat granulosa cells to LH or HCG stress in cell culture system: to analyse the signal transduction pathway in the two	Dr. Kalpana Luthra All India Institute of Medical Sciences New Delhi	9.12
718.	Developing epitope based immunogen using different stages of <i>P.vivax</i> using inbuilt immuno adjuvants and delivery in microspheres	Dr. D.Nageswara Rao All India Institute of Medical Sciences New Delhi	_
719.	Gene expression profile analysis of human esophageal cancer using cDNA microarrays	Dr. Ranju Ralhan All India Institute of Medical Sciences New Delhi	_

720.	Effect of alternations in intracellular cacium ion concentration on ORL1 (opioid receptor-like1) opioid receptors in the rat nervous system during morphine tolerance	Dr. S.K.B.Ray All India Institute of Medical Sciences New Delhi	2.26
721.	Elucidation of molecular genetics of acute leukemia in India	Dr. Renu Saxena All India Institute of Medical Sciences New Delhi	3.78
722.	A study of the expression and targeting of inhibitor(s) of apoptosis - an <i>in vitro</i> and <i>in vivo</i> study	Dr. Neeta Singh All India Institute of Medical Sciences New Delhi	0.40
723.	Mitochondria in apoptosis and human cancer	Dr. Neeta Singh All India Institute of Medical Sciences New Delhi	2.59
724.	Evaluation of topical cyclosporin A drops in control of acute ocular inflammation in Steven Johnson's syndrome	Dr. R.B.Vajpayee All India Institute of Medical Sciences New Delhi	0.77
725.	Azathioprine <i>versus</i> coticosteroids for the treatment of <i>Parthenium</i> dermatitis - a double blind randomized controlled trial	Dr. K.K.Verma All India Institute of Medical Sciences New Delhi	3.71
726.	Genetic polymorphism of drug metabolizing enzymes cyp2d6, cyp2c19, cyp2c9 and GST genes in patients developing toxicity to specific antiepileptic drug-phenytoin	Sh. S.Vivekanandhan All India Institute of Medical Sciences New Delhi	1.11
727.	Jai vigyan mission project on community control of thalassaemia syndromes - awareness,screening,genetic counselling and prevention	Dr. Vasantha Muthuswamy Indian Council of Medical Research New Delhi	5.57
728.	Construction and screening of <i>L.donovani</i> 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	-

729.	Molecular characterization of <i>Leishmania</i> parasites isolated from dermal lesions of PKDL patients in india	Dr. Poonam Salotra Institute of Pathology New Delhi	4.02
730.	Mechanism and regulation of CD4+ T cell apoptosis by recombinant malarial proteins in mouse splenocytes	Dr. Paushali Mukherjee International Centre for Genetic Engineering and Biotechnology New Delhi	6.40
731.	Therapeutic intervention of anthrax : a molecular medicine approach	Dr. Rakesh Bhatnagar Jawaharlal Nehru University New Delhi	9.08
732.	Production of recombinant vaccine against anthrax using yeast expression system	Dr. Rakesh Bhatnagar Jawaharlal Nehru University New Delhi	7.17
733.	Comparative genomics approach to identify pathogenesis - related genes in <i>Entamoeba</i> <i>histolytica</i>	Dr. Sudha Bhattacharya Jawaharlal Nehru University New Delhi	8.04
734.	To investigate neurochemical regulation of REM sleep and cellular changes after REM sleep deprivation	Dr. B.N.Mallick Jawaharlal Nehru University New Delhi	4.05
735.	Innate immune recognition of filarial parasites by phagocytes	Dr. Vineeta Bal National Institute of Immunology New Delhi	10.34
736.	Expansion of adult human bone marrow and cord blood stem cells for reconstituting marrow and for reprogramming into hepatocytes	Dr. Ashok Mukhopadhyay National Institute of Immunology New Delhi	3.76
737.	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 Noida	8.88
738.	Screening of heparin from marine molluscs	Dr. A.Shanmugam Centre of Advanced Study in Marine Biology Parangipettai	1.59
739.	Genetic markers:vulnerability to common neuro-psychiatric diseases	Dr. Suman Kapur Birla Institute of Technology and Science Pilani	-

740.	Design and synthesis of novel non-nucleoside reverse transcriptase inhibitors for the treatment of AIDS and opportunistic infections associated with AIDS including tuberculosis	Dr. Dharmarajan Sriram Birla Institute of Technology and Science Pilani	1.51
741.	Genetic polymorphism of drug metabolising enzymes in South Indian population	Dr. C.Adithan Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	-
742.	Biological implications of oxidative stress and the effects of treatment	Dr. Bobby Zachariah Jawaharlal Institute of Postgraduate Medical Education and Researc Pondicherry	1.03 ch
743.	Immunological and molecular studies on the mosquito humoral factors involved in the susceptibility/regulation of <i>Wuchereria bancrofti</i> infection and development in <i>Culex quinquefasciatus</i>	Dr. K.P.Paily Vector Control Research Centre Pondicherry	4.27
744.	HIV-1 subtyping and detection of HIV-1 recombinants in India	Dr S.P.Tripathy National AIDS Research Institute Pune	_
745.	Genomic characterisation of hepatitis E and A viruses circulating in India for 25 years	Dr. Vidya A.Arankalle National Institute of Virology Pune	1.50
746.	Genomic analysis of hepatitis A virus isolates from different geographic locations of India	Dr. S.D.Chitambar National Institute of Virology Pune	1.50
747.	Molecular charcterisation of vectoral competence of <i>Anopheles stephensi</i>	Dr. D.N.Deobagkar University of Pune Pune	27.30
748.	Preparation of an enzostrip for semi-quantitative determination of urinary oxalate	Dr. C.S.Pundir Maharshi Dayanand University Rohtak	0.94
749.	Handigodu disease - phase II	Dr. Natraj Sagar General Hospital Sagar	_

750.	Analysis of the immunotherapeutic response of turmeric extract towards malignancy, taking both tumour cells and lymphocytes as targets	Dr. A.K.Chakravarty University of North Bengal Siliguri	1.78
751.	Inhibition of tumour specific angiogenesis of endothelial cells by curcuminoid derivatives	Dr. Girija Kuttan Amala Cancer Hospital and Research Centre Thrissur	0.39
752.	Role and regulation of bruton's tyrosine kinase and its association with apoptosis pathway in the activated platelets	Dr. Debabrata Dash Institute of Medical Sciences Banaras Hindu University Varanasi	7.29
753.	Studies on the status of gastric mucosal defensive factors <i>per se</i> and on physical and chemical factors-induced gastric ulceration in experimental diabetic rats <i>vis a vis</i> some Indian medicinal plants	Dr. R.K.Goel Institute of Medical Sciences Banaras Hindu University Varanasi	6.23
754.	The pathogenetic and prognostic role of Epstein Barr viral oncogenes in lymphomas in an Indian population	Dr. Rekha Rozario Christian Medical College and Hospital Vellore	3.75
755.	Mechanism of action of <i>oduvanthalai</i> leaf poison	Dr. Sathya Subramani Christian Medical College and Hospital Vellore	4.95
	Public	cation and Information	
756.	Scientometric studies - an ICMR sponsored study	Dr. K.Satyanarayana Indian Council of Medical Research New Delhi	_
757.	A study of emerging technology trends in the development of vaccines\diagnostics as reflected from current patent analysis	Dr. K.V.Swaminathan Waterfalls Institute of Technology Transfer New Delhi	_
758.	WISTA: vaccines/diagnostic	Dr. K.V.Swaminathan Waterfalls Institute of Technology Transfer New Delhi Medicinal Plant Unit	5.29

759.	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	4.67 e
760.	Quality standards of Indian medicinal plants and preparation of monograph thereof	Dr. M.Rajani BV Patel Pharmaceutical Education and Research Development Centre Ahmedabad	4.97 e
761.	Chemical, chromatographic and toxicological evaluation of ayurvedic herbal drugs- pre and past sodhana process	Dr. Kamala K.Vasu BV Patel Pharmaceutical Education and Research Development Centre Ahmedabad	4.57 e
762.	Medicinal plant monographs on diseases of public health importance - filaria	Dr. R.K.Shenoy T.D.Medical College and Hospital Alappuzha	_
763.	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. Karan Vasisht Panjab University Chandigarh	0.32
764.	Medicinal plant monographs on diseases of public health importance - kala-azar	Dr. R.C.Mahajan Postgraduate Institute of Medical Education and Research Chandigarh	_
765.	Quality standards of Indian medicinal plants	Dr. A.Saraswathy Captain Srinivasamurthy Drug Research Institute for Ayurveda Chennai	4.31
766.	Medicinal plant monographs on diseases of public health importance - malaria	Dr. S.Pattanayak B-91, Swasthya Vihar Delhi	_
767.	Medicinal plant monographs on diseases of public health importance - liver diseases	Dr. S.S.Handa 522-A, Block-E Sushant Lok Phase-I Gurgaon	_
768.	Quality standards of Indian medicinal plants and preparation of monographs thereof	Dr. P.K.Mukherjee Jadavpur University Kolkata	1.42

769.	Quality standards of Indian medicinal plants and preparation of monographs thereof	Dr. Indira Balachandran Centre for Medicinal Plants Research Aryavaidyasala Kottakal	7.93
770.	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	_
771.	Heavy metals and persistent pesticide analysis of selected medicinal plants - phase II	Dr. Y.K.Gupta Industrial Toxicology Research Centre Lucknow	2.98
772.	Quality standards of Indian medicinal plants and preparation of monographs thereof	Dr. A.K.S.Rawat National Botanical Research Institute Lucknow	6.71
773.	Medicinal plant monographs on diseases of public health importance - immunomodulators	Dr. S.S.Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	_
774.	Medicinal plant monographs on diseases of public health importance - diabetes mellitus	Dr. B.N.Dhawan 3, Ramakrishna Marg Lucknow	_
775.	Medicinal plant monographs on diseases of public health importance - Co-Ordinating unit	Dr. A.K. Gupta Indian Council of Medical Research New Delhi	_
776.	Review monographs on Indian medicinal plants	Dr. A.K. Gupta Indian Council of Medical Research New Delhi	32.6
777.	Quality standards of Indian medicinal plants and preparation of monographs thereof - co-ordinating unit	Dr. A.K. Gupta Indian Council Of Medical Research New Delhi	7.51
778.	Quality standards of Indian medicinal plants and preparation of monograph thereof	Dr. A.M.Majumdar Botany Group Agharkar Research Institute Pune	3.51
779.	Medicinal plant monographs on diseases of public health importance - anti-inflammatory drugs	Dr. R.H.Singh Institute of Medical Sciences Banaras Hindu University Varanasi	_

APPENDIX IV

RESEARCH FELLOWSHIPS Funded During 2005-2006

Name of the Fellow/Institute

National Tuberculosis Institute

Smt. Irum Tabassum

Bangalore

Epidemiology and Communicable Diseases

Mycoplasma pneumoniae

Development of an immunodiagnostic

assay using recombinant p1 protein of

Title of the Project

SI.

No.

1.

2.	Immunogenicity of tetanus toxiod conjugates of anti-idiotypes that mimic <i>Klebsiella pneumoniae</i> surface polysaccharides	Ms. Sonia Bohnchal Bhardwaj Punjab University Chandigarh	
3.	Streptococcal inhibitor of complement protein : its distribution, isolation and functional characterization from Indian GAS isolates	Sh. Vivek Sagar Postgraduate Institute of Medical Education and Research Chandigarh	
4.	Cysteine proteinase activity in <i>Trichomonas</i> <i>vaginalis</i> isolates from symptomatic and asymptomatic patients and clinical samples : its correlation with free nitrogen radical levels	Ms. Manisha Yadav Postgraduate Institute of Medical Education and Research Chandigarh	
5.	Stage specific analysis of <i>in vitro</i> drug resistance in promastigote and amastigote stages of <i>Leishmania donovani</i> isolates of India	Ms. Ranjini Valiathan Postgraduate Institute of Medical Education and Research Chandigarh	
6.	Cytokine responses in symptomatic <i>vs</i> asymptomatic amoebiasis patients	Sh. Devendra Bansal Postgraduate Institute of Medical Education and Research Chandigarh	
7.	Molecular epidemiological surveillance and evaluation of virulence factors in nontypable <i>Haemophilus influenzae</i>	Sh. C Sasanka Sekhar Postgraduate Institute of Medical Education and Research Chandigarh	
8.	Study of potential beneficial effects of biotherapeutics on experimental <i>Clostridium difficile</i> infection	Smt. Sukhminderjit Kaur Postgraduate Institute of Medical Education and Research Chandigarh	
9.	To study the expression of major virulence factor: <i>Streptococcal</i> adhesins (SFB) in Indian isolates and its pattern of antibody response in humans	Sh. Anil K. Sharma Postgraduate Institute of Medical Education and Research Chandigarh	

- 10. *Entamoeba histolytica* adherence lectin (GAL/GALNAC) mediated activation of immune competent cells
- 11. Detection of canine distemper virus related bone disease in pet owners
- 12. Enhancing the efficacy of recombinant protein vaccines and DNA vaccines for human lymphatic filariasis
- 13. Surveillance for influneza viruses activity in Chennai, standardization of RT-PCR/RFLP analysis for rapid identification of influenzae viruses and studying antigenic strain variation
- 14. Analysis of molecular basis of pyrazinamide resistance in mycobacteria
- 15. Genotypic testing for drug resistant mutations in HIV strains in South India-Pilot study
- 16. A study of the clinical presentation of tuberculosis in HIV positive patients and its correlation with CD4 and CD8 counts
- 17. Dermatological manifestations in HIV infection and its correlation with CD4 count
- A study of various clinical manifestations in HIV patients with CD4 count less than 200 amongst Indian population
- 19. Basic studies on the mechanism of infection in cerebral malaria pathology mediated by *Plasmodium berghei* antigen
- 20. Role of apoptosis in the pathogenesis of influenza virus, correlation of virological and immunological parameters : study in human and murine model
- 21. Study of extracellular proteinase and phospholipase activities of clinical and environmental isolates of *Cryptococcus neoformans,Candida albicans* and non-albicans

Smt. Monika Sharma Postgraduate Institute of Medical Education and Research Chandigarh

Ms. D. Latha Anna University Chennai

Sh. Balakrishnan A Setty Centre for Biotechnology Chennai

Sh. A. Khaleef Athullah Sheriff King Institute of Preventive Medicine Chennai

Smt. E. Ezhilkatharine Tuberculosis Research Centre Chennai

Smt. S. Lakshmi Tuberculosis Research Centre Chennai

Dr. Amit Mann Base Hospital Delhi

Dr. Gulhima Chawla Base Hospital Delhi

Dr. Renu Susan David Base Hospital Delhi

Sh. Vinay Kumar Godina Dr. B.R. Ambedkar Centre for Biomedical Research Delhi

Sh. Vikarm Srivastava Vallabhbhai Patel Chest Institute Delhi

Sh. S.R. Nawange Rani Durgawati Vishwavidyalaya Jabalpur

APPENDIX IV

- 22. Studies on occult hepatitis B virus infection and naturally occurring surface gene variants of hepatitis B virus and its clinical significance in eastern Indian population
- 23. Studies on interspecies transmission of rotaviruses
- 24. Studies on the identification of Th1 stimulatory proteins of a recent field isolate of *Leishmania donovani* for their prophylactic evaluation against experimental visceral leishmaniasis
- 25. Characterisation of *Brugia malayi* adult parasite molecules that might potentially facilitate reinfection in infected host previously treated with antifilarials
- Characterization of semipurified molecules of *Brugia malayi* adult worm extract in relation to pathophysiology of filariasis in rodent
 B. malayi model
- 27. Characterization of extended spectrum beta lactamase producing *Klebsiella spp.* isolated from intensive care unit
- 28. Relationship between *Helicobacter pylori* genotypes and different gastroduodenal diseases
- 29. Effect of chromium on dengue virus infection in mice
- 30. Phenotypic switching and its frequency in primary *C. neoformans* isolates from infected patients
- 31. A prospective study to evaluate the role of *Clostridium perfringens* in diarrhoea versus controls and their phenotypic and genotypic characterization
- 32. Characterization of 30 kDa adhesin protein (p30) of *Mycoplasma pneumoniae*

Sh. Anup Banerjee ICMR Virus Unit Kolkata

Dr. Souvik Ghosh National Institute of Cholera and Enteric Diseases Kolkata

Sh. Ravindra Garg Central Drug Research Institute Lucknow

Sh. Rajivlochan Gaur Central Drug Research Institute Lucknow

Sh. Saurabh Dixit Central Drug Research Institute Lucknow

Sh. Rajesh Kumar Mondal K.G's Medical University Lucknow

Sh. Ashish Saxena Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow

Ms. Richa Shrivastava Central Food Technological Research Institute Mysore

Ms. Neena Jain All India Institute of Medical Sciences New Delhi

Ms. Lovely Joshy All India Institute of Medical Sciences New Delhi

Sh. Avanish K. Varshney All India Institute of Medical Sciences New Delhi

- 33. Prevalence and association of transfusion transmitted virus and hepatitis C virus in patients undergoing hemodialysis in northen India
- 34. Expression and use of TTV recombinant protein to detect anti TTV antibodies in serum
- 35. Development of a conjugate vaccine for enteric fevers
- 36. A study of thyroid functional status in HIV infected persons and to compare thyroid function at various stages of HIV infection and correlate with CD4 and CD5 counts
- 37. Study of mutation in the HBV genome in fulminant hepatitis patients and its clinical significance
- 38. Molecular characterization of hepatitis B and C viral infections and their associaton with the risk of hepatocellular carcinoma study from a north Indian hospital
- 39. Studying the effect of oxidative stress and manipulation of iron metabolism on drug resistance in *Candida albicans*
- 40. Epidemiological study of the antiretroviral drug resistant HIV-1 strains by monitoring antiretroviral drug resistance in protease and reverse transcriptase gene of HIV-1 infected patients
- 41. Genotypic characterisation of hepatitis C virus (HCV) and its significance in patients with chronic liver disease (CLD)
- 42. Molecular characterization of dengue virus strains by sequence analysis of envelope region
- Study of hepatitis B virus (HBV) genotypes and their clinical significance in patients with HBV-related liver diseases

Dr. Somia Bashir All India Institute of Medical Sciences New Delhi

Dr. Yukti Sharma All India Institute of Medical Sciences New Delhi

Ms. Sanyukta Sengupta All India Institute of Medical Sciences New Delhi

Dr. Debasish Saha Army Hospital (Research & Referral) New Delhi

Sh. Abdul Malik Jamia Milia Islamia New Delhi

Mr. Mohammad Asim Jamia Milia Islamia New Delhi

Dr. Aparna Chandra Kansal Jawaharlal Nehru University New Delhi

Sh. Sanjeev Saini Maulana Azad Medical College and Associated Hospitals New Delhi

Sh. Vikas Verma Maulana Azad Medical College and Associated Hospitals New Delhi

Smt. Rajni Kumaria Maulana Azad Medical College and Associated Hospitals New Delhi

Sh. Saket Chattopadhyay Maulana Azad Medical College and Associated Hospitals New Delhi

- 44. Study of non structural protein encoding gene of hepatitis C virus
- 45. Characterization of extended spectrum B-lactamases (ESBI) and B-lactmases of clinical strains of *Yersinia enterocolitica* isolated from India
- 46. Multilocus variable number tandem repeat analysis for typing of *Yersinia enterocolitica* isolated from India and other parts of the world
- 47. Biodiversity of actinomycetes and their fungal activity against human pathogenic yeasts
- 48. Studies on nosocomial infection with special reference to acinetobacter

Reproductive Health and Nutrition

- 49. Clinical-biochemical profile of the referred sick newborns at admission and its relationship to outcome in terms of morbidity and mortality
- 50. Role of p53 in experimental oxidative stress mediated apoptosis in spermatogenic process
- 51. Regulation of male fertility by monensin
- 52. Impact of maternal hypothyroidism on androgen receptor gene expression in the ventral prostate during pre-pubertal and pubertal period in rats
- Impact of sex steroids on insulin receptor expression and glucose oxidation in target tissues of male albino rat

Sh. Deepak Kumar Maulana Azad Medical College and Associated Hospitals New Delhi

Sh. Sachin Sharma University of Delhi South Campus New Delhi

Smt. Pooja Gulati University of Delhi South Campus New Delhi

Ms. Sangeeta Bansilal Raina University of Pune Pune

Sh. Abhishek Gaur Institute of Medical Sciences Bananas Hindu University Varanasi

Dr. Ruchi Rai Moti Lal Nehru Medical College Allahabad

Dr. Parminder Kaur Panjab University Chandigarh

Ms. Malti Singh Panjab University Chandigarh

Ms. P.J. Arokya Mary Sashi Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai

Sh. Muthusamy Thirupathi Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai

- 54. Effects of experimental diabetes and insulin replacement on epididymal structure and function
- 55. Clinical effectiveness of co-trimoxazole versus amosycillin for pneumonia in children a randomized controlled trial
- 56. Transcutaneous bilirubinometer in neonatal practice
- 57. *Chlamydia trachomatis* infection : a prospective study of its incidence in pregnant and non pregnant women and its effect on pregnancy in treated and untreated cases
- 58. Nutritional and hypoglycemic effect of fruit pulp and leaves of *Annona squamosa* (custard apple)
- 59. A randomised comparative trial of two different dose regimens of misoprostol for medical termination of pregnancy up to 8 weeks
- 60. Control of tuberculosis : a socio-cultural and gender based study in Manipur
- 61. An anthropological study on current prevalence, nature and etiology of childhood and adolescent obesity in Delhi
- 62. Long-term (2 year) effects of a reduced-fat diet intervention in type 2 diabetes mellitus
- 63. A study on nutrition and health status in relation to some bio social factors among the major tribes of Imphal and Churachandpur district, Manipur
- 64. Understanding families coping with thalassemia : a psychosocial investigation

Sh. Soudmani Singh Dr. A.L. Mudalar P.G. Institute of Basic Medical Sciences University of Madras Chennai

Dr. S.M. Rajesh Base Hospital Delhi

Dr. Shalini Singh Base Hospital Delhi

Dr. Shilpa Garg Base Hospital Delhi

Sh. R.K. Gupta Dr. B.R. Ambedkar Centre for Biomedical Research Delhi

Dr. Ritu Goyal University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi

Dr. Mary Grace 'D' Tungdim University of Delhi Delhi

Dr. Sonali Walia University of Delhi Delhi

Ms. Neelima Gundupallee The Nizam's Institute of Medical Sciences Hyderabad

Sh. A.K.S. Sarangthem Regional Institute of Medical Sciences Imphal

Ms. Tanuka Roy Indian Institute of Technology Kharagpur

N COUNCIL OF MEDICA

- 65. Characterization of a sperm outer surface-lectin receptor and its physiological significance
- 66. Isolation and characterisation of a sperm forward mortility stimulating factor from goat blood serum and its role in male fertility regulation
- 67. Studies on the effect of supplementation of variable dietary components (protein & carbohydrate) in the diet on excitatory neurotransmitters in relation to brain regions and immune response in young and aged mammals
- 68. Studies on the antioxidative effects of sesame lignans in diabetes induced rats
- 69. Studies on the significance of maturation dependent 33 kDa glycoprotein of mammalian epididymis in human fertility/infertility
- 70. To evaluate the efficacy of misoprostol for the induction of labour at term
- 71. Study on the functional role of epididymal proteins in sperm maturation
- 72. Identification and characterization of sperm specific antigen/s by using vasectomy induced antisperm antibodies
- 73. Proteome profile of domain specific proteins acquired during epididymal maturation
- 74. Genomic study related to Y chromosome microdeletions in infertile males

Sh. Kaushik Das Indian Institute of Chemical Biology Kolkata

Sh. Sudipta Saha Indian Institute of Chemical Biology Kolkata

Ms. Sudipta Pal University College of Science Kolkata

Dr. Krishna Chattopadhyay University College of Science and Technology Kolkata

Sh. Abhishek Chandra Central Drug Research Institute Lucknow

Dr. Aruna Nigam Era's Lucknow Medical College & Hospital Lucknow

Sh. E. Prabagaran National Institute for Research in Reproductive Health Mumbai

Ms. Monali Shashikant Wakle National Institute for Research in Reproductive Health Mumbai

Dr. Amol Ratnakar Suryawanshi National Institute for Research in Reproductive Health Mumbai

Mr. Abid Shadaan National Institute for Research in Reproductive Health Mumbai 75. Gene reguation of endometrial apoptosis

76. Studies on molecular mechanism of aggregation of amyloid beta peptide (1-40) and its modulation by amino acid stereo specificity and dietary components (garlic), relevance to Alzheimer's disease

- 77. Diabetes associated male reproductive dysfunction : role of oxidative stress and its nutritional amelioration
- Studies on nutritional and immunomodulatory effects of omega-3 and omega-6 rich oils in animal models
- 79. Xenobiotic-induced biochemical perturbations in pancreas and their interactive role in the onset of diabetes: development of dietary amelioration strategies
- 80. Studies on influence of raw and heat processed garlic and onion on bile metabolism
- 81. Studies on the bioavailability of micronutrients from selected Indian foods
- 82. Studies on the beneficial influence of spices on gastrointestinal system
- 83. Aspergillus carbonarius strain improvement and process development for the production of xanthophyll
- 84. Secretion of progesterone and expression of hypoxia inducible factor-1 alpha during hypoxia induced by cobalt chloride in MA-10 cells
- 85. Role of hypoxia on progesterone and vascular endothelial growth factor secretions in tumor leyding MA-10 cell

Smt. Mathura Yatin Narkar National Institute for Research in Reproductive Health Mumbai

Ms. Veer Bala Gupta Central Food Technological Research Institute Mysore

Ms. Shrilatha Balakrishnan Central Food Technological Research Institute Mysore

Sh. B.T. Diwakar Central Food Technological Research Institute Mysore

Sh. G. Vasudeva Kamath Central Food Technological Research Institute Mysore

Sh. S.K. Vidyashankar Central Food Technological Research Institute Mysore

Smt. S. Hemalatha Central Food Technological Research Institute Mysore

Ms. N.S. Usha Prakash Central Food Technological Research Institute Mysore

Sh. K.R. Sanjay Central Food Technological Research Institute Mysore

Dr. Bidut Prava Mohanty All India Institute of Medical Sciences New Delhi

Ms. Garima All India Institute of Medical Sciences New Delhi

- 86. Determination of the efficacy of reflexology therapy in the management of mastalgia and nodularity of the female breast by estimating the physio-chemical parameters
- 87. Some epidemiological studies on unwanted pregnancy
- An investigation on chromosome mosaicism and aneuploidy on early embryos through preimplantation genetic diagnosis
- Efficacy and safety of tranaexamic acid for dysfunctional uterine bleeding and its comparison with cyclical progesterone therapy
- 90. Comparison of diane 35 plus finasteride combination with diane 35 plus spironolactone in the treatment of hirsutism
- 91. Mitochondrial genome and Y chromosome analysis in male infertility
- 92. Active management of the third stage of labour at cesarean sections: a randomised comparison of sublingual misoprostol with syntocinon
- 93. Regulation of granulosa cell steroidogenesis by a novel secretory protein of *Mycobacterium tuberculosis*, its mechanism of action and possible role in modulating ovarian function in patients of extra-genital tuberculosis
- 94. Role of uterine artery embolisation in management of symptomatic uterine fibroids
- 95. Study of hepatic enzymes in neonates with perinatal asphyxia
- 96. Clinical predictors of mortality in neonates requiring mechanical ventilation
- 97. GnRH agonists and antagonists in assisted reproductive techniques

Ms. Charulata Jindal All India Institute of Medical Sciences New Delhi

Ms. Shahina Begum All India Institute of Medical Sciences New Delhi

Sh. Ashish Kumar Fauzdar All India Institute of Medical Sciences New Delhi

Dr. Vidushi Kulshreshtha All India Institute of Medical Sciences New Delhi

Dr. Sumitra Das All India Institute of Medical Sciences New Delhi

Mr. Rakesh Kumar All India Institute of Medical Sciences New Delhi

Dr. Vimalamma Nellore All India Institute of Medical Sciences New Delhi

Dr. Nishat Ahmad All India Institute of Medical Sciences New Delhi

Dr. Kanupriya Army Hospital (Research & Referral) New Delhi

Dr. Naveen Rana Army Hospital (Research & Referral) New Delhi

Dr. Rahul Yadav Army Hospital (Research & Referral) New Delhi

Dr. Ratna Vasishta Army Hospital (Research & Referral) New Delhi

- 98. Incidence and prevalence of candidiasis lichen planus and leukoplakia in diabetes
- 99. Incidence and severity of periodontal disease in diabetes
- 100. Infant feeding practices with special reference to exclusive breastfeeding for first six months an intervention study
- 101. Development of card based kit for rapid detection of aflatoxin in food stuff
- 102. Analysis of mutation in sry gene and chromosomal anomalies in infertile patients and its clinical importance
- 103. Development of counseling module for mutritional, lifestyle and psychosocial management of patients with type 1 diabetes
- 104. DNA and liver vector based immunocontraceptive vaccine
- 105. A study to evaluate deficits of FSH & testosterone signal transductions in the Sertoli cells of infant rats in the phase of adequate hormones for determining causes of some forms of idiopathic male infertility
- 106. Evaluation of the effects of various intervention strategies to counteract damages induced in the testis due to cryptorchidism: studies in rats
- 107. Androgen and estrogen receptor expression in male rats during transition from repubertal to adulthood : modulation following hormonal intervention
- 108. Characterization of an antimicrobial compound from a lactic acid bacterium for application in food safety

Dr. Vivek Tyagi Deen Dayal Upadhyay Hospital New Delhi

Dr. Kavita Jhigan Deen Dayal Upadhyay Hospital New Delhi

Ms. Vandana Sabharwal Institute of Home Economics New Delhi

Sh. Faraz Rashid Jamia Hamdard (Hamdard University) New Delhi

Sh. Mohammad Shahid Jamia Milia Islamia New Delhi

Ms. Sonia Kakar Lady Irwin College New Delhi

Dr. Sangeeta Choudhury National Institute of Immunology New Delhi

Dr. Jibanananda Mishra National Institute of Immunology New Delhi

Sh. Mukesh Kumar National Institute of Health and Family Welfare New Delhi

Mr. Mahesh Kaushik National Institute of Health and Familiy Welfare New Delhi

Sh. Santosh Kumar Tiwari University of Delhi South Campus New Delhi

- 109. Estimation of serum magnesium in normal pregnancy as a predictor of gestational hypertension
- 110. Investigating activation of NAD(P)H oxidase and characterization of its components in the implanting embryos
- 111. Identification of potential interacting partners of transcription factor state during embryo implantation
- 112. Characterization of NOX-5 in mouse spermatozoa and its assembly with photoregulatory elements
- 113. Dietary antioxidants in habitual foods of different population groups and the prevalence of coronary heart disease risk factors
- 114. Glycaemic response to selected pulse based products
- 115. Effect of nutrition and lifestyle intervention programme on atherogenic profile of patients and increased risk of cardiovascular disease
- 116. *In vitro* studies of the embryos of *Scotophilus heathi* and *Cynopterus sphinx*
- 117. Effect of some medicinal plants with anti-diabetic potential on male reproductive health and pregnancy outcome

Non-communicable Diseases

- 118. To delineate biochemical changes due to oxidative stress induced cataract formation : *In vitro* and *in vitro* study
- 119. Chlorpyrifos toxicokinetics in acute poisoning cases
- 120. Electromyographic and biomechanical analysis of VDU operators in relation to postdural stress and musculoskeletal discomfort

Smt. Usha Kumari Patna Medical College and Hospital Patna

Sh. Rajesh Kumar Jha Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram

Ms. Shiny Titus Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram

Dr. Sunita Agnihotri Rajiv Gandhi Centre for Biotechnology

Dr. K. Kodanda Reddy Sri Venkateswara University Tirupati

Ms. Shalini Sharma Government Meera Girls' College Udaipur

Ms. Ankur Singh Government Meera Girls' College Udaipur

Ms. Anjana Tiwari Banaras Hindu University Varanasi

Ms. Akanksha Singh Banaras Hindu University Varanasi

Sh. Dearshi Urvish Gajjar Illadevi Cataract and IOL Research Centre Ahmedabad

Sh. Ramavati Ramsevak Pal National Institute of Occupational Health Ahmedabad

Ms. Era Poddar National Institute of Occupational Health Ahmedabad

- 121. Role of environmental chemicals in human male reproductive system
- 122. Carcinoma of the breast: evaluation of risk factors and biomarkers
- 123. Combination chemoprevention of hamster buccal pouch carcinogensis by bovine milk lactoferrin and tea polyphenols
- 124. Effect of melatonin and α-ketoglutarate on biochemical circadian rhythms (*in vivo* and *in vitro*) in hepatocellular carcinoma
- 125. A study of serum her-2/neu expression in carcinoma breast along with other prognostic factors like CEA, CA 15-3 and tissue telomerase activity
- 126. Homocystein metabolism: a study in cerebral venous thrombosis
- 127. A hospital based study on progressive and regressive changes in oral precancerous lesions
- 128. Role of zinc and selenium in arsenic toxicity: an experimental and environmental study
- 129. Studies on biochemical mechanisms of carbofuran neurotoxicity
- 130. Influence of loss of heterozygosity of the Wilm's tumour suppressor gene (wt1) on expression of IGF-2, IGF-1, IGF-beta 1 and angiogenic factors in DCIS and infitrating breast carcinoma
- 131. Effect of polychlorinated biphenyal (Aroclor 1254) on Leydig cell steroidogenesis and beneficial effects of vitamin supplementation
- 132. Activation of WNT signal transduction target genes, cylin D1 and CD44 and its role in *Helicoter pylori* induced gastric neoplasia

Sh. Minal Devendra Mankad National Institute of Occupational Health Ahmedabad

Sh. R.Kumuraguruparan Annamalai University Annamalai Nagar

Sh. K.V.P. Chandra Mohan Annamalai University Annamalai Nagar

Sh. Kadiyala Babu Dakshayani Annamalai University Annamalai Nagar

Sh. Thrivenik Bhat Kidwai Memorial Institute of Oncology Bangalore

Sh. Pinnelli Venkata Bharat Kumar National Institute of Mental Health and Neurosciences Bangalore

Dr. Binti A Jhuraney National Tuberculosis Institute Bangalore

Sh. Ashok Kumar Panjab University Chandigarh

Sh. Amit Kamboj Panjab University Chandigarh

Sh. Sachin Gupta Postgraduate Institute of Medical Education and Research Chandigarh

Sh. Murugesan Palaniappan Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai

Sh. Udhaya Kumar Gopal University of Madras Chennai

- 133. Effect of histone h1 on cell mediated immune response in experimental breast cancer
- 134. A randomised double controlled comparative study of continuous paravertebral block and continuous epidural analgesia for post operative pain relief in hip surgeries
- 135. To identify predictors of relapse in alcohol dependence syndrome in relation to life events
- 136. Clinical study of operative conditions and hemodynamic response in cholecystectomy in general anaesthesia *versus* combined spinal epidural anaesthesia technique
- 137. Role of emotional intelligence in psychosocial problems and coping strategies among the children and spouses of alcoholism patients
- 138. Pesticide induced oxidative stress and immunotoxicity : mode of attentuation by certain drugs
- 139. Role of free radicals in functional changes in vascular responsiveness on mercury exposure in rabbits
- 140. Study of quenosine modification in tRNA during tumor growth in mice
- 141. Studies on oxidative DNA damage induced by organophosphate pesticides, chlorpyrifos and parathion in rats and search of a suitable biomarker
- 142. A study of some genetic risk factors in premature cardiovascular disease
- 143. Anti-angiogenic role of T11TS/SLFA-3 in brain tumor abrogation
- 144. Oxidative injury in cerebral diseases

Ms. Ganapati Vani University of Madras Chennai

Dr. Pankaj N. Surange Base Hospital Delhi

Dr. Shubhra Base Hospital Delhi

Dr. Pallavi Kwatra Hindu Rao Hospital Delhi

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Smt. Chandra Banerjee Dr. B.C. Roy Postgraduate Institute of Basic Medical Sciences Kolkata

Dr. Sibani Sarkar Indian Institute of Chemical Biology Kolkata

145. Chromosomal aberrations and sister chromatid exchanges in the symptomatic individuals exposed to arsenic through drinking water in West Bengal
146. Assessment of oxidative stress on male reproductive

function after chronic arsenic exposure

- 147. Study of the effect of antiulcer active principle isolated from *Neem bark* extract on gastric mucosal apoptosis induced by indomethacin and reactive oxygen intermediate
- 148. To investigate the role of nitric oxide, apoptosis and mitochondria in the experimental models of Parkinson's disease
- 149. Studies on the effect of dapsone on aflatoxin B1-initiated hepatocarcinogenesis and its modulation
- 150. Cellular and molecular mechanisms of heat shock proteins in isochemical reperfusion injury
- 151. Environmental monitoring and occupational health status of workers in asbestos-cement based industries : an epidemiological and cytogenetic approach
- 152. Isolation, characterization and applicability of bacterial strains from earthworm gut in endosulfan metabolism
- 153. Neuro-genotoxicity assessment of co exposure of lead and ethanol: an *in vitro* study
- 154. Imprinting of cerebral and hepatic cytochrome P450s (CYPS) in rat offsprings following prenatal expsure of indane
- 155. Flow cytometric and cytogenetic analysis of cancer cervix
- 156. Cancer chemopreventive properties of resveratrol : a mechanistic approach

Ms. Julie Mahata Indian Institute of Chemical Biology Kolkata

Smt. Subarna Roy Gupta Regional Occupational Health Centre (Eastern) Kolkata

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Ms. Seema Kumari Central Drug Research Institute Lucknow

Ms. Namrata Manhas Central Drug Research Institute Lucknow

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Smt. Kiran Verma Industrial Toxicology Research Centre Lucknow

Ms. Santosh Yadav Industrial Toxicology Research Centre Lucknow

Sh. Ashu Johri Industrial Toxicology Research Centre Lucknow

Dr. Madhulika Singh Industrial Toxicology Research Centre Lucknow

Ms. Neetu Kalra Industrial Toxicology Research Centre Lucknow

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- 157. A study on modulation of proinflammatory cytokines and anti-oxidative profile in experimental arthirtis by *Nyctanthes arbor* tirstis
- 158. Genetic association studies for susceptibility to gallstone disease
- 159. A pilot study to assess the popularity, effectiveness and adverse effects of various complementary and alternative medicines (CAN) tried by patients with advanced gastrointestinal tract malignancy in northern India
- 160. Genetic polymorphism in patients with calcium oxalate urolithiasis
- 161. Laser spectroscopic and biochemical investigations on clinical samples in cancer of human uterine cervix
- 162. A comparative evaluation of gingival crevicular blood glucose levels and periodontal status in office screening test
- 163. Study of patho-physiology of simple writer's cramp using neuro-physiological methods
- 164. Role of acyclovir prednisolone combination in treatment for Bell's palsy
- 165. Role of transforaminal epidurography in diagnosis and management of failed back surgery syndrome
- 166. An analytical penspective of missing data analysis in clinical trial of thyroid cancer
- 167. A study of risk factors for cancer of the pancreas
- 168. Genetic and metabolic investigations in obstructive sleep apnea syndrome

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Ms. Charulata Jindal K.G's Medical University Lucknow

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Sh. Hemant Kumar Bid Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow

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Dr. Mamta Khandelwal All India Institute of Medical Sciences New Delhi

Sh. Prem Chandra All India Institute of Medical Sciences New Delhi

Dr. Shallu All India Institute of Medical Sciences New Delhi

Sh. Bharat Bhushan All India Institute of Medical Sciences New Delhi

- 169. Assessment of alcohol and tobacco abuse in adolescent children in government schools in the National Capital Territory of Delhi
- 170. c667t and a 1298c mutations in methylene tetra hydrofolate reductase gene in patients with myocardial infarction in comparison with healthy controls
- 171. Effect of antioxidant supplementation on pain, antioxidant profile and oxidative stress in chronic pancreatitis
- 172. Study of clinico-pathological and immune profile of patients of chronic invasive fungal sinusitis
- 173. Response of glioblastoma cell lines to chemotherapeutic agents, with reference to molecular indicators of genomic instability in normoxic and hypoxic condition
- 174. A study of the expression of II-13 and II-4 receptors in primary meningeal tumors
- 175. Sentinal node staging of early breast cancer (TNM-stage-T 1&2, NO) using lymphoscintigraphy and gamma detecting probe
- 176. p-glycoprotein expression in relation to 99m technetium tetrofosmin mammoscintigraphy in patients with breast cancer and assessment of torfemifene as a modulator of multidrug resistance in patients with breast cancer
- 177. Comparison of the changes in foveal avascular zone before and after 532nm ND-YAG macular grid laser photocoagulation in cases of clinically significant macular edema
- 178. Prospective randomized controlled clinical trial comparing the outcomes of preoperative biliary decomposition versus surgery alone in malignant obstructive jaundice with serum bilirubin level of > 10mg%
- 179. A comparative study of restanosis rate in bare metal and drug eluting stents

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Dr. Mukta Sharma All India Institute of Medical Sciences New Delhi

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Dr. Aditya Verma Army Hospital (Research & Referral) New Delhi

Dr. Manish Nanda Army Hospital (Research & Referral) New Delhi

Dr. Shilpi Mohan Army Hospital (Research & Referral) New Delhi

- 180. Comparative study of clinical profile in cancer breast in premenopausal and post menopausal age groups and of respones and efficacy of various treatment regimens in ERPR negative groups in terms of 5 years survival
- 181. Carcinomia oesophagus : results of multimodality treatments
- 182. Clinicopathological presentation management and survival pattern in carcinoma gall bladder
- 183. A study of the plasma hemocysteine levels and methyline tetra hydrofolate reductase (MTHFR) c677T polymorphism as a risk factors in coronary artery diseases in Indians
- Assessment of the protocol for evaluation of patients with bilateral profound sensorineural hearing loss
- 185. To evaluate and compare the efficacy between laryngeal mask airway-classic, laryngeal mask airway-proseal and the endotracheal tube in patients undergoing diagnostic gynaecologic laproscopic surgery
- 186. Pretreatment with thiopental : prevention of pain associated with propofol injection
- 187. A comparative study of click evoked otoacoustic emmisions and distortion product otoacoustic as a screening tool for noise induced hearing loss
- 188. Prospective long term assessment of cochlear implantation in pre lingually deaf children done in army hospital (R&R) in terms of threshold (T) and maximum comfort (C) levels and speech perception developments
- 189. Evaluation of intraoperative acute normvolemic hemodilution (ANH) in open heart surgeries
- 190. Study of efficacy of CO2 laser surgery in the management of oral-pharyngeal and laryngeal lesions

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Dr. V. Natesh Army Hospital (Research & Referral) New Delhi

Dr. Tasskin Rehman Hazarika Army Hospital (Research & Referral) New Delhi

Dr. Nirupam Awasthi Army Hospital (Research & Referral) New Delhi

- 191. Comparative evaluation of conjunctival autograft versus limbal graft in the surgery of primary pterygium
- 192. Evaluation of endoscopic sinus surgery with and without partial middle turbinate resection in patients of chronic sinusitis
- 193. Study of candidate genes associated with breast cancer susceptibility
- 194. Studies on the regulatory role of hyaluronan binding protein-1 (HABP-1) on cell migration and its downstream signalling
- 195. Radiomodulation by bibenzimidazole
- 196. Indicators of psychopathology on the Rorschach ink blot test : a normative study on the Indian population
- 197. Evaluation of single stage ossicular chain reconstruction in patients operated for chronic suppurative otitis media
- 198. To study the role of mitomycin C in preventing adhesion formation following endoscopic sinus surgery
- 199. Evaluation of results of obliterating mastoid cavity using vascularized temporalis myofascial flap with open cavity mastoid operations
- 200. Pharmacogenomics of selected genes in upper serodigestive tract cancers in a South Indian population
- 201. Studies on the molecular mechanism of osteopontin regulated pormatrix metalloproteinase-9 activation and tumor growth
- 202. Germline mutation analysis of BRCA2 gene in hereditary breast ovarian cancer families in Kerala

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Ms. Hema Rangaswami National Centre for Cell Sciences Pune

Ms. S. Vani Regional Cancer Centre Thiruvananthapuram

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- 203. Role of xenobiotic metabolizing gene polymorphism in lung cancer susceptibility
- 204. Role of curcumin on the regulation of telomerase activity in lymphoma/leukemia cells
- 205. Retinoid metabolism during devlopment of liver cirrhosis

Basic Medical Sciences

- 206. Genomic diversity in leprosy bacillus
- 207. Hepatoprotective effect of andrographolide on liver cancer
- 208. Chemical investigation, extraction, standardization and pharmacological analysis of three medicinal plants *i.e. Diospyros montana, Ficus lyrata* and *Xylosma longifolium*
- 209. Allele specific sequencing of human mu opiate receptor: genetic correlation with opiate use and abuse
- 210. Studies on the isolation and mechanism of action of hypoglycemic compound(s) from *Murraya koengii*
- 211. Comparative effects of fenugreek (*Trigonella foenum graecum*) seed polyphenols and (-) epigallocatechin gallate (EGCG) on ethanol-induced liver damage in rats
- Evaluation of chemopreventive potential of *Jasminum grandiflorum* linn. (*jathi malli*) in 7, 12-dimethylbenz (a) anthracene induced mammary carcinogenesis
- 213. Studies on bioavailability enhancement of albendazole by solid dispersion and cyclodextrin-complexation techniques for the effective treatment of parenteral stages of human and veterinary helminthiases

Ms. L. Sreeja Regional Cancer Centre Thiruvananthapuram

Sh. Vijendra Kumar Mishra Banaras Hindu University Varanasi

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Sh. Achyut Narayan Kesari Allahabad Agricultural Institute Allahabad

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Sh. K. Kolanjiappan Annamalai University Annamalai Nagar

Sh. R. Kalaiselvan Annamalai University Annamalai Nagar

- 214. Evaluation of the chemopreventive efficacy of ethanolic *neem* leaf extract and its constituents on experimental gastric carcinogenesis in Wistar rats
- 215. Modulatory effect of piperine on lipid metabolism in hypercholesterolemic rats
- 216. Biochemical and physiological effects of exogenous recombinant leptin on hepatic fibrogenesis induced by chronic alcohol supplementation
- 217. Antidiabetic and antioxidant effect of pterostilbene on streptozotocin induced diabetic rats
- 218. Effect of naringin on isoproterenol induced myocardial infarction in rats
- 219. Effect of ursolic acid on chronic-ethanol induced toxicity in rats
- 220. Effect of umbelliferone (7-hydroxycoumarin) on glycaemic control in normal and streptozotocininduced diabetic rats
- 221. Isolation and characterization of active principle from *Caseaaria esculenta* (roxb.) root and its effect on glycaemic control in normal and streptozotocin induced diabetic rats
- 222. Screening of some halophytes and mangroves for antimicrobial activity
- 223. Neuro and psychopharmacological studies of *Enhydrina schistosa* venom, its photooxidised venom product and screening of herbal drugs for antivenom property
- 224. Evaluation of ginsenosides andrographolide and POVRVP for their beneficial effects in diabetic related complications using diabetogenic and hyperinsulinemic animal models
- 225. Formulation and evaluation of microspheres of ketoprofen and ketorolac tromethamine for controlled release

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Sh. Anil Kumar M. Dandu Al-Ameen College of Pharmacy Bangalore

Sh. Sam Thomarayiet Mathew Al-Ameen College of Pharmacy Bangalore

- 226. Oral delivery of cyclosporin G, an immunosuppressive peptide by entrapment as liposomes and nanoparticles
- 227. Formulation and clinical evaluation of ultradeformable liposomes in the treatment of psoriasis
- 229. Molecular modulation of hyperlipidemia induced oxidative stress and LDL receptor expression by *Dunaliella salina* derived beta-carotene
- 230. Studies on lactase expression and glycosylation in developing rat intestine
- 231. Studies on comparative phytochemistry and toxicological effects of different varieties of *Lantana camara* var. *aculeate* feeding to guinea pigs
- 232. Role of neurofilament phosphorylation in chronic aluminium neurotoxicity in rat
- 233. Role of CREB phosphorylation and muscarinic signal transduction in dichlorvas induced memory deficits
- 234. Neuroprotective effect of *Bacopa monniera* extract on ischemia-reperfusion induced brain injury
- 235. Detection of most common mutation (his 1069g 1n) in Wilson disease by PCR based RFLP technique: correlation between lymphocyte cuatpase activity and their phenotypes
- 236. Effect of garlic and carotenoids on oxidative stress due to isoniazid and rifampicin in rat liver
- 237. To evaluate the expression of perforin, granzyme B and fas ligand in the peripheral blood as a non-invasive diagnostic tool for acute renal allograft rejection

Smt. K.V. Sandhya Al-Ameen College of Pharmacy Bangalore

Ms. Vanaja Kenchappa Al-Ameen College of Pharmacy Bangalore

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Sh. Sandeep Kumar Postgraduate Institute of Medical Education and Research Chandigarh

Sh. Ravinder Pal Postgraduate Institute of Medical Education and Research Chandigarh

Ms. Shiwali Karnal Postgraduate Institute of Medical Education and Research Chandigarh

- 238. Utilization of plant derived antioxidants for designing safer NSAIDS prodrugs of diclofenac
- 239. Design and development of lantadenes as antitumor agent
- 240. Design and development of prodrugs of tea polyphenols as potential anticancer agents
- 241. Cytotoxic effect of polychlorinated hydrocarbons (PCHS)-perchloroethylene and the protective potential of *Terminalia chebula* retz., (botanical) with reference to tocopherol
- 242. Development of peptide (GHK) incorporated collagenous material for the treatment of wound healing process
- 243. Peptide vaccine against a beta protofibrils for Alzheimer's disease (AD)
- 244. A study towards molecular screening in women with PCOD from Chennai base population -Estimation of ob protein (serum leptin), ob mRNA expression in obese subjects
- 245. Modulatory role of *Centella asiatica* on age related alterations in neurotransmitter levels and apoptosis in rat brain
- 246. Modulatory role of *Centella asiatica* on age related alterations in neurotransmitter levels and apoptosis in rat brain
- 247. Therapeutic intervention of I-carnitine and dl alpha lipoic acid on aggregation of amyloid beta protein and associated pathogenesis during aging with special reference to Alzheimer's disease

Ms. Benu Manon University Institute of Pharmaceutical Sciences Chandigarh

Sh. Manu Sharma University Institute of Pharmaceutical Sciences Chandigarh

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Ms. M. Anusuya Devi Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai

- 248. Contribution of connexin 26 mutations in childhood deafness of Indian population
- 249. Therapeutic efficacy of propolis along with paclitaxel against 7, 12 dimethyl benz (a) anthracene induced experimental breast cancer in female
- 250. Chemopreventive and therapeutic effect of soybean isoflavone genistein in human hepatocellular carcinoma cell culture and in experimental hepatocellular carcinoma
- 251. Effect of *Ocimum sanctum* on noise induced alterations in brain free radical scavenging enzymes and neurotransmitters
- 252. Impact of *Terminalia arjuna* linn on proliferation, differentiation and mineralization of rat bone marrow stem cells and human osteoblast like cells
- 253. A study on the imbalance between the expression and activity of inducible and endothelial nitric oxide synthases (NOS) under oxalate stress condition and its potential impact on the expression of tamm horsfall
- 254. Evaluation of cytoprotective efficacy of pentacyclic triterpene and its ester against cyclophosphamide induced cardiotoxicity
- 255. Evaluation of chemopreventive potential of two medicinal plants in 1,2-dimethyl hydrazein induced colon carcinogenesis in male albino rats
- 256. Evaluation of antidiabetic activity of *Abelmoschus esculentus* and *Marsilea quadrifolia* in streptozotocin induced diabetic male Wistar rats

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Sh. Arul Albert Basker Entomology Research Institute Chennai

Sh. Subash Babu Pandurangan Entomology Research Institute Chennai
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- 257. Construction of a novel shuttle vector system for enhanced expression of Mycobacterium tuberculosis antigens
- 258. Design and development of iron (iii) hexacyanoferrate Sh. S.M. Senthil Kumar based amperometric sensor electrode for estimation of reduced glutathione in clinical samples
- 259. Efficacy of Centella asiatica as a free radical scavenger and on the fate of heat shock protein during adriamycin induced myocardial injury
- 260. Molecular mechanism of action of Holarrhena antidysenterica against enteropathogenic Eschrichia coli
- 261. Antiulcer activity of Pterocarpus santalinus (red sandal wood) on experimental gastric ulcer-an in vivo and in vitro study
- 262. Gastroprotective effect of Terminalia arjuna on gastric ulcer-an experimental study
- 263. To study the role of molgramostim {granulocyte macrophage colony stimulating factor (GM-CSF)} in enhancing the seroconversion post hepatitis-B vaccination in cases of leukemias and lymphomas in pediatric age
- 264. Evaluation of neuroprotective role of Hypericum perforatum extract in global cerebral ischemia in mice
- 265. Biochemical studies on the antidiabetic effect and mechanism of action of Terminalia chebula in experimental animals
- 266. A search for some new anti-tumor drugs based upon the natural alkaloid-noscapine
- 267. Synthesis and characterization of antisense oligonucleotides for gene targeted anticancer therapy

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Ms. Neerupma Dhiman Dr. B.R. Ambedkar Centre for **Biomedical Research** University of Delhi Delhi

Sh. Atul Pathak Institute of Genomics and Integrative Biology Delhi

- 268. Detailed studies on mechanism of action of the hypoglycemic compounds obtained from the bark of *Ficus bengalensis*
- 269. Biochemical and biophysical investigations of structural polymorphisms in β2-adrenergic receptor
- 270. Evaluation of the mechanism of action of aspirin as a cardioprotective agent in experimentallyinduced hypercholesterolemic rats
- 271. Remote preconditioning-protects the myocardium from reperfusion injury
- 272. Studies on the role of acetoxy drug, protein transacetylase of human placenta in the modifications in the development of therapeutic agents against hormone sensitive cancers
- 273. Role of oxidative stress in the induction of bronchial hyper responsiveness and its modulation by dietary antioxidant vitamin C and E in guinea pigs
- 274. Therapeutic effectiveness of propolis extract and its active principle against carbon tetrachloride induced liver damage in rats
- 275. Therapeutic effectiveness of propolis extract and its active principle against carbon tetrachioride induced liver damage in rats
- 276. Role of nutritional supplements along with chelating agents against aluminium induced toxicity : *in vitro* and *in vivo* approach
- 277. Psychopharmacological investigations on the benefits of Indian systems of medicine in the modulation of mental dysfunctions
- 278. Role of calcium and calpain (calcium-activated cysteine protease) in Duchenne muscular dystrophic cell death: an insight into apoptosis
- 279. An evaluation of genetic and molecular factors contributing to premature ovarian failure in Indian population

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Dr. Sadhana Shrivastava Jiwaji University Gwalior

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Sh. G. Jaya Prakash Institute of Genetics and Hospital for Genetic Diseases Hyderabad ICMR ANNUAL REPORT 2005-2006

280.	Epidemiology and genetics of dilated cardiomyopathy	Ms. Boda Ushashree Institute of Genetics and Hospital for Genetic Diseases Hyderabad
281.	Studies on activation of neutrophils by galectin-1	Sh. R.K. Gupta Devi Ahilya Vishwavidyalaya Indore
282.	Functional characterization of human serum lectins	Sh. Krishna Chaitanya Gulla Devi Ahilya Vishwavidyalaya Indore
283.	Investigation on some Indian medicinal plants for anti-fibrotic activity	Sh. T.A. Sheikh Regional Research Laboratory (CSIR) Jammu Tawi
284.	Investigations on anti-allergic / anti-asthmatic activity of <i>Allium cepa</i>	Ms. Kesar Jehan Peerzada Regional Research Laboratory (CSIR) Jammu Tawi
285.	Studies on a human placental bioactive sphingolipid mediated signal transduction in order to establish its role on the pigment recovery in vitiligo	Sh. Suman Kumar Singh Indian Institute of Chemical Biology Kolkata
286.	Purification and characterisation of toxins from Russel's viper venom of Eastern Indian origin	Ms. Gargi Malty Indian Institute of Chemical Biology Kolkata
287.	Study of health status and health maintenance among communities of Cachar district, Assam: comparison between eco-zones	Smt. Sujata Kar Indian Statistical Institute Kolkata
288.	Molecular basis of inhibition of experimental hepatocarcinogenesis by <i>Frianthema portulacastrum</i> linn	Ms. Mitali Basu Jadavpur University Kolkata
289.	A new approach against cancer through chemoimmunotherapy	Sh. Shovanlal Gayen Jadavpur University Kolkata
290.	Study of the potential of antisense insulin-like growth factor (IGF2) phosphorothioate oligomers as a future drug for liver cancer	Smt. Sharma Ghosh Jadavpur University Kolkata
291.	Screening, characterization and production of novel antibiotics from marine actinomycetes isolated from the deltaic Sundarbans	Sh. Malay Saha Jadavpur University Kolkata

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- 292. Production and purification of clinically important enzymes and enzyme inhibitors produced by marine microorganisms of the deltaic Sundarbans
- 293. Exploring herbal antioxidant formulations from Indian system of medicine
- 294. Studies on the biochemical effects of food additive (erythrosine B) in relation to brain serotonergic system and immune response
- 295. Study of acute leukemia
- 296. Structural and functional evaluation of cardioactive factor(s) Cobra (*Ophiophagus hannah*) venom
- 297. Development of adaptogenic and immunomodulatory agents from Indian medicinal plant *Tinospora sinensis* and *Evolvulus alsinoides*
- 298. Oral delivery of peptides with improved bioavailability
- 299. A study on the role of cyclooxygenase-2 in healing of gastric ulcer in rodents
- 300. Molecular and celluar mechanisms of neuroprotective effect of neurotrophins following cerebral ischaemia/reperfusion injury
- 301. Proteome analysis and characterization of cell-wall antigens of *Aspergillus fumigatus* and monoclonal antibodies production for their role as immunotherapeutics
- 302. Testing teratogenicity by rat whole embryo culture
- 303. Evaluation of novel therapeutic molecules against latent tuberculosis

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Sh. Ashok Kumar Chaturvedi Central Drug Research Institute Lucknow

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304. Current approaches towards nephrotoxicity testing : an analysis Lucknow 305. Study of angiogenic effects of 1-lysine mono hydrochloride and neurotrophic factors in middle cerebral artery occlusion rat model of stroke Lucknow 306. Frequency of angiotensin converting enzyme (ACE) gene insertion deletion (i/d) polymorphism and methylene tetrahydrofolate reductase (MTHFR) gene mutation in insulin dependent (ID) and Lucknow non-insulin dependent (NID) 307. Molecular characterization of the Wison's disease Lucknow 308. Characterization, maintenance and expansion of human corneal epithelial stem cells Lucknow 309. The evaluation of the chemopreventive, chemoprotective and radioprotective properties of naringin in mice Manipal 310. Evaluation of the chemoprotective and radioprotective properties of Aegle marmelos (Bael) in vivo and in vitro Manipal 311. Evaluation of wound healing properties of hesperidin in the artificially wounded mouse exposed to gamma radiation Manipal 312. Design and evaluation of novel drug delivery systems of anti-malarial drugs Mumbai 313. Pharmacological evaluation of indigenous plants for antiallergic and antiasthmatic activity Mumbai 314. Investigation of purinergic neurotransmission in smooth muscle : effect of ATPase inhibition on synaptic potentials in the mammalian vas Mumbai deferens 315. Genetic factors contributing to osteoporosis : study of polymorphism in human vitamin D and estrogen receptor genes

Ms. Diva Shukla Central Drug Research Institute Lucknow

Dr. G.M. Merlin Margaret Industrial Toxicology Research Centre Lucknow

Ms. Priti Ojha Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow

Ms. Monika Vishnol Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow

Ms. Monika Vishnoi Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow

Sh. T. Koti Reddy Kasturba Medical College and Hospital Manipal

Sh. Ponemone Venkatesh Kasturba Medical College and Hospital Manipal

Sh. K.V.N. Malikarjuna Rao Kasturba Medical College and Hospital Manipal

Sh. N.K. Tayade Bombay College of Pharmacy Mumbai

Sh. P. Suresh Kumar Bombay College of Pharmacy Mumbai

Ms. Parakashtha Ghildyal Indian Institute of Technology Mumbai

Ms. Sumegha Mitra National Institute for Research in Reproductive Health Mumbai

- 316. Molecular role of steroid acute regulatory (STAR) gene in steroidogenesis
- 317. Screening for novel antioxidant bioactives from endophytes of medicinal plants
- 318. Molecular mechanism-based screening for putative antiangiogenic compounds from medicinal plants : role in development of anticancer drugs
- 319. Turmerin an 'on the spot' antioxidant antidote for Snake bite
- 320. Role of p53 on human cathepsin-I expression
- 321. Regulation of human cathepsin expression by multiple mRNA species
- 322. Role of ENOS gene polymorphism in coronary artery disease in the Indian subjects
- 323. Evaluation of drugs with antioxidant property in *in vitro* and in middle cerebral artery occlusion model of acute ischemic stroke in rats
- 324. The interrelationship between sleep-wakefulness and body temperature role of medical preoptic area
- 325. Studies on immunoexpression of anti-apoptotic and transcription marker molecules in ovariectomized rat hippocampus
- 326. Biochemical studies on regulation of c-myc promoter by targeting triple helix forming oligonucleotides
- 327. Physico-chemical characterization of *Plasmodium vivax* heat shock metalloprotease
- 328. Genetic polymorphisms and expression of MTHFR & RFC-1 genes in coronary artery disease

Ms. Heena U Shirwalkar National Institute for Research in Reproductive Health Mumbai

Sh. M.V. Tejesvi University of Mysore Mysore

Sh. G. Thippesvamy University of Mysore Mysore

Sh. M. Chetan Kumar Adichunchangiri Cancer Research Centre Nagamangala

Sh. Rahul Katara All India Institute of Medical Sciences New Delhi

Ms. Shivani Mittal All India Institute of Medical Sciences New Delhi

Dr. Kamna Srivastava All India Institute of Medical Sciences New Delhi

Ms. Seema Briyal All India Institute of Medical Sciences New Delhi

Sh. R.A. Vetrivelan All India Institute of Medical Sciences New Delhi

Sh. Kanhaiya Sharma All India Institute of Medical Sciences New Delhi

Ms. Akanchha All India Institute of Medical Sciences New Delhi

Sh. Asim Anees Siddiqui All India Institute of Medical Sciences New Delhi

Md. Afaque Alam All India Institute of Medical Sciences New Delhi

329.	Outcome of HBsAg positive renal transplant recipients	Dr. Durga Shankar Army Hospital (Research & Referral) New Delhi
330.	To study the role of human recombinant erythropoietin in reducing blood transfusions in very low birth weight infants	Dr. Madasu Anjan Army Hospital (Research & Referral) New Delhi
331.	Monoclonal antibodies to <i>Chlamydia trachomatis</i> : characterization, specificity, sensitivity and reactivity of desired clones in clinical samples	Sh. Amit Kumar Institute of Pathology New Delhi
332.	Cell culture contamination with mycoplasma in basic and applied biomedical research	Sh. Ashok Kumar Institute of Pathology New Delhi
333.	Biochemical studies on aflatoxin induced oxidative stress using mice as animal model	Ms. Farah Naaz Jamia Hamdard (Hamdard University) New Delhi
334.	Solid lipid nanoparticles as surrogate carrier for bioactive agents	Ms. Deepti Pandita Jamia Hamdard (Hamdard University) New Delhi
335.	Role of boron in ameliorating oxidative stress and liver cell necrosis: implications in liver diseases	Ms. Humaira Farooqi Jamia Hamdard (Hamdard University) New Delhi
336.	Production of bioactive gonadotropin by insect cell using baculovirus expression vector system	Ms. V. Pooja Jamia Hamdard (Hamdard University) New Delhi
337.	Protection against typhoid by <i>Terminalia belerica</i> and <i>Punica granatum</i> : molecular, antioxidative and immunomodulatory evaluation	Sh. Arfat Madani Jamia Hamdard (Hamdard University) New Delhi
338.	Role of the chemical constituent of an indigenous plant in the chemopreventive potential of skin carcinogenesis in animal model system	Ms. Sonia Sharma Jamia Hamdard (Hamdard University) New Delhi
339.	Ameliorative properties of plant flavonoid galangin on hepatocarcinogenic and genotoxic effects induced by chemical agents in animal models	Dr. Anuradha Sehrawat Jamia Hamdard (Hamdard University) New Delhi

APPENDIX IV

- 340. Development of new drug delivery system with sodium-hydrogen exchanger modulators and evaluation of their role in epilepsy
- 341. Antidiabetic properties of *Trigonella foenum* graecum related to membrane structure and function
- 342. Elucidation of the role of neuropeptide, neurokinn B and its analogues on molecular and biochemical correlates in aging brain functions
- 343. Analysis of expression of human p35 and p40 genes and their assembly to form bioactive human interleukin-12 in a mammalian cell line and its bioreactor optimization in culture
- 344. Studies on the mechanisms of gene regulation by transcriptional activators in yeast
- 345. The role of oxidative stress and cellular transcription factor ap-1 in pre and post operative cases of breast carcinomas
- 346. Neural repair by glial cell line derived neurotrophic factor (GDNF) in experimental model of Parkinson's disease
- 347. Role of stat family of transcription factors in regulation of transcription in the brain
- 348. Cytogenetic and molecular biological study of sporadic and familial breast cancer patients from Goa
- 349. Biochemical variation among hill peoples of Lahaul-Spiti and Kulu districts of north Himachal Pradesh
- 350. Relationship between candidate genes of hypercholesterolemia and the risk of coronary heart disease in South Indian population
- 351. Rational design, synthesis and biological evaluation of some novel cholesterol lowering agents

Sh. Atif Ali Jamia Hamdard (Hamdard University) New Delhi

Mohd. Rizwan Siddiqui Jamia Milia Islamia New Delhi

Sh. M. Anil Kumar Jawaharlal Nehru University New Delhi

Sh. Anand Kumar Verma Jawaharlal Nehru University New Delhi

Ms. Sonal Sawhney Jawaharlal Nehru University New Delhi

Ms. Priyanka Verma Lady Hardinge Medical College and Associated Hospitals New Delhi

Ms. Shalini Singh Maulana Azad Medical College and Associated Hospitals New Delhi

Ms. Anjana Kalita National Institute of Immunology New Delhi

Ms. T.M. Deshpande Goa University Panaji

Ms. Rupinder Kaur Bansal Punjabi University Patiala

Dr. Padmaja Narayanan Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry

Sh. M.K. Kathiravan Poona College of Pharmacy Pune

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- 352. Conformational analysis of anticancer drug mitoxantrone, its analogues and their complexes by NMR spectroscopy and molecular modeling techniques
- 353. Dendrimer mediated genetic immunization against hepatitis B
- 354. Microbial triggered targeted oral drug delivery for colorectal cancer
- 355. Development and characterization of intestinal M-cell targeted microsphere for the oral vaccination against hepatitis B
- 356. Synthesis and characterization of antisense oligonucleotides for skin associated genetic disorders
- 357. Isolation and screening of antimicrobial peptides from insects
- 358. Exploring the structural requirements of peptide/protein antagonists of cxcr4 and ccr5 to inhibit the co-receptor mediated cellular entry of HIV-1
- 359. Study of microtubule assembly by some microtubule nucleation promoters
- 360. Genetic transformation studies in *Cucumis sativus* for expressing immunogenic proteins

361. 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

- 362. Studies on *Selaginella involvens* with special reference to its immunomodulatory and anti-oxidant properties
- 363. Studies on monocyte-macrophage differentiation

Ms. Manpreet Kaur Narang Indian Institute of Technology Roorkee

Sh. Tathagata Dutta Dr. Hari Singh Gour Vishwavidyalaya Sagar

Sh. Anekant Jain Dr. Hari Singh Gour Vishwavidyalaya Sagar

Sh. Premnarayan Gupta Dr. Hari Singh Gour Vishwavidyalaya Sagar

Ms. Gyati Shilakari Dr. Hari Singh Gour Vishwavidyalaya Sagar

Sh. N. Chandrasekhar Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram

Sh. P. Sanchidanandan Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram

Ms. Nisha Elizabeth Thomas Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram

Ms. Sindhu C. Unni Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram

Ms. S.R. Sangeetha Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram

Ms. V. Gayathri Tropical Botanic Garden and Research Institute Thiruvananthapuram

Ms. A. Radhika University of Kerala Thiruvananthapuram

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DIAN COUNCIL OF MEDICAL RESEARCH

- 364. Inhibition of viral carcinogenesis by selected medicinal plants
- 365. Biochemical studies on antidiabetic activity of *Syzygium alternifolium* seeds
- 366. Development of liposomal dry powder inhalers for lung diseases
- 367. To develop novel nonviral gene delivery system: targeting specific cell and enhancing gene expression
- 368. Study of the role of rab 11 during eye development in Drosophila
- 369. Study the anticarcinogenic effect of *Terminalia* arjuna, Andrographics paniculata and Asparagus racemosus in Dalton's lymphoma ascites bearing mice
- 370. Reno protective actions of aldose reductase inhibitors in experimental diabetic nephropathy
- 371. Investigations on biosynthesis, continuous production and kinetics of urokinase (UK) employing immobilized mesangio-proliferative glomerulo nephritis (MPGN) kidney cells

Publication and Information

372. The transfer of public domain science to patented technology : a case study with major inventions as reflected by patents

Sh. K.B. Hari Kumar Amala Cancer Hospital and Research Centre Thrissur

Sh. M.D. Rajasekhar Sri Venkateswara University Trupati

Sh. Mahavir Bhupal Chougule M.S. University of Baroda Vadodara

Sh. V.I. Kulkarni M.S. University of Baroda Vadodara

Sh. A.K. Tiwari Banaras Hindu University Varanasi

Ms. Nibha Verma Banaras Hindu University Varanasi

Sh. G. Jayaprakash Andhra University Visakhapatnam

Ms. Bhavani Devi Ravuri Andhra University Visakhapatnam

Dr. Sonica Pawa Indian Council of Medical Research New Delhi

Expenditure on Fellowships during the year Rs. 383.00 lakhs

LIST OF PUBLICATIONS OF ICMR INSTITUTES

Acosta, C.J., Galindo, C.M., Ali, M., Elyazeed, R.A., Ochiai, R.L., Danovaro-Holliday, M.C., Page, A.L., Lee, H., Puri, M.K., Agtini, M.D., Punjabi, N.H., Canh do, G., Sur, D., Nizami, Q., Manna, B. and Bhattacharya, S.K. A multi-country cluster randomized controlled effectiveness evaluation to accelerate the introduction of Vi polysaccharide typhoid vaccine in developing countries in Asia: rationale and design. *Trop Med Int Health* 10 (2005) 1219.

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