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ANNUAL REPORT of ICMR HEADQUARTERS (2003-2004)

APPENDICES

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Annual Report

2003-2004

Indian Council of Medical Research
New Delhi

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Director-General`s Message

The Indian Council of Medical Research has made significant strides in its mandate of 'Research for Better Health'. The Council has lived up to country's expectations on all major fronts of its activity: research and development of vaccines and drugs for infectious diseases like tuberculosis, malaria, filariasis, HIV/AIDS, research in the areas of modern biology like molecular biology, genomics, bioinformatics, fertility regulation, cancer and other non-communicable diseases, consultancy and human resource development, national and international collaborations and biomedical informatics and communication.

During the period under report, the Memorandum for the Expenditure Finance Committee (EFC) of ICMR has been approved by the Government of India and Rs.870 Crores have been allocated for the 10th Plan. The research activities will now be pursued with greater vigour as more funding would be available. To optimize resource utilization, the Council is using the Combined Approach Matrix being used by Global Health Forum for Health Research for setting research priorities in various disciplines.

The Council continued to play an important role in detecting new and emerging infections in India like the Chandipura virus encephalitis in Andhra Pradesh and Gujarat and outbreak of mysterious fever in Siliguri. The investigations carried out in collaboration with CDC, Atlanta on biological specimens collected from Siliguri in 2001 revealed that the outbreak was due to Nipah virus.

An Inter-Agency collaboration has been started on herbal drugs between the Department of ISM/AYUSH, CSIR and the ICMR, popularly known as the "Golden Triangle'. A National Centre for Primate Breeding and Research is being established at Sasunavgher, Maharashtra. The Centre would function as a base for research, biological testing and breeding of primates.

In order to improve access to scientific journals by various institutes of the ICMR, a J-Gate Custom Content for Consortia-ICMR @ JCCC has been set up. It will provide online access to more than 2000 biomedical journals and 12000 journals covered under J-Gate and will enhance sharing of journals available in ICMR Institutes.

The publication output of ICMR continues to be outstanding. The scientists of the Council's Institutes published a total of 434 research papers during 2003 as compared to 330 in 2002. The average impact factor per paper of ICMR improved to 2.180 from 2.030 in 2002. During the financial year 2003-04, over 1000 research projects were funded. Around 900 scientific, technical and supporting staff were trained during the period. Eight patents including one US patent were filed during the year.

The quality of publications of ICMR such as the Indian Journal of Medical Research and Annual Report has improved. A biennial award scheme has been initiated for popular medical books published in Hindi.

I am happy to present the Annual Report of the ICMR for the financial year 2003-04 giving highlights of activities during this period.

Nirmal Kumar Ganguly
Director-General

Contents

An Overview

The Indian Council of Medical Research (ICMR) has entered 93rd year in the service of nation. The Council continues to direct its resources in conducting research towards finding feasible solutions to problems being encountered in addressing India's health problems.

The Memorandum for the Expenditure Finance Committee for utilizing the funds received from Departments of Health and that of Family Welfare have been approved. The research activities outlined in the 10th plan document could now be pursued with greater vigour. This was not possible up to now as the ICMR's annual allocations in the first two years of the 10th plan were almost equal to the last year of 9th Plan. It is expected that in the remaining part of the 10th plan this shortfall would be compensated with an adequate increase in the allocations.

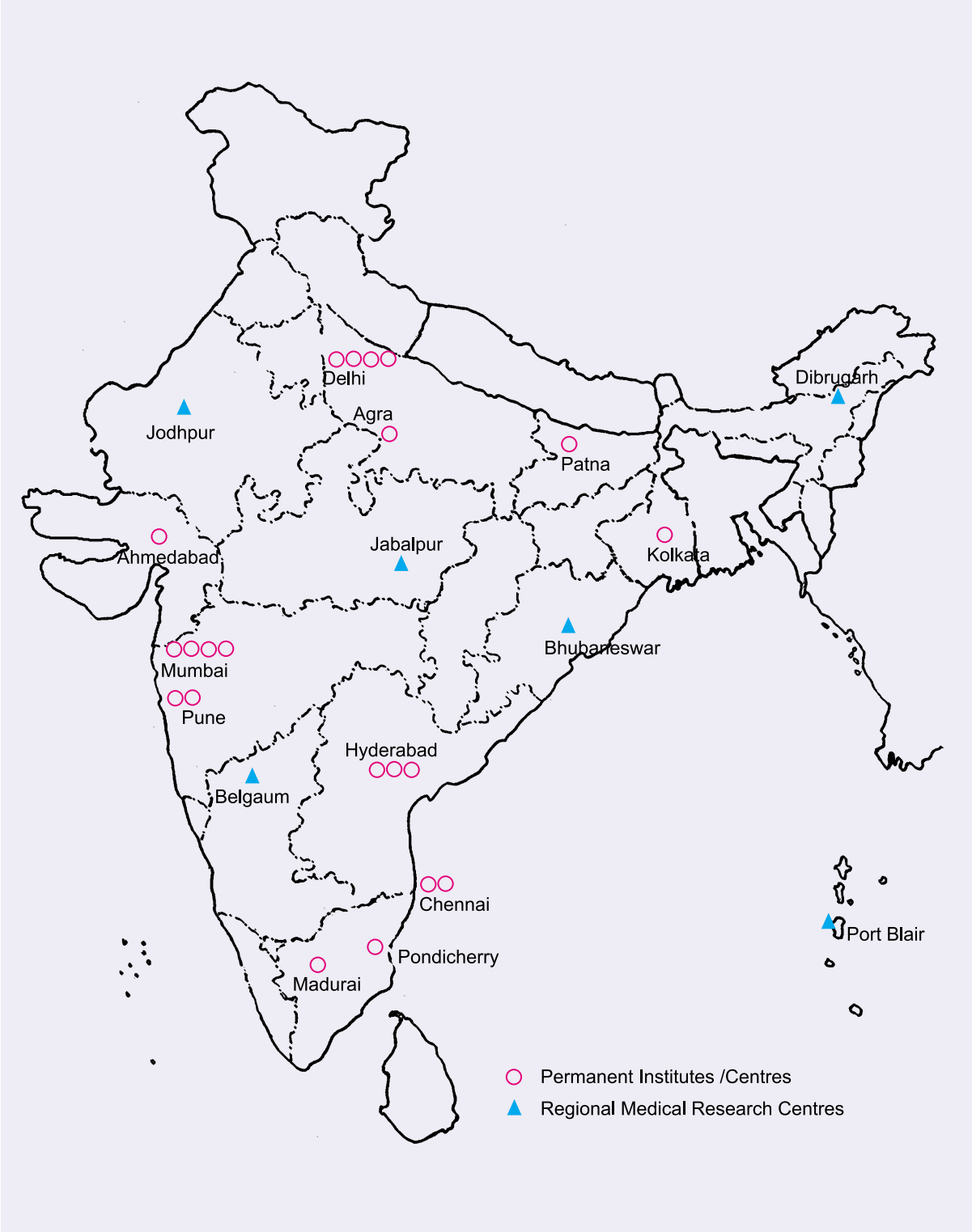
The Council has stepped-up its funding for the extramural research programme for which close to 25% of the budget is being earmarked. As part of its Extramural Research Programme, the Council supported over 1000 projects during the year 2003-04. Laboratory studies constituted about 40%, clinical studies 30%, epidemiological and operational studies 20%. Of Rs. 34 crores being spent in this programme, laboratory, clinical, epidemiological and operational studies constituted about 30% each. A large share of funding (46%) went to research institutions, about 30% to medical colleges and 13% to universities. As part of this programme, large number of scientific (350), technical (500) and supporting staff (60) were trained.

Having improved the infrastructure in the Institutes/Centres in previous years, the focus this year has been on a larger allocation for supplies and consumables so that the equipments could be put to optimal use. The Council is spending a quarter of its budget on pay and allowances. It has not been possible to shift some of the expenditure being made under "Plan" to "Non-Plan" due to the static Non-Plan outlay. With the improvement in infrastructure for conducting research in the Institutes, it has been possible for them to attract larger number of Ph.D. students as compared to earlier years. The Council continues to support human resources development through its training courses (regular as well as short term) in various institutes.

Playing its stewardship role as a health research organization, the Council has used the Global Forum for Health Research (GFHR) Combined Approach Matrix for setting research priorities in various disciplines. The estimation of disease burden using Murray and Lopez method for some infectious and non-infectious diseases was pursued. Due to variation in the completeness and quality of data available on disease incidence and prevalence coupled with statistics obtained from the programme and research studies with the problems associated in assigning disability and age weights, alternative strategies to estimate disease burden are being thought of. Application of methods developed by Centre for Economic Policy Research for tracking financial flows for health research in India indicated that the existing system of keeping accounts did not permit disaggregation of expenditure on health research. Thus differentiation of the spend on service sector from research at tertiary level health care facilities can not be done.

NEW AND EMERGING INFECTIONS

The ICMR is playing an important role to detect new and emerging infections in India like the Chandipura virus encephalitis in Andhra Pradesh and parts of Gujarat. Investigations carried out with the help of CDC, Atlanta, USA have indicated a strong possibility of the Siliguri Outbreak of mysterious fever of 2002 to be due



ICMR INSTITUTIONAL NETWORK

to Nipah virus. In its attempt to step-up research on these pathogens, the Microbial Containment Complex, Pune has been completed and is now ready for commissioning. It is a state of the art laboratory to assist the scientists of ICMR and other agencies in conducting research on exotic and dangerous pathogens. Microbial Repositories of malaria and leishmaniasis parasites, Mycobacteria, HIV and other viruses and *V.cholerae* were strengthened and catalogues of strains available in some of these registries have been prepared.

REPRODUCTIVE AND MATERNAL HEALTH

Nisin, a food preservative has been demonstrated to also have antifertility activity for the first time. A reproductive health programme for adolescents has been initiated besides home based management of young infants in five states of the country.

PUBLICATIONS

The Indian Journal of Medical Research – the ICMR's flagship medical journal has now a

contemporary new look. The Medicinal Plants Unit has brought out the first volume of the quality standards of Indian medicinal plants as well as the first three volumes on Indian Medicinal Plants.

RESEARCH PERFORMANCE INDICATORS

An important indicator of performance of any research organization is the quality and quantity of publications including the impact factors of its research publications. During 2003, a total of 417 research papers were published of which 268 were in SCI/JCR journals. The average impact factor per paper improved to 2.180 from 2.030 of 2002.

ICMR @ JCCC

In order to improve the access of scientific journals to various institutes of the ICMR a J-Gate Custom Content for Consortia – JCCC (*http://www.jccc-icmr.informindia.co.in*) has been set up to provide access to over 500 journals subscribed currently by the ICMR's network of Institutes/Centres. It provides on-line access to more than 200 free biomedical journals and also nearly 12000 e-journals covered under J-Gate. The ICMR has subscribed to JCCC for all laboratories with the aim of sharing resources of journals available in ICMR institutes.

COLLABORATIONS

An Inter Agency Collaboration for development of herbal medicine has been set up

between the Department of ISM/Ayush, CSIR and the ICMR – popularly known as the 'Golden Triangle'. The JICA-NICED collaboration has entered into Phase-II and a grant-in-aid totalling about Rs. 90 crores has been approved. This would further strengthen the collaboration in improving techniques and molecular biology research. Another example for the international collaboration is the progress made in setting up of a National Centre for Primate Breeding and Research at Sasunavgher, Maharashtra. This Centre would function as a base for research, biological testing breeding of primates and human resources development.

Communicable Diseases

Infectious diseases continue to remain a major public health problem of the country. An added cause of concern is the emergence of tuberculosis (TB) in association with human immunodeficiency virus (HIV) infection. Malaria, Kala-azar and dengue pose serious threats to populations across the country whereas diarrhoeal diseases account for significant mortality of children/infants in various parts of the country. Attempts have been made to completely eradicate poliomyelitis from India.

The ICMR has a network of Institute/ Centres totally devoted to research in the field of communicable diseases. Priority is being given to development and evaluation of diagnostic tools, drugs and vaccines for emerging and re-emerging communicable diseases. The Council has integrated its efforts with the national health programmes to meet the growing challenges.

BACTERIAL DISEASES

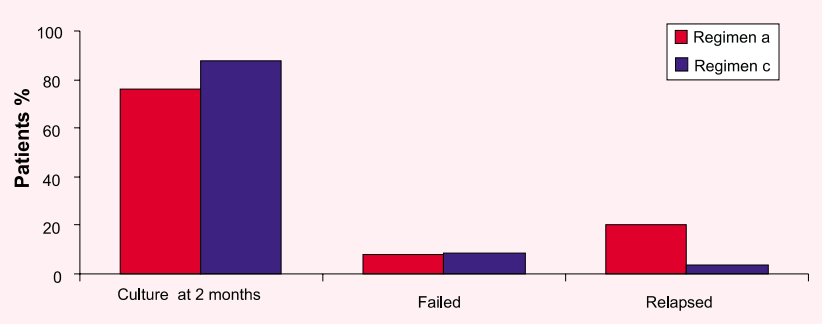
TUBERCULOSIS

Tuberculosis continues to remain number one killer in India. The prevalence of tuberculosis is increasing because of the concomitant HIV infection. The Council has a Tuberculosis Research Centre (TRC) at Chennai engaged in research studies on various aspects of tuberculosis such as diagnostic tests, drug resistance, development of newer regimens for treatment of TB and molecular biological studies.

Clinical Studies

Ofloxacin-containing Short Course Treatment Regimens for Pulmonary Tuberculosis

The TRC, Chennai in collaboration with state government hospitals and the Chennai Corporation had initiated a randomized clinical trial to test the efficacy of intermittent ofloxacin-containing regimens for the treatment of patients with smear positive pulmonary tuberculosis in May 2001 in Chennai and Madurai. The test regimens were ofloxacin, isoniazid and rifampicin three times a week for four months with either pyrazinamide or ethambutol for the first two months, *i.e.* regimen (a) 2 OHRZ thrice weekly/ 2OHR thrice weekly, and regimen (b) 2OHRE thrice weekly / 2OHR thrice weekly. These regimens were compared with regimen (c), a control regimen of isoniazid and rifampicin three times a week for six months with ethambutol and pyrazinamide for the first two months (2EHRZ thrice weekly/ 4HR thrice weekly). The results in 265 patients [(167 allocated to regimen (a) and 98 to regimen (c)] are summarised in Fig. 1. Due to the study design that employed a staggered allocation to



Regimen a: ofloxacin, isoniazid and rifampicin three times a week for four months with pyrazinamide for the first two months
Regimen c: isoniazid and rifampicin three times a week for six months with ethambutol and pyrazinamide for the first two months

Fig. 1. Results of a randomised trial comparing 4-month intermittent ofloxacin-containing regimen with 6-month control regimen in the treatment of patients with smear-positive pulmonary tuberculosis.

the three regimens, only 25 patients were allocated to regimen (b). Since the relapse rate in the test regimen was unacceptably high, the study has been terminated after an interim analysis.

Sputum culture conversion at two months was lower and relapse rates were higher among patients treated with the 4-month thrice-weekly ofloxacin-containing regimen compared to those treated with the 6-month regimen. These results suggest that the intermittent ofloxacin regimen is unlikely to be successful.

Revised National Tuberculosis Control Programme (RNTCP) Regimens for Tuberculosis Patients with HIV Infection

Study was initiated in 2001 to assess the efficacy of RNTCP treatment regimens among HIV-infected persons with pulmonary or lymph node tuberculosis in Chennai and Madurai. Patients with pulmonary or lymphnode 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). Till date 271 patients have been admitted to the study and of the 165 patients followed up for 12 months after treatment, 10 have relapsed (4, 5 and 1 patients from the 6-month and 9-month category I regimen and category III regimen respectively).

Epidemiological Studies

Monitoring the Performance of DOTS Strategy in Tiruvallur District

TRC has been involved in monitoring the DOTS programme in a population of about 600,000 in Tiruvallur district, Tamil Nadu for the past 5 years. The new smear positive case detection, sputum conversion and cure rate achieved in this population are given in Fig.2. All the parameters showed an increasing trend over the years.

Relapse of Tuberculosis in Patients Treated in the RNTCP in Tiruvallur District

Sputum specimens were collected and examined at 6, 12 and 18 months after completion of anti-TB treatment from a cohort of pulmonary tuberculosis patients registered from the 2nd quarter of 2000 to the 4th quarter of 2001 to assess the relapse rate in patients treated under the RNTCP. Of the 534 patients registered 503 were followed up, and of these 62 were found sputum positive giving a relapse rate of 12% during an 18-month period after completion of treatment. Multivariate analysis

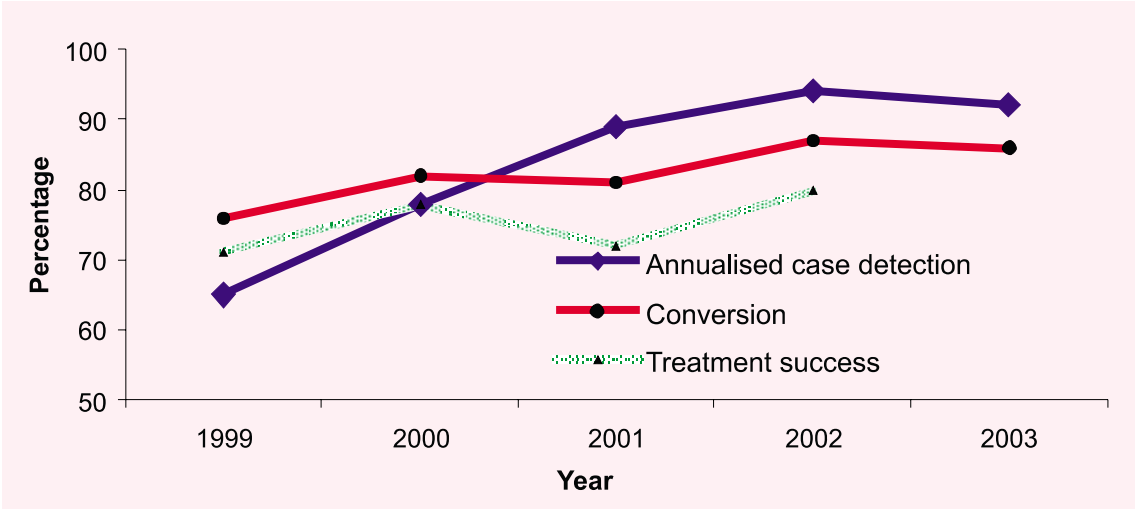


Fig. 2. Programme indicators for the period 1999-2003 in Thiruvallur district.

showed drug irregularity, initial drug resistance and smoking to be associated with the occurrence of relapse. Only one patient had multi-drug resistant TB at the time of relapse.

Tuberculosis among the Nicobarese in Car Nicobar

An intensified tuberculosis control programme was carried out in 1986 in Car Nicobar among an isolated community of Nicobarese, a mongoloid tribe. All the smear positive TB cases detected during the survey were given treatment with nine month short course chemotherapy (SCC), and smear negative radiologically positive TB cases with a two drug regimen. INH chemoprophylaxis was administered to children aged 5-14 yr for a period of six months. After the end of the intensified control programme, the antituberculosis activities in this island were carried out as per District Tuberculosis Programme (DTP). Assessment of the impact of this programme on tuberculosis situation in this island 15 yr post intensified control programme by measuring the prevalence of tuberculosis in children < 14 yr and in sputum positive cases among the older age groups was undertaken.

A total of 15,575 individuals were assessed from 15 villages of Car Nicobar Island, which included 4543 children. Of the 4351 children, who were satisfactorily tested and read, 22.5% were without a BCG scar. The frequency distribution of tuberculin reaction sizes among children without a BCG scar is presented in Fig.3 which shows a bimodal distribution with the secondary mode at 19 mm.

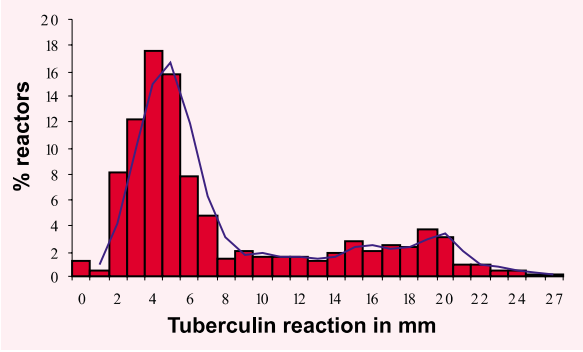


Fig. 3. Frequency distribution of tuberculin induration sizes in children aged 0-14 yr in Car Nicobar.

The observed prevalence of infection among children without a BCG scar was 16.4%, whereas the standardized prevalence was 17.0%, with population distribution in 1986 as the standard. The annual risk of TB infection (ARTI) based on observed prevalence of infection among children without a BCG scar was 2.4% whereas that based on standardized prevalence was 2.5%. The ARTI among the children with a BCG scar was 2.4%.

Of the 11,032 individuals aged > 15 yr, 95.8% were interviewed for presence of chest symptoms and 9.1% had them. A total of 77 smear positive cases (S+) were detected with a prevalence of 7.28/1000 among this population. The findings of the study show that the prevalence of tuberculosis infection and smear positive TB cases has increased significantly since 1986.

Involving the Private Health Sector in Tuberculosis Control

A feasibility study to involve private medical practitioners in the RNTCP was initiated. A total of 48 practitioners were enrolled in the study. Of the 808 chest symptomatics referred for sputum examination 172 have been diagnosed to have tuberculosis. All these patients have been started on treatment. Of 73 new smear positive patients 75% were cured. The study shows that it is feasible to integrate the private health care sector in the public tuberculosis control programme.

Drug Susceptibility at the Time of Failure of Treatment in RNTCP

Initial resistance to anti-TB drugs may be one reason why some patients fail to respond to anti-TB treatment. A study was carried out to find the degree of initial drug resistance in patients treated in Tiruvallur district. Among 1363 patients treated in category 1 of the RNTCP, 69 were declared to have failed treatment; on culture 14 of them were found negative for *M. tuberculosis*. Of the remaining 55 patients, 11 had organisms resistant to isoniazid (H) and rifampicin (R), 16 to H alone and 15 were susceptible to H and R. Sputum could not be collected in 13.

Estimating Unit Provider Cost for Treating Patients with Tuberculosis

All government health facilities situated in one tuberculosis unit of Tiruvallur district were visited to evaluate daily practice of tuberculosis diagnosis and treatment. Administrators in these health facilities were interviewed to gather data on diagnosis, treatment and monitoring of tuberculosis patients. In addition, relevant financial records from all health facilities were scrutinised. The cost per cure of a tuberculosis patient was analysed by considering the provider costs for diagnosis and treatment of TB under DOTS programme for the year 2000.

The calculation of unit cost was done separately for radiological and laboratory procedures. The cost of treatment per patient was calculated using a combination of variables like personnel, capital and consumables (supplies and drugs) and the cost for each was estimated. The cost for the provider was extended for cure of an individual patient. Unit cost for procedure was calculated on the basis of Rs. 10 for sputum smear microscopy and Rs. 25 for radiography. Drug cost for Category I was Rs. 392; Category I with extension Rs. 495; Category II Rs 584; Category II with extension Rs. 687 and Category III Rs. 277. The overall unit provider cost to treat a tuberculosis patient was Rs. 13462 for Category I, Rs. 13654 for Category II and Rs. 13347 for Category III.

Application of Lot Sampling of Sputum Acid-Fast Bacilli (AFB) Smears for Assessment of Sputum Microscopy Centres

RNTCP guidelines suggest lot sampling of sputum AFB smears to assess the performance of microscopy centres. An attempt was made to test the feasibility of adopting lot sampling of AFB smears and to assess the performance of microscopy centres employing field-level Senior Tuberculosis Laboratory Supervisors (STLS) with no prior knowledge of principles of quality assurance of AFB microscopy and RL-based laboratory technicians with training on quality assurance for blinded checking of AFB smears.

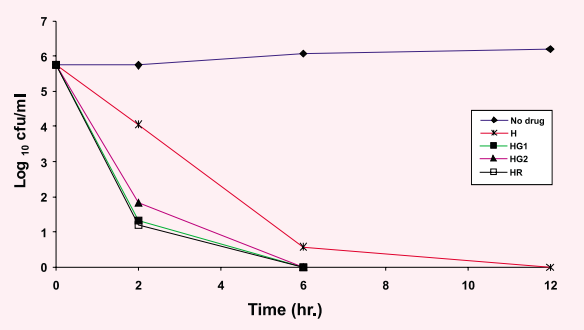
It was observed that lot sampling of AFB smears is feasible under field conditions. Assessment of microscopy centres was more valid with controllers trained in principles of quality assurance of sputum AFB microscopy than with laboratory supervisors with no such training and working in the field.

Laboratory Studies

Bactericidal Action of Gatifloxacin, Rifampicin and Isoniazid on Cultures of M. tuberculosis

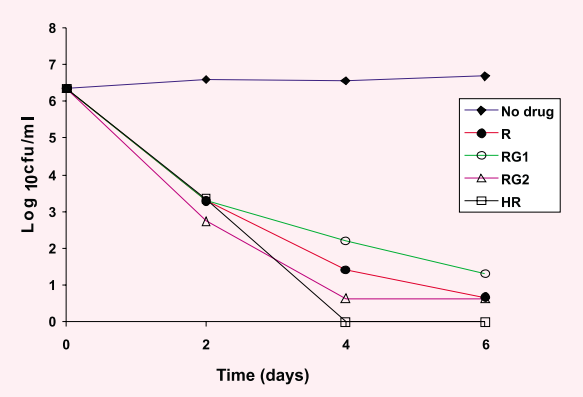
Gatifloxacin is a new 8-methoxy quinolone with more potent activity against *M. tuberculosis* than other quinolones. The drug also has a favorable pharmacokinetic profile in humans with oral bioavailability of almost 96%. Considering its potential in reducing the treatment duration of tuberculosis and in the treatment of MDR TB, a study was carried out to determine the bactericidal activity of gatifloxacin alone and in combination with isoniazid and rifampicin on both logarithmic and stationary phase cultures of *M. tuberculosis* H37Rv.

On actively growing population (logarithmic phase), the bactericidal activity of gatifloxacin at 4µg/ml was found to be similar to that of isoniazid. Gatifloxacin showed synergistic activity with isoniazid at concentrations of 0.25µg/ml and 4µg/ml. On stationary phase cultures, gatifloxacin at 4µg/ml concentration was more active with a fall of 2.17 log cfu at the end of the second day. It also enhanced the activity of rifampicin and was similar to the activity of isoniazid-rifampicin combination. These findings suggest that gatifloxacin has a potential use as a bactericidal and sterilizing drug in the chemotherapy of tuberculosis (Figs. 4 & 5).



H – isoniazid; R – rifampicin; G1 – gatifloxacin 0.25µg/ml; G2 - gatifloxacin 4µg/ml

Fig. 4. Bactericidal activity of gatifloxacin with isoniazid against logarithmic phase of *M. tuberculosis*.



H – isoniazid; R – rifampicin; G1 – gatifloxacin 0.25µg/ml; G2 – gatifloxacin 4µg/ml

Fig. 5. Bactericidal activity of gatifloxacin with rifampicin against stationary phase of *M. tuberculosis*.

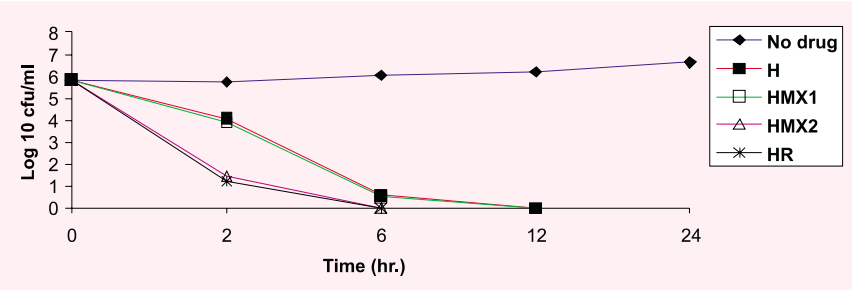
Bactericidal Action of Moxifloxacin, Rifampicin and Isoniazid on Cultures of M. tuberculosis

Moxifloxacin is a fourth generation quinolone used for the treatment of bacterial diseases. Study was carried out to examine its bactericidal activity alone and in combination with isoniazid and rifampicin on the logarithmic and stationary phase cultures of *M. tuberculosis* H37Rv.

In logarithmic culture, moxifloxacin (4mg/ml) showed synergistic activity along with isoniazid resulting in 0 cfu even at 6 hr. It showed greater sterilizing activity with rifampicin, similar to the sterilizing activity achieved with isoniazid-rifampicin combination. Moxifloxacin along with isoniazid and rifampicin showed greater bactericidal and sterilizing activity (Figs. 6 & 7).

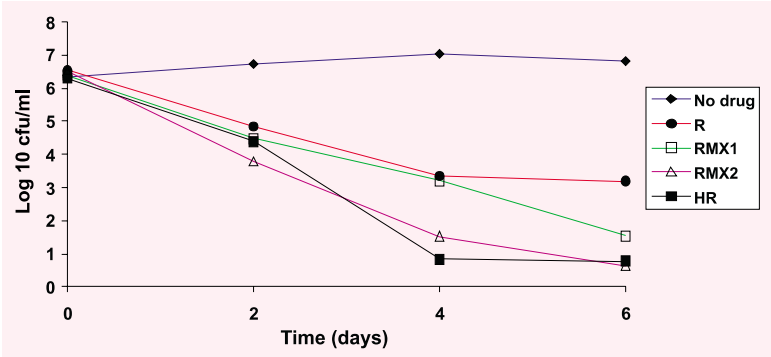
Comparison of Ziehl-Neelsen (ZN) and Auramine Phenol (AP) Staining to detect AFB in Direct and Deposit Smears

In drug resistance surveys, sputum samples are collected in cetyl pyridinium chloridium (CPC)-sodium chloride solution and transported to central laboratories for bacteriological



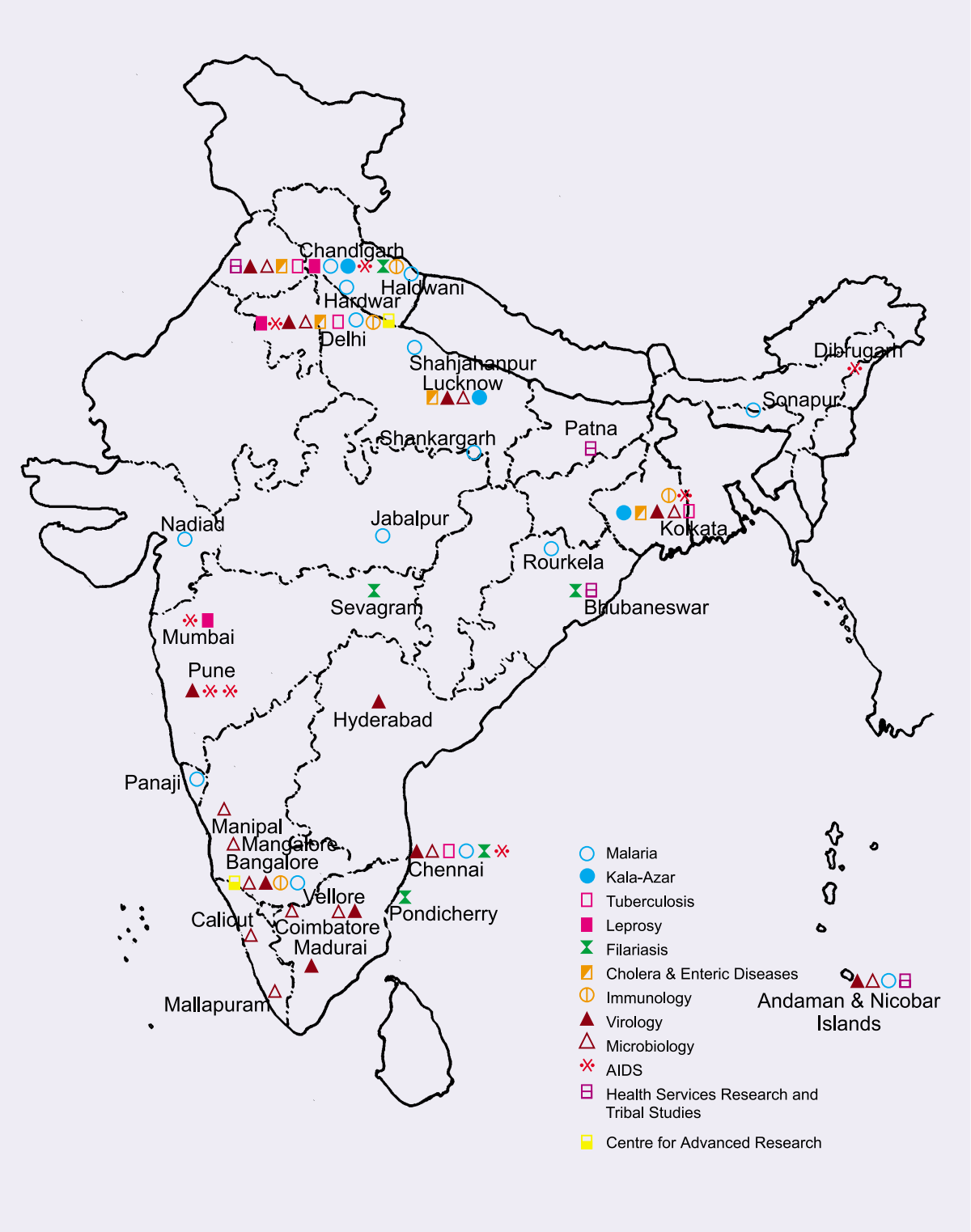
H – isoniazid; R – rifampicin; MX1 – moxifloxacin 0.25µg/ml; MX2 – moxifloxacin 4µg/ml

Fig. 6. Bactericidal activity of moxifloxacin against logarithmic phase of *M. tuberculosis*.



H – isoniazid; R – rifampicin; MX1 – moxifloxacin 0.25µg/ml; MX2 – moxifloxacin 4µg/ml

Fig. 7. Bactericidal activity of moxifloxacin with rifampicin against stationary phase of *M. tuberculosis*.



MAJOR ICMR RESEARCH PROJECTS IN COMMUNICABLE DESEASES

examination. Due to unknown reasons the rate of detection of AFB in direct smears is significantly reduced using AP and ZN staining methods. The direct and deposit smears prepared from 583 samples collected in CPC were compared with culture results. It was found that washing the deposits of sputum samples preserved in CPC with water increased the detection rate of AFB in AP and ZN methods.

Molecular Biological Studies

Cloning Genomic DNA Fragments from M.microti and Screening for Promoter Activity

Obtaining promoters and inserts of *M. microti*, a member of *M. tuberculosis* complex and getting information about mycobacterial gene regulation and expression could be a lead in designing new recombinant DNA vaccines for TB and in finding various factors that control host specificity.

In this study genomic DNA fragments from *M. microti* were digested and cloned in *E. coli* mycobacteria promoter probe shuttle plasmid vector pJEM13 with *lacZ* gene and an attempt was made to screen for promoter activity.

Repeated ligation and transformation did not yield blue colonies indicating absence of promoter activity. However, the appearance of white colonies indicates the expression of kanamycin resistant genes. Of the white colonies, six were selected for extraction of plasmid DNA and for the presence of inserts by standard procedures. Three plasmids (pAZM1-8 kb, pAZM2-4 kb and pAZM3-1.7 kb) with different size of inserts were obtained. The clone pAZM1 was large enough to carry more than one gene and it would be an interesting clone to study in detail.

Temperate Luciferase Reporter Phage for Diagnosis of Tuberculosis

Luciferase reporter phage (LRP) assay is simple, rapid and highly specific for measuring cell viability. Since, already existing LRP constructs from lytic phages are not sensitive to detect less than 10^4 organisms/ml, there is a need for a better phage construct for the diagnosis of *M. tuberculosis*. A LRP construct phAETRC11 has been developed at TRC from a lysogenic phage che12.

The light output measured as relative light units (RLU) with lytic phage phAE129 and lysogenic phage phAETRC11 are shown in Figs. 8 & 9.

Experiments are in progress to test positive sputum samples with lysogenic phage LRP construct.

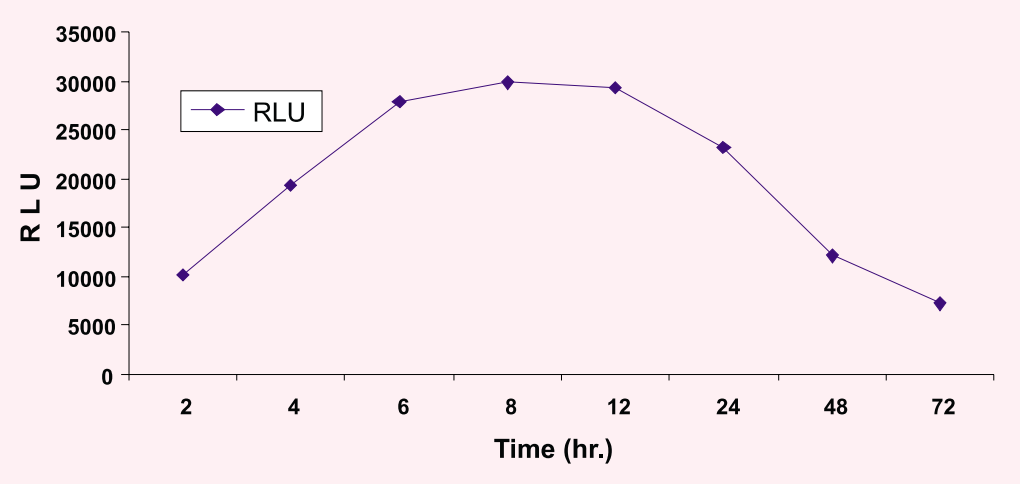


Fig. 8. Kinetics of phAE 129.

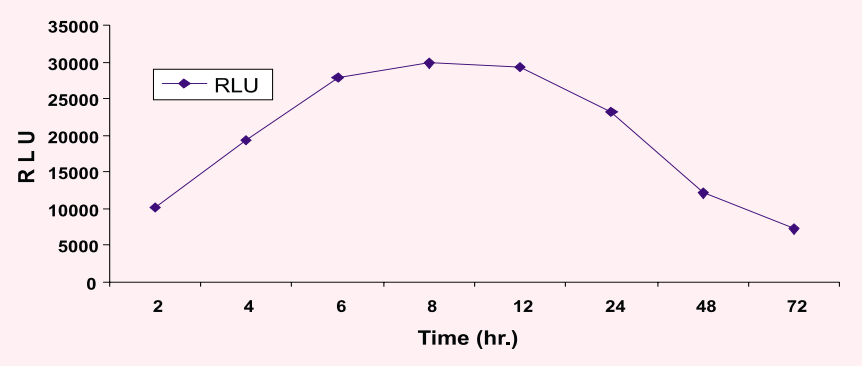


Fig. 9. Kinetics of phAETRC 11.

Molecular and Immunological Characterization of M. tuberculosis Strains with Single Copy of IS6110

Restriction fragment length polymorphism (RFLP) studies done at TRC have shown that most prevalent (40%) strains of *M. tuberculosis* from south India contain a single copy of IS6110 insertion sequence. These widely spread strains of *M. tuberculosis* are of importance in studying their virulence and role in immunity. Studies showed that these antigens induced T-cell activation. To explore for newer antigens from the recent and highly prevalent pathogens, which can be further utilized for purification and in diagnosis, the humoral immune response to these antigens was studied in 30 normal healthy PPD positive and 30 pulmonary tuberculosis patients' plasma by ELISA and Western blot.

In the SDS-PAGE protein profiles of the 13 sonicate antigens (S1-S13), S10 and S12 showed maximum differential protein bands in low molecular mass region of 10-30 kDa. ELISA results showed significant increase in *M. tuberculosis* specific IgG antibodies in TB plasma for H37Rv, followed by PPD, S1 and S10 antigens (Fig.10). Immunoblot analysis of S10 and S12 (Fig. 11) sonicate antigens showed very specific recognition pattern at low molecular mass region by TB plasma alone but showed either cross reactive or minimal recognition patterns for the antigens S1, S2 and H37Rv. The percentage

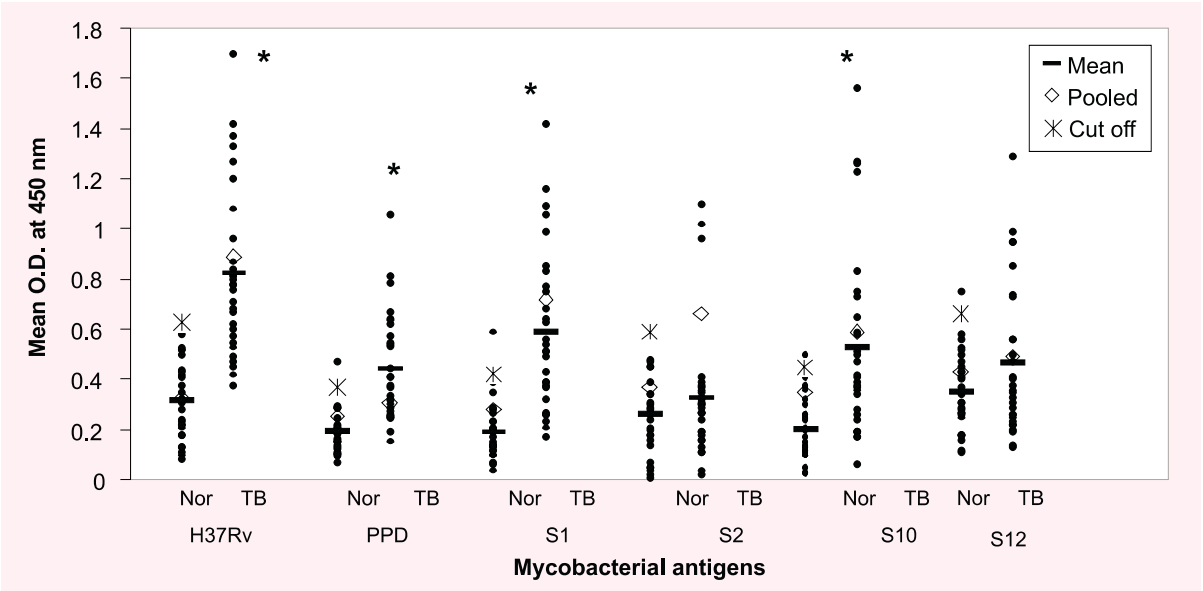


Fig. 10. Total IgG levels in normals and TB patients against various mycobacterial sonicate antigens.

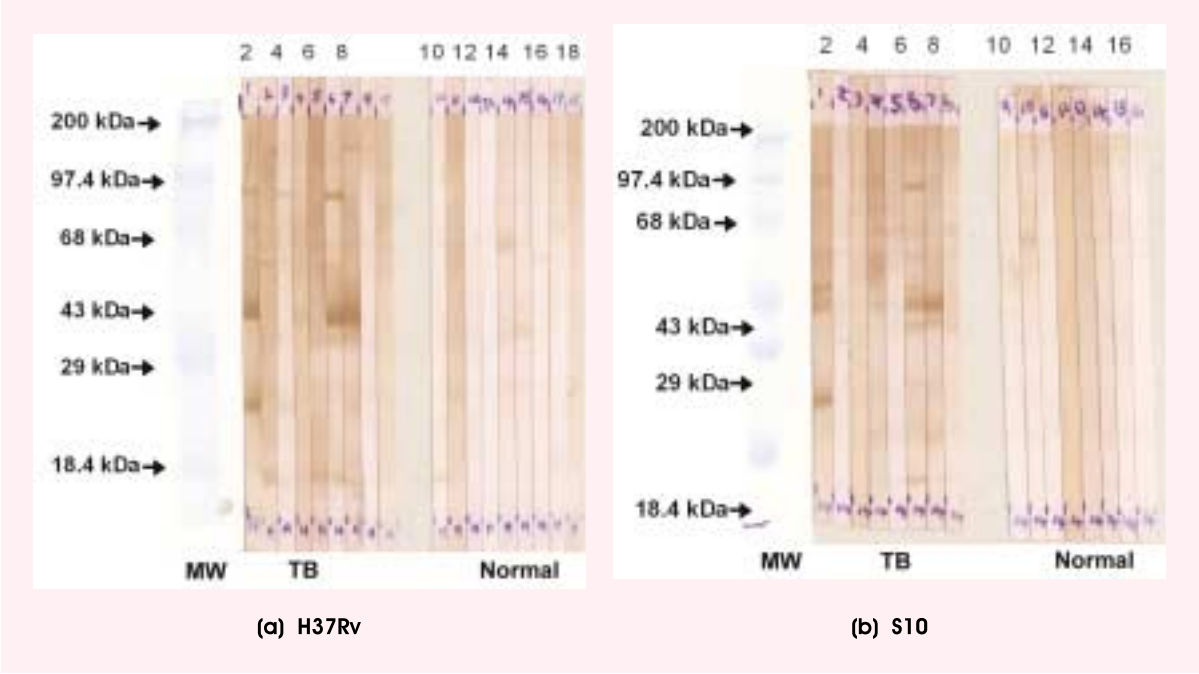


Fig. 11. Immunoblot analysis of mycobacterial sonicate antigens.

positivity of protein bands in TB plasma for antigen S10 ranged from 12-77%. The maximum positivity was observed for 16 and 45kDa (77%) followed by 38kDa (66%) protein bands. The sonicate antigen S10 was found to be discriminatory by ELISA and Western blot and thus can be a good candidate for further purification of its individual proteins that needs to be evaluated for diagnosis.

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

M. tuberculosis is an intracellular pathogen that is remarkably well adapted to survival in the human host. Tubercle bacilli can remain dormant within tissue for decades and then cause reactivation disease when the immune system of the host is suppressed. A study was conducted at AIIMS, New Delhi with the objective of developing and establishing *M. smegmatis* (non-pathogenic and rapid growing mycobacterial species) as a suitable surrogate model to study the hypoxia response of *M. tuberculosis* and the involvement of DevR-devS genetic system therein. This objective was achieved in four phases. In the first phase, an *in silico* analysis was performed of the unfinished genome sequence of *M. smegmatis* and *devR*, *devS* and other genes upregulated and implicated in the hypoxia-induced response in *M. tuberculosis* were found to be present. In the second phase, the expression of the DevR-DevS genetic system in aerobic and hypoxic cultures of *M. smegmatis* was assessed. The levels of *devR* and *devS* gene products at RNA and protein levels increased 5 fold in *M. smegmatis* cultures under hypoxia and the elevated levels were maintained upto the end of the experiment suggesting a continuous role for them during hypoxia. In the third phase, the suitability of *M. smegmatis* to evaluate the activity of hypoxia-responsive *M. tuberculosis* promoters was demonstrated using *lacZ* and green fluorescent protein-based reporter assays. Thus establishment of *M. smegmatis* as a suitable surrogate model to study the hypoxia response of *M. tuberculosis* and the involvement of DevR-DevS genetic system therein has been demonstrated.

LEPROSY

The Central JALMA Institute for Leprosy (renamed as Central JALMA Institute for Leprosy and Other Mycobacterial Diseases) has been undertaking research programmes with a major focus on leprosy, tuberculosis, HIV infection and other infections like filariasis associated with the endemicity of leprosy and other mycobacterial diseases. The focus of the Institute is towards a better understanding of disease process of these infections as well as on developing technologies for diagnosis, detection of drug resistance, molecular epidemiology, drug permeability and metabolism in mycobacterial diseases, surgical management, psycho-social aspects and treatment of leprosy.

Immunological Studies

Immunogenic Activities of Lipids and Glycolipid Antigens from *M. leprae*

With a view to understand the mechanism of T-cell interaction with *M.leprae* antigens, studies have been initiated in leprosy patients with synthetic phosphoantigen, *M.leprae* soluble antigen and mitogen. The status of γδ T cells was analysed by flow cytometer. No significant difference was observed in the stimulation of γδ T cells in borderline tuberculoid (BT-33%) and lepromatous (LL-44%) patients (Fig.1). These findings are being analysed in relation to T-cell activation by intercellular free calcium.

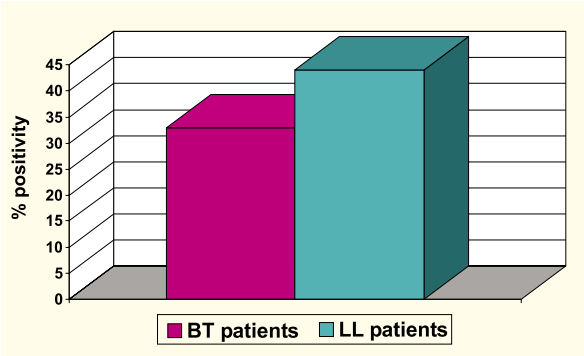


Fig. 1. γδ positive T cells in leprosy patients.

Flowcytometry for Detection of Anti-M. leprae Antibodies

Flow cytometry as a modern tool is being used for various purposes including detection of antibodies. This technique has been explored for detection of anti-*M.leprae* antibodies using *M.leprae* coated beads and NT-P-BSA coated gelatin as solid phases for antigens. The comparison of these results with respective ELISAs showed that the overall sensitivity of detection by flowcytometry and ELISA were similar. These findings thus indicate that flowcytometry could be another alternate tool to ELISA for detection of antibodies.

Surgical Studies

JALMA Flap for Restoration of Volume of First Web Space in Ulnar Palsy in Leprosy

Ulnar nerve palsy is common in leprosy and results in clawing of fingers and hollowing of the first web space due to atrophy of adductor pollicus and first dorsal interosseous. Correcting of finger clawing makes the hollowing deformity more obvious when the patient opens the hand fully or greets someone. In the past surgeons have tried different strategies but the success was very short lived and the graft was either absorbed or rejected due to foreign body reaction. Keeping these in mind, a viable adipocutaneous flap based on the cephalic vein and the major tributary of the radial artery from the lower forearm was taken and transferred to the depression of the first web space. This procedure has been named as 'JALMA Flap'. Of the total, 75% cases showed improvement. The scar over the radial side of the forearm appears to be a big cosmetic problem for which a two hole procedure to harvest the graft is planned.

Therapeutical Studies

Uniform MDT Regimen for Leprosy Patients

The regimen comprising dapsone and clofazimine administered daily and once a month supervised dose of rifampicin (multibacillary regimen x 6 months) for all types of leprosy cases proposed by WHO is being tried at CJIL, Agra in the Ghatampur field area. Of the total patients included 40% are PB and MB (with only 4% smear positive).

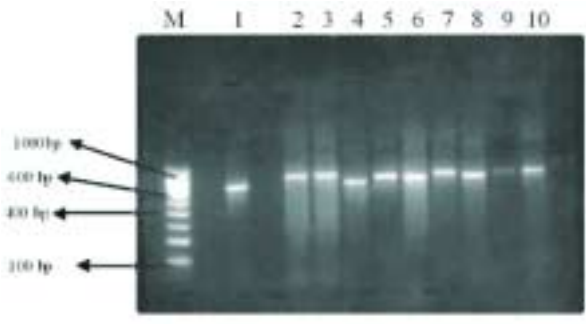
Molecular Biology of Mycobacteria

Probes for Detection of Drug Resistance

Multicentric studies have identified novel mutations in the rpoB, inhA and other gene loci encoding for rifampicin and INH resistance in Indian isolates of *M. tuberculosis.* Based on this information, probes were designed and their application studies are continuing. Using the strategy of line-probe assay, a system has been developed for detection of mutations *in inhA* locus of *M. tuberculosis.* The technique has been tested on isolates of *M. tuberculosis* and the results show good concordance with sequence data. The probes accurately detect the mutations and the results are available within 48-72 hr. of getting the specimens/isolates. Overall, this system shows concordance of about 60% with microbiological data as other loci like katG and ahpC also are also responsible for INH resistance.

DNA Fingerprinting of Mycobacteria

Studies were carried out at CJIL to develop and apply different DNA fingerprinting methods for various species of mycobacteria. During the year, a MIRU-VNTR based method for *M. tuberculosis* was established. The results of one locus have been found to be promising (Fig.2). The technique has been found to be discriminatory for identifying the differences among isolates of *M. tuberculosis* and has been tested on more than 100 strains from CJIL repository.



M : Molecular weight marker (100bp ladder),
Lane 1: H37Rv Lane 2-10: Different *M.tuberculosis* isolates

Fig. 2. DNA fingerprinting of mycobacteria.

Proteomic Analysis of Expression of Proteins after infection with Mycobacteria

The mechanism of survival of the mycobacteria in the hostile environment of macrophages is fundamental to the understanding of their virulence and pathogenicity. The genes/proteins involved in their survival have been partly defined. During the year, experiments were conducted at CJIL to standardize and analyze the protein profile of cell lysates of mycobacteria grown within and outside macrophages. Macrophage lysate was also analysed to serve as control. Initial findings showed overexpression of 65-70 kDa proteins (Fig.3). The origin of these proteins is being investigated.

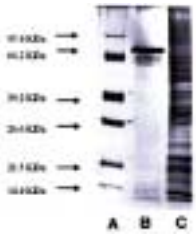


Fig. 3. A: Molecular weight markers; B: cell lysate of infected cells; C: mycobacterium cell lysate.

Identification of T cell Signaling Pathways using *M. leprae* Derived Antigens

Leprosy, a chronic infectious disease shows multifactorial manifestations ranging from strong cell mediated immune (CMI) response in tuberculoid from (BT/TT) or weak CMI with immunological anergy in lepromatous from (BL/LL). Repeated stimulation with mycobacterial antigen either *in vivo* or *in vitro* causes activation induced cell death or T cell anergy in these patients. A study aimed at understanding the T cell defect in leprosy patients at the biochemical level is ongoing at AIIMS, New Delhi. The involvement of caspases in cell death and expression of apoptotic markers *viz.*, CD95 and CD95L; CD40 and CD40L on T/B cells as well as monocytes/macrophages of leprosy patients was studied and the effect of particulate formulations of mycobacterial antigens and immunomodulations in the reversal of apoptosis in BT/TT and BL/LL patient group was assessed. Caspase 8/3 activity was maximum in BL/LL

patients in constitutive state followed by decreased activity in BT/TT and normal subjects. Caspase 8/3 activity increased significantly from constitutive state after 5 days of *in vitro* antigen stimulation (inducible state). Both the antigens were equally potent in inducing apoptosis in leprosy patients. The reversal of apoptosis (down regulation of caspase activity) using the particulate formulations of both antigens was observed in BL/LL group. The expression of apoptotic markers on T/B cells of leprosy patients increased significantly after 5 days of antigen stimulation. However, percent expression of CD95, CD95L by T cells of BL/LL patients decreased significantly when the particulate formulations were used. The decreased percent expression of CD40/CD40L in B/T cells was observed in BT/TT patients. It was noticed that the particulate formulations of antigens with immunomodulators slowed down the apoptosis and hence T cell anergy in leprosy by stimulating the cells to proliferate.

Epidemiological Studies

Epidemiological Studies on Leprosy in Agra

Studies on understanding the prevalence, incidence and profile of the disease in Agra district continued during the year. Besides survey of rural areas, the leprosy situation in Agra city was assessed. An overall prevalence of 15/10000 has been found in Agra city. The prevalence of leprosy among females was 16.4 as compared to 12.5 among males. Of the cases identified, 33.7% were single skin lesion cases, 51.5% PB cases and 14.5% MB cases.

Relationship between Filarial Infection and Leprosy

A study has been initiated in Ghatampur, Kanpur to find out the relationship, if any, between the endemicity of leprosy and filarial infection. A survey of three villages and a population coverage of 3600 have been completed where the filarial disease rate has been found to vary from 0.2 to 2%. In the same population, the microfilaraemia rate has been observed to range from 4 to 10% (Fig.4). Leprosy prevalence is also quite high in the same area.

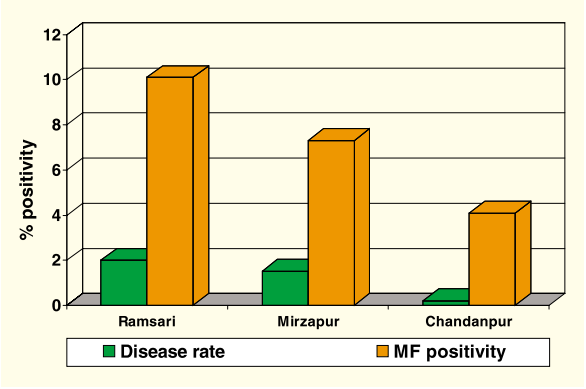


Fig. 4. Correlation between filarial disease and microfilarial positivity rates.

Larger population will be examined for assessing the correlation.

Field Programme for Epidemiological Studies at Ghatampur

An epidemiological study has been initiated in Ghatampur area of district Kanpur to study the disease profile in the community, identify the differences in the incidence of disease in relation to age, sex, relation and type of contacts, genetic factors, effect of hygiene, socio-economic status on the prevalence of disease and effect of treatment regimens in the field specially on the transmission of the disease. So far, a population of 1,22,346 has been examined and a total of 1912 leprosy cases have been identified. The overall prevalence is 156/10,000 showing very high endemicity in this area. Of the total 31.8% cases are children up to 15 yr of age which indicates continued transmission. Slit skin smear test was done in 86%. Skin smear was positive in 11% case. However, smear positivity of 2+ or more was found only in 1.4% of the total cases examined (Fig. 5).

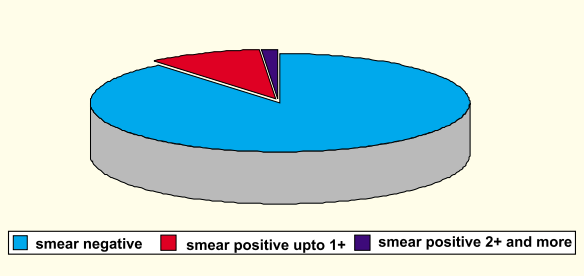


Fig. 5. Skin smear status of leprosy patients at Ghatampur.

DIARRHOEAL DISEASES

Diarrhoeal diseases contributing to at least 1.5 million deaths in children, still remain a major public health problem in India. The Council is supporting studies to strengthen facilities for identifying new pathogens, to provide guidelines for management of acute and persistent diarrhoea and to understand the mechanism of pathogenesis of diarrhoeal diseases. Most of the research in this area is in progress at the Council's National Institute of Cholera and Enteric Diseases (NICED), Kolkata.

Community Based Study

Impact of Albendazole on the Nutritional Status and Diarrhoeal Incidence among Children in Kolkata

Helminthic infections are a very common childhood problem in India causing malnutrition which is an important predisposing factor for diarrhoeal disease. A study has been undertaken by NICED, Kolkata to assess the impact of periodic deworming on the nutritional status and diarrhoeal incidence among children (2-5 yr of age) and to assess the feasibility of periodic anthelminthic administration by existing health workers.

In this double blind randomised community based intervention study in Tiljala slum area, 702 children were identified and enrolled.

Significant increase in mean weight of children receiving albendazole was noticed at 3 months, 6 months and 9 months (Fig.1). The children also suffered from significantly reduced (28%) episodes of diarrhoea. Health workers could satisfactorily administer the correct dosage and there were no adverse effects. Thus periodic mass deworming may be adopted at the community level or as an integral part of school health services to improve growth and reduce the incidence of diarrhoea in children.

Vibrio cholerae

Molecular Characterization of CTX Prophages of Vibrio cholerae

The prime virulence factor cholera toxin (CT), expressed by the toxigenic *V.cholerae* is an AB_5 like toxin encoded by a lysogenic phage known as CTXf. The potential of CTXf to convert nontoxigenic strains to toxigenic trait is a major concern.

Toxigenic traits of non-O1, non-O139 strains isolated and maintained in the archive of NICED, Kolkata were studied at NICED,

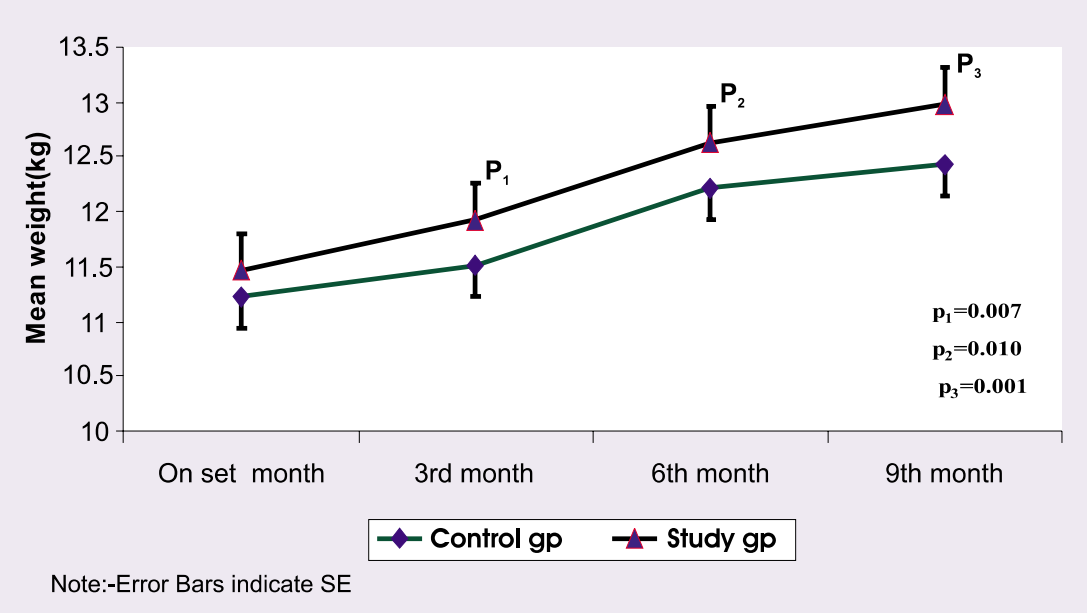


Fig. 1. Trend of weight gain in children receiving albendazole.

Kolkata. A total of 503 non-O1, non-O139 strains isolated from acute diarrhoeal cases from 1992 to 2002 were revived and analyzed by PCR based assay for the presence of *ctxA*, the gene responsible for expression of CT subunit-A protein as well as *cep* gene responsible to express CTXf coat protein. Both the target genes (*ctxA* and *cep*) are conserved in their nucleotide sequence among the known alleles of CTX prophages. During 2003, a total of 69 *V.cholerae* non-O1, non-O139 strains were isolated from acute diarrhoeal cases and were also included in the study.

During the study period, PCR primers specific to *cep* were developed and specificity of the primers was initially tested against known *ctxA* positive *V. cholerae* strains before being used for PCR based screening along with well referred *ctxA* primers. PCR amplicons were obtained against reference strains carrying respective types of prophages (Fig.2). Furthermore, amplicons were cloned into plasmid vector so as to serve as specific DNA probe that may be utilized in characterization of the prophages present in *V.cholerae* strains by Southern hybridization analysis.

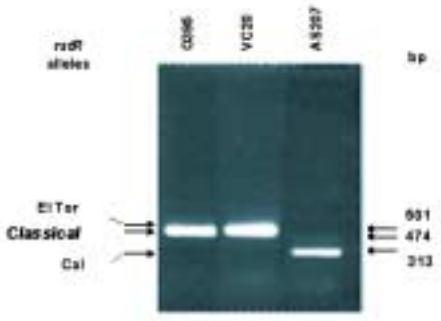


Fig. 2. Agarose gel electrophoresis patterns of PCR amplicons obtained with rstR allele specific primers. PCR amplicons specific to classical (O395, 474 bp), El Tor (VC20, 501 bp) and Cal (AS207, 313 bp) rstR types are indicated.

PCR based analysis showed that all the (more than 20) O1 and O139 clinical strains constantly gave positive amplicons against both *ctxA* and *cep* PCR assay whenever used as a positive control. However, none of the clinical non-O1, non-O139 strains (total 503) was found to possess either *ctxA* or *cep*. Interestingly, 2 out of 69 clinical non-O1, non-O139 strains isolated from diarrhoeal cases during 2003 gave both *ctxA* and *cep* amplicons. During 2003, comparative isolation of non-O1, non-O139 strains to that of O1 *V. cholerae* appeared to be higher than that of the previous years. During July 2003, isolation of non-O1, non-O139 strains exceeded that of O1 *V.cholerae* from clinical cases.

Study was also carried out with *V.cholerae* non-O1, non-O139 strains isolated from environmental origin. Results showed that 3 of 360 strains isolated during 1984-85 possess new type of prophage. Analysis of the nucleotide sequences of both repressor (*rstR*) and phage-receptor (*orfU*) of these prophages showed their identity to each other.

An environmental strain (VCE22) isolated in 1984 was also seen which gave positive amplicon in the PCR assay with *cep* specific primers but not with primers specific to *ctxA* (Fig.3). This result in conjunction with Southern hybridization analysis established the presence of truncated CTX prophage (without *ctxAB*) in the strain VCE22 (O36). Therefore, targeting *cep* rather than *ctxA* is more important for the tracking of *V.cholerae* CTX prophage which is known to exist either in complete or incomplete form within *V.cholerae* strains. Studies are in progress to characterize CTX prophages present in non-O1, non-O139 *V.cholerae*.

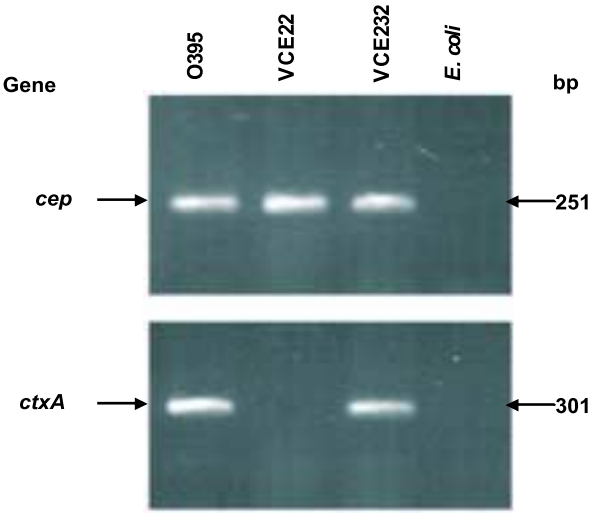


Fig. 3. Agarose gel electrophoresis patterns of amplicons obtained in PCR assays with cep and ctxA specific primers against *V. cholerae* strains. PCR amplicon obtained against *V. cholerae* O1 classical strain O395, environmental isolates of *V. cholerae* non-O1, non-O139 strains VCE22 and VCE232 are indicated.

Shigella Sonnei

Nalidixic Acid Resistance among Shigella sonnei Isolates

Shigella infection has been occurring both in epidemic and sporadic form in Andaman and Nicobar Islands and is mainly due to *S. flexneri* 2a and *S. dysenteriae* type 1. Nalidixic acid resistant *S. sonnei* appeared as a predominant strain during 2001 – 02. *S. sonnei* infection has not been common in developing countries including India. However, it appears to be emerging as a common and a predominant infection in Andaman islands.

S. sonnei isolates were characterized using molecular biological tools such as plasmid profiling, randomly amplified polymorphic DNA (RAPD) and pulsed-field gel electrophoresis (PFGE) to understand the clonal relatedness of this emerging strain in comparison with strains isolated earlier. A total of 16 *S. sonnei* strains were characteized.

The plasmid profile of nalidixic acid resistant and nalidixic acid sensitive strains is shown in Fig.4.

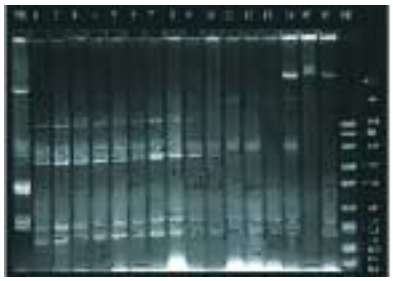


Fig. 4. Plasmid profiles of nalidixic acid resistant (1-9) and sensitive (10-16) strains of *Sh. Sonnei*.

All the resistant strains had similar plasmid profile, irrespective of their time of isolation and source. These strains thus belong to a single clone and possess seven plasmids. One nalidixic acid sensitive strain (lane 10) showed almost a similar profile, but had an additional plasmid (~7 kb). Plasmid profile of no other nalidixic acid sensitive strain had any similarity with that of the resistant strains. The profile of each of the sensitive strains was different.

RAPD patterns of both nalidixic acid resistant and sensitive strains are shown in

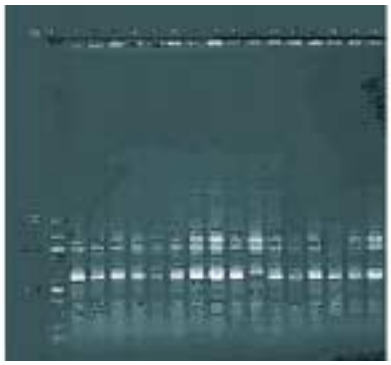


Fig. 5. RAPD profiles of nalidixic acid resistant (1-9) and sensitive (10-16) strains of *Sh. Sonnei*.

Fig.5. Patterns of all strains except those in lanes 10, 12 and 14 are similar. All the resistant strains showed similar profile (lane 1-9). The RAPD profile of a recently isolated sensitive strain (lane10) showed almost a similar profile, but the band of ~6.5 kb was absent. Other nal^S strains presented the closely related profiles.

PFGE profiles of both nalidixic acid resistant and sensitive strains were similar (Fig.6). The tested strains include nine resistant and three sensitive strains.

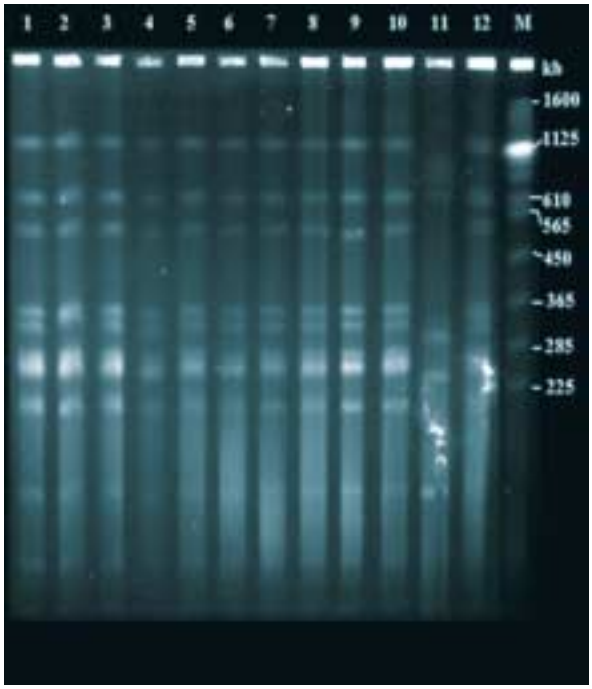


Fig. 6. PFGE profiles of nalidixic acid resistant (1-9) and sensitive (10-12) strains of *Sh. Sonnei*.

Shigella dysenteriae

Up-regulation of Mucosal Immune Response by Porin of Shigella dysenteriae *type 1*

Mice and human have phenotypically distinct populations of B cells, termed B-1 and B-2, that have been proposed to represent entirely separate B cell lineages. Porins possess immunopotentiating properties and are possible vaccine candidates. Studies were conducted at NICED for activating B-1 cells by porin purified from *Shigella dysenteriae* type 1. The study showed that coexpression of toll-like receptor (TLR) 2 and TLR6 is essential as a combinatorial repertoire for recognition of porin by the B-1 cells. Among the two key TLRs (TLR2 and TLR4) TLR2 was found to participate in porin recognition. mRNA for myeloid differentiating factor, an effector molecule associated with TLR-mediated response, was enhanced 1.8-fold suggesting its involvement in the activity of porin. Both the B-1 cell populations expressed strongly the mRNA for NF-*k*B in presence of porin that was 2.4-fold more than untreated controls, conforming to the earlier finding that coexpression of TLR2 and TLR6 resulted in robust NF-*k*B activation for signaling. Porin treatment of B-1 cell populations of C57BL/6 mice, and C3H/HeJ mice in particular, selectively up-regulated the expression of the co-stimulatory molecules. CD80 expression got enhanced on the B-1a cells whereas CD86 got solely expressed on B-1b cells.

Escherichia coli

Association of cytolethal distending toxin locus cdtB with enteropathogenic E. coli

Cytolethal distending toxin (Cdt) is a novel class of bacterial genotoxin that induces characteristic elongation of eukaryotic cells followed by progressive cellular distention and death. Cdt is considered as an important factor in intestinal pathogenesis as this toxin is able to induce tissue damage and fluid accumulation in the descending colon of orally infected suckling mice.

The three genes, cdtA, cdtB and cdtC arranged in an apparent operon are required for the production of active Cdt. Presence of cdt in different bacterial species and analysis of its flanking regions suggest that this gene has been acquired from heterologous species by horizontal gene transfer or through a phage.

To investigate the incidence of *cdt* harbouring *E.coli*, a total of 284 stool specimens collected from acute diarrhoeal patients of all age groups admitted to the Infectious Diseases Hospital and B.C. Roy Memorial Hospital for Children, Kolkata were examined. The incidence level of *E.coli* harbouring *cdtB* in Kolkata was 1.4%. All the 4 strains having *cdtB* gene were identified as EPEC since they harboured *eae* and *bfpA* (Table 1). A total of 138 EPEC strains collected over a period of 4 yr from 1998 to 2001 were screened by colony hybridization assay.

Table 1. Serotyping and virulence gene profile of *E.coli* strains harbouring *cdtB*

Strain	Serogroup	PCR result									
		cdtB	*est*	*elt*	*eae*	*bfp*	EAF	*astA*	EAgg	*stx1*	*stx2*
GB 1371	O86a	+	-	-	+	+	+	-	-	-	-
VTE 1456	O142	+	-	-	+	+	ND	-	-	-	-
VTE 1488	O86a	+	-	-	+	+	ND	-	-	-	-
GB 1807	O127a	+	-	-	+	+	ND	-	-	-	-
DO 5491	O86a	+	-	-	+	+	+	-	-	-	-
FO 6580	OUT	-	-	-	+	-	-	-	-	-	-
F 17290	O157	-	-	-	+	-	-	-	-	-	-
GB 469	O127a	+	-	-	+	+	+	-	-	-	-
NT 3363	O127a	+	-	-	+	+	+	-	-	-	-

OUT, untypable; ND, not done

Five strains (2.7%) hybridized with *cdtB* probe of which 2 gave negative results in the CDT-PCR (Table 1).

In the serological analysis with somatic antisera, 33.3% of the strains were identified as O86a and O127a. Since no *E. coli* strain was encountered that harboured only the *cdtB* locus, it appears that there is a association of *cdtB* among EPEC strains. The study showed that except for one, all the patients infected with *E.coli* harbouring *cdtB* were children in age group 4 months - 6 yr. Five of the 9 children had blood in their stool.

The reciprocal titer of Cdt with strains belonging to the O86a and O142 serogroups was higher than O127a (Table 1). These strains were isolated from patients with bloody diarrhoea. The strains that expressed Cdt were found to be sorbitol non-fermenters. To determine the DNA sequence of the *cdtB* locus from 3 representative strains (GB1371, GB 1807 and VTE 1456), the amplified *cdtB* gene was purified and sequenced in both the directions. Analysis of the *cdtB* of these strains showed that all of them were identical and closely related with the sequences of U03293 and AF373206. When the phylogenetic tree was rooted through U03293, all the Kolkata strains formed one group along with AF373206, which was reported from Iran (Fig.7).

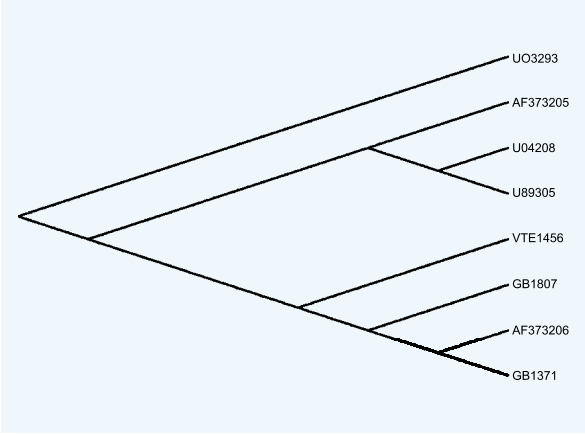


Fig. 7. Phylogentic analysis based on the sequence comparison of cdtB genes of three representative strains (GB 1371, GB1807 and VTE 1456) with other sequences available in the GenBank. The tree was constructed using CLUSTAL X and viewed with TREE VIEW software after rooting through U03293 cdt sequence.

The study is the first systematic report, applying conventional and molecular approaches for screening and characterization of *E.coli* strains harbouring *cdtB* locus associated with acute diarrhoea in India.

Ultra Structures Associated with Intestinal Cell Adherence of Enteroaggregative Escherichia coli (EAEC)

Study was undertaken to demonstrate the ultra microscopic structure of attachment and penetration of EAEC strains into intestinal cells at various culture conditions and to compare the attachment to intestinal cells by EAEC strains in diarrhoeal and healthy children. Results revealed that the bacterial cells adhered to the intestinal cells. The brush border of epithelium was destroyed by the bacteria and internalization of the bacteria was observed inside the epithelial cells (Fig.8). No difference was found between strains from diarrhoeal and healthy children indicating that bacterial and *in vitro* cell interaction had no effect on disease progression and persistence.

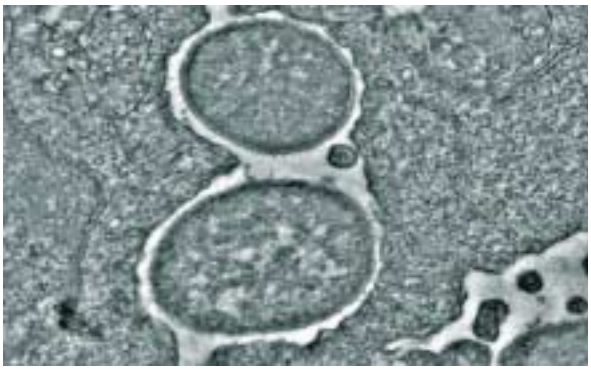


Fig. 8. Internalisation of EAEC bacteria in *in vitro* intestinal cell culture.

Helicobacter pylori

Multiplex PCR Assay for Rapid Detection and Genotyping of Helicobacter pylori

The gastric pathogen *Helicobacter pylori* causes gastritis and peptic ulcer disease and is an early risk factor for development of gastric adenocarcinoma. Because it is fastidious and microaerophilic, it cannot be cultured in clinical or research laboratories in "resource poor"

developing countries. None of the methods to detect *H. pylori* infection including the recently developed *H. pylori* stool antigen test and PCR restriction analysis using RNA polymerase gene (*rpoB*) can give a clue on the virulence genes of *H. pylori* strains harboured by the host. Development of a multiplex PCR assay was reported by NICED, Kolkata by which, *vacA* signal sequence (s1 and s2) and mid-region (m1 and m2) alleles and presence or absence of *cagA* gene can be detected in a single reaction, directly from gastric biopsy samples within 4 hr after endoscopy, without need for culture or genomic DNA extraction. This can save several weeks time, expensive reagents and instrumentation.

Seventy-nine *H. pylori* strains, isolated from India, Japan, Spain, Australia, the UK and USA were used to develop the multiplex PCR assay. Ninety fresh biopsies were collected randomly from patients with duodenal ulcer, gastric ulcer, non-ulcer dyspepsia, duodenitis, gastritis, adenocarcinoma and 3 healthy volunteers for further evaluation of this method. Each person's infection status, inferred from multiplex PCR, was further tested and culture and genotype data obtained from biopsy multiplex PCR was evaluated by PCR using DNA extracted from cultured strains, isolated from the respective patients.

Using this multiplex PCR 65 previously isolated Indian strains were characterized. Forty-four of them carried slml $cagA^+$ allelic combination, 16 carried slm2 $cagA^+$ and 5 carried s2m2 $cagA^-$.

The multiplex PCR developed by NICED will be of great value in clinical microbiology and *H.pylori* population studies, especially for rapid screening of many samples to detect *H. pylori* infection, to determine *vacA* and *cagA* status, to identify multiple infections in host and to detect variant alleles.

Yersinia enterocolitica

Mode of Action of Y. enterocolitica Heat Stable Enterotoxin in Rat Intestinal Epithelial Cells

A study was carried out to evaluate the mechanism of action of heat stable enterotoxin secreted by *Y. enterocolitica*. The enterotoxin (YSTa) was purified from the culture filtrate and fractions were tested for enterotoxicity by suckling mice assay. It was found that purified YSTa raised $[Ca^{2+}]i$ in a dose dependent manner and the optimal level of $[Ca^{2+}]i$ was achieved by incubating cells with YSTa. The enterotoxin was found to stimulate phospholipase C activity and induced rise in intracellular calcium level in presence and absence of calcium in extracellular environment. YSTa also stimulated IP_3 mediated calcium mobilization.

Entamoeba histolytica

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

Amoebiasis, a parasitic infection in man due to the protozoan *E. histolytica*, is an invasive enteric illness that can spread to multiple tissues, particularly mucosa and submucosa of host intestine. Because, collagen is major component of the extracellular matrix and basal lamina of human intestine, it is thought that collagenase which was detected in pathogenic *E.histolytica* is one of the important factors of tissue lysis during invasive amoebiasis. Till date no study has been conducted on the expression of collagenase genes in *E.histolytica*. Attempts were made by NICED, Kolkata to clone and

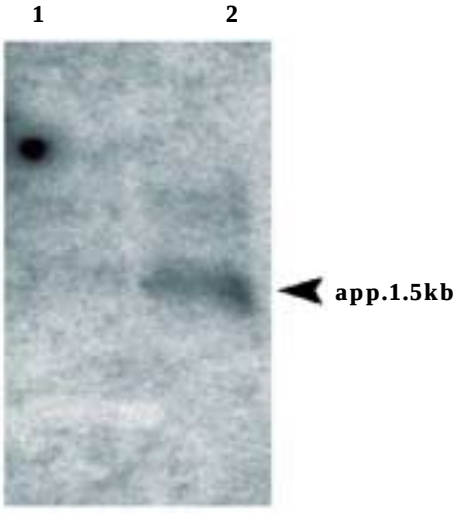


Fig. 9. Northern hybridization pattern of *E. histolytica* RNA from non-activated and collagen type I and Ca^{2+} activated trophozoites.

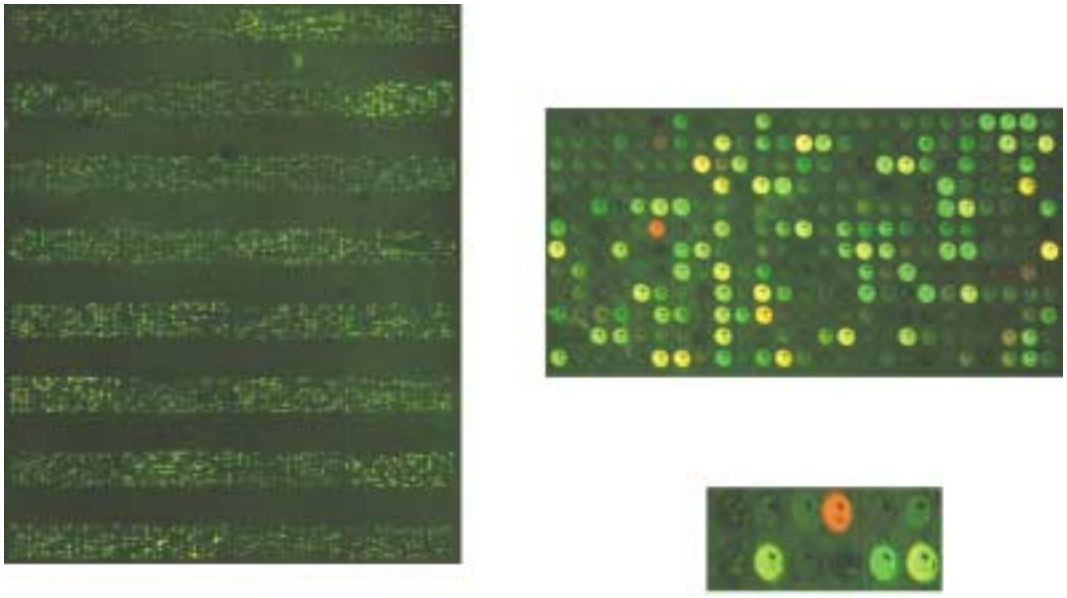


Fig. 10. Identification of *E. dispar*-selective gene expression on the microarray. Hybridizations of Cy3- and Cy5-labelled cDNA are represented as green and red signals respectively. Genes expressed at roughly equal levels appear as yellow spots.

sequence some of the genes that are differentially expressed during activation with human collagen type I and Ca^{2+} and compare homology analysis with the sequences in Gen Bank.

Global expression of genes in *E.histolytica* during collagen activation was analysed for the first time by genomic DNA microarray developed using 6144 clones from a random fragment genomic DNA library of *E.histolytica*. At least 14 genes, which showed reproducible overexpression in collagen-activated trophozoites after hybridization were sequenced (Fig.9). Most of these genes are important for the pathogenesis of *E. histolytica*. The hybridization of collagen-activated *E.histolytica* and normal *E.dispar* cDNAs and also between non-activated *E. histolytica* and *E. dispar* cDNAs are shown in Fig.10. The study is in progress.

Rotavirus

Emergence of a new genotype of bovine Group B Rotavirus

A surveillance study was conducted over a period of seven months in organized farms and cattle market in West Bengal to ascertain the role of rotaviruses as an etiological agent of diarrhoea. During this study, out of 175 diarrhoeic samples, 10.3% and 1.7% were positive for group A and B rotaviruses respectively. These 3 group B rotavirus (GBR) strains collectively referred to as Kolkata strains (DB101, DB176 and DB180) and were detected by RNA electrophoresis in polyacrylamide gel and confirmed by RT-PCR (Fig.11). Gene segment 9 and 11, coding for the VP7 and the NSP5 proteins respectively were sequenced to know variation among bovine group B rotaviruses. Comparison of sequences of Kolkata strains with other bovine GBR VP7 sequences showed a high level of diversity between them. The data indicated that these strains might be genetically distinct from other bovine GBR. Multiple alignments of all GBR VP7 amino acid sequences showed greater divergence among themselves. This divergence of the sequences clusters in several discrete regions. The distinct amino acid substitutions of VP7 sequences of Kolkata strains also differ from other bovine GBR which confined to these clusters of discrete regions. The data suggest that clustering of diverse regions may be the putative basis for genotype differentiation of group B rotaviruses.

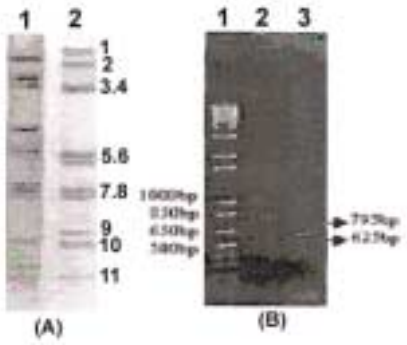


Fig. 11 (a). Electropherotyping of rotavirus dsRNA in 10% PAGE. Lane-1 and 2 represent electrophoretic migration pattern of bovine group A (4-2-3-2) and B (4-2-2-3) rotavirus strains detected during the study.

(b). RT-PCR products of the bovine Group B rotavirus isolates. Lanes 2, 3 represent the amplified VP7 gene (795bp, partial length) and NSP5 gene (625bp, full length), Lane 1, 1 kb plus molecular weight marker.

The diverse nature of Kolkata strains was also supported by the sequence analysis of NSP5 genes. NSP5 gene of Kolkata strains showed 54.9-60.9% and 49.1-50.6% identity with ADRV, CAL, IDIR and 80.5% and 82.5% with KB63 at nucleotide and amino acid level respectively.

The sequencing and sequence analysis of VP7 and NSP5 data showed that the Kolkata strains exhibit a novel type of GBR sequences, although their basic structural features are same as other GBRs. Based on the differences in sequences of VP7 gene one may postulate that Kolkata strains represent a new genotype from other bovine group B rotaviruses. Phylogenetic analysis of all GBR VP7 and NSP5 protein sequences also confirmed that three Kolkata strains form a separate cluster further supporting the distinct nature of these strains (Fig.12 & 13).

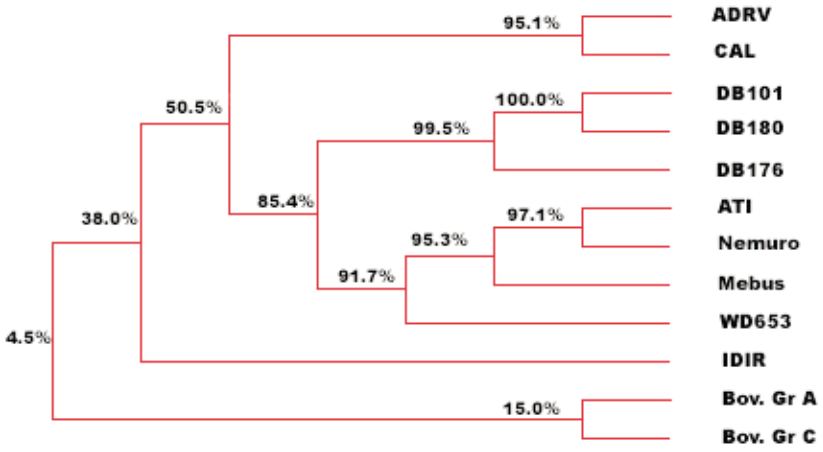


Fig. 12. Phylogenetic tree of VP_7 amino acid sequences of all the group B rotaviruses. Numbers at nodes represent the homology percentage.

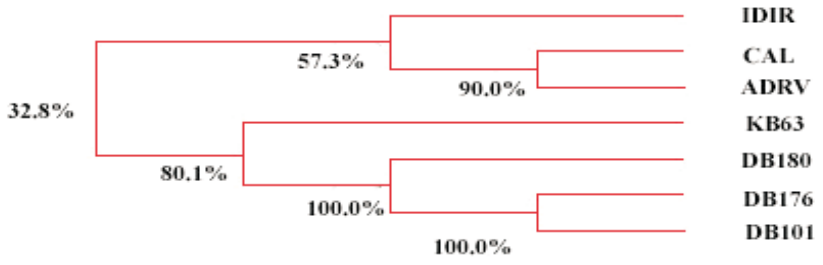


Fig. 13. Phylogenetic tree of NSP_5 amino acid sequences of all the group B rotaviruses. Numbers at nodes represent the homology percentage.

Molecular Characterization of Long Electropherotype and Subgroup I Strain isolated from Manipur

RMC321, the long electropherotype and subgroup I strain isolated from Manipur, which showed porcine characteristics in most of the genes sequenced so far, was partially characterized for the remaining three gene segments VP1, VP2 and VP3. As it revealed porcine characteristics in 7 of 8 genes sequenced earlier, it was decided to complete the characterization of all the 11 segments of RNA of this particular strain. RMC321 was found to have very close genetic relationship with porcine strain (HP140) in VP1, VP2 and VP3. Both of them shared 97.2% identity in VP1, absolute identity in VP2 and 96% identity in VP3. These were the highest identities RMC321 shared with any known strain for the respective genes. Both the strains clustered together in the phylogenetic tree of VP1 (Fig.14), VP2 and VP3. The results indicate that the overall genetic constellation of Manipur strain is very close to porcine rotaviruses. Only the VP7 gene seemed to have originated from a human rotavirus genetic constellation. The data indicate that VP7 may hold the passport for cross-species transmission.

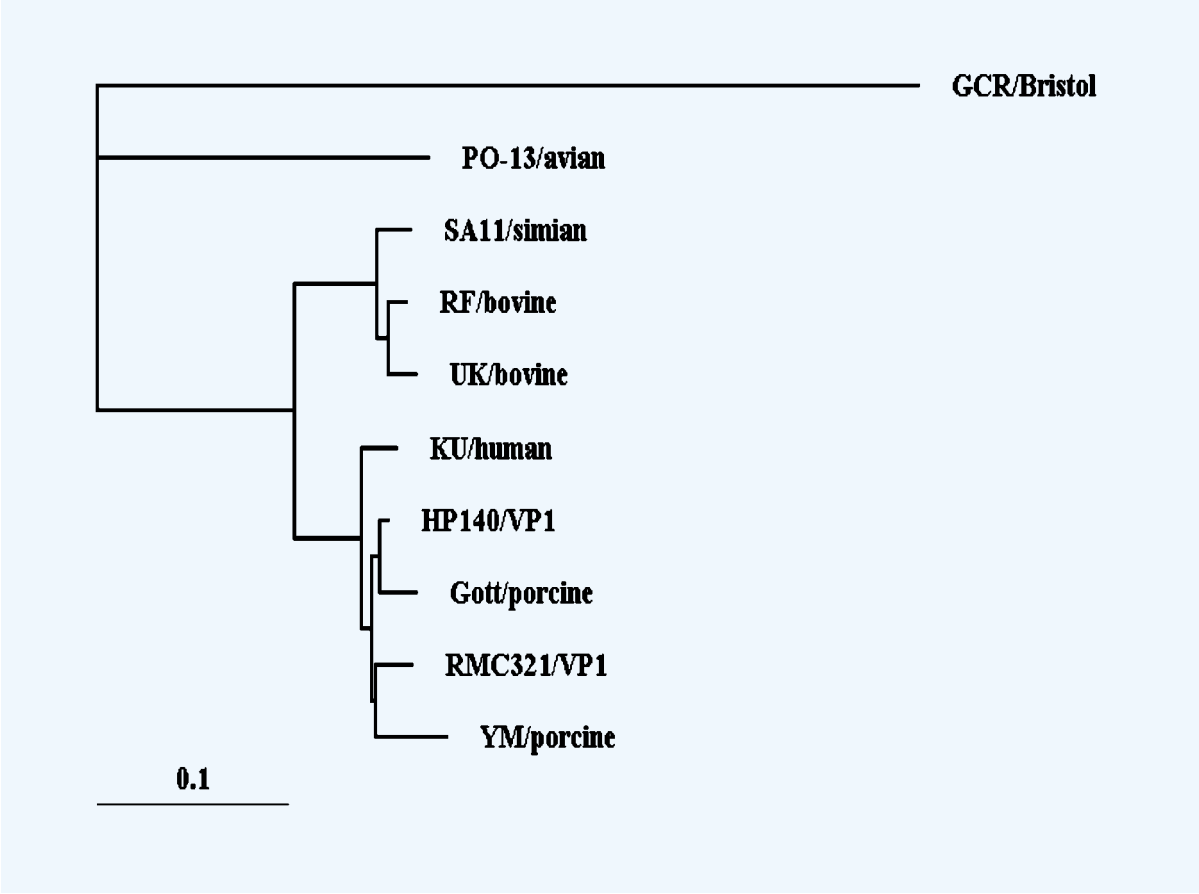


Fig. 14. Phylogenetic tree of partial VP1 amino acid sequences of human and animal strains along with the Manipur (RMC321) and porcine (HP140) strain. RMC321 clustered with porcine rotaviruses.

OTHER MICROBIAL INFECTIONS

LEPTOSPIROSIS

In Andamans, leptospirosis caused by *Leptospora grippotyphosa* occurs mostly as outbreaks during post-monsoon period. Involvement of respiratory system is a common complication manifesting as haemoptysis and is associated with high morbidity and mortality.

Leptospiral Proteins Expressed during Acute and Convalescent Phases of Human Leptospirosis

An understanding of leptospiral protein expression during acute and convalescent phases is helpful to develop new immunoprotective and serodiagnostic strategies. Quantitative immunoblot analysis was performed using paired sera (acute and convalescent) from confirmed cases, serologically negative, normal healthy controls and patients with other diseases by the RMRC, Port Blair. Leptospiral protein 32 was found to be predominantly expressed with higher seroconversion, which may be useful for serodiagnosis and serosurveys.

Development of Latex Agglutination Test for Diagnosis of Leptospirosis

Characterization of different types of antigens (whole cell lysate, heat extracted and detergent soluble) from serovars/strains of leptospires prevalent in India was done at RMRC, Port Blair. As a first step three strains of leptospires belonging to serogroups *grippotyphosa*, *andamana* and *semaranga* respectively were used. Different antigenic preparations were made from these strains. The latex agglutination test developed was considered positive when there was clear agglutination and negative when there was no agglutination (Fig.1).

Fig. 1. Positive and negative agglutination patterns in indigenously developed latex agglutination test.

Microscopic agglutination test (MAT) showed a sensitivity of 86.7% and a specificity of 90%. Fifteen percent cross reactivity was observed among the sera from typhoid patients whereas 10% false positive results were found in hepatitis B virus positive sera. No cross reactivity was reported in samples collected from malaria.

New Serovar of a New Serogroup of Leptospires

While investigating outbreaks of leptospirosis in Andaman islands, four isolates were recovered from patients. Three of them were identified as belonging to serogroup *grippotyphosa*. However, serological tests done on the fourth isolate (Fig 2 & 3) did not yield conclusive evidence to place it in any of the known serogroups.

Fig. 2. Isolate DS-2 under light microscope (Fontana stained smear).

Fig. 3. Electron microscopic view of isolate DS-2.

The isolate coded as DS2 showed typical morphology and characteristic motility of the genus *Leptospira* on field microscopic examination. DS2 as well as the pathogenic

reference strains Wijnberg, Jez Bratislava did not show growth at 13^{0}C and in the presence of 8-azaguanine even at 21 days of incubation indicating the pathogenic nature of the isolate.

The results of the serological experiments on the isolate did not fulfill the criteria laid down by the International Committee on Systematic Bacteriology to place the isolate into any serovars/serogroup. Therefore, the isolate has been designated as a new serovar Portblairi and placed in a new serogroup Sehgali.

Genomic Fingerprinting of the Serogroup of Leptospires

The strain DS2 that was identified as a new serovar Portblairi of a new serogroup Sehgali was characterised using PCR followed by sequencing of the PCR product RAPD and fluorescent amplified fragment length polymorphism (FAFLP)

Fingerprints generated using primer PB1 revealed that the isolate DS2 shared highest percent identity (85%) with the two strains Ballico and RGA which belong to genospecies *L. interrogans* (Fig.4 & 5).

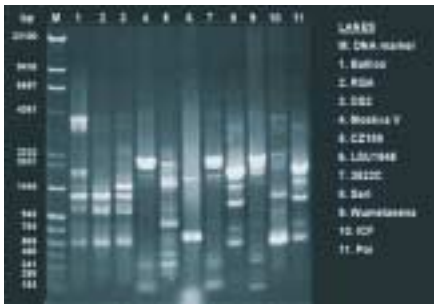


Fig. 4. RAPD fingerprints of isolate DS2 and reference strains belonging to six species generated with the primer PB1.

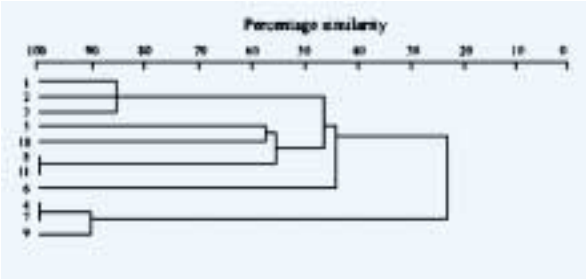


Fig. 5. Neighbour joining tree constructed using RAPD data (PB1 primer) of DS2 and ten reference strains belonging to 6 genospecies.

The fingerprints generated with the primer set B11 and B12 also showed that the isolate DS 2 has highest genetic similarity of 87% with the strains Ballico and RGA (Fig. 6 & 7).

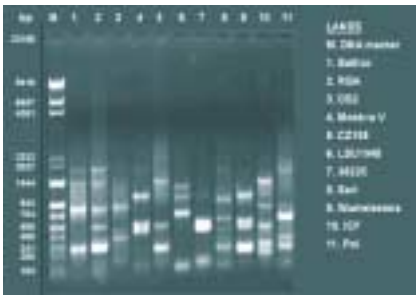


Fig. 6. RAPD fingerprints of isolate DS2 and reference strains belonging to six species generated with the primer B11 and B12.

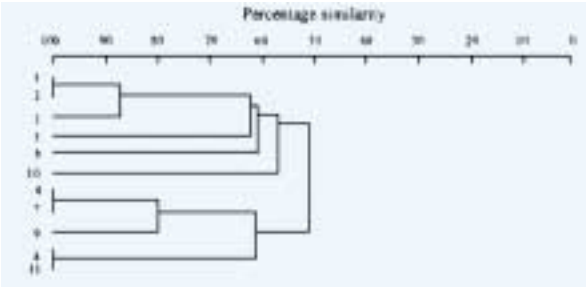


Fig. 7. Neighbour joining tree constructed using RAPD data (B11 and B12 primers) of DS2 and ten reference strains belonging to 6 genospecies.

FAFLP using two sets of primers generated a total of 76 fragments ranging in size from 50-500 base pairs. Analysis of the binary data of ten reference strains belonging to six genomomic species revealed six amplitypes (genotypes). The isolate DS2 was closely related to the amplitype formed by the reference strains belonging to the genomic species *L. interrogans sensu stricto.* (Fig.8).

The species *L. interrogans sensu stricto* has highest collection of serovars of different serogroups (87 serovars belonging to 15 sergroups) The strain DS2 is to be considered as a new entry into it. All the isolated leptospires causing pulmonary haemorrhage so far have been identified to be belonging to *L. interrogans sensu stricto* but belong to different serovars and serogroups.

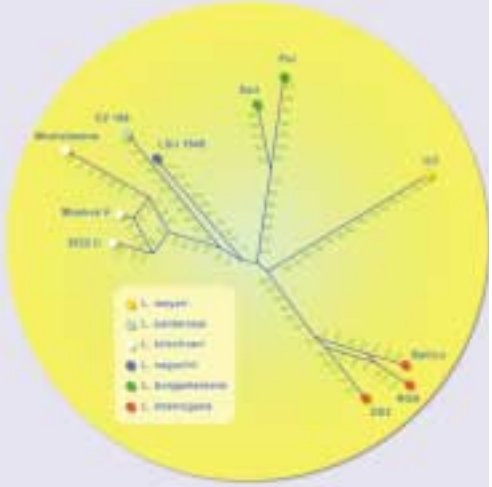


Fig. 8. Network tree constructed using FAFLP data of the new isolate (DS2) and reference strains belonging to six genospecies of leptospires.

Fluorescent Amplified Fragment Length Polymorphism (FAFLP) - A Useful Tool in Molecular Epidemiology of Leptospirosis

Genetic characterization using high resolution technologies is a possible method to throw light into the molecular epidemiology of infectious diseases. Phylogenic relatedness among leptospiral isolates recovered during investigation of three major outbreaks and from several sporadic cases occurring in Andaman Islands was analyzed at RMRC, Port Blair using FAFLP technique.

Out of the 21 isolates collected from epidemic and sporadic cases in Andamans during 1996, 1997 and 1999, serotyped and characterized using FAFLP, 13 were found to belong to serogroup *grippotyphosa*, 3 to *australis*, 2 to *icterohaemorrhagiae* and one each to *hebdomadis*, *canicola* and *sejroe*. Selective PCR with six sets of primers generated a total of 26 polymorphic fragments ranging in size from 50-500 base pairs (Fig.9).

The phylogenetic tree (Fig.10) showed that all the isolates were grouped into two main clusters or amplitypes or genotypes with genetic distance of 33% between these. Each main cluster had several sub clusters. The first cluster (cluster I) has several sub - clusters, of which one (I – A) is a tight grouping of eight isolates with 100% similarity. All these isolates belonged to serogroup *grippotyphosa* but four of them showed close relation to serovar *ratnapura* and remaining four to serovar *valbuzzi*.

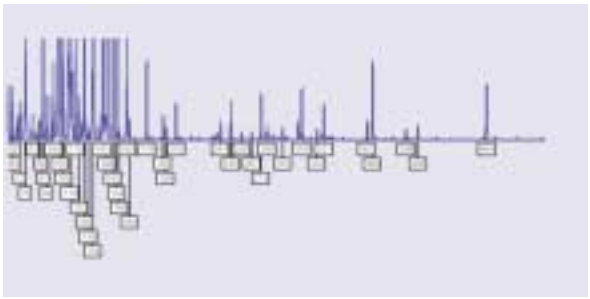


Fig. 9. Genescan of isolate FIS02.

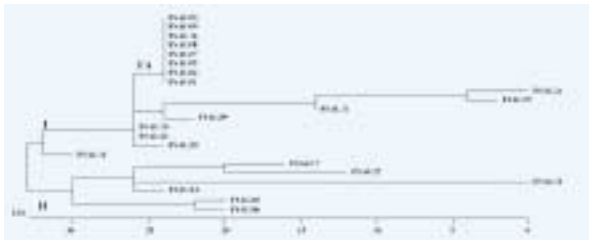


Fig. 10. Neighbour joining tree constructed with FAFLP data of leptospiral isolates from Andamans.

All these isolates except one were recovered during epidemics. However, these epidemics were at different times and in different places. Out of 21 patients from whom isolates were obtained, six had severe illness with complications such as renal failure, abnormal liver function or pulmonary involvement. Out of these six isolates from patients with complications five fell into this cluster (I – A). There were only two isolates from North Andaman epidemic and both were serovar *valbuzzi* and were in subcluster I – A. The isolates obtained from Manglutan during 1999 epidemic and those from sporadic cases in South Andaman showed great genetic diversity. Their serogroups were also diverse.

The subtype I – A, with eight strains isolated at different times and places falling under it with absolute genetic similarity appears to be the dominant strain causing outbreaks. All these isolate were of serogroup *grippotyphosa*. The earliest isolates included in the study were obtained in 1996 and 1997 in North Andaman. It seems that this clone (amplitype - I-A) evolved

in North Andaman, where it was causing outbreaks of Andaman haemorrhagic fever (local name for leptospirosis with pulmonary involvement) since 1988, spread to South Andaman by 1999, as it was responsible for some of the cases during the 1999 outbreak in South Andaman.

PARASITIC DISEASES

MALARIA

Malaria caused by *Plasmodium falciparum* is a disease with serious consequences. Malaria control is a complex problem particularly in view of the insecticide resistance developed by the vector species and also vector behaviour and emergence of drug resistance in *P. falciparum*. Most of the studies on malaria are being carried out by the Council's Malaria Research Centre (MRC) at Delhi, Vector Control Research Centre (VCRC) at Pondicherry and various Regional Medical Research Centres (RMRC) of the Council.

Studies on Species Complexes of Malaria Vectors

Major malaria vectors are complexes of several sibling species which differ in their vector competence. Hence studies are being undertaken on the identification of new sibling species, their bionomics and development of simple diagnostic tools for use in disease control programme.

An. fluviatilis Complex

The MRC has discovered a new species in *An. fluviatilis* complex—species V from Haridwar, which is fourth species in the complex. The new species is characterized by presence of two fixed inversions in chromosome arm 2 and 3.

The PCR assay developed by MRC for differentiation of the three known members of *An. fluviatilis* complex *i.e.*, species S, T, and U was field validated using cytologically identified members of the complex collected from various parts of India representing different sympatric associations.

Studies on P. vivax-refractory An. culicifacies

To understand molecular basis of refractoriness in *P. vivax*-refractory *An. culicifacies*, molecular characterization of pro-phenoloxidase and serine proteases was undertaken. Full open reading frame of serine protease gene was cloned, sequenced and expressed using expression vector pET *43a* and *E. coli* host BL21(DE-3). The gene of serine protease was found to be present in both refractory and susceptible strains.

Prospecting for Botanical Pesticides

Bioactivity, larvicidal, adulticidal and mosquito repellent properties of various herbal extracts/fractions/formulations were determined against mosquitoes particularly the malaria vector *An. stephensi* using standard protocol. Of the 331 samples tested, 46 showed larvicidal activity, 11 insecticidal activity against adult mosquitoes and 5 repellent activity for more than one hour.

Resistance Monitoring in Malaria and Dengue Vectors

The MRC was identified for carrying out studies to establish the diagnostic doses against two pyrethroid insecticides, alpha-cypermethrin and bifenthrin. *An. culicifacies species C*, *An. stephensi* and *Ae. aegypti* were tested using standard WHO protocols. *An. culicifacies* registered 98% mortality against alpha-cypermethrin and *An. stephensi* and *Ae. aegypti* registered 99% mortality against bifenthrin. Similarly for *An. stephensi* 94% mortality was registered against 0.05% alpha cypermethrin and 99% against 0.25% bifenthrin. Likewise *Ae. aegypti* registered only 91% mortality at 0.05% alphacypermethrin and 99% at 0.25% bifenthrin.

Laboratory and Field Evaluation of Biocide/Insecticide Formulations

VectoBac Wdg (Bti) Formulation

A new biolarvicide formulation of *Bti viz.* VectoBac wdg provided by Sumitomo Chemicals

was evaluated against immatures of different mosquitoes in laboratory. In the laboratory bioassays the formulation was most effective against larvae of *C. quinquefasciatus*, followed by *Ae. aegypti*, *An. stephensi* and *An. culicifacies*.

Pirimiphos Methyl

Efficacy of pirimiphos methyl, an organophosphorus insecticide, was evaluated against immatures of *Anopheles* and *Culex* spp. in laboratory and under field conditions in different types of breeding habitats. In the laboratory bioassays, it was found to be most effective against larvae of *An. stephensi* followed by *An. culicifacies* and *Cx. quinquefasciatus*. Under field conditions, pirimiphos methyl at dosages of 100 and 200 g.ai /hectare, produced 100% reduction in the larval density of *Anopheles* and *Culex* mosquito spp. in clean and polluted water habitats respectively within 24 hr. However, up to one week pirimiphos methyl at dosages of 200 & 300 g.ai /hectare produced 80% to 100% reduction in the density of immatures in clean and polluted water habitats.

Clinical Drug Trials

Therapeutic efficacy studies with first and second line antimalarials namely chloroquine and sulfa-pyrimethamine (SP) were conducted in falciparum malaria according to standard WHO protocols in Orissa, North eastern states and across international borders.

The analysis of data showed good efficacy of chloroquine and SP in Keonjhar town and Padampur (Keonjhar). However, high failure rates (upto 50%) were observed in Bisra and Kuarmunda CHCs (Sundergarh). In Assam failure rate of 34% and 30% was observed in Sonapur (Kamrup) and Kathiatali (Nowgaon) respectively with chloroquine, however, efficacy of the drug was good in Boko (Kamrup district).

The efficacy of chloroquine was also evaluated along Indo-Nepal border in Darjeeling (West Bengal). Cumulative failure rates were 66 and 33% respectively in Sukna and Naxalbari Block PHCs. Results of the study indicate the need to review the drug policies especially along international borders where there is free population movement. As a new initiative in therapeutic studies molecular markers were used to differentiate fresh infection from recrudescence in *P. falciparum* isolates from Assam and Orissa.

Therapeutic efficacy of chloroquine in *P. vivax* malaria was investigated in Gautam Budh Nagar (U.P.), Navi Mumbai and Chennai. In 287 patients the curative efficacy of chloroquine was found to be 100%.

Drug Development

In view of decreasing efficacy of existing anti-malarial drugs especially in *P. falciparum* malaria new molecules/herbal products were screened at MRC for possible anti-malarial activity. *In vitro* and *in vivo* antiplasmodial and *in vitro* cytotoxicitiy activity of xanthones isolated from the roots of *Andrographis paniculata* were conducted. Sixty two percent reduction in parasitemia was observed in *in vivo* studies.

Nitric oxide (NO) is known to possess antiparasitic activity towards *Plasmodium* species. Inhibitory effect of NO was studied on the activity of plasmepsin in *P. vivax*, the pepsin- like aspartic protease believed to be involved in the cleavage during hemoglobin degradation in *P. falciparum*. The results provide novel insights into the pathophysiological mechanisms, and will be useful for designing strategies for selectively upregulating NO production in *P. vivax* infections for antimalarial chemotherapy.

Development of Field Sites for Malaria Vaccine Trial

Rourkela and Jabalpur field sites are being developed by MRC for testing of vaccines.

Rourkela

In a collaborative project with ICGEB, longitudinal epidemiological studies of villages in forest and plain areas characterized by hyper- and meso-endemic malaria situations respectively are being conducted. It includes determination of malaria incidence, API, IPR, CPR and attack rates due to *P. falciparum*. In

addition, malaria prevalence during different transmission seasons was measured through cross-sectional point prevalence surveys in all the study villages.

Entomological surveys were carried out and a total of 14 anopheline species from forest and 10 species from the plain area were recorded. *An. culicifacies* was widely prevalent throughout the year in both forest and plain areas with prevalence rate of 38.8 and 24.9 % respectively. *An. fluviatilis* was restricted to the forest area and its prevalence rate was 6.3 %. Transmission load in the study area measured through entomological inoculation rate (EIR) was nil in strains whereas in forest area it was 0.0, 0.085 and 0.35 infective bite per person per night during low, intermediate and high transmission seasons respectively.

Studies on host immune response have shown that overall anti-$MSP1_{19}$ IgG profile was higher in study subjects of forest areas than plains in both low and high transmission seasons. The age-dependent increase in specific antibody levels was noticed in individuals of these areas in both seasons. Results also suggest that there was a boosting in antibody production against this molecule by natural infections among these individuals.

Highly polymorphic nature of *P. falciparum* isolates in respect of MSP1 and MSP2 gene was observed with more than 60% of the isolates harbouring more than one parasite genotype suggesting that multiplicity of infection is mostly greater than 1.

For the success of development and testing of malaria vaccine it is important to know diversity existing among the parasite populations of the area. Sequence diversity studies carried out on these isolates revealed sequence variations in $MSP\text{-}1_{19}$, TRAP and EBA 175 rII. In EBA 175 rII, out of 20 variations, 15 were new, not reported earlier from any geographical region of the globe. Binding efficiency and inhibition assay revealed that these new mutations in EBA rII region do not affect the binding efficiency of parasite to human erythrocytes thus supporting the view that a vaccine based on these constructs is feasible to work universally.

Jabalpur

Field and laboratory studies aimed at investigating parasite infection, host immune responses, parasite and mosquito characteristics are being conducted in Jabalpur. The relationship between immune responses and genetic diversity will be analyzed in the context of level of parasitaemia and clinical illness (fever, anemia, cerebral malaria, and placental infection).

Genetic Polymorphism in Human Plasmodia Species

Understanding genetic structure of the human plasmodia species and information on the genetic diversity existing among the parasite populations are important for the developments and testing of malaria drugs/vaccines. Therefore, isolates are being characterized for genetic/ molecular markers.

Analysis of microsatellite markers and single nucleotide polymorphism (SNPs) in house keeping genes have been initiated to get information on genetic relatedness of the geographically diverse populations and to understand gene flow in the species. More than 90% *P.falciparum* isolates studied from Orissa comprised multiple infection of genetically different genotypes. All the microsatellite markers studied were observed to be highly polymorhic with allele number ranging between 4 to 10 and allele size between 66-250 bp. $L_{35}e$, house keeping gene was observed to show good number of SNPs.

Analysis of *P. vivax* field isolates has been initiated to study distribution of two populations of *P. vivax*, old world (Asia and Africa) and new world (Europe and America) on the basis of small subunit RNA and data indicate the presence of both the populations among the Indian isolates.

Analysis of T-helper epitopic regions (Th2R and Th3R) of CSP of *P.falciparum* isolates from different geographical regions of India have shown variations to be regionally unbiased, however, variations could be categorized into four groups. The variations in two groups of both Th2R and Th3R showed sequence identity with the variation in other geographical regions

of the world. Therefore, prototype variants from different groups could be included in subunit polyvalent vaccine against sporozoites, which could be of global use.

Diagnostics for Malaria Parasite

A *P. falciparum* blood stage antigen, (glycophospholipid antigen) was isolated from *in vitro* parasite culture supernatant. Analysis of chemical composition of the antigen revealed the presence of sugars such as galactosamine, galactose, mannose, glucose, rhamnose and frucose. Lipid as core structure comprised docosahexanoyl and docosanoyl and phosphate as phosphorylcholine.

Malaria in Pregnancy

Epidemiological and clinical data on malaria during pregnancy in Indian subcontinent are very scarce. Therefore, a prospective study was undertaken at district hospital, Mandla (M.P.) in an area where both *P. vivax* and *P.falciparum* coexist. The results revealed that at delivery, the parasitaemia in maternal peripheral blood, placental and umbilical cord blood was 12%, 26% and 12% respectively. Both *P.vivax* and *P.falciparum* were recorded from placenta and umbilical cord blood. The mean birth weight of 51 babies born to mothers with infected placentae was significantly low as compared to 150 babies born to mothers without infection. Moreover, a large number of asymptomatic pregnant women of all parity groups had subpatent parasitaemia with *P.falciparum*. The findings have important practical implications for the development of an effective intervention strategy and programme to reduce the impact of malaria in pregnant women.

Parasite Bank

The Malaria Research Centre has a well established Parasite Bank. The Bank has stock of human and non-human plasmodia which are cryopreserved and used for various in-house studies and also provided to other institutes. In addition, the bank has well characterized isolates for chloroquine sensitivity, cytoadherence, molecular marker and erythrocytic invasion properties.

Geographical Information System (GIS)

Mapping of distribution of all 58 anopheline species was completed during the year. A CD has been produced consisting of 58 maps each showing the GIS predicted distribution in India, along with the blow up map of GIS predicted districtwise in favourable areas and the validation of GIS predicted distribution through reported surveys. This data can be used to identify malaria risk free areas and for delineation of the areas favourable for any species.

In Mewat region, (Gurgaon) GIS was used to i) delineate five malaria paradigms namely, irrigation command, catchment, mining, urban and flood prone areas at macro level; (ii) identify eco-epidemiological characteristics of each paradigm and (iii) identify the receptivity for malaria paradigm/s. Paradigm wise receptivity revealed that during 1996 (an epidemic year), different paradigms responded differently. Although all paradigms showed upward trend, maximum amplification occurred in urban/ semi urban paradigms. During the last two inter-epidemic periods (1993 and 1998), flood prone paradigm, irrigation command area II and non-catchment area continued to retain active pockets of malaria.

Epidemiological Studies

Dynamics of Malaria in Rajasthan

Malaria continues to be the major cause of morbidity and mortality in the desert districts of Rajasthan. During the year 2003 there have been 73,808 cases of malaria in six desert districts including 3,691 of *P. falciparum*. As malaria appears in Rajasthan in the form of seasonal morbidity, a comprehensive study of the epidemiology of unstable malaria in 26 villages of Jaisalmer and Jodhpur districts was undertaken by DMRC, Jodhpur. The observations have indicated that during beginning of malaria season about 63 to 80% malaria in different settings is imported through in-migration. Migration thus plays role of primary risk factor of malaria. Availability of more cattle leads to increase in zoophilic index of vector species such as *An. stephensi* which

reduces risk of malaria transmission. Rainfall above normal combined with imported malaria forms set of epidemic risk factors of malaria in desert. Just in the beginning of monsoon season, people who had left for green pastures for their cattle and sheep in the post monsoon season of previous year return home. A part of this population harbours malaria which becomes primary risk factor in rainy season. Due to rains mosquito breeding sites increase in number and also life expectancy of vectors increases due to optimum ambient humidity levels. Vectors thus act as secondary risk factor and increase in their density in more and more areas leading to a number of areas becoming receptive to malaria infection. In the areas where malaria is brought by in-migrants, local transmission starts. In favourable seasons few local foci also act as disseminating centres of infection (Fig.1).

Fig. 1. Dynamics of malaria in desert.

Malaria in Tribals of Madhya Pradesh

Following an outbreak of malaria in Betul district in the year 2000 which claimed several lives, RMRC, Jabalpur investigated the epidemic. In October 2000 rapid fever surveys revealed that slide positivity rate was >50% with over 90% *P. falciparum*. Spleen rate among children (2 to 9 yr) was over 70%. Only 10% of *An. culicifacies* population was susceptible to DDT.

Post intervention follow up revealed steady decline in malaria situation. There was 98% and 99% reduction in SPR and SFR respectively in 2003 (Fig.2). Spleen rate showed 88% reduction (Fig.3). Sharp reduction (63%) in anopheline

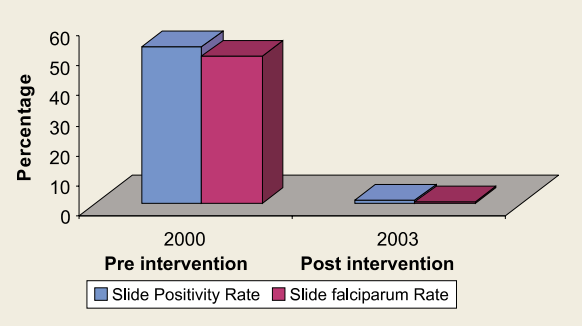


Fig. 2. Malaria prevalence in study area of Betul.

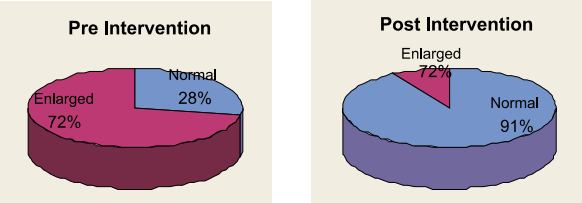


Fig. 3. Spleen enlargement in study area of Betul.

density was recorded in 2003 as compared to 2000. The study revealed that similar intervention measures may be used to contain malaria in other tribal areas.

A study on transmission dynamics of malaria was pursued in two tribal areas namely Baigachak, characterized by thick evergreen monotonous forest of *Saal* and Kanha, characterized by mixed forest of *saal* and *teak*. Slide positivity rate and slide falciparum rate were significantly high in *Baiga* as compared to Kanha area (Fig.4).

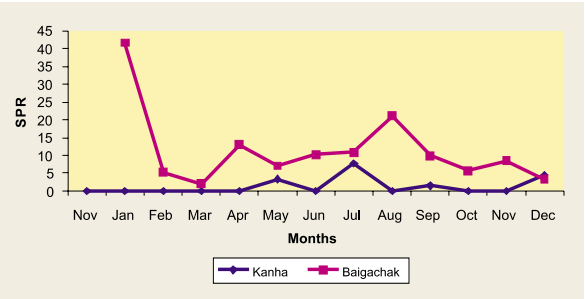


Fig. 4. Monthwise slide positivity rate in study area.

Density of anophelines was significantly higher in Kanha than the Baigas. *An. culicifacies* was found resistant against DDT and was susceptible to deltamethrin. *An. culicifacies*

sibling species composition shows that species C is predominant in both the areas. Only few specimens were identified as species A/A1 from Baigachak area.

FILARIASIS

Around one third of the world's population at risk of lymphatic filariasis infection lives in India. India is a signatory to the World Health Assembly resolution (1997) on elimination of lymphatic filariasis as it is a major tropical disease and remains a significant health problem in India. Filariasis due to *Wuchereria bancrofti* is the predominant type in the country accounting for 98% of cases. Filariasis caused by *Brugia malayi* is limited to a few pockets in Assam, Orissa and Kerala. Studies on filariasis are being carried out mainly by the Council's VCRC at Pondicherry, Centre for Research in Medical Entomology (CRME), Madurai and RMRC, Bhubaneswar.

Molecular Studies in Filariasis

Molecular Epidemiology and Genomics of Filariasis

At VCRC, Pondicherry genetic variation of *W. bancrofti* populations from different geographic regions of India was investigated at spatially hierarchical levels *viz*., a) parasite isolates collected from different geographic regions, b) parasites within a region, c) within a mf carrier and d) parasites under chemotherapeutic (DEC) pressure, through RAPD fingerprinting and population genetic structure analysis. The genetic heterogeneity of populations of this parasite at geographic level was reported last year. Heterogeneity at regional and local levels has been analyzed during the year.

Regional Variations

Genetic variation among 34 parasite populations from within a region constituting Pondicherry town and the nearby villages (around 5-10 kms) *viz*., Thondamanatham, Sethurapet (adjacent to each other), and those at a distance of 40-50 kms *viz*., Alampoondi, Chinnanergunam and Athipakkam, is presented in Fig.1. The isolates from this region formed 2 lineages with three populations *viz*., from Soukupet, Sethurapet and Thondamanatham forming one single most ancient lineage than the other. The second lineage comprised 2 sub-lineages with rural populations from Alampoondi village forming the earliest branching populations. The second lineage is highly heterogeneous comprising parasite populations from Pondicherry as one cluster and Chinnanergunam and Athipakkam populations forming another. While Athipakkam village populations showed high homogeneity, that from Channanergunam village branched into two clusters. The single population from Pondicherry (P3) presented itself as separate sub-lineage.

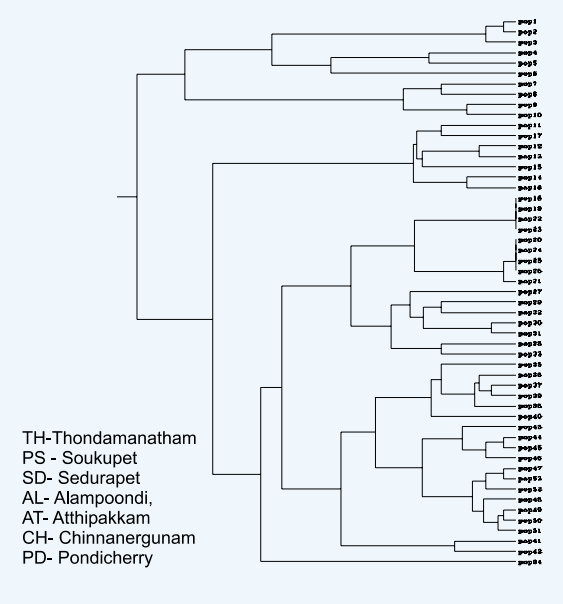


Fig. 1. Phylogenetic analysis of *Wuchereria bancrofti* from Pondicherry and surrounding areas.

Local Variations

When 20 parasites were analyzed, isolates were found to form two main clusters, one isolate forming one lineage while second lineage comprised the remaining 19 isolates, which formed 4 sub-clusters. This indicates that in an urban area like Pondicherry the parasite populations show great genetic variations and that there are at least 5 genotypes of *W. bancrofti* circulating among the human host populations. The genetic heterogeneity in this area could be

due to several reasons such as-a) the migration of infected individuals from surrounding lymphatic filariasis endemic areas for trade, employment and medical treatment, and b) long term chemotherapy. Hectic commercial and construction activities are going on in Pondicherry, known for good medical and educational facilities which attracts traders, labourers, patients as well as students who migrate temporarily/permanently from the surrounding districts of Tamil Nadu (endemic for lymphatic filariasis) and Andhra Pradesh. This leads to pooling and mating of different genotypes of the parasite from different geographic regions.

Variation within a mf Carrier

The worm burden in an individual carrier and their genetic diversity has important implications in chemotherapy and clinic outcome. The utility of RAPD was tested for understanding the genetic diversity of parasites within a mf carrier. The diversity of parasites generated for the mf populations in a mf carrier of age 30 yr is presented in Fig.2. The population structure showed high divergence with at least 5 major clusters. Subsequently, mf from carriers of different age groups were analyzed for diversity. A 14 yr old mf carrier showed 3 clusters. On the other hand, mf from carriers of 34 and 45 yr were more heterogeneous with longer branch lengths and falling under distant genetic clusters revealing that the parasite heterogeneity increases with age of the carrier.

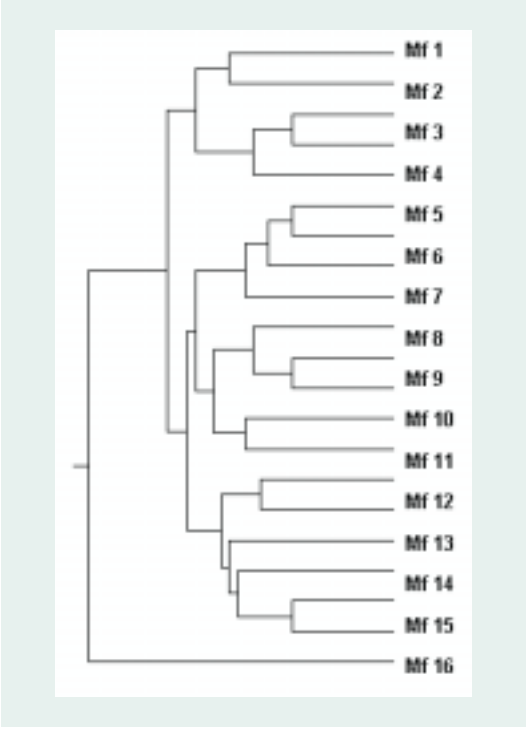


Fig. 2. Dendrogram of mf population in a microfilaria carrier.

Chemotherapy and Genetic Variation

Long chemotherapy is likely to lead to genetic divergence among parasite populations, often leading to the selection of resistant ones. Preliminary analysis was carried out to assess the occurrence of genetic divergence among mf populations due to treatment with conventional anti-filarial drug diethylcarbamazine (DEC). The populations of mf collected from two individuals before and after treatment were analyzed. The analysis showed that the mf that survived treatment formed a separate cluster, indicating that the drug treatment plays a role in the selection of certain population, which does not respond to the drug.

Thus, the results showed that the RAPD fingerprints generated for different isolates are bar code like profiles for *W. bancrofti* isolates of different geographic regions, as they clustered according to their geographical origin. Thus it appears that there is limited gene flow between parasite populations of different geographic regions. The only exception is Rajahmundry populations, forming two groups, one independent (cluster 5) and the other (cluster 3) with rural populations constituting the second major lineage. The parasite populations grouped into 12 clusters with varying numbers of genotypes in each cluster, *viz.*, rural/urban, with/without chemotherapy and or human migration. Most of the rural parasite populations are genetically homogeneous, except those that were under anti-filarial drug pressure. This indicates that long-term chemotherapy programmes lead to genetic restructuring of parasite population which has bearing on the selection of drug resistant populations. The study also showed that the rural parasite populations from Thondmanatham and Sethurapet are the most ancestral populations followed by the Calicut

populations indicating that the *W. bancrofti* parasites moved from rural to urban areas and are now drifting from southern most part of the country to the central region and then towards northern regions.

Molecular Tools for Detection of Parasites in Vectors

Evaluation of Simple and Rapid DNA Extraction Method for Xenomonitoring of W. bancrofti Infection in the Vector Mosquitoes

At the VCRC, a PCR assay has been developed for detecting lymphatic filarial parasites in vectors utilizing a simple, less expensive and rapid method for extracting DNA from infected vectors. In order to test the utility in the operational programmes, the method was validated in an ongoing filariasis control programme. The results of the validation showed that the method was efficient in detecting the infection in the vector mosquitoes. It has certain advantages over the latter method in that the infection can be detected in large pools in low-level infection areas and can be employed in operational programmes.

Immunological Studies

Identification of Molecular Markers for Diagnosis of Infection and Morbidity in Lymphatic Filariasis

For effective management of filariasis it is essential to understand the pathogenesis of the disease and to develop markers for morbidity. At RMRC, Bhubaneswar pro and anti-inflammatory molecules quantified for development of markers included TNF-α, TNF-α receptors type1 and type2, IL-10, IL-6, IL-8, LPS binding protein and sICAM-1. The levels of two TNF-α receptors could differentiate elephantiasis and hydrocele; acute disease and chronic filariasis differed in terms of levels of TNF-α. IL-6 and IL-8 were shown as best markers of disease morbidity since subjects with asymptomatic infection were significantly different from those with acute or chronic disease and thus could be differentiated from each other. Immunomodulators which decrease pro-inflammatory cytokines such as IL-6, IL-8 and TNF-α can now be used for clinical management of filariasis. Clinical trials are being planned for further studies.

Immunological Responses in W. bancrofti and B. malayi Infections

Study of immunological (immunoglobulin and cytokine) responses in *W. bancrofti* and *B. malayi* infections in endemic areas of India was carried out by PGIMER, Chandigarh in collaboration with VCRC, Pondicherry and T.D. Medical College, Alleppey. The results showed that none of the *W. bancrofti* mf carriers became antigen negative till 365 post treatment day, although no mf were detected in 42% and 13% of them on 180 and 365 post treatment day respectively. Significant antigenemia was detected in 54% endemic normals as compared to nil in non-endemic subjects. Cytokine response analysis revealed no significant difference in pre- and post treated samples of mf carriers.

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

A study carried out on different immunological factors across the clinical spectrum of filariasis in an endemic area carried out at Mahatma Gandhi Institute of Medical Sciences (MGIMS), Sevagram concluded that immunomonitoring of filarial cases lead to a significant decrease in filarial specific IgG4 antibodies in all the three groups *viz.* microfilaraemic, chronic and occult filarial cases after treatment with DEC. While there was no significant decrease in filarial IgG1 and IgG2 subtypes, filarial IgG3 antibodies increased significantly in chronic filarial cases after DEC treatment.

Studies on Mass Chemotherapy

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

Transmission interruption through annual single dose mass drug administration (MDA) is

the recommended strategy to eliminate lymphatic filariasis (LF) and is being widely used in many countries. DEC or ivermectin alone or in combination with albendazole are the drugs being used under the MDA programme. The impact of these drugs on microfilaraemia prevalence and transmission in relation to the number of annual treatments has tremendous implications for the LF elimination programmes. Therefore, a community level longitudinal study is being carried out by VCRC, Pondicherry, in rural areas of Villupuram district in Tamil Nadu, to evaluate the effectiveness of 8-10 cycles of mass administration of DEC alone or ivermectin alone or DEC+ivermectin or DEC+albendazole on (a) microfilaraemia prevalence (b) transmission of infection and (c) prevalence of chronic disease. So far, eight rounds of annuals mass administration of DEC and ivermectin, six rounds of DEC+ivermectin and two rounds of DEC+albendazole have been given and evaluated. Each drug or combination of drugs was given in five villages each.

The effect of MDA on microfilaria (mf) prevalence was assessed by night blood survey of all members of 7% randomly selected households in each village. The blood surveys were carried out prior to each round of MDA. The impact on transmission is measured through changes in infection and infectivity rates of vector mosquitoes, collected in each village. The entomological surveys are carried out after each round of drug administration. The effect of MDA on chronic disease was evaluated by comparing its prevalence between pre-intervention and post-seventh intervention period.

During the eighth round of MDA, the compliance with MDA was 60% in DEC arm, 64% in ivermectin arm, 61% in DEC+ivermectin arm and 69% in DEC+albendazole arm. Eight rounds of MDA of DEC reduced the mf prevalence from pre-intervention level of 13.2% to 2.18%, which is equivalent to 84% reduction. Ivermectin reduced it from 14.5% to 3.1% (Fig.3). The geometric mean intensity (GMI) of mf fell from the pre-treatment level of 0.66 to 0.04 in DEC arm and from 0.62 to 0.07 in ivermectin arm (Fig.4). The vector infection rate was reduced from pre-intervention level of around 18.0% in both the arms to 3.0% in DEC arm and to 2.8%

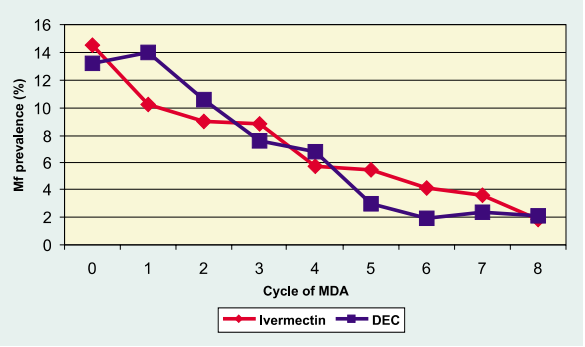


Fig. 3. Impact of eight rounds of MDA on mf prevalence.

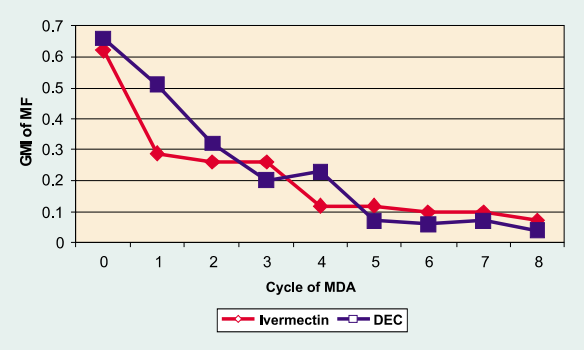


Fig. 4. Impact of eight rounds of MDA on GMI of mf.

in ivermectin arm. The infectivity rate declined from pre-intervention level of 1.0% to 0.18% and 1.70% to 0.31% in DEC and ivermectin arms respectively. The transmission intensity index (TII) declined from pre-control level of 0.73 to 0.10 in DEC arm and 0.85 to 0.15 in ivermectin arm.

After six rounds of administration of DEC+ivermectin, the mf rate declined from pre-intervention level of 14.7% to 2.0%, GMI of mf from 0.62 to 0.05, vector infection rate from 13.4% to 4.1%, vector infectivity rate from 1.40% to 0.34% and TII from 0.42 to 0.14.

Mass administration of two rounds of DEC+albendazole reduced the mf rate from 8.10% to 4.06%, GMI of mf from 0.31 to 0.11, vector infection rate from 13.1% to 7.5%, vector infectivity rate from 1.0% to 0.39%. However, TII increased from 0.20 to 0.30.

Evaluation of the effect of the ninth round treatment with DEC and third round treatment with DEC+abendazole is in progress.

During the year, the impact of MDA on chronic disease prevalence has also been evaluated. Seven rounds of mass administration of DEC reduced the prevalence of lymphoedema from pre-intervention level of 3.7% to 3.2% and hydrocele prevalence from 20.5% to 5.1% while ivermectin reduced the prevalence from 4.6% and 3.9%. Five rounds of DEC+ivermectin reduced the prevalence of lymphoedema from pre-intervention level of 5.7% to 2.2% and hydrocele prevalence from 23.1% to 14.6%. More detailed analysis on the impact of MDA on chronic disease is in progress.

Operational Feasibility and Impact of Co-administration of Albendazole and DEC in Controlling Lymphatic Filariasis

Elimination of lymphatic filariasis by the year 2015 is a national goal for India. Transmission control through MDA with annual single dose of anti-filarial drug(s) is the main strategy being implemented by the state public authorities. In India, during the year 2003, a total of 20 districts implemented the MDA with DEC covering a population of 53.18 million and in 7 districts co-administration of DEC with albendazole was done covering a population of 18.19 million. The reported coverages ranged from 89.1% to 96.5% in the DEC districts and from 54.8 to 94.3% in the DEC +alb districts. At VCRC, the evaluation covers four districts, two each from Tamil Nadu (DEC – Thiruvannamalai; DEC+alb – Thanjavur) and Kerala (DEC – Kozhikode; DEC+alb – Allapuzha) covering a population of about 8.5 million.

During the year 2003, surveys relating to impact evaluation were carried out just prior to the third round of MDA, providing results for impact of two rounds of MDA.

The coverage of drug distribution and consumption for Tamil Nadu (Fig.5a) and Kerala (Fig.5b) are shown. The drug consumption rate was 63.1% in the DEC district compared to 55% in the DEC + alb district in Tamil Nadu. Although, there was no significant difference between the districts in the 3rd round, the pattern shows that in the DEC district consumption rate was higher in all the three rounds. While the coverage in the rural areas was significantly higher compared to urban area in the DEC district, it was similar in both the DEC + alb districts (Fig.6 a & b). The comparison of coverage of drug distribution and consumption did not show any significant difference between the sentinel and spot check sites in the districts of Tamil Nadu during 2003. The reason for non-consumption of drug after receiving the same by the community was also analyzed. Fear of side reaction and forgetfulness (unable to perceive the importance of MDA) were the important reasons, for which the people did not consume the drug in spite of receiving the same (In Tamil Nadu). In Kerala, the drug consumption rates were again higher in the DEC district compared to the DEC + alb district in the 3rd round (Fig. 5b). Over 50% of the target population did not receive the drug in the DEC + alb district compared to only 20% in the DEC district in Kerala. A large proportion of those who received the drug (approximately 50%) in DEC district (Kozhikode) did not consume the drug.

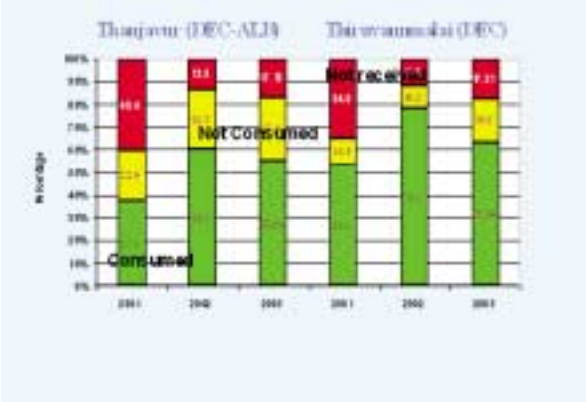


Fig. 5 a. Coverage of drug distribution and consumption in Tamil Nadu.

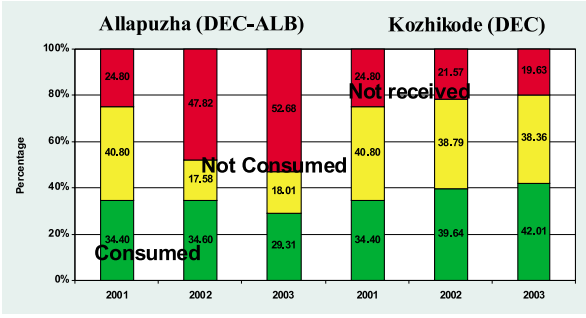


Fig. 5 b. Coverage of drug distribution and consumption in Kerala.

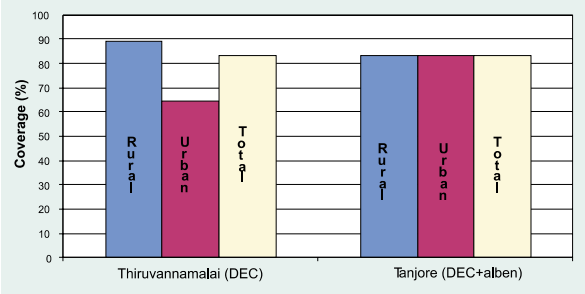


Fig. 6 a. Assessed consumption of drug in the sentinel sites in the intervention districts in 2003.

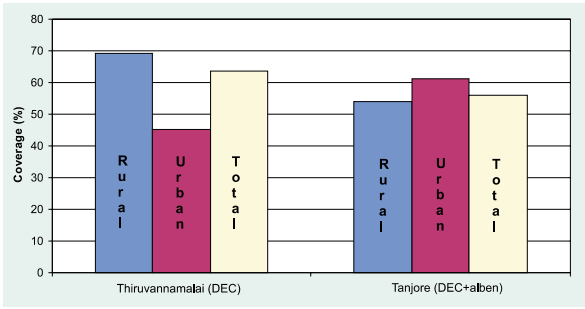


Fig. 6 b. Assessed consumption of drug in the sentinel sites in the intervention districts in 2003.

The change in mf prevalence after two rounds of MDA compared to the baseline is shown in Fig.7. There was a significant decrease in mf prevalence in both the DEC and DEC + albendazole districts in Tamil Nadu, while this was not so in either of the districts in Kerala. Although, the age specific patterns between base line and post 2nd round showed marked change in the DEC +alb district compared to the DEC district (Figs.8a & b) in Tamil Nadu, the relative change in the percentage reduction between the two arms in the sentinel sites was not significantly different. These results suggest the need for further rounds of MDA and continued impact evaluation. The prevalence of geo-helminth parasite significantly reduced between baseline and post 2nd round MDA in both DEC and DEC + alb districts in Kerala and DEC + alb district in Tamil Nadu. There was significant decline in the parsite prevalence in the post second round compared to post first round only in the DEC + alb district of Kerala. Overall, the pattern suggests that both the drug arms have some impact on geo-helminths prevalence, however, the results are marked only after the first round of MDA (Fig.9). Preliminary cost

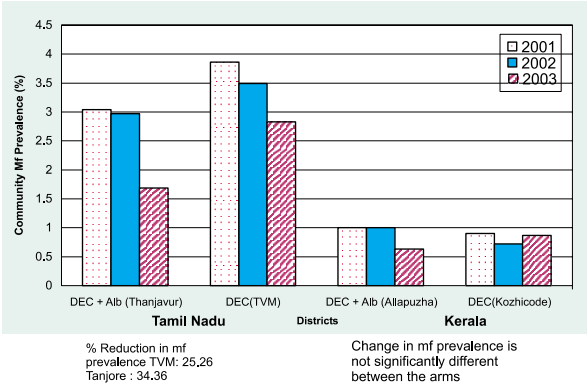


Fig. 7. Changes in mf prevalence after two rounds of MDA.

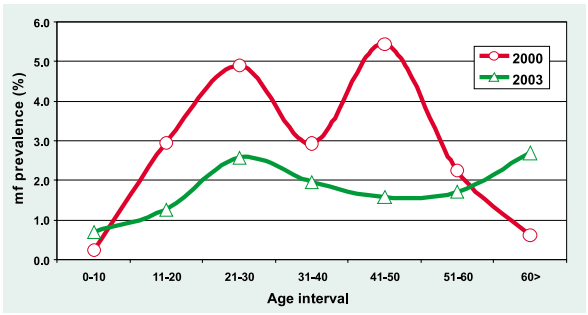


Fig. 8 a. Age specific prevalence of mf in Tanjore (DEC+alben) after two rounds of MDA.

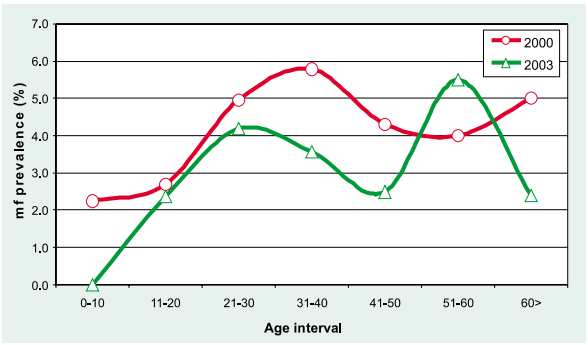


Fig. 8 b. Age specific prevalence of mf in Thiruvannamalai (DEC) after two rounds of MDA.

analysis for the two study districts for the first two rounds for drug distribution in Tamil Nadu showed that the cost/person distributed was Rs.1.41 and the cost/person consumed was Rs.2.02 for the DEC + alb district in the second round. These values were higher than that for DEC alone (cost/person distributed Rs.0.61 and cost per person consumed Rs.0.69).

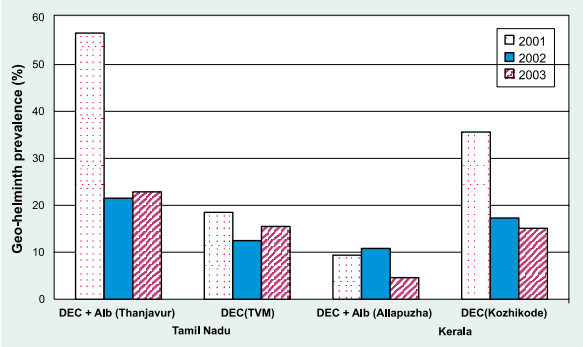


Fig. 9. Geo-helminth prevalence.

It was concluded that it is operationally feasible to distribute the drug in the MDA programme to about 80% of target population in Tamil Nadu, but not due to the inclusion of albendazole. In contrast, in Kerala, the coverage of distribution and compliance were much lower compared to Tamil Nadu and the DEC districts showed a higher coverage rate compared to DEC+albendazole. This suggests that the operational feasibility is different in different states, although feasibility of distribution reached the desired level in Tamil Nadu. In both the states, a considerable proportion of target population did not consume the drug after receiving it. Operational feasibility in terms of drug consumption has still not reached desired level and will require appropriate social mobilization as well as strengthening of distribution mechanism and training of grass root level workers, so that the community acceptance is enhanced.

The results clearly indicate that the co-administration of albendazole with DEC does not influence the consumption rate in any way in both the states. Deworming report is too low and that too is restricted to the 1st round in Kerala. Therefore, this appears to have no influence whatsoever on the drug consumption rate.

The administration of DEC alone or with albendazole appeared to be safe. Though the number of episodes of minor reactions was higher in DEC+albendazole group, these cannot be attributed to the drug(s) alone. The information available so far does not indicate a conclusive benefit of DEC+ alb over DEC alone.

Effect of Daflon-500 in the Treatment of Filarial Lymphoedema: A Double Blind Hospital Based Study

Study was conducted at VCRC, Pondicherry to evaluate the effect of Daflon-500 +DEC or DEC alone (administered for 90 days) on reduction of filarial lymphoedema volume. The recruited cases were followed up to a period of 36 months from the starting of drug therapy. The oedema volume changes in these groups are shown in Figs.10a &b. The results of extended follow up at 36th month showed 68% reduction in DEC alone arm and 82% reduction in DEC+Daflon arm compared to the baseline. However, there was no significant difference in mean oedema volume between the arms at 36th month.

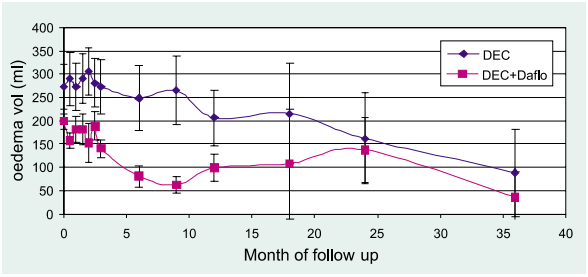


Fig. 10 a. Mean oedema volume during pre and post treatment in two drug arms.

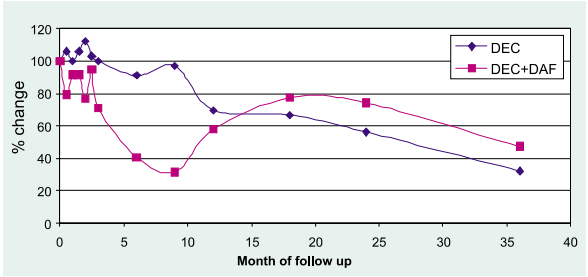


Fig. 10 b. Change in oedema volume during pre and post treatment in two drug arms.

Mode of Action of Albendazole

Studies were initiated at RMRC, Bhubaneswar to evaluate the mode of action of albendazole against filarial parasites since the drug is known for poor absorption in the intestine and plasma concentrations do not reach levels conducive for anti-filarial activity. The results revealed that albendazole was very effective in

patients with concomitant helminthic infection than in subjects with only filarial infection. This indicates that the antifilarial ativity of albendazole was mediated through elimination of geohelminths. This observation is expected to make radical changes to the ongoing global initiative for control of filariasis in disease endemic countries including India.

Management of Filariasis with Antibiotics and DEC

At RMRC, Bhubaneswar morbidity management of filariasis has been addressed from the point of view of patients as well as from an etiological angle. The first component was addressed by evaluation of different prophylactic methods such as use of long acting antibiotics-penicillin and doxycycline and/or foot-care and maintenance of hygiene. Three regimens were evaluated: foot-care with oral antibiotics, foot-care with DEC and foot-care with topical antibiotics. The first regimen significantly decreased the lymphoedema compared to the other two regimens while regimen I and III significantly decreased the frequency of acute filariasis. Results of the study are expected to contribute to improved clinical management of disease in endemic regions of the country.

LEISHMANIASIS

Kala-azar has once again become a major public health problem in Bihar and some parts of West Bengal and UP. Large number of cases of kala-azar are not responding to sodium antimony gluconate (SAG) therapy. Problems in diagnosis, specially in rural areas continue to delay early initiation of treatment in many patients. Effective control of kala-azar involves efficient case finding, diagnosis and systematic treatment of infected individuals. With the main aim of strengthening control activities based on these three principles, ICMR's Rajendra Memorial Research Institute of Medical Sciences (RMRI) at Patna is engaged in research on kala-azar. Studies are also ongoing through extramural research programmes in other institutes/medical colleges of the country.

Epidemiological Studies

Hospital based Surveillance System for Kala-azar

Study is being conducted by RMRI, Patna for identifying the spectrum of kala-azar, associated infections and therapeutic response in relation to clinical, epidemiological and socio-economic characteristics. Of the 737 kala-azar patients included in the study, most were in the age group 5-19 and 20-50 yr (Fig.1) and the incidence in males was two times higher than in females because of several factors (*viz*., clothing pattern, sleeping habits and occupation). All patients were screened clinically, haematologically and parasitologically and given various anti-leishmanial regimens for treatment. In Bihar, the second poorest state in India, poverty plays a major role in perpetuation of the disease, contributing to malnutrition, illiteracy (60%), and poor housing (82%). Further, presence of peri-domestic animal shelters around houses (63%) and vegetation (77%) facilitate breeding of sandfly vector. Clinical and laboratory characteristics were similar in age groups <12 yr and >12 yr of age. The increasing unresponsiveness of visceral leishmaniasis (VL) patients to conventional anti-leishmanial drugs *e.g*. SAG and pentamidine has definitely posed a major therapeutic challenge in combating the disease.

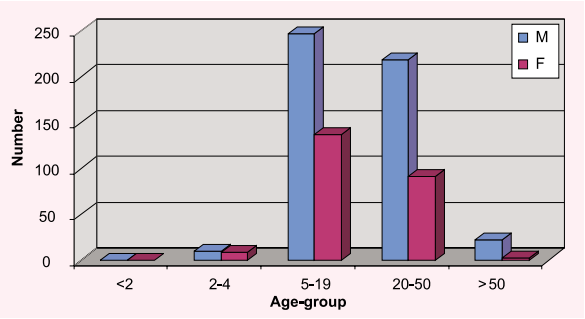


Fig. 1. Age-sex distribution of patients.

Clinical Studies

Safety and Efficacy of Injectable Paromomycin in Patients with Visceral Leishmaniasis

A multicentric clinical trial has been initiated to evaluate the safety and efficacy of parenteral

paromomycin compared to amphotericin B, its cure rates and pharmacokinetics in adults and children with VL.

Till date, a total of 145 patients have been enrolled in the trial of which 62 have completed 6 months of follow up.

Clinical Trial with Miltefosine

A WHO-sponsored study to confirm the efficacy and safety of Miltefosine in VL patient is ongoing at RMRI, Patna. The Institute is coordinating with various pathological centres.Periodical visits to different centres were made and the facts and figures were reported to WHO clinical monitors. Apart from this, a total of 150 confirmed VL cases were recruited at the Institute for the trial. Recruitment, treatment and one- month follow up (in 1106 patients) and six months follow up (in 969 patients) has been completed. Sixty one patients relapsed before 6 months of follow up while serious adverse effects were recorded in 11 of them.

Immunological Studies

Role of CD2 Antigen in T-cell Signal Transduction in Visceral Leishmaniasis

Studies are ongoing to understand the role of CD2 antigen in T-cell activation in visceral leishmaniasis patients.

CD2 was shown to play a critical role in the CMI response to *Leishmania* by contributing to the amount of IFN-γ produced by T-cells in VL patients. Addition of CD2 in culture medium induced more PKC-α signals in T-cells from these patients, indicating that CD2 transduces a functionally important signal for T-cells to converge into Th1 effectors.

Role of Leishmania Isolates of Responsive and Unresponsive Patients in IFN-γ & IL-4 Production in vitro

A study was undertaken at RMRI, Patna with the objective to evaluate the producton *in vitro* of the disease protective (IFN-γ) and promoter cytokine (IL-4) when similar sets of T-cells were stimulated by *Leishmania* isolates in patients responsive and unresponsive to SAG. The results from five patients have shown that responsive parasites might play better role in cytokine (IFN-γ) production which was directly proportional to parasitic load of patient from whom T-cells had been collected. The study will be continued with more samples.

Diagnostic Studies

Study was carried out for the detection of *L. donovani* "axenic" amastigote specific antigen by patients' sera through immunoblotting for diagnosis of kala-azar at PGIMER, Chandigarh. The study revealed that detection of response to amastigote antigen is a better marker for diagnosis than detection of antibody response to promastigote antigen either by ELISA or immunoblotting.

In separate studies validation and multicentric evaluation of *L. donovani* freeze dried DAT antigen for the diagnosis of kala-azar in the field was carried out at CDRI, Lucknow. The resullts revealed that FD as well as AQ antigen showed 96.5% sensitivity and 100% specificity compared to rk39 strip test which exhibited 86% sensitivity and 100% specificity. Production of large batches of FD antigen might be highly commercially viable and economically feasible for the diagnosis of VL in millions of poverty ridden endemic populations under adverse field conditions. The outcome of the study is of national relevance for kala-azar elimination.

PCR Based Diagnosis of VL from Suspected Cases of Kala-azar in Bihar

Several methods have been used in the diagnosis of leishmaniasis but none is completely satisfactory when used alone. A study has been taken up at RMRI with the objectives to develop a new gene target (NTS / ITS region of rRNA gene) for the diagnosis of VL and to compare the results of the PCR (aspirates / blood) with the results of conventional diagnostic methods and other target genes.

A total of 183 clinical aspirates (169 splenic and 14 bone marrow aspirates) have been collected from suspected kala-azar patients. Test is being developed and evaluated.

Efficacy of DNA Vaccination in Leishmaniasis

Studies were carried out at Indian Institute of Chemical Biology, Kolkata to determine the efficacy of DNA vaccination against experimental visceral leishmaniasis. The antigenicity of the KMP-11 molecule was explored by cloning the gene from the genomic DNA of the virulent AG83 parasites. The extent of KMP-11 expression in the virulent and avirulent strains of *L. donovani* was successfully determined. Marked differential expression of the KMP-11 gene expression was noted among the avirulent strains of parasites. The findings with laser confocal microscopy corroborated the findings found at the RNA level.

Entomological Studies

Antileishmanial Bacterial Metabolites from the Gut Microbiota of Female P. argentipes

Development of resistance in *Leishmania* species against conventional drugs like SAG and lethal side effects of other drugs and their cost resulted in search for new antileishmanial products from microorganisms.

The gut of 20 *P. argentipes* were aseptically removed, pooled, minced and inoculated in nutrient media to isolate the intestinal microbiota. The mixed populations of microbiota were then pure cultured and isolates obtained were tested for antileishmanial activity. Out of 20 isolates, 6 showed strong and 2 weak antileishmanial effect.

Identification and Characterization of L. donovani Antigen of Infected P. argentipes

Study was conducted for determination of peptides responsible for infection in *P. argentipes* by observing their immunoreactivity against kala-azar. Protein concentration of the sandfly whole extract range was determined. The protein profile obtained from SDS-PAGE showed several major proteins with mol. wt. ranging from 29 to 160 kD. For identification of immuno -reactive peptides Western blotting is in progress.

Control of Indian Kala-azar Vector, P. argentipes

This study was undertaken with the objectives to isolate symbiotic bacterial flora of *P. argentipes* from different geographic regions of India and to develop a shuttle plasmid and transformation system for genetic modification of sandfly symbionts to be used in field conditions.

Out of 20 colonies of bacterial isolates from the gut of *P. argentipes* tested to see their effect on growth of *L.donovani* individually in the culture medium RPMI 1640 with 20 % of FCS, the effect on growth of parasite due to presence of two isolates was found comparable with the control of the same medium with good number of parasites. This indicates the possibility for the existence of commensalistic relationship between bacteria of gut of *P. argentipes* and *Leishmania* promastigotes.

Basic Studies

Biochemical and Molecular Characterization of Leishmania Isolates from SAG Responsive and Unresponsive Patients from Bihar

Study was carried out to identify the molecular variation in different isolates of SAG responsive and unresponsive kala-azar patients of different parts of Bihar. Different strains of leishmania isolates were obtained from the leishmania bank at the institute. After primary isolation and culture adoptation, mass cultures of isolates were done to get sufficient amount of pure culture.

PCR-RFLP patterns showed some variation in few SAG responsive and unresponsive isolates, which need further confirmation with more isolates of SAG responsive cases. Efforts have been made to get some more SAG responsive isolates from other organizations for meaningful conclusions.

Genetic Heterogeneity of Ribosomal Internal Transcribed Spacer (ITS) in Clinical Isolates of L. donovani by DNA Polymorphism

Study was conducted to investigate intraspecific variation among different clinical isolates of

L. donovani from different endemic and geographical regions of Bihar. After primary isolation and culture adaptation, mass cultures of 33 isolates were obtained from the leishmania bank at the institute. These isolates were subjected to DNA isolation, amplification, gel electrophoresis and Southern blot analysis. Some intraspecific variation has been observed among the isolates of different endemicity and geographical regions of Bihar which needs further confirmation.

Remote Sensing for Mapping Sandfly Distribution in Bihar

At RMRI, Patna the study has been conducted to find the association of specific vegetation cover, water bodies, human settlements and other land use features with vector abundance through conventional ground surveys as well as satellites.

Out of six models generated, the best one provides detailed mapping of sandfly density in endemic sites. This model derived from the environmental variables and land cover features *i.e.* temperature, humidity, dry fallow and minimum normalized difference vegetation index enables one to produce a map of distribution of *P. argentipes* in endemic sites and can be used to predict the vector density in those areas not covered by the initial data. The map produced from the study could be of great use for planning and identifying areas of high vector abundance for vector control programme such as localized and intensive indoor residual insecticide spraying. Although, this model was based on data pertaining to one PHC/block of the state, it can be used for prediction of vector density in other high endemic areas of Bihar and other parts of the country as well.

Evaluation of the Impact of DDT and Malathion Spraying on Kala-azar Control Programme

The objective of the study was to evaluate the efficacy of indoor residual spraying of DDT and malathion on kala-azar control programme. DDT spraying status of the selected villages and post spray evaluation of first round DDT spray was carried out in different months after about 4-5 month spray in July 2001. Density of the indoor collected flies was found in the range of 0.52 to 17.66 during post spray evaluation, while the parity rates were in the range of 11 to 34. Vector species *P. argentipes* was prevalent during study period. Insecticide susceptibility tests in district Vaishali registered 18-53% mortality indicating presence of DDT- resistant foci.

In 2002-2003 no spraying was conducted in the study area. Man hour density, abdominal and parity stages were studied and compared with post-sprayed period. High percentage of parous flies after one year of spraying indicated the impact of the insecticide spray on the sandfly population by affecting the longevity of the sandfly. Similarly, relatively decreased populations of indoor-resting stage sandfly (semi-gravid and gravid) in the interiors during the post spray evaluation period compared to evaluation after one year of spray indicates that deposits of indoor residual spray are not allowing the sandfly to rest on the surface. It could also be possible that sprayed insecticide deposits on sandfly are preventing it from entering into the sprayed houses.

However, a comparative study on the post spray and after one year of spray reveals that desired epidemiological impact of DDT spray is not being achieved possibly due to development of tolerance in *P.argentipes* against DDT.

Other Studies

Study of Grassroot Level Functionaries of Kala-azar in Bihar

Study is ongoing at RMRI, Patna to examine the existing pattern of functioning of health care services for kala-azar related to organizational and implementation aspects and to identify shortfalls, if any. Three known highly endemic districts and PHC's in each district were randomly selected. All medical officers and health workers of nine PHC's were interviewed through semi-structured questionnaire. Of the health workers interviewed, 84% supervisors told that they were overburdened due to various activities. Almost 96% supervisors faced

problems when contacted by kala-azar patients pertaining to lack of facilities at PHC (83%), shortage of medicines (91.7%) and bone-marrow/ splenic aspirations being not available. Only 10.5% supervisors knew about splenic aspirations being used as a tool for diagnosis of kala-azar. Similarly, 58% health workers narrated that their sub centres were running in rented building and the condition was poor/very poor (63% respondents), nearly 22% told that no staff meeting was held for specific kala-azar programme. Some (5%) were even unaware about the vector of kala-azar. Though 64% health workers told that educational and awareness activities for kala-azar control programme were performed at local levels, district team never turns up for IEC programmes. Almost 98.3% health workers/ supervisors and 75% medical officers need training for kala-azar (Fig. 2) though they were working for so many years in the PHCs in endemic areas. A large number (50-70%) of health workers/supervisors suggested that regular supply of drugs, diagnostic facilities, regular DDT spraying and kala-azar awareness activities may make kala-azar programme popular in the community.

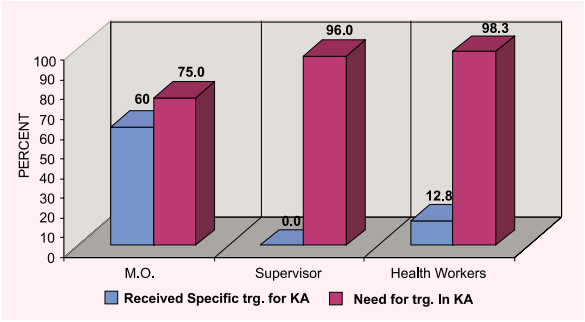


Fig. 2. Status of training received & need in kala-azar.

Risk Factors for Kala-azar in Endemic Areas of Bihar

A study was taken up at RMRI, Patna to investigate the socio-economic risk factors for kala-azar in endemic villages. By multivariate analysis, past history of other diseases in last one year, family history of kala-azar, mud-plastered walls, granary inside house, presence of bamboo trees around houses and DDT unsprayed houses in last six months were found as significant risk factors of kala-azar. These finding will be useful for Kala-azar Control Programme for implementing intervention strategies.

Socio-cultural and Demographic Studies

Study is continuing at RMRI, Patna to prepare a site for future vaccine trials and to document information on socio-cultural, demographic, epidemiological and entomological aspects of the disease. As per the protocol, study was conducted in endemic Kurhani block in Muzaffarpur district (Bihar). A cluster of ten villages having history of kala-azar, comprising 3493 households covering 21312 population with sex ratio 877 females per 1000 males has been selected. Illiteracy is very high (61%) and only 30% population is engaged in one or other occupation. A total 458 cases in last 10 years were found in the study area but during the study period *i.e.* December 2003, a total of 62 cases were found (39 males and 23 females). Bone marrow was the most popular test (50.2%) followed by aldehyde test (36.9%) and splenic aspiration (9.6%). SAG was the first line of drug used in 95.6% of the cases in this area followed by pentamidine (3.1%) and amphotericine (1.3%). Majority of the cases (97.4%) were reported cured after the treatment while 1.0% were receiving the treatment at the time of survey. Private practitioners were the first choice of kala-azar patients followed by primary health centre and government hospitals. Around 6.3% were treated by the village quacks (untrained doctors).

VIRAL DISEASES

ENCEPHALITIS

Epidemic Investigations

Andhra Pradesh: An outbreak of suspected viral encephalitis reported among children (9-14 yr) from Karimnagar and Warangal district of Andhra Pradesh during June-September 2003 was investigated by NIV, Pune. A total of 329 encephalitis cases with 183 death (CFR 55.6%) were reported between June and September 2003. The typical clinical manifestation in confirmed CHP encephalitis group included rapid onset of fever followed by vomiting, altered

sensorium, convulsion, diarrhoea neurological deficit and meningeal irritation.

Screening for JE, West Nile, paramyxo, corona, measles, dengue, rabies, influenza viruses and mycoplasma yielded negative results. In the encephalitis group, all 10 CSF samples were negative for virus isolation. Three of 22 throat swabs, 1 brain aspirate and 2 blood clots were positive for virus isolations. In the fever group, 1/8 throat swab yielded virus in RD cell line. The culture isolates showed presence of bullet shaped particles, 150-165 nm long, 50-60 nm wide, showing distinct surface projections 9-11 nm in size and a stain filled canal at the base of the virus particles, all features suggestive of rhabdoviruses. Isolates obtained from different cases were identified as CHP virus.

Maharashtra : An outbreak of encephalitis was reported among children (1 to 10 yr) at Nanded between June-July 2003. Forty cases with 10 deaths (within 9 hours of hospitalization) were reported. Case distribution appeared to be sporadic. Serological investigations revealed presence of IgM antibodies to Chandipura virus.

West Bengal : An outbreak of unknown aetiology affecting children (<10 yr) was investigated in Murshidabad district of West Bengal during June 2003. Fever, altered sensorial, vomiting, convulsions and death in a short period were the prominent clinical manifestations. The NIV team collected 34 blood samples and 30 throat swabs. Sixteen of the 30 throat swabs were positive for influenza A virus by RT-PCR. Two of the 16 positive specimens yielded influenza A virus sequences. Four isolates were obtained in tissue culture, which were identified as influenza A.

Uttar Pradesh : An outbreak of encephalitis in children from Saharanpur district was investigated during September- October 2003. Moderate to high fever for 3-4 days, vomiting, altered sensorial, convulsion in a few cases and unconsciousness leading to death in a majority of cases were the prominent clinical features. The case fatality rate was 80%. The cases were scattered throughout the district. No neurological sequalae was observed in recovered cases. No etiological agent has been detected so far from samples collected from the outbreak.

SEVERE ACUTE RESPIRATORY SYNDROME (SARS)

During April 2003, reports of SARS epidemic caught global attention. During this period, serum, and urine from suspected cases were referred to NIV for PCR analysis.

Nested RT – PCR identified 3 probable and 4 suspected cases in India. All these cases had travel history to exposed countries.

JAPANESE ENCEPHALITIS (JE)

Epidemiological Studies

During the current year 140 specimens from suspected cases (86 male, 54 female) of JE were received. (Karnataka-119, AP-17, TN & Kerala-1 each, Not known-2). Diagnosis of JE by IgM MAC-ELISA was confirmed in 44 cases of which 41 were children <10 yr. Most of the JE positive cases were diagnosed in November (28); of the 159 bird sera collected from Bellary (Karnataka), two sera from paddy birds had antibodies to JE virus.

Immunological Studies

Identification of Neutralization Epitopes on JE Virus Envelope Protein

The selection of 16 neutralization escape mutants using two strains of JE and three MAbs was reported earlier. Characterization of mutants showed that there was a loss of neutralization with more than one type of MAb and loss of virulence by intra cerebral (IC) route in adult mice. Sequencing of the E gene of the 16 mutants identified single amino acids at different sites in the two strains – glycine at 153 to tryptophan in the Vellore strain and glutamine 138 to lysine in the Bankura strain. The sites were in the region of dimerization and had the potential to cause major changes in the tertiary structure of the E protein thereby justifying the huge changes seen in the mutant phenotype.

Development of Attenuated JE Virus Strain

The isolation of two attenuated mutants of JE virus - persistently infected cultures has been

reported earlier. To check the stability of the phenotype, mutants were passaged 20 times in PS cells and checked again for loss of virulence. Both mutants were still avirulent in infant mice by the intraperitoneal route. One mutant 6H protected the mice against intracerebral challenge with JE virus.

Molecular Characterization of Live Attenuated JE Vaccine Strain ML-17

The ML-17 is the live attenuated pig vaccine virus used in Japan. Two recombinant clones MS-14 and MS-15 had been generated using JaOArS982 backbone with substitutions detected in the ML-17 sequence. Adult CD1 mice were inoculated intra-peritoneally with recombinant viruses, ML-17 and JaOArS982. The ML-17 strain showed complete loss of virulence and MS-14 and MS-15 exhibited partial loss of virulence indicating that substitutions in the PrM region were important for the attenuation of ML-17 JE vaccine strain.

Characterization of Human Immune Response to Selected Genes of Japanese Encephalitis Virus

A project was undertaken at Indian Institute of Science, Bangalore to characterize the human B and T cell immune response to the membrane, capsid, NS1, NS2b, and NS5 genes of JE virus with the aim to design an effective vaccine.

All five JEV genes proposed to be studied for their ability to elicit human immune response were cloned from viral RNA and inserted into expression vectors. It was observed that the viral nonstructural protein 3 (NS3) was highly immunodominant for stimulation of T cell responses. Fixed whole cell preparations of insect cells individually expressing recombinant prM, E, NS1, NS3 and NS5 proteins of JEV detected NS3-specific memory T cells in up to 86% of a JE-endemic cohort whereas prM, E and NS1 each elicited reactions in approximately 45% and NS5 in only 13% of the cohort. NS3 stimulated interferon-γ production in both CD4+ and CD8+ T cells. It was observed that non-structural proteins are frequently targeted by T cells in natural JEV infections and may be efficacious supplements for the predominantly antibody-eliciting E-based JEV vaccines. Both $CD4^+$ and $CD8^+$ T cell subsets specific to the nonstructural (NS) protein 3, with IFN-γ production were significantly higher in healthy donors compared to patients. A striking inverse association between IFN - γ levels and the severity of post-encephalitic sequelae in patients implicated a role for IFN-γ in recovery. The immunogenicity of NS3 was focused to amino acids 193 to 324, which contained five of the eight helicase motifs of NS3. Complete identity of amino acids 219 to 318, contained within the above segment, across 16 JEV isolates suggested that NS3-specific epitopes tend to cluster in relatively conserved regions that harbour functionally critical domains of the protein.

Development of a Candidate DNA Vaccine for JE

The effect of colloidal gold as an adjuvant and incorporation of an additional gene, NS1 (a non-structural protein important for inducing cell-mediated immune response) on the immunogenicity of pCDNA3.1-PrM-Et was studied. Combined immunization with 3.1PrM-Et and 3.1-NS1 boosted the immune response and neutralizing antibodies were detected in mice. However, colloidal gold had no effect on improving the immune response. The DNA vaccine will be tested for protection in a prime-boost model using either baculovirus expressed E protein or SFV replicon expressing PrM-Et protein as boost.

Analysis of Virus Cell Interactions

To study the significance of various cell organelles in virus replication, cells infected with JE and dengue viruses were stained for golgi and virus antigen. Both JE and dengue virus proteins were found to co-localize with golgi showing that the golgi played an important role in the processing of flaviviral proteins.

WEST NILE VIRUS

Molecular Epidemiology

WN virus is highly prevalent in India and limited information is available about antigenic

as well as genetic variations among isolates from different hosts and geographical areas. WN virus isolates obtained from four different mosquito species and a human patient during the same season in 1980 were analyzed for the sequence divergence in the genomic region spanning portions of nucleocapsid and envelope protein including the entire region encoding the premembrane and membrane proteins. The sequence analysis showed absolute sequence similarity among all the five isolates independent of the host. As compared to the Egyptian prototype strain (Eg 101), nucleotide substitutions occurred at 194 positions leading to 9.5% amino acid changes at different locations. The amino acid changes were dispersed throughout the fragment. However, major substitutions were located in the C – terminal portion of nucleocapsid region forming the signal sequence.

Alignment with respective sequences of strains from other countries revealed that most of the amino acid substitutions among Indian isolates were not found in other strains. These unique amino acid changes will form a marker for identification and can be helpful in understanding the geographical movement of WN virus strains from Southern India. Indian isolates showed about 21% divergence from American and European strains and 33% divergence from those of African strains (lineage II) (Fig. 1) suggesting that these strains can form a separate genetic cluster within the genetic lineage I. The study indicated that WN virus strain isolated from Southern India is different from those reported by American, European and African countries.

Seroepidemiology

Bird sera (159) collected from Bellary (Karnataka) were tested by HI test against West Nile (WN) virus. Six paddy birds and 3 cattle egrets were found positive for antibodies to only WN virus. Thirty two pig sera collected during investigation of epidemic in Bhandhra were tested in mouse NT for detection of N antibodies to WN virus. Seven of the 32 sera were positive and two were partial positive.

DENGUE

Epidemiologcal Studies

A total of 3260 suspected cases of dengue (DEN) from Karnataka, AP and TN were tested for IgM antibodies by MAC-ELISA against

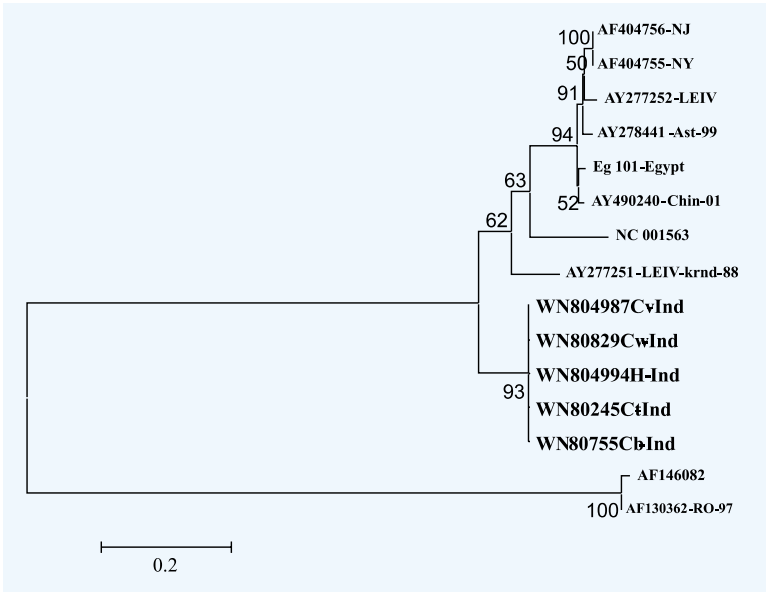


Fig. 1. Phylogenetic tree constructed by using the sequence of 921 bp genomic fragment of Indian isolates and Eg 101 along with respective sequences of strains reported from other countries (GenBank).

DEN-2 antigen, Of these 2704 were classical dengue fever cases and 242 DHF/DSS cases. DEN positive cases were diagnosed during all months with maximum cases during May to October with a peak in July. Cases were seen in all age groups and in both sexes, 53.6% cases were adults and remaining children below 15 yr.

During a survey of *Ae.aegypti* in relation to dengue outbreak in rural areas in Karnataka, it was observed that this species was breeding in 63 villages. Few villages in Kodagu and Dakshina Kannada districts of Karnataka with confirmed DEN cases, were negative for *Ae.aegypti*. In these villages *Ae. albopictus* was the predominant species indicating its possible involvement in DEN transmission.

Vector surveillance in the endemic area of Mumbai showed that there was a higher prevalence of *Ae. aegypti* in dry season (October–May) compared to wet season (June – September), indicating that *Ae. aegypti* is mainly water storage dependent in that area.

Molecular Epidemiology

Complete sequence of E gene was obtained for 6 strains of dengue 2. The strains were obtained from different regions of India – TN, Jammu, Haryana and Maharashtra. The Vellore strain of 1960 was very close to the 1957 strain from South India and a Trinidadian strain. The strains isolated in 1990s were closer to the Chinese strains. This indicated a shift in the circulating genotype within the country from the American to the Asian genotype.

Use of Sodium Azide for Preservation of Mosquito Larvae

Sodium azide was found to be effective as a preservative for storage and transport of field collected mosquito larvae for detection of DEN virus. Using this preservative, 48 of the 132 larval pools collected from Gujarat showed presence of DEN virus antigen.

Development of Monoclonal Antibodies (MAb) against DEN Viruses

MAbs were generated against the three serotypes of DEN viruses. Eleven clones were obtained, of which 2 were found reacting specifically against only DEN viruses.

Role of Ae. albopictus in Maintaining Alternate Cycle of Dengue

Studies continued on reporting maintenance mechanism of dengue virus in nature. Having reported transovarial transmission as possible mechanism of virus sustenance, another possible mechanism of dengue virus maintenance through an alternative cycle between *Ae. albopictus* and monkeys was pursued. Different ecotypes representing zoos/parks, hilly terrain, typical urban settings and high altitude area were chosen and investigations with respect to their acting as sentinel points of vectors and virus were accomplished. Monthly observations made from 2001 to 2004 showed that tree hole breeding of *Ae. albopictus* and *Ae. aegypti* was present in zoos/parks around Jodhpur. During the month of September, these species also showed positive IFA results indicating vertically transmitted dengue antigen within them. Further studies of involvement of monkeys in the alternate cycle of dengue are to be initiated.

Development of Surveillance Mechanism for Dengue in Jodhpur

Under the WHO project on studies on dengue and dengue haemorrhagic fever in Rajasthan, investigations were undertaken at RMRC, Jodhpur in selected settings of Jodhpur town on the basis of geographical reconssaince (GR). All the 60 wards of Jodhpur were divided into 7 settings representing different ecotypes relevant from epidemiological point of view. Entomological, virological and serological parameters were investigated to study association of these with the characteristics of areas. Maximum adult house index (AHI) was observed (54%) in low-socio economic, plain areas, while highest breeding index was observed in urban areas inside city. Maximum number of dengue fever cases (20) were observed from urban inside city area. GR based study settings are shown in Fig. 2.

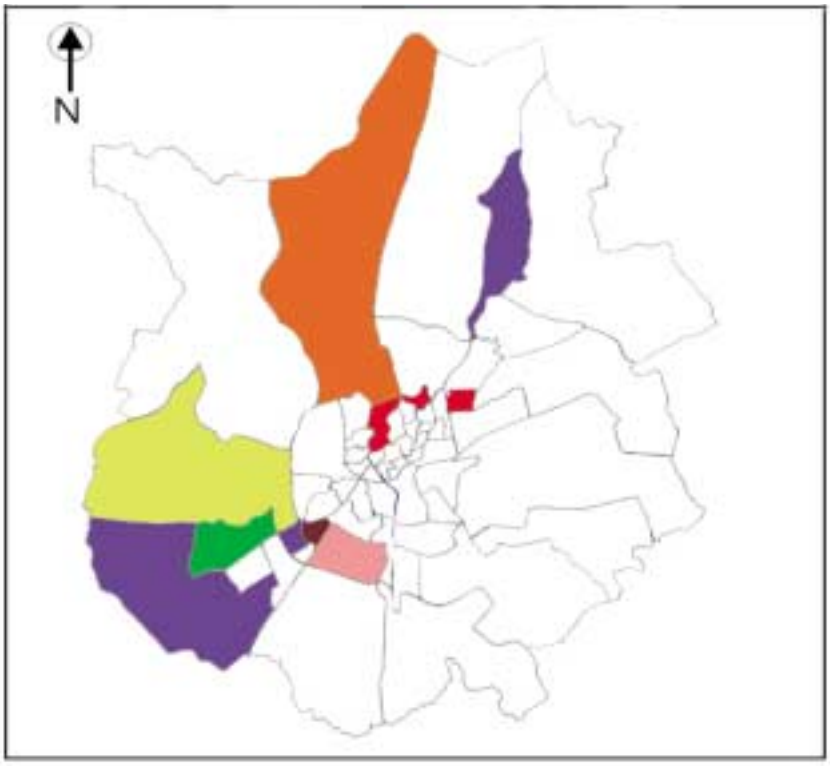


Fig. 2: Map of Jodhpur city depicting GR based study areas for dengue vector survey

CHANDIPURA VIRUS

Molecular Studies on Chandipura Virus

In an outbreak of encephalitis reported among children in AP during 2003, Chandipura (CHP) virus was found to be the etiological agent. As a follow up of this investigation, molecular studies on CHP viruses isolated during this outbreak were carried out. G, N and P genes were amplified and sequenced for five CHP isolates (one from a fatal cases of encephalitis, 2 from recovered encephalitis cases and 2 from fever cases) and one from a febrile case reported in 1965, to assess if emergence of a divergent strain was responsible for the pathogenesis of the virus. The isolates obtained during the present epidemic were closely related to the 1965 isolate, Percent nucleotide identity (PNI) being 95.6-96.1% (G gene), 96.5-97.6% (N gene) and 95.8-96.8% (P gene). Thus, appearance of a much divergent strain of CHP virus was not responsible for the encephalitis epidemic potential of the virus with very high mortality. Phylogenetic analyses based on three different genes showed that the brain-derived isolate clustered with the 1965 isolate whereas the other three isolates grouped together, irrespective of the type of the viral gene (Fig. 3). No segregation of the isolates from encephalitis and fever cases was noted indicating thereby probable

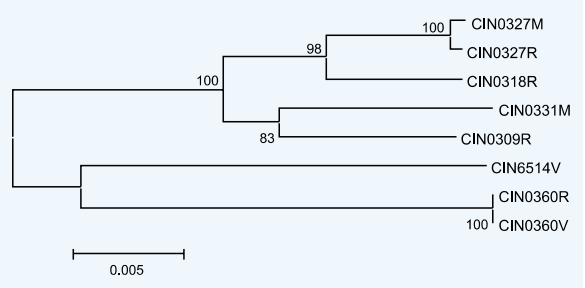


Fig. 3. G gene based phylogenetic analysis of CHP virus isolates.

importance of host factors in influencing the outcome of the infection.

The comparison of the deduced amino acid sequences of G protein documented 7 substitutions for the epidemic isolates as compared to the 1965 isolate. Importance of the amino acid substitutions in the G protein in the pathogenesis of CHP virus infection remains to be determined. The N and P proteins were highly conserved.

Development of Monoclonal Antibodies against CHP Virus

Splenocytes from CHP virus immune BALB/c mice were fused with SP20 cells. Hybrids obtained were selected using virus-neutralizing assay. This ensured that MAbs against non-neutralizing and cross-reactive nucleoprotein were not obtained. Seven MAbs could be generated having neutralizing activity against CHP virus. Titres of the MAb tissue cultures ranged from 1:4 to 1: 63000. None of the antibodies neutralized closely related vesicular stomatitis virus. These antibodies have been used for developing antigen capture ELISA. IgM and IgG capture ELISA were developed for CHP virus using in-house prepared reagents.

Propagation of CHP Virus in Chick Embryos

Three Indian CHP virus isolates were propagated in 10 day old chick embryo. Results demonstrated that chick embryo was susceptible to CHP virus and the virus could be grown to high titres for the development of diagnostic reagents and vaccine.

Cytokine Profile among Chandipura Encephalitis Patients

Fourteen children presenting with encephalitis and admitted to a tertiary care hospital were studied. Concentrations of IL-2, INF-γ, IL-6 and TNF-α in mitogen stimulated PBMC supernatants were assessed in ELISA. High levels of INF-γ along with significantly high levels of IL-2 in the later state of the disease suggest the role of Th1 cells in recovery. Absence of variations in IL-6 levels in both the groups indicate the absence of its specific role in disease progression or recovery. Non-significantly elevated levels of TNF-α in the later stage of the disease compared to the early stage (where mortality is high) suggests its antiviral effect.

Serological Survey of Domestic Animals

A serological survey of domestic animals (pig, goat, cattle, sheep and dog) was carried out in Karimnagar and Warangal (AP) to determine the prevalence of antibodies to CHP virus. A total of 180 animal sera were collected from 5 villages in Karimnagar (92) and 7 villages in Warangal (88) in July 2003.

All the animal survey sera were tested by *in vitro* neutralization test in Vero cell culture to detect antibodies to CHP virus. Thirty-three of the 180 sera had N antibodies to CHP virus. Analysis of sera according to the species indicated that the highest seroprevalence was observed in pig followed by buffalo, cattle, goat and sheep. Three of the 6 dog sera were positive for N antibodies to CHP virus.

Experimental Transmission

Laboratory transmission studies have shown that, *Phlebotomus* sandflies infected with Chandipura virus can transmit the virus orally to swiss albino mice and can also transmit the virus transovarially (TOT).

Studies have indicated that *Ae.aegypti* can transmit the Chandipura virus not only from mosquitoes to mouse and vice versa but also by TOT and venereal routes.

HEPATITIS

Hepatitis A

Molecular Epidemiology

Three outbreaks of hepatitis in children <15 years, two from Maharashtra and one from Kerala were attributed to hepatitis A and obtained from Maharashtra were typed as IIIA on the basis of phylogenetic analysis. Children from Maharashtra, (172) judged to be susceptible to HAV on the basis of absence of anti-HAV antibodies were vaccinated with killed hepatitis A vaccine.

Nucleotide sequence data obtained on partial RNA polymerase and VP1/2A regions of 31 HAV isolates collected over a period of 10 yr (1992-2001) were analyzed. Extensive heterogeneity among HAV strains recovered from hepatitis A patients was evidenced by presence of (i) sub genotypes IB and IIIA, (ii) their mixed infection in individual hepatitis A patients and (iii) by diverse (partial) RNA polymerize region in HAV isolates of genotype IIIA investigated in this study.

Cytokine Levels

Both the Th1 and TH2 cytokine levels were measured in the sera and the supernatants of mitogen-stimulated supernatants of lymphocyte cultures of acute hepatitis A pediatric patients leading to recovery. Mean levels of IFN-γ and IL2 were significantly higher compared with that of IL-10 and IL4 respectively suggesting possible involvement in the elimination of HAV by inducing a direct anti-viral effect.

Hepatitis B

Development of a Real time PCR Assay for Quantitation of HBV DNA

Real time PCR assay was standardized using primers and probe designed according to HBV pre-core region. Pre-core-core clone plasmid was used as a DNA standard in this assay. Serial dilutions from 10 -10^9 copies / reaction showed a linear relationship in the standard curve. Comparison with the commercially available assay is underway.

Hepatitis B Vaccination among the Nicobarese

The RMRC, Port Blair initiated a pilot project of hepatitis B vaccination using indigenously developed recombinant DNA vaccine (*Shanvac-B*) in tribals (aged <45) in two villages of Car Nicobar Island having a total population of 2376.

Follow up revealed that the vaccine was well tolerated and had no side effects. None of the subjects had any anaphylactic reaction. The sero-protection rates and geometric mean titers of anti-HBs are summarized in Fig. 4. Four of the 1096 individuals were positive for HBsAg over a two-year period indicating breakthrough infection.

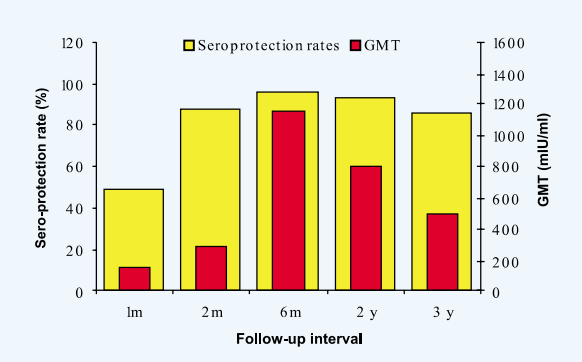


Fig. 4. Sero-protection rate and geometric mean titre of anti-HBs among vaccinated Nicobarese at different intervals.

Hepatitis C

Development of PCR Assay for Quantitation of HCV RNA

Primers and probes corresponding to HCV 5'NCR were designed and used to standardize real time RT-PCR assay for HCV RNA quantitation. Standard RNA was prepared by PCR amplification, TA cloning and run off transcription. Standard curve showed linear relationship from 9-10^9 RNA copies/ reaction. Comparison with the commercially available assay is underway.

Analysis of Interferon Sensitivity Determination Region (ISDR) of HCV

Studies were undertaken to find out the correlation between outcome of antiviral

interferon (IFN) therapy or IFN plus riboviron combination therapy and the amino acid sequence of small region, IFN sensitivity-determining region of the HCV nonstructural protein 5A. No correlation could be confirmed between the outcome of IFN therapy and the ISDR, PKR and V3 sequences in the individuals infected with HCV genotype 3b and 1b. However, therapy responders, infected with genotype 1b, showed glutmine to arginine conversion at position 289 (PKR domain). Responders from genotype 1a group showed more than 5 changes in ISDR, PKR and V3 together while those in nonresponders were less than three.

Epitope Mapping of HCV

Epitope mapping of HCV was done using random M13 phage display library. Subtractive biopanning was carried out by using pool of IgGs from normal and HCV infected individuals. Total 52 clones isolated from three different panning experiments resulted in identifying 7 different epitopes or antigenic determinants, three in core region, two in NS5A region, one in E1/E2 region and one in E1 region. These peptides would be synthesized and checked in ELISA.

Possible Association between HLA Class I and Class II Genes and HCV Infection

In order to assess the association of genetic factors with HCV infection, distribution of HLA class I and class II alleles in anti-HCV positive individuals was determined. Allele frequencies of DQB1 *06 and DRB1 *11 in Maharashtrian HCV infected individuals. were significantly more common. This is the first report on the association of HLA allele subtypes with HCV infection in Indian population.

Hepatitis E

Study of T Cell Epitopes of Hepatitis E Virus

Cellular immune responses to HEV have not been studied. A project was undertaken at Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow to study the lymphoproliterative responses to HEV capsid protein [open reading frame (ORF) 2; 660 amino acids].

Twenty-five patients with acute viral hepatitis E and 15 healthy controls were studied. Eighty-one overlapping 20-mer peptides corresponding to amino acid sequence of capsid protein of human HEV (Burmese strain) were synthesized. Significant proliferative response to recombinant ORF2 protein was observed in 72% patients compared to 40% controls. Peripheral blood mononuclear cells of patients with acute HEV infection showed significant proliferative responses to ORF2 protein of HEV. The responses were most pronounced against the C-terminal region and the region extending over amino acids 73-156 of the ORF2 protein. The finding may be useful for future development of a vaccine against HEV hepatitis.

Sequencing of Swine HEV Whole Genome, Expression of ORF-2 Protein and Development of ELISA

Full–length genomic sequence of Indian swine HEV was determined. The genome consisted of 7240 nucleotides (nt) with the 5'NTR (25 nt), ORF-1 (5121 nt), ORF-2 (2022 nt), ORF-3 (342 nt) and 3'NTR (70 bases) excluding the poly A tract at 3' terminus. An insertion of a single nucleotide (C) at position 5159 affecting both ORF2 and ORF3 translations was present. The hypervariable region identified between aa 680-796 showed only 74.3% identity with genotype IV prototype sequence. Whole genome-based phylogenetic analysis confirmed that Indian swine HEV belonged to genotype IV and was divergent from other isolates of same genotype (83.7-84.7% identities). Complete swine ORF2 protein was expressed in SF9 cells (insect cells) using Bac-to-Bac Baculovirus expression system (Invitrogen). Western blot analysis showed that 72hr-168hr-harvest time was optimum and the sizes of the expressed proteins were of 72kDa, 55kDa and 33kDa. Though Swine (genotype IV) and human (genotype I) HEV ORF-2 protein differed by 9% at amino acid level, comparison of both proteins in ELISA based on 552 samples showed almost identical results.

Development of DNA and DNA Prime / Protein Boost Vaccines

The complete ORF2 gene (capsid) of HEV type 1 was cloned in pcDNA3.1 vector. BALB/c

mice were immunized with this plasmid by two routes; intramuscular and intradermal. DNA prime protein boost effect was studied in intradermally immunized mice. Purified recombinant ORF2 type 1 protein with Freund's complete adjuvant was used for protein boost. Two week post recombinant protein immunization boosting effect was observed in the mice earlier immunized with DNA.

RESPIRATORY INFECTIONS

INFLUENZA

Epidemiological Studies

Seasonality of influenza virus infection in Pune was studied. An increased influenza activity was noted in two peaks, February to April and July-August. Thirty Seven influenza virus isolates comprising 23 typeA and 14 type B isolates were obtained (Fig. 5). Type A isolates were identified as A/Panama/2007/99 (H3N2) and type B as A/Beijing/184/93 (B/yamagata lineage) strain.

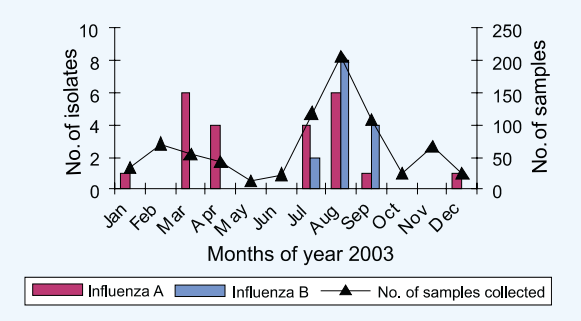


Fig. 5. Month-wise specimen collection and influenza virus isolates.

RT-PCR for Detection of Influenza A, B and Respiratory Syncytial Virus

A semi-nested RT-PCR for the detection of influenza A, B and RSV was standardized and used to screen clinical samples collected and tested for viral antigen by other methods during previous years.

Detection of H5 Subtype of Influenza A

Nested RT-PCR for detection of H5 subtype of influenza using primers recommended by WHO and those designed at NIV was standardized. This test could easily be used for rapid detection of influenza H5 subtype.

MAb Based Immuno Fluorescence Test for Detection of RSV Infection

One hundred thirty one nasophyrangeal aspirates were screened, employing indigenously developed RSV MAbs and commercial Chemicon kit. Eight samples showed presence of virus/viral antigen for influenza A, four for influenza B, two for RSV, one for parainfluenza-1, two for parainfluenza-3 and one for adenovirus.

Molecular Detection of Human Metapneumo Virus

Human metapneumo virus (HMPV) is a newly discovered respiratory pathogen in India. Specimens from 26 pediatric and 18 adult cases with acute respiratory infection from Pune, Maharashtra were screened for the presence of HMPV RNA. Only 19.2% children were positive for the viral RNA. Out of five HMPV RNA positive four were <1 yr old and one was >1 yr. Phylogenetic analysis based on the M gene showed grouping of the Indian HMPV isolates into two distinct genetic lineages (Fig. 6).

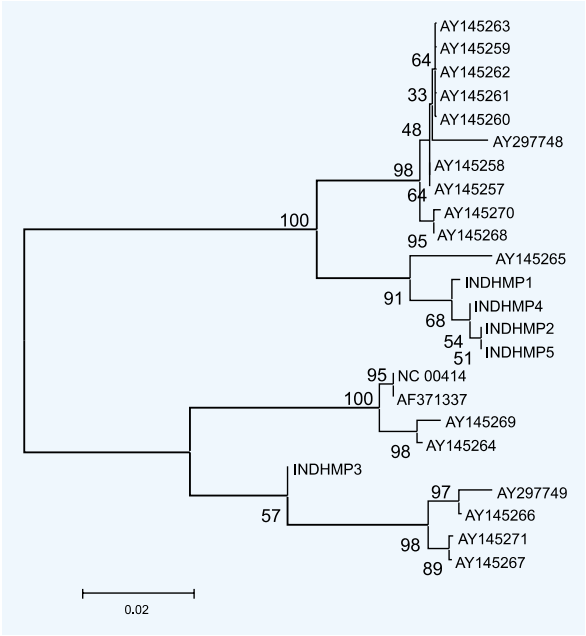


Fig. 6. Phylogenetic analysis of partial M gene (216 base fragment) sequences of 24 HMPV isolates.

Genetic Analysis

During May-June 2003 an outbreak of encephalitis was reported among children (<10 years) in Murshidabad, West Bengal. A number of influenza A (H3N2) virus isolates were obtained from encephalitis as well as febrile cases. HA and NA genes from these isolates and from mild cases from Pune isolated during the same period were amplified in RT-PCR and sequenced. All the isolates exhibited unique substitutions at different positions documenting antigenic drift. Seven of eight Indian isolates had N-D substitution at position 126. Analysis of the deduced amino acid sequences of the NA protein clearly documented lack of association of amino acid substitutions with the outcome of encephalitis. Phylogenetic analyses revealed that clustering of viral sequences was a function of time of isolation and not type of clinical disease in the patient.

MEASLES

During an outbreak of suspected measles at Vitha village, Sangamner *taluka* in Ahmednagar, (Maharashtra) blood throat swab, urine and skin swab samples were collected and transported to the laboratory for serological and virological studies. The outbreak was confirmed by RT-PCR and sequencing. Of the 26 serum samples from suspected measles cases 42.3% were positive. Two throat swab were subjected to RT-PCR and sequencing using N gene based primers. Primary data using blast analysis indicated that these measles virus strains belonged to D8 genotype.

POLIOMYELITIS

The major thrust area of research at the Enterovirus Research Centre (ERC), Mumbai is poliomyelitis. Since the beginning of the global polio eradication programme, ERC has been regarded as a major laboratory support to the program in India. The WHO Polio Laboratory Network consists of a total of 145 laboratories. In India, AFP surveillance is supported by a total of 8 laboratories. The WHO has designated ERC as one of the specialized laboratories in the Global Polio Laboratory network which is fully accredited for the period 2004-05 by the WHO.

Primary diagnosis of cases of acute flaccid paralysis in Maharashtra, Madhya Pradesh, Goa, Chhattisgarh, Delhi and Western Uttar Pradesh is undertaken by ERC. Polioviruses detected by other laboratories are also submitted to ERC for further studies. All polioviruses are differentiated as either wild virus or of Sabin vaccine origin (Vaccine-like). Wild polioviruses are sequenced to determine genetic relationship of viruses. The information is used to identify virus transmission patterns. The knowledge is helpful in understanding virus transmission routes, reservoir areas and to fine tune disease control strategies.

Virological Diagnosis of Acute Flaccid Paralysis

It is not always possible to differentiate clinically cases of acute flaccid paralysis (AFP) caused by poliovirus infection from those due to other causes. Virological diagnosis therefore is required. In 2003, a total of 4850 stool samples from 2397 AFP cases were studied for detection of wild polioviruses. Of these 770 were from Maharashtra and 515, 221, 96, 778 and 7 from Chhattisgarh, Delhi, Western UP and Goa respectively. Ten cases were from other states. Two stool samples were collected from 97% cases except in Western Uttar Pradesh (79%). Virus isolation results of 95% samples were sent to National Polio Surveillance project within 28 days.

In 2003, wild poliovirus type 1 was isolated from 3 cases in Maharashtra detected in Thane, Nanded and Sangli. Wild poliovirus type 1 was isolated from 10 cases in MP, 3 in Delhi and 65 in Western UP. Wild poliovirus type 3 was isolated from 8 cases in Western UP.

Intratypic differentiation of poliovirus isolates (1516) received from various parts of the country was done. In 2003 a total of 225 wild poliovirus cases were reported in India. State-wise distribution of wild poliovirus cases in India in 2003 is given in Fig. 7. In 2001, wild poliovirus transmission was confined mainly to UP and Bihar. In 2002, a total of 1600 poliomyelitis cases

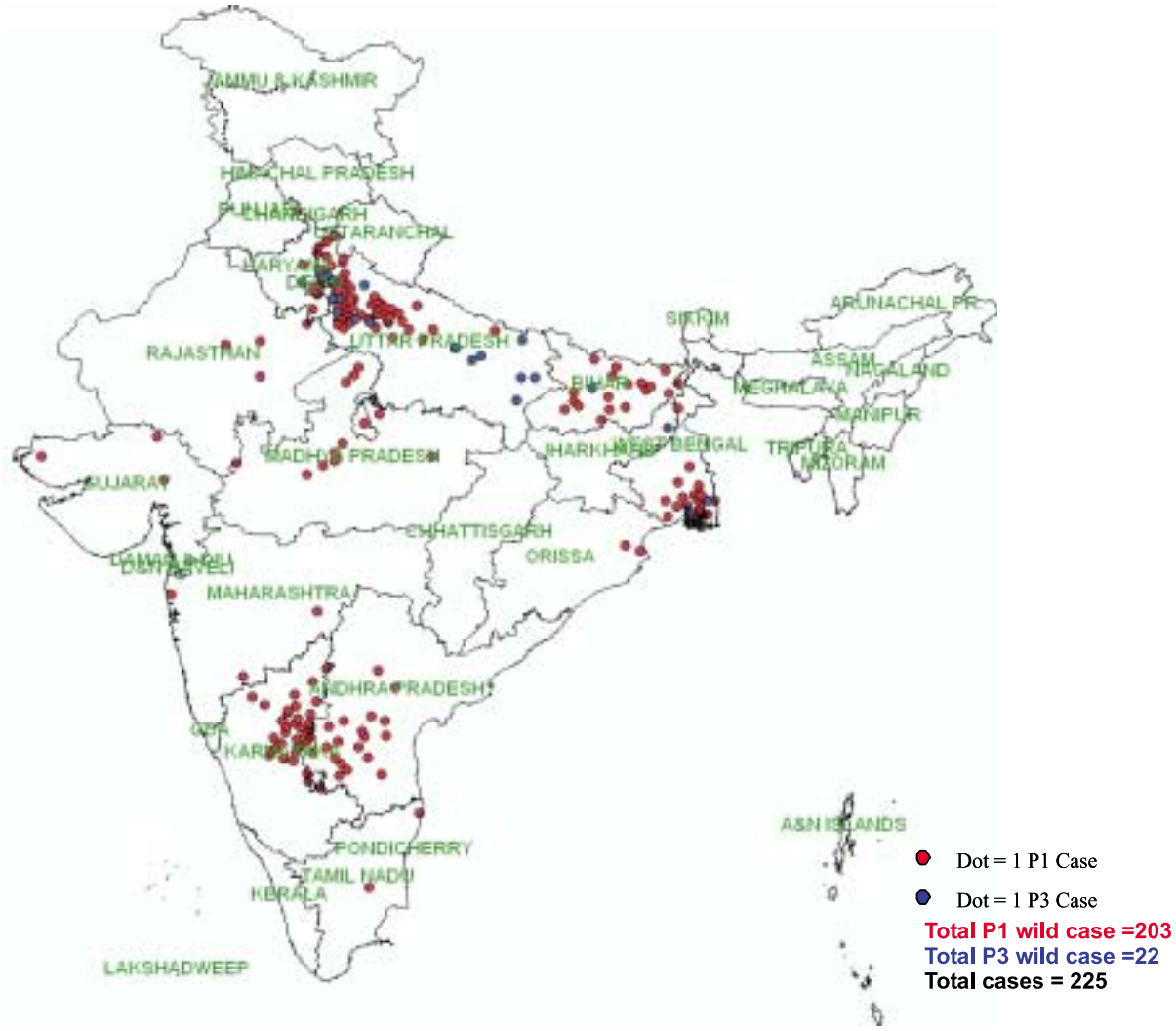


Fig. 7. Geographic distribution of virologically confirmed poliomyelitis cases in India, 2003.

were reported from India. Poliomyelitis cases were reported in states that had achieved zero polio status in previous year(s). Orissa reported polio cases after 3 consecutive polio-free years. Gujarat, West Bengal. Rajasthan and MP suffered from polio outbreaks in specific districts. Virus spread to adjacent districts causing additional cases. In Maharashtra, 3 paralytic poliomyelitis cases were reported in 3 geographically separated districts. There was no evidence of secondary spread of the wild poliovirus in the state. The last wild virus polio case in Maharashtra was in October 2003, in MP in November 2003 and in Chhattisgarh in July, 2002. Goa has been polio free since October, 1998.

Molecular Epidemiology of Wild Poliovirus

Complete VP1 nucleotide sequences of wild poliovirus isolates were determined for high resolution of virus transmission pathways. Phylogenetic analysis to determine genetic relatedness of the wild virus isolates was carried out using PHYLIP computer program. DNA-distances calculated by Kimutra 2-parameter model were used to generate neighbour-joining trees. Virus isolates were grouped into genetic clusters (lineages). Fig. 8-10 show the distribution of different genetic clusters (color coded dots) of poliovirus type 1 in India in 2001, 2002 and 2003. In 2002 wild poliovirus spread

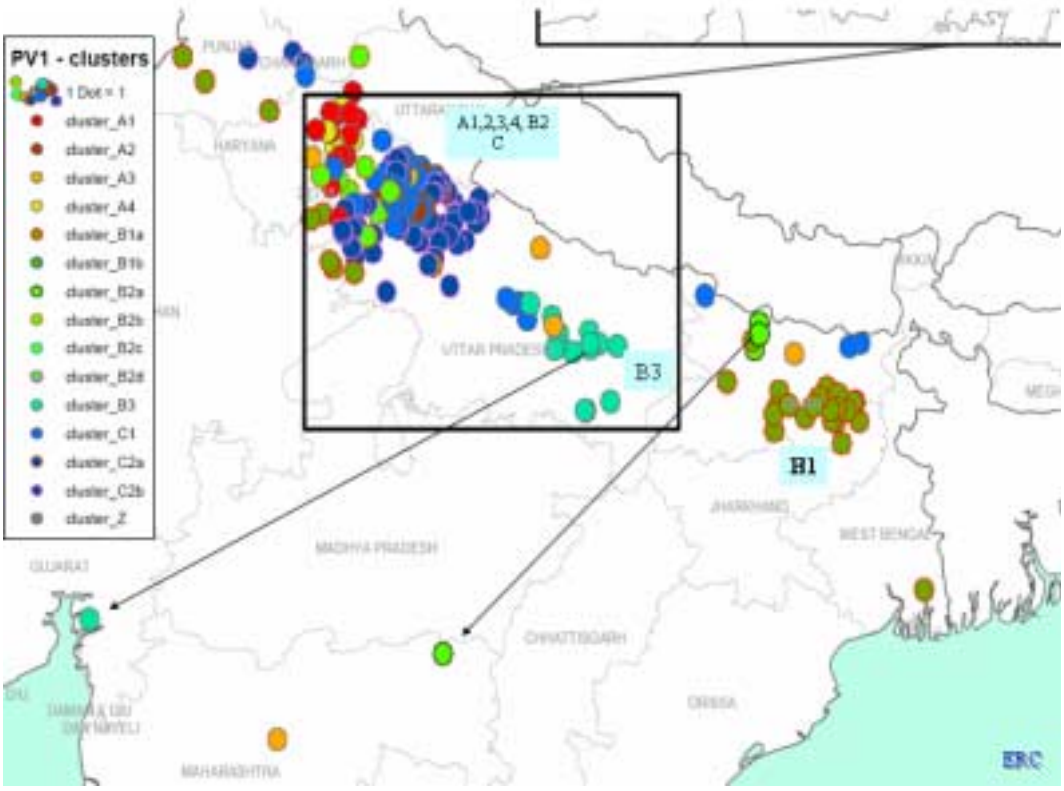


Fig. 8. PV1 SOAS-INDIA Geographic distribution by cluster 2001.

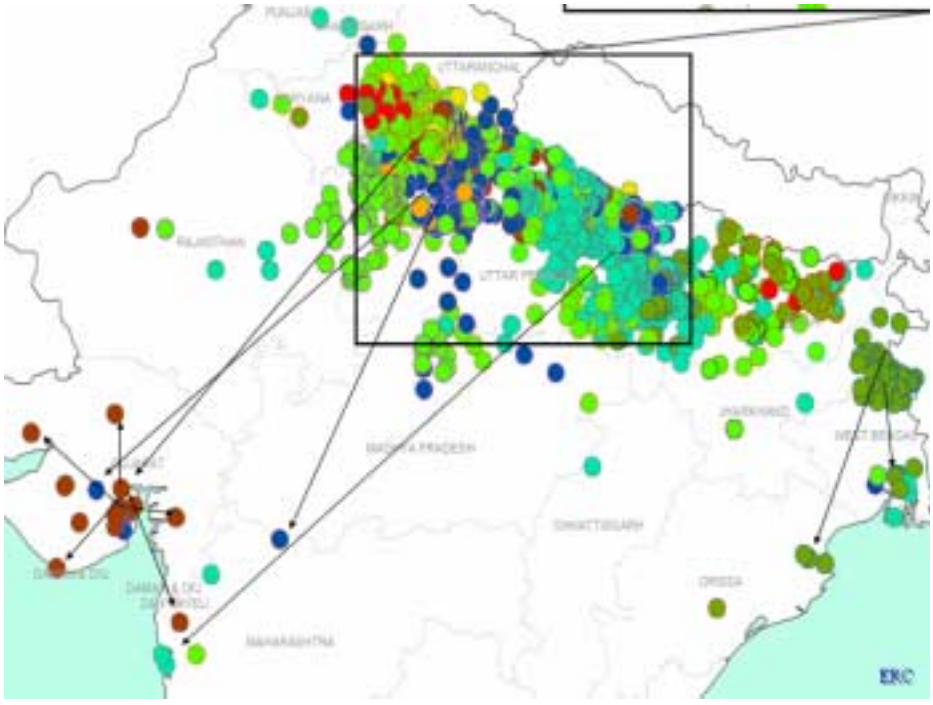


Fig. 9. PV1 SOAS-INDIA Geographic distribution by Cluster 2002.

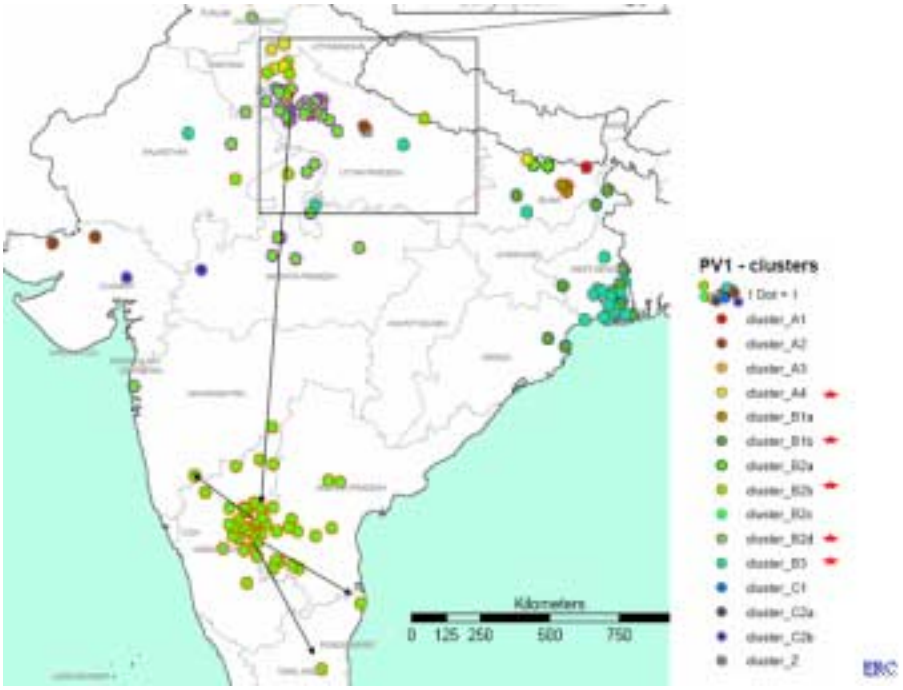


Fig. 10. PV1 SOAS-INDIA Geographic distribution by Cluster 2003.

from UP and Bihar to other polio-free states in the country. Noticeable are the polio cases in Gujarat that occurred because of reintroduction of wild virus from western UP. In fact wild polioviruses of two different genetic clusters were isolated in Gujarat. There was an upsurge of polio cases in Murshidabad district in West Bengal. The virus was then isolated from cases in Pakur district in Jharkhand. The wild virus was later isolated from cases in Orissa. The state was free from polio since 1999. In contrast, wild polioviruses of 4 different genetic clusters were isolated in Maharashtra. These observations indicate multiple reintroduction of wild poliovirus from UP to Maharashtra. However, there were no secondary cases and virus transmission met with dead end. Other states that suffered resurgence of poliomyelitis included MP and Rajasthan. As can be observed from the genetic clusters spot map for 2003, more than six months of intensive vaccination campaigns were required in these states to stop transmission of the reintroduced wild poliovirus.

In 2003, a new focus of intense transmission of wild poliovirus developed in Karnataka. The first case was recorded in May 2003 followed by an epidemic-like situation. Genetic sequencing identified the origin of the virus in Western UP, most likely in Meerut district. Wild virus from Karnataka spread to Andhra Pradesh, Tamil Nadu and Maharashtra. Wild virus circulation was continuing at the end of 2003.

Environmental Surveillance for Wild Poliovirus in Mumbai

Sewage samples were collected from F, G and M municipality wards of Mumbai every week for isolation of wild poliovirus. In 2003 no confirmed paralytic poliomyelitis case was reported in Mumbai. Wild poliovirus type 1 was isolated from 19, 16 and 10 sewage samples out of 52 samples collected from these wards respectively. Wild type 3 poliovirus was isolated in one sample each from F and M wards. Fig. 11 shows the week-wise isolation of wild poliovirus from sewage samples. The frequency of wild virus in sewage increased as the number of wild poliovirus cases in the country increased during the second half of the year.

Molecular sequencing of the wild viruses isolated in sewage samples indicated

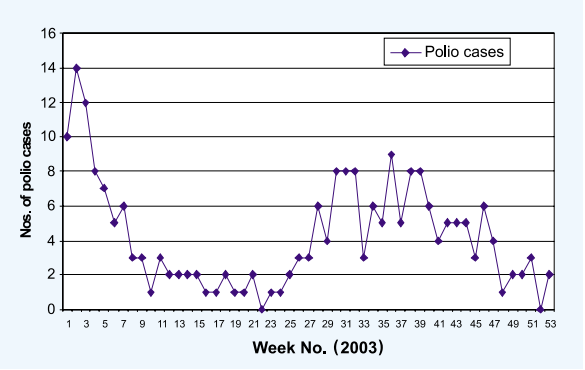


Fig. 11. Confirmed poliomyelitis cases in India, 2003 and wild polioviruses detected by environmental surveillance in Mumbai.

introduction of viruses of different genetic clusters from other high-risk areas where poliomyelitis cases were reported in preceding weeks. Continuous reseeding of wild virus into Mumbai poses a high risk of poliomyelitis to the resident population. In 2002, wild virus of one genetic cluster was isolated from sewage samples for over 5 months indicating local circulation of the virus. This virus was responsible for 2 polio cases in the city. The study has provided important information about wild virus transmission in the country

Vaccine Associated Paralytic Poliomyetitis (VAPP)

Sabin vaccine poliovirus viruses were isolated from 22, 27 and 13 AFP cases reported in Maharashtra in 2001, 2002 and 2003 respectively. All cases except those administered OPV after onset of paralysis and where final clinical diagnosis was established were considered for analysis of VAPP. Since the cases were reported as AFP no differentiation was made between those that had residual weakness at 60 days follow-up from those that had recovered. The range of VAPP in children less than 5 yr was found to be 91 to 208 cases.

Molecular sequencing of 5' untranslated region vaccine-like isolates was carried out to identify reversion mutants in poliovirus 1, 2 and 3 isolates. However, correlation of reversion at major attenuation site to wild type and post-paralysis residual weakness in patients did not correlate well.

Search for Vaccine Derived Polioviruses (VDPV)

In recent years paralytic poliomyelitis cases due to circulating VDPV have been recognized in either sporadic or outbreak form. VDPV are Sabin vaccine strains showing more than 1% sequence divergence from the vaccine virus. The nucleotide sequence substitutions arise during transmission of the virus from person-to person. It has been observed that VDPV yields non-standard results in the strain-specific ELISA used for intratypic differentiation of poliovirus isolates. VP1 sequencing of such isolates confirms the presence of VDPV.

All poliovirus isolates from year 2003 have been sequenced giving discordant results in the ELISA and probe hybridization methods. No vaccine-like isolate that has 1% or more sequence divergence from Sabin vaccine viruses has been found. The nucleotide sequences of the complete capsid (VP4, VP2, Vp3 and VP1) of these isolates to identify the mutations leading to changes in antigenic sites and altered ELISA reactivity has been determined.

Studies on Non-Polio Enterovirus (NPEV)

Enterovirus 71 is known to cause hand, foot and mouth disease in children, meningitis, encephalitis and also polio-like paralysis. An EV71 isolate was identified in stools collected from an a FP case in 2002. VP1, VP4 and 5'UTR nucleotide sequences of the isolate were compared with isolates from other countries. Indian isolate was found to have unique sequence qualifying to be in a separate genetic group (Fig. 12).

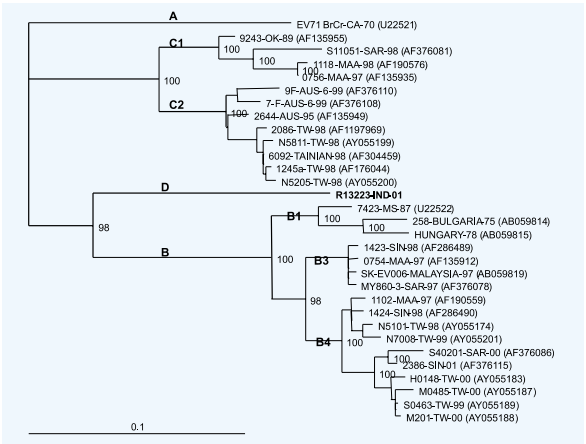


Fig. 12. Genetic relationship of EV71 isolates using VP1 sequences.

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

AIDS pandemic is spreading unchecked in almost every part of the world. Currently, more than 34 million individuals are infected with human immunodeficiency virus (HIV). Although majority of infections are due to HIV type-1 (HIV-1) strains, a significant number of cases with HIV type-2 (HIV-2) infections has been reported in many countries. In India 3.5 million people are HIV seropositive as estimated by National AIDS Control Organization (NACO). The presence of HIV-2 has been reported from different parts of India and in most of the cases it is associated with HIV-1 infection. However, isolation and neutralisation of two HIV-2 isolates from Pune was also reported in 1999. Since the beginning of national serosurveillance of HIV in the eastern part of India, only HIV-1 infection has been reported. The National AIDS Research Institute (NARI) and NIV at Pune, NICED, Kolkata and TRC, Chennai have been conducting several studies on epidemiological, clinical, immunological and socio-behavioural aspects of HIV/AIDS.

Epidemiological Studies

Comparative Research Study of the Reality® Female Condom and Version 4 of the Reddy Female Condom

A randomized crossover study was carried out to assess acceptability of Reddy's and Reality female condoms (Fig. 1) in low risk women at two sites—NARI, Pune and YRG Care, Chennai. After obtaining a written informed consent from both the partners, 30 couples having low risk for HIV infection and using some contraceptive method were enrolled at each of the two sites for assessment.

The data is being analyzed for functional performance of study condoms in terms of clinical breakage, non-clinical breakage, total breakage, complete slippage and total clinical failure. With respect to acceptability, participants did not indicate a clear preference for either of the two condom types. There were no statistically significant differences in the performance measures between the Reddy version 4 and Reality female condoms.

Fig. 1. Reality and Reddy female condoms.

HIV Incidence and Participant Retention Protocol

Study was conducted at NARI, Pune to determine the current incidence and retention of HIV among a cohort of 400 newly identified high risk women as well as among 400 HIV-uninfected partners of HIV-infected persons and to assess risk factors for HIV.

Till date 286 HIV-negative women and 315 HIV sero-discordant couples have been enrolled in the study. In-depth interviews at the follow up visits and focused group discussion session with infected male participants indicated that main barriers to retention among high risk women were informing the husband or family and others, undue suspicion arising out of repeated clinic visits, lack of time due to household and family responsibilities, not remembering the dates and lack of community acceptance to couples frequently going out together. However, all participants expressed interest in participation in microbicide trials.

A total of 21 index cases died. Cause of death included TB, AIDS related illness, anaemia, cardiorespiratory arrest, diarrhoea and meningitis in 11 cases. Cause of death was not known in 10 cases. There was no documented HIV antibody seroconversion to date in the HIV-negative women's cohort, however, four uninfected partners have seroconverted in the couple's cohort. A total of 315 couples contributed 203.2 person-years of follow up providing an incidence estimate of 1.97 per 100 person-years.

In the follow-up of HIV infected index cases, during 68 person-years of follow-up, 28 participants required 36 hospitalizations. The hospitalization rate was 53 per 100 person years. Twenty-one index cases were hospitalized once, six were hospitalized twice, and one was hospitalized thrice. Participants with a CD4 cell count below 200/mm^3 were 7.7 times more likely to be hospitalized compared to others.

Phase I / II Vaginal Microbicide Study using Praneem Polyherbal Formulation

A phase I / II vaginal microbicide study using Praneem polyherbal formulation (vaginal tablet), an indigenously developed product with potential anti-microbial properties has been initiated at NARI, Pune to test its long-term toxicity in HIV negative low risk women (cohort A) and HIV negative commercial sex workers (cohort B), to assess its efficacy in prevention of STDs and HIV infection and to assess its acceptability among participating women and their partners. Till date, of the 37 participants screened, 20 have been enrolled for the study.

Serosurveillance of HIV in Different Population Groups in Agra

As a part of the surveillance study, screening of blood samples is being carried out at CJIL, Agra from different high risk population groups such as HIV-suspected patients referred from different hospitals, commercial sex workers resident at Government Protection Homes, foreign students, individuals opting for voluntary HIV testing, cases referred by the District Jail and District Magistrate. Of the 289 samples screened during 2003, 121 were positive. Interestingly, all these positives were among either HIV suspected patients or individuals opting for voluntary HIV testing. None of the foreigners was positive. These trends indicate increased level of awareness about HIV in the community and among people managing the problem.

Phase I HIV-1 C MVA Vaccine Trial (NARI-IAVI-NACO study)

Community work plan was developed with a view to sensitize the community about the proposed vaccine trial and to initiate dialogue with certain groups in the community to identify volunteers for the study. Meetings with the partner non-government organizations and community advisory board members were conducted to discuss issues related to recruitment of volunteers in the proposed vaccine trial.

The vaccine trial protocol has been finalized with close interaction between scientists from NARI and IAVI. The screening and enrolment, consent forms and study information brochures and other materials have been finalized. A new vaccine trial clinic and a modern laboratory facility to carry out various laboratory assays pertaining to vaccine trial have been created and both the facilities are now functional (Fig. 2a & b).

Fig. 2 a. Vaccine Trial Clinic.

Fig. 2 b. Vaccine Trial Laboratory.

Clinical Studies

Study of Clinical Utility and Effect of a Tumor Necrosis Factor Inhibitor (pentoxyphylline) on Immune Profile in Patients with HIV Infection

Study of clinical utility and effect of a tumour necrosis factor inhibitor (pentoxyphylline) on immune profile in patients with HIV infection was carried out at PGIMER, Chandigarh. Forty patients with HIV infection were administered 400 mg pentoxiphylline thrice daily. Follow up evaluation was carried out at 4,8,16 and 24 weeks. Two patients reported opportunistic infections - one each had cryptococcal meningitis and therefore tuberculosis, soon after institution of the therapy. They have all been followed up for at least 12 weeks and barring 2 all have shown subsidence of major symptoms they reported with at presentation. They gained weight (3.9 kg) over the period of follow up. There was a significant increase in CD4 counts. No adverse effects of the drug were observed suggesting that it can reduce the incidence of opportunistic infections and delay the initiation of antiretroviral therapy. Hence this may be a valuable therapy for individuals who are unable to afford anti-retroviral medication.

Response to DOTS Therapy in HIV Seropositive and HIV Seronegative Tuberculosis in Pune

Study was carried out at NARI, Pune to determine the response to thrice weekly anti-TB DOTS treatment in HIV serpositive and seronegative pulmonary tuberculosis patients.

The TB cure rate at the end of 6 months of DOTS therapy was 85.8 % in HIV seronegative and 52.7% in HIV seropositive TB patients. During treatment 0.8% HIV seronegative and 14.5% HIV seropositive patients expired. The cure as well as mortality rates during anti-TB treatment were higher in the HIV seropositive patients.

Study on Mother to Child Transmission

A study is being carried out at the BJ Medical College, Pune in collaboration with Johns Hopkins University, USA. The plasma samples of the pregnant women enrolled in the study and cord blood samples were processed for determining HIV-1 viral load. During the year, 227 samples (in addition to 34 from pregnant women enrolled in 2002) were processed for viral load estimation.

Analysis of Generic Antiretroviral Formulations Manufactured in India

India is a major producer of generic HIV antiretroviral drugs. These are widely used in developing countries since they are less expensive than those produced elsewhere. However, data describing the integrity of these drugs are not available. Therefore, the content of efavirenz (600 mg), nevirapine (200mg), zidovudine (300mg), stavudine (30 mg), lamivudine (150 mg), didanosine (250 mg) and a combination pill containing nevirapine, stavudine and lamivudine in the same dosages obtained from three Indian sources (Aurobindo Pharma, Ranbaxy and Cipla) was analyzed by TRC, Chennai and compared with proprietary medications manufactured in USA.

Six tablets/capsules of each antiretroviral drug were processed and analyzed in duplicate. The concentration of the drugs was calculated from a set of calibration standards of known concentration. The drugs compared well with the proprietary formulations and the variability ranged from 0.01 to 8.3%. All the formulations were within 5% range of the stated contents as compared to the proprietary drugs except for stavudine and lamivudine which were slightly higher, but withing 10% range.

Immunological Studies

Activated CD3+T lymphocytes in HIV Infection

The activation of T lymphocytes harbouring latent virus triggers the multiplication of HIV at the later stage of disease progression. During the year CD3+HLA-DR+ T lymphocytes were estimated in 746 HIV infected individuals and 67 healthy controls. The data shows that activated T lymphocytes circulate at all stages

of HIV infection and the activation is more predominant in HIV infected females. Sixty four per cent HIV infected women showed elevated levels of activated T lymphocytes as compared to 52 % HIV infected males. The importance of these levels in HIV infection is being further analyzed.

Identification of HIV-1-specific gag, nef and env Epitopes Recognized by Indian Patients

A study was carried out to identify HIV-1 C epitopes recognized by the Indian patients. Peripheral blood mononuclear cells from 47 HIV-1 infected Indian subjects were screened for HIV-1 gag, nef and env-specific T cell responses by IFN-γ ELISPOT assay using pools of overlapping peptides. Thirty of them showed response to one or more HIV-1 antigens, 21 to at least one antigen (16 against gag, four against nef and one against env), seven against two antigens (four against gag and nef, two against gag and env and one against env and nef) and two against all three antigens.

The gag and nef were the most targeted antigens; 83% of the responders showed response to gag and 36% to nef (Fig.3). There was no association between HIV-specific T cell response and the pasma viral load or CD4 counts. Fifteen gag (10 in p24 and 5 in p17), 10 nef and one env (gp41) epitopes were identifed using a combination of peptide matrix ELISPOT and CTL prediction software. Three putative gag (AEWDLHPV, GPIAPGOM, RPGGKKRYM) and one nef epitope (WIYTHQGYF) were recognized by

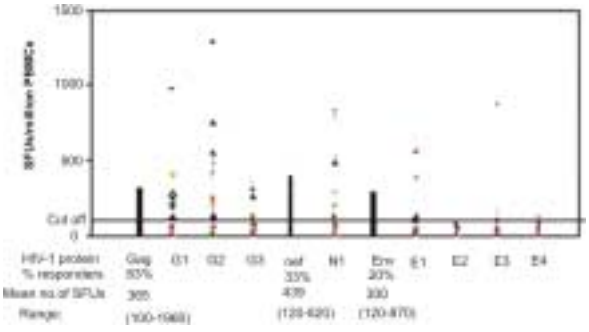


Fig. 3. HIV-1 C gag.nef and env-specific IFN-γ secretion measured in ELISPOT assay.

more than one study subject. Additionally, five nef and one env epitope were recognized in association with more than one HLA type expressed by a single study subject. Five p24 epitopes were highly conserved across the clades while one p17 epitope was subtype C-specific. The epitopes identified in the study will be important in designing HIV vaccine candidates eliciting strong and sustained CTL response.

Assessment of Utility of Absolute Lymphocyte Count (ALC) as a Marker of HIV-1 Disease Progression

Efforts are ongoing to find a cheaper and widely available method to predict and monitor HIV progression and to monitor response to therapy. The ALC estimations are cheaper, widely available and could be easily automated. The cost of CD4 count estimation is 45 times higher than ALC. Therefore, utility of ALC for monitoring disease progression has been analyzed on a subset of data and found to be satisfactory. The efficiency of ALC was assessed in a large database containing paired values of ALC and CD4 counts from 2419 patients at NARI. The CD4 counts were estimated using flowcytometry and the ALC were estimated using the blood cell analyzer. Using this data, an equation has been derived to calculate CD4 counts using respective ALC values. The CD4 counts obtained were compared with the actual CD4 counts and the sensitivity of the equation to correctly predict CD4 counts was calculated. In addition,various cut offs of ALC were also evaluated for prediction of CD4 and<200 dn <350/ cells/mm^3.

CD4 counts were found to be significantly correlated with ALC (Fig.4). Amongst the various ALC cut offs, ALC<1500 cells/mm^3 predicted CD4 cell counts<350 cells /m^3 with a sensitivity and specificity of 72 and 78% respectively. Greater sensitivity and specificity of prediction will allow use of ALC as surrogate marker for CD4 counts. However, the equation was not found useful to predict CD4 counts <200 cells / mm^3 with a poor sensitivity of 49%.

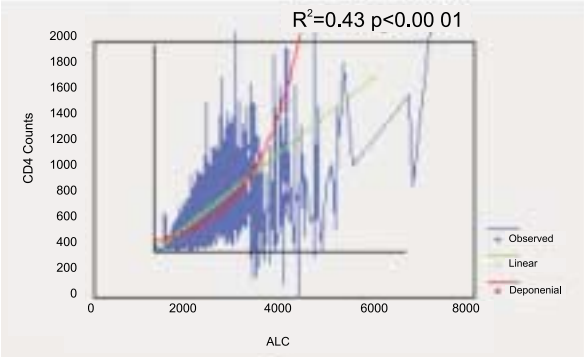


Fig. 4. Correlation between CD4 counts and ALC in HIV seropositives.

Role of Dendritic Cells in Presentation of Antigen to the Immune System

Dendritic cells (DCs) are the potent antigen presenting cells of the immune system. A study has been initiated to sensitize lymphocytes from normal healthy individuals to HIV antigens by using antigen pulsed dendritic cells as stimulator cells with the aim to study the response of healthy adults to HIV antigens and in identifying epitopes recognized by healthy adults but not by HIV infected persons.

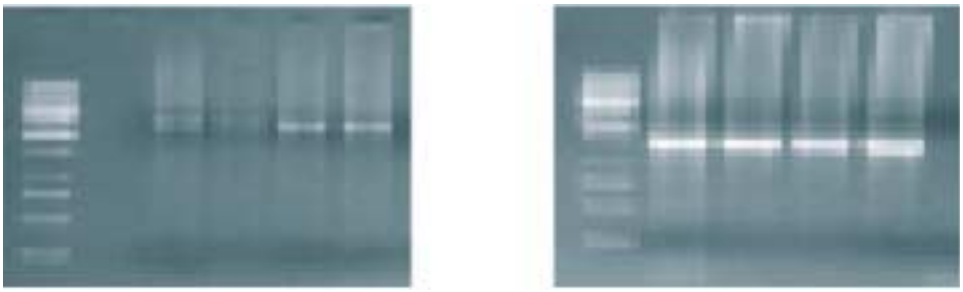
The (CTL) response of p24 antigen stimulated cells was determined by chromium release assay using autologous PBMCs pulsed with p24 antigen as a target (Fig. 5). One clone showed 69% HIV-1 gag specific CTL response at a ratio of 50:1.

Development of a Candidate Vaccine based on Multiple CTL Epitopes for gag and env Antigens from Indian HIV -1 Subtype C Viruses

Study was carried out on a multi-epitope vaccine containing immunodominant HIV-1C antigens. Amplification and cloning of gag and env genes from 4 of the 6 seropositives identified in HIV seropositive cohort at NARI has been completed (Fig. 6). The sequencing of these clones is underway.

These sequences will be further used for obtaining consensus sequences and will be used for generating overlapping peptides for Indian HIV-1 C gag and env. The epitopes recognized by Indian patients will be determined by ELISPOT assay and CTL epitope prediction

Fig. 5. *In vitro* stimulation of T cells by p24 pulsed dendritic cells.



2.5 kb Env Gene 1.5 kb Env Gene

Fig. 6. Amplified gag and env genes by PCR.

software. These epitopes will be used for construction of multiepitope vaccine.

Influence of Active Tuberculosis on Chemokine and Chemokine Receptor Expression in HIV-infected Persons

Chemokine receptors (CCR5 and CXCR4) have been identified as major co-receptors that act in combination with CD4 surface molecules for HIV docking and entry. Interactions between chemokine receptors and their corresponding ligands could therefore block and down-regulate co-receptor expression and effectively inhibit HIV life cycle. There is a paucity of information regarding the influence of active tuberculosis on the expression of the chemokine receptors, and circulating levels of the β-chemokines adn macrophage inflammatory protein-1 alpha and beta (MIP-1α, MIP-1β). At TRC, Chennai CCR5 and CXCR4 expressing CD3+ and CD4+ T cells (by flowcytometry) and plasma levels of MIP-1α, MIP-1β and RANTES (by ELISA) were estimated in 14 HIV-TB, 14 HIV, 10 TB and 1 normal individuals. The proportion of total T cells, particularly helper T cells, expressing CCR5 and CXCR4 was significantly lower in HIV seropositive patients, irrespective of the presence or absence of tuberculosis as compared to normal and TB groups. On the other hand, plasma levels of MIP-1α, MIP-1β and RANTES tended to be higher in HIV patients than in normals. The HIV-TB patients showed higher production of chemokines than HIV patients. There was no statistically significant correlation between viral load and cellular expression of chemokine receptors or plasma β chemokine levels in these individuals. The data suggest a down-regulation in *in vivo* expression of CCR5 and CXCR4 on CD4+ cells in HIV patients with and without tuberculosis in India. A trend towards increased production of MIP-1α, MIP-1β and RANTES was observed in HIV patients when compared to normal controls; among HIV patients, those with TB had higher plasma chemokine levels than those without.

Apoptosis of PBMCs in Patients with HIV and TB

HIV infection leads to a progressive loss of CD4 lymphocytes, which results in decreased general immunity and increased susceptibility to opportunistic infections and malignancies. Study was carried out at TRC, Chennai to evaluate the extent of apoptosis in the peripheral blood mononuclear cells (PBMCs) of HIV-infected patients with and without TB to test the dual signal hypothesis of cell proliferation and apoptosis. PBMCs from HIV, TB and HIV-TB patients and healthy controls were obtained. Genomic DNA and RNA were extracted from fresh PBMCs as well as from PBMCs stimulated *in vitro*.The results of the study show that both HIV infection and TB induce apoptosis of PBMCs.

Socio-Behavioural Studies

Stigma Attached to HIV/AIDS: Implications for Health Care and Social Adjustment

A multi-centric study, coordinated by ICMR, was conducted with the broad objective of assessing the nature of stigma, discrimination and denial to HIV/AIDS positive individuals in different settings and its effects in relation to seeking health care and social adjustment. The findings of the study will fill important gaps in the current knowledge and provide critical information for the design of stratagies for overcoming the effects of HIV/AIDS related stigma.

The qualitative and quantitative research techniques being used to elicit responses include in-depth interviews of HIV sero-positive/AIDS patients, care givers at hospitals, and at homes, counsellors and interviews of respondents representing the general population.

The major preliminary findings of the study conducted by NIRRH, Mumbai indicate that 43% of persons living with HIV (PLWHIV) have not revealed their sero-positive status to any of their family members, to colleagues at workplace or in the community. The main reasons given were-fear of being thrown out of the house or the community; fear of losing the job and fear of being neglected. Fifty seven per cent of PLWHIV shared their HIV status with either of their spouses, parents relatives and friends. The reactions at home included - did not believe; were shocked; got scared; stopped talking and frequent quarrels including physical abuse. The

community reacted by keeping a distance; stopped inviting them to social functions; verbal abuse and total neglect. In the hospital/clinic setting, PLWHIVs perceived reactions, 50% experienced a sympathetic attitude mostly from doctors while others perceived negative reactions. The stigma related actions and reactions expressed by ward boys and *ayahs* were fear, anger and hate.

Eighty per cent of the employed respondents had not revealed their HIV status at workplace, the reasons reported were fear of losing their job, sarcasm and neglect. Regarding modes of transmission of HIV, around 50% felt that they had contracted the infection through high risk sexual behaviour. Around 40% female respondents, all housewives felt that they contracted the infection from their husbands and 10% respondents expressed that blood transfusion was the cause of their getting infection by HIV virus. With regards to counselling, majority felt that better counselling, particularly post-test counselling, should be provided to the infected people as well as to their family members, particularly their spouses and close relatives. Other suggestions included support in terms of free medicines, government shelter homes, free education and food for their children.

The study in HIV seropositive individuals carried out at TRC, Chennai showed that actual stigma experienced by those infected with HIV was much less (26%) as compared to the fear of being stigmatized or perceived stigma (97%). Stigma was found to have a highly significant negative correlation with quality of life in the psychological domain and a significant negative correlation in the environmental domain. However, individuals who did experience actual stigma seemed more determined to live and experience an above moderate quality of life. The findings of this study will serve to motivate HIV infected individuals to rise above stigma, avoid internalizing their stigmatized feelings and work toward a better quality of life. Health providers need to address these issues in their care for HIV infected individuals.

Studies are also ongoing at NARI, Pune to understand HIV related stigma and discrimination amongst urban, rural and industrial population of Pune.

Gender Differences in Perceived Health related Quality of Life among Persons Living with HIV

During the past decade there has been a lot of focus on improving the quality of life of HIV infected persons. A clinic based study of 203 HIV infected individuals (102 female and 101 male) at TRC, Chennai showed that females scored significantly higher in the psychological domain and males scored significantly higher in the sociological domain. The CD4 counts of the patients did not influence the quality of life among males as it did in females in all the four domains. The findings of this study highlight the need for gender specific motivation strategies in improving the quality of life in HIV infected persons.

Understanding Women's Reproductive Health Concerns in the Context of AID/HIV

A study is ongoing among adolescent girls and their mothers from slums of Pune, working women in the hostels, comparable group of adolescents and their mothers in the same area. The base line study was helpful in understanding the needs of women. The second phase of the study involved need based intervention and was initiated this year. Specific interventions included maintaining health cards during health camps, menstrual diary card records for three months, growth measurements, *etc.* Other interventions would cater to the needs of the women. The specific objectives in this phase include women's empowerment through development of reproductive health related innovatiove and indigenous package of information, education and communication and to develop an advocacy model for women's health programs. It was observed that myths and misconceptions existed and regarding reproductive health, family planning, sexuality, STDs including HIV/AIDS *etc.* among adolescents, their mothers and working women.

Studies on HIV/AIDS and Drug Abuse in Manipur

Study has been initiated by NICED, Kolkata to record the descriptive epidemiology of intravenous drug users (IDUs) and their behavioural status, to study the sero-prevalence of HIV, HBV and HCV among IDUs and to assess the trend of HIV infection among them. Studies showed that most of IDUs belonged to age group 21-25 yr. Highest prevalence of HIV was found in 31-40 yr age group. About 17% of the IDUs were found to be unemployed while 34% were students. Heroin was the most commonly used drug (55%) followed by spasmoproxyvon and narcotic analgesics. Highest prevalence of HIV was seen in IDUs who injected for more than 15 yr. No HIV infection was found among fresh IDUs.

Another study is being carried out by NICED, Kolkata in collaboration with a NGO operating a needle exchange program among IDUs. The study indicated the usefulness of needle exchange program in reducing the complication of infections associated with unsafe injection practices among IDUs. About 80% of the drug users injected the drugs, with an average injection rate of two per day and less than 10% shared injection equipment. Due to health education through the project, condom use among IDUs has increased to over 90% when visiting commercial sex workers (CSW). The prevalence of HIV in IDUs was low. In contrast, HBV prevalence was 18%. HCV prevalence increased from 7% in 1997 to 66% in 2002 and 80% in 2003. The prevalence of HIV and HBV in commercial sex workers (CSWs) was 9% each. Most CSWs entertained 3-4 clients a day and most of them used condoms. Thirty six cases were found to be having active tuberculosis. NICED has liased with the state health services and arranged for their treatment under RNTCP.

Impact of Counselling on Coping Behaviour of HIV Positive Cases in Different States

Counselling with HIV positive cases aims to enhance the medical, social and emotional management of the condition by way of strengthening coping mechanisms of the individuals. In order to look into the quality of counselling and its impact on the coping behaviour of HIV infected people, study was carried out at Delhi, Mumbai, Channai and Ranchi. At each centre about 200 HIV positive and 200 control cases and 50 counsellors have been studied by using standard psychological tools for anxiety, depression and coping behaviour and structured questionnaires. The data of the study is being analyzed.

Reproductive Health

Research in the area of reproductive health is being pursued by the National Institute for Research in Reproductive Health (NIRRH) located at Mumbai and the Human Reproduction Research Centres (HRRC) of the Council.

At NIRRH, several new epididymal testicular proteins with role in sperm maturation and function have been identified and characterized. Molecules with dual roles of contraceptive and anti-microbial activity have been purified from the hemolymph of Indian mud crab, *Scylla serrata* and are being assessed. Nisin, a food preservative has been demonstrated for the first time to also have antifertility activity.

An HIV receptor/binding protein on spermatozoa (a 160 kDa sperm protein that is bound specifically by gp120 HIV envelop glycoprotein as well as cell free HIV) was identified by Western blot analysis suggesting an alternative mode of HIV entry into spermatozoa which is devoid of conventional CD4 receptors.

Reproductive health programme for adolescents has been initiated by the Institute. The knowledge, attitudes and need of the adolescents are being studied and a programme for their long term need will be provided.

FERTILITY REGULATION

BASIC RESEARCH

Identification and Characterization of Epididymal Antigens

(i) Using neonatal tolerization

Sperm antigens play a crucial role in reproduction and these proteins are mostly acquired either from the testis or the epididymis. Neonatal tolerization was used for raising monoclonal antibodies to rare or minor antigens. Monoclonal antibodies so generated as probes using epididymis specific antigens were identified. One of the five epididymis specific monoclonal antibodies obtained was characterized. Immunochemical characterization of the cognate protein revealed a tissue specific and cell type specific pattern (Fig. 1).

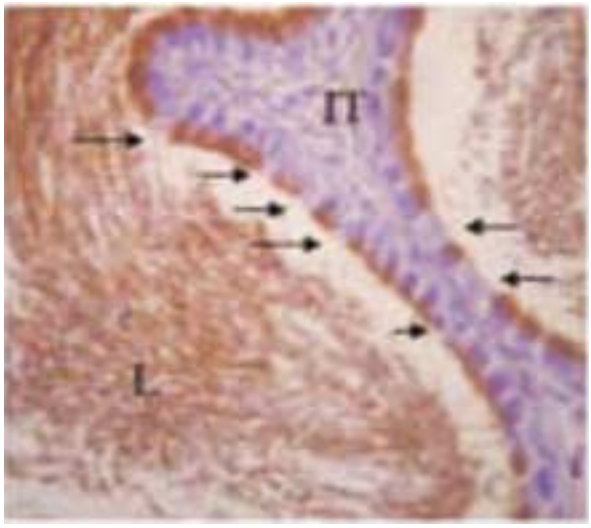


Fig. 1. Tissue and cell type specific localization of the protein.

The protein identified was found to be developmentally expressed from day 30 onwards and is androgen regulated. Two forms of the protein were found to exist, one held by ionic bond which leaches out along with 2M NaCl [peripheral] and the other which falls out with a detergent Triton X- 100 [integral]. The antibody identified a protein of ~ 48kDa on a non reducing gel suggesting the presence of disulphide bonds. Immunogold labeling indicated that the protein is localized on the mid piece and tail region of the rat spermatozoa (Fig. 2).

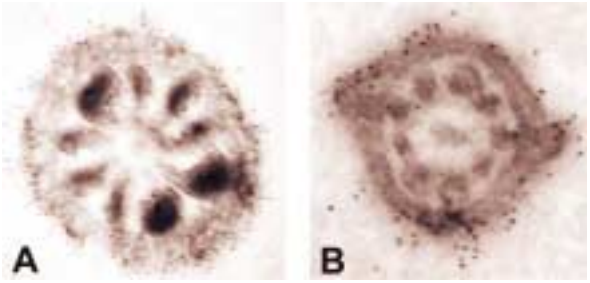


Fig. 2. Immunogold labelling of the protein on the midpiece (A) and sperm tail (B) using antisperm antibodies.

(ii) Using antisperm antibodies

Using vasectomised mouse model, monoclonal antibodies were generated for use as tools to identify and characterize functionally relevant and conserved testicular and epididymal proteins. One of the monoclonal antibodies D5E5 identified a ~70kDa testis specific antigen (Fig. 3).

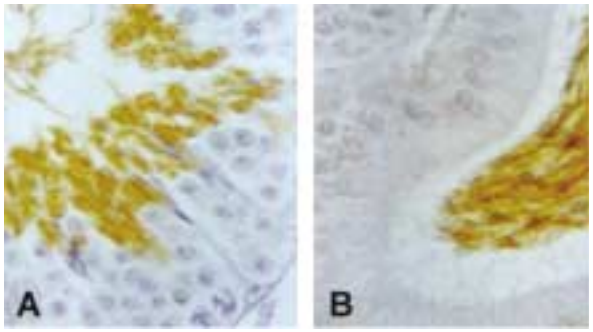


Fig. 3. Immunohistochemical localization of the protein in mouse testis (A) and epididymis (B).

The cognate antigen is expressed post-meiotically in a stage specific manner starting from elongating spermatids at stage 8 of spermiogenesis upto mature spermatozoa. Immunofluorescence (IIF) studies showed that the antigen is localized on the tip of acrosome as well as principal piece of tail (Fig. 4). The antigen is conserved across the species on rat, bull, marmoset and human spermatozoa as seen by IIF and exhibits species specific domain localization.

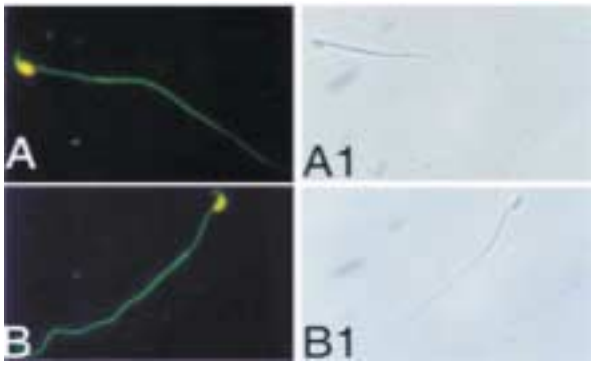


Fig. 4. Immunofluorescent localization on the mouse testicular (A) and epididymal sperm (B). A1 and B1 are corresponding phase contrast images.

Its testis specificity, acrosome and tail localization suggest an important role in reproduction.

Studies with 80 kDa Human Sperm Antigen and its Synthetic Peptides

An 80 kDa human sperm (80 kDa HSA) protein responsible for inducing immunological infertility has been identified, purified and characterized. Active immunization of male and female rats with 80 kDa resulted in infertility. The N-terminal peptide and peptides obtained by digestion of 80 kDa using endoproteinase Lys-C (peptides 1-4) and Glu-C (peptides 5-6), did not show any homology with any other protein in the database. These peptides were synthesized and conjugated to keyhole lymphocyte haemocyanin and used to generate polyclonal antibodies in rabbits. A good immune response was observed with peptides NT, 1, 2 and 4.

Passive immunization of rats with 10 or 40 µg of the immunoglobulin fraction of antibodies to NT and peptide 1 resulted in inhibition of pregnancy in 45-70 % of the animals, respectively. In immunized rats, the epididymal spermatozoa were found to be agglutinated and antibodies were localized in the epididymis and not in the testis suggesting that antibodies do not cross the blood testis barrier.

Studies also indicate that in the epididymis the protein appears from day 40 onwards, suggesting that it may be androgen regulated.

Role of a Novel Androgen Regulated Hox-B2 *containing Gene Expressed in the Epididymis*

A partial sequence showing homology to the conserved region of *Hox-B2* was identified from a monkey epididymal library. In an attempt to identify epididymal proteins which play a functional role in sperm maturation, a clone was identified from the monkey cDNA library using monoclonal antibody raised against washed human spermatozoa with sequence homology to the conserved region of *Hox-B2*. The gene was expressed in adult rat, monkey and human epididymis and not in immature rat epididymis, suggesting that it is a conserved protein and is regulated by androgens. Both in the castrated as well as ethane dimethane sulfonate (EDS) treated rat model, the protein expression in the epididymis disappeared and following

supplementation with testosterone was restored to near normal levels. In developing rats, the protein was expressed from day 40 onwards, concomitant with the secretion of testosterone, also confirming its androgen regulation. The protein was expressed only in the epididymis with maximal expression in the cauda epididymis. Northern blot analysis revealed a single transcript in the monkey cauda epididymis. Attempts to obtain a full length sequence using 5'RACE resulted in a 900 bp upstream region, which has been cloned into the pGEM-T vector and is currently being sequenced.

Regulation of Endometrial Apoptosis

The human endometrium is characterized by cyclic appearances of proliferative and apoptotic changes in a steroid dependent manner. However, the precise role of steroid hormones associated with these changes remains unclear. In studies done at NIRRH, Mumbai, the female common marmoset (*Callithrix jacchus*) has been utilized as a model to study the endometrial changes in response to steroid hormones. Studies were carried out in normally cycling and ovariectomized females treated with graded doses of estradiol and progesterone. Using the TUNEL method, apoptosis was observed in the endometrial samples collected during the mid-luteal phase of the normal menstrual cycle. Expression of Bax, an apoptotic protein, was coincident with TUNEL and optimum plasma progesterone levels. In simulated cycles, the number of apoptotic and Bax positive cells was higher in the estradiol and progesterone treated group as compared to that in the estradiol alone or progesterone alone treated groups (Fig. 5). Thus, programmed cell death in the endometrium of common marmosets occurs during the mid-luteal phase and is regulated by estrogen, progesterone and Bax protein.

Role of FSH Binding Inhibitor in Ovarian Pathophysiology

The FSH binding inhibitor (FSHBI) is an intraovarian peptide of molecular weight < 4 kDa that inhibits FSH binding to granulosa cells *in vitro*. *In vivo*, the peptide induces atresia in

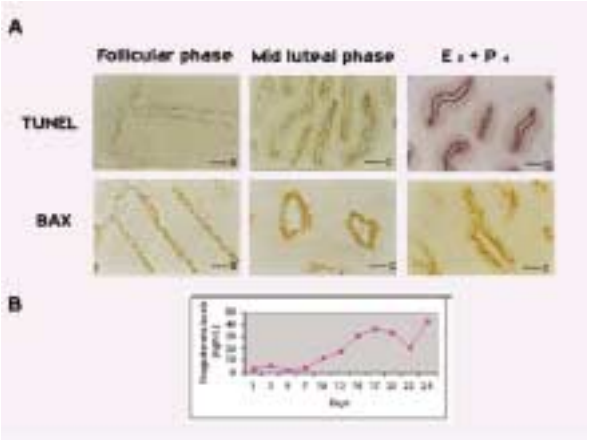


Fig. 5. (A) Detection of apoptosis by TUNEL and expression of Bax in marmoset endometrium during follicular phase, mid luteal phase and in the endometrium of ovariectomized marmoset after treatment with oestradiol (E) and progesterone (P). (B) Progesterone levels in marmosets during ovarian cycle.

mice and impairs fertility in marmosets. The N – terminal 8-amino acid fragment (Octapeptide, OP) of FSHBI exerts antifertility effects similar to that observed with the native peptide. In an attempt to study the expression and levels of OP/FSH BI in ovarian follicles, rabbit polyclonal antibodies were raised against OP and its titre assessed by ELISA. The antiserum was used for localization of OP/FSHBI in mouse ovarian follicles. While OP/FSHBI was expressed specifically in granulosa cells, the expression was higher in atretic follicles. However, no localization was noted in other mouse tissues such as liver, kidney, spleen, adrenal and uterus (Fig. 6).

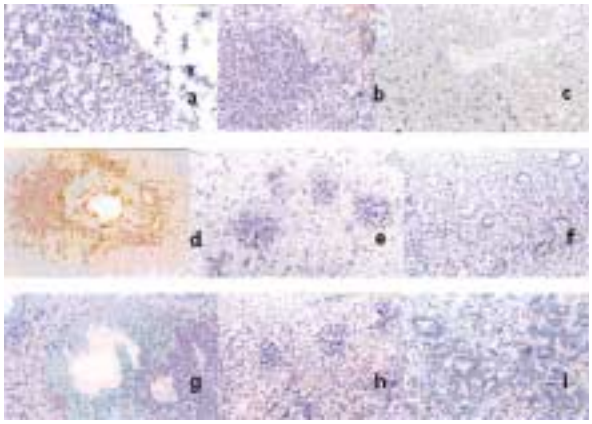


Fig. 6. Localisation of OP in mouse tissues: (a) adrenal, (b) spleen, (c) liver, (d,g) ovary, (e,h) kidney, (f,i) uterus; (a-f)-OP; (g-i) NRS control.

Oocyte-Granulosa Cell Interaction during Early Folliculogenesis

The paracrine factors secreted by oocytes and somatic cells possibly regulate many of the events of early follicular development in mammals. However, factors responsible for stimulating follicles for differentiation and development are not well defined. A study was undertaken to delineate these factors using a mouse model. Morphology of the ovary and immunohistochemical localization of growth differentiation factor-9 (GDF-9), proliferating cell nuclear antigen (PCNA) and apoptosis were studied on days 2, 4 and 6 in neonatal ovaries.

GDF-9 was located in oocytes of primary follicles while, PCNA was expressed in granulosa cells of secondary follicles. Apoptosis, as revealed by TUNEL technique, was not observed during early folliculogenesis (Fig. 7). These studies suggest that GDF-9 secreted by oocytes of primary follicles possibly interacts with granulosa cells to induce proliferation in these cells. Studies are also in progress to understand the role of growth factors in regulation of early folliculogenesis.

Structure-Function Studies on Gonadotropins and their Receptors

Gonadotropins play a critical role in both male and female reproduction. They bind to specific high affinity receptors present on the plasma membrane of respective gonadal cells.

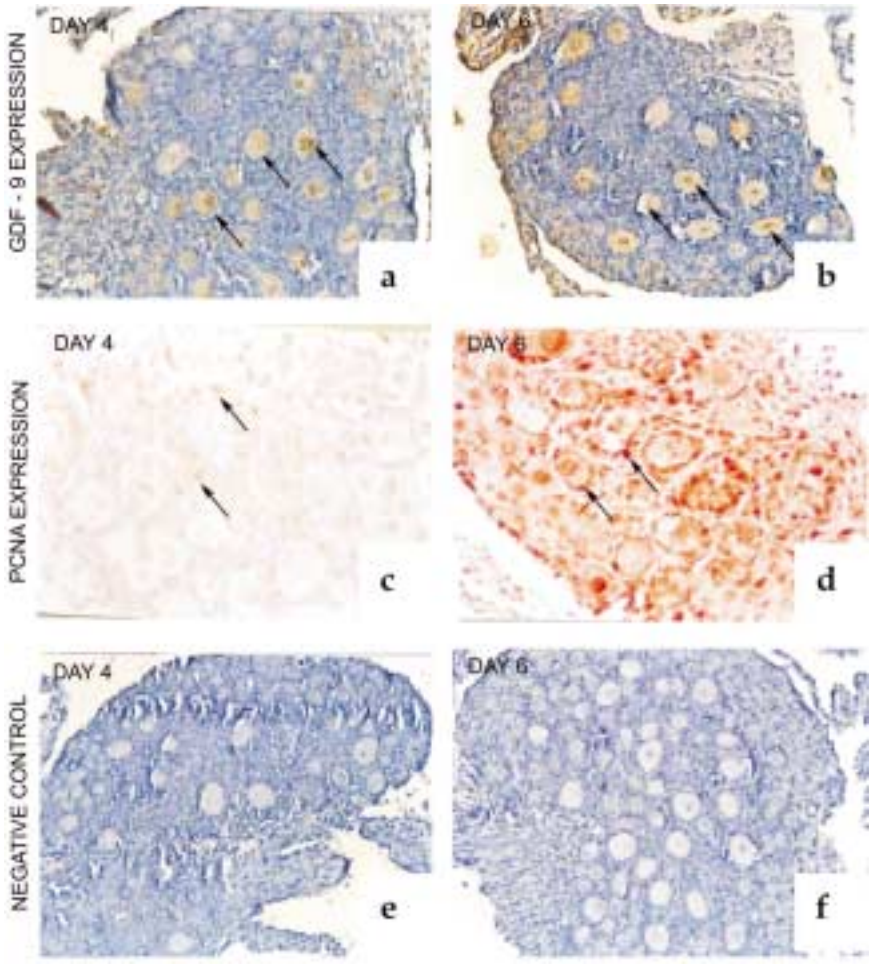


Fig. 7. Immunohistochemical localization of GDF-9 (a,b) and PCNA (c,d) in oocytes of primordial follicles in day 4 and day 6 mouse ovaries. GDF-9 is expressed in oocytes of primary follicles (a) and preantral follicles (b). PCNA's expression in granulose cells of primary follicles (c) and preantral follicles (d). Negative control (e,f).

Understanding the structural basis of this interaction would facilitate the designing of small molecules exhibiting gonadotropin-antagonistic activities. Ten different synthetic peptides corresponding to the probable surface oriented regions of extracellular domain of FSH receptor (FSHR) were studied for their ability to modulate FSH induced cAMP levels in an *in vitro* FSH bioassay. Of these peptides 15-31, 79-89, 184-195, 216-235 and 285-300 exhibited an inhibitory effect indicating their involvement in signal transduction. Antipeptide antibodies raised to these peptides also inhibited the binding of hormone to its receptor indicating their ability to recognize the corresponding region on the receptor surface. Ability of the antipeptide antibodies to bind and neutralize the receptor function are being studied in depth.

CLINICAL RESEARCH

Acceptability and Continuation Rates of Two Monthly Injectable Contraceptive - Norethisterone Enanthate

To increase the range of contraceptive choices for couples in the reproductive age, a study has been initiated to evaluate the acceptability and continuation rate of two-monthly injectable contraceptive norethisterone enanthate (NET-EN).

Study was undertaken: (i) to assess user acceptability and continuation rates of NET-EN; (ii) to evaluate the incidence of menstrual irregularities and other side effects; (iii) to assess the socio-behavioural aspects with respect to socio-economic and cultural diversity and (iv) study return of fertility in eligible women. The main emphasis of this study is on good counselling by qualified and trained staff in an attempt to ensure better continuation rates.

The study is being conducted at 10 centres with a target of 1200 women from different parts of the country. So far 1070 women have been enrolled. The emphasis on counselling has ensured a good continuation rate. During the first 18 months of the study, 311 women completed 12 months of use. The preliminary observations show a cumulative continuation rate of 83.3% and 67.1% at 6 and 12 months of use respectively (Fig. 8).

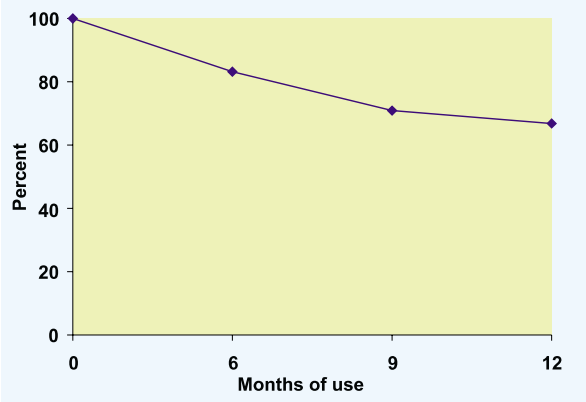
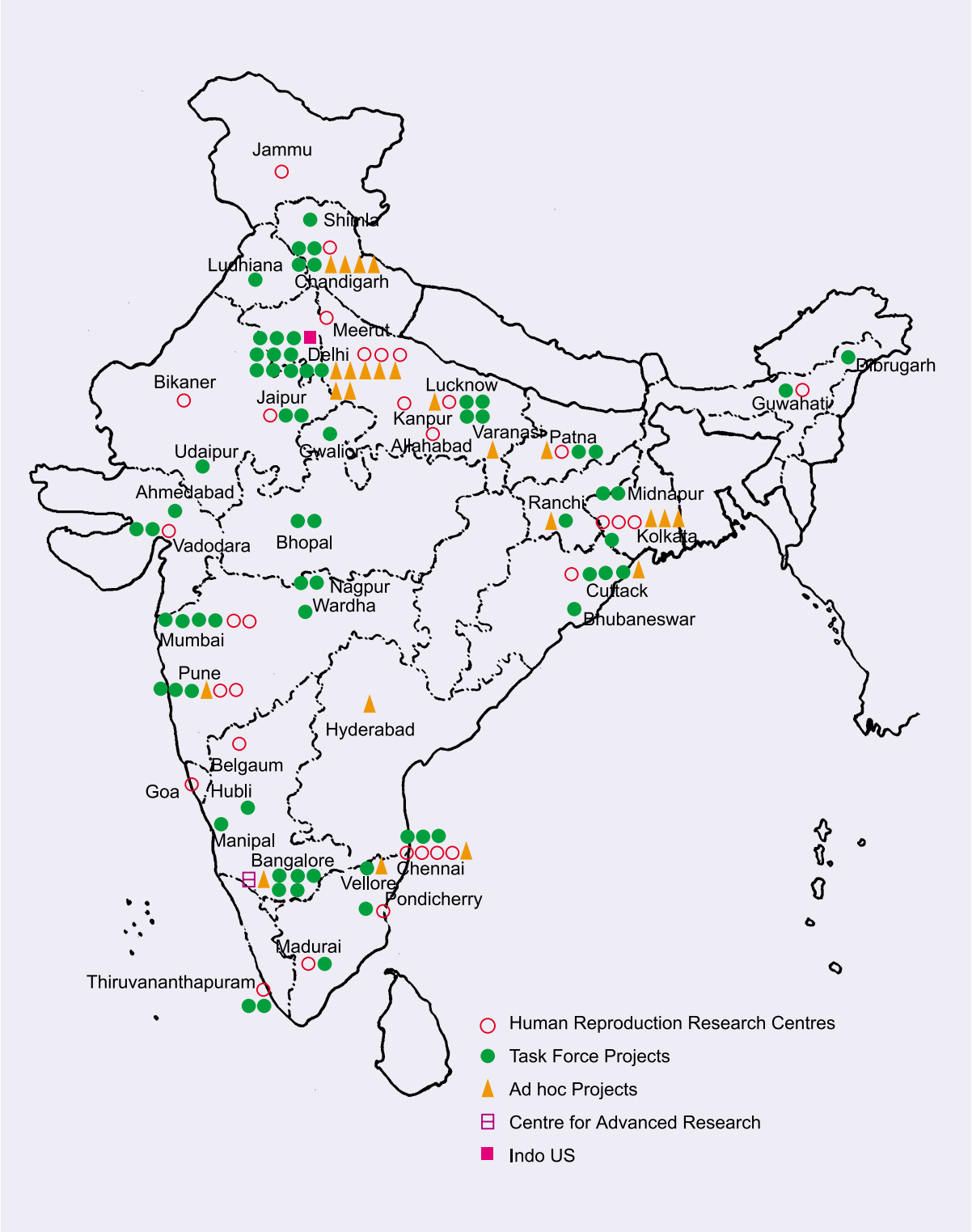


Fig. 8. Cumulative continuation rate of NET-EN.

Improving Male Involvement in Family Welfare

In India, men play a dominant and many a times a decisive role in regulating women's access to reproductive health. In an attempt to: (i) understand family planning knowledge, perception, attitude and practices of men; (ii) plan appropriate intervention strategies for enhancing male involvement; and (iii) evaluate the impact of the interventions on the reproductive health care of the family, a study was designed to include situational analysis in both control and experimental areas; intervention phase to increase awareness and knowledge regarding reproductive health issues and services in experimental area; and impact evaluation after three years in both the areas. Analysis of the impact analysis revealed that the knowledge of correct use of condom (14.1%), withdrawal (27.6%) and rhythm (27.5%) had increased significantly (Fig. 9) and the knowledge of condom use for dual purpose *i.e.* in prevention of pregnancy and infection had increased by 6.3% in experimental area. Inter-spouse communication with regard to obtaining family planning information increased by 5.4%, permanent methods by 3.9% and spacing methods by 0.6% in experimental area (Fig.10). Overall contraceptive use had increased by 1% in control and 17.1% in experimental area (Fig.11). Female sterilization was widely accepted in control area, while condom use was higher in the experimental area.



MAJOR ICMR RESEARCH PROJECTS IN REPRODUCTIVE HEALTH

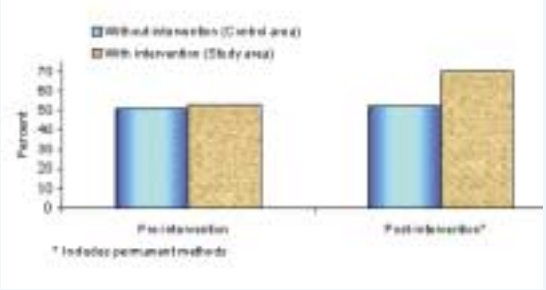


Fig. 9. Impact: knowledge of correct use of contraceptive methods.

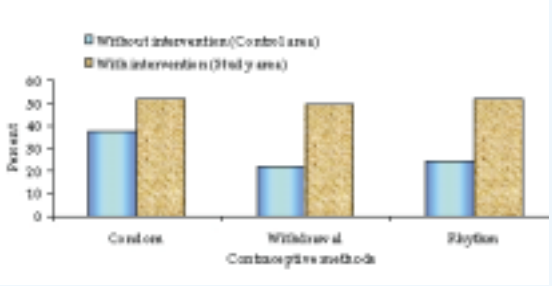


Fig. 10. Impact: Inter-spouse communication.

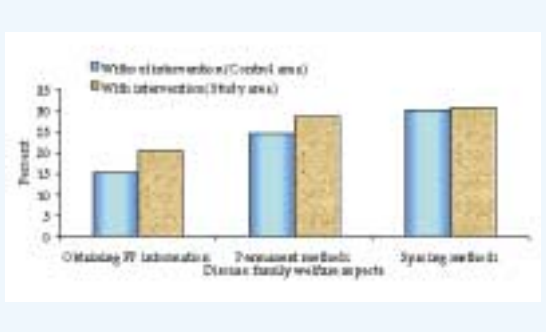


Fig. 11. Contraceptive use by couples.

Emergency Contraception with CuT 200B IUCD and Levonorgestrel

No contraceptive by itself is perfect in its use or efficacy. Therefore, so long the search for an ideal contraceptive continues there will be need for a second chance for protection against pregnancy. Lack of access to emergency contraception may subject women to unsafe abortions, which contribute significantly to maternal mortality and morbidity. Yuzpe regimen and levonorgestrel (LNG) 0.75 mg two doses are the most widely researched and available methods besides IUCD CuT 200B.

Women requesting for emergency contraception after a single act of unprotected intercourse in the current menstrual cycle were offered as per their request 0.75 mg LNG (two doses) or IUCD Cu T 200 B if seeking within 72 and 120 hr of unprotected intercourse respectively. Women were advised to abstain or use barrier methods till the onset of next menstrual period. Of a total of 1868 women who came to the clinic seeking EC, only 37.0% could be offered. Rest of them could not be offered due to various reasons *viz.* came after stipulated date (29.9%), overdue/pregnant at the time of seeking EC (33.2%), more than one unprotected act in the current cycle (14.4%) and women who did not meet eligibility criteria for the study (22.6%). A total of 648 women accepted EC—63.6% accepted LNG and 36% Cu T 200B. Among the women enrolled for EC, 69.8% women sought EC (either LNG or IUCD) within 48 hr of unprotected act.

Women sought EC mainly (38-58%) for non-use of any family planning method, 15-23% for condom breakage/slippage, 10-12% forgot to use condom and 4 - 11% for IUCD expulsion/ displacement. Forced sex was the reason given by only 1.7% women (Fig. 12).

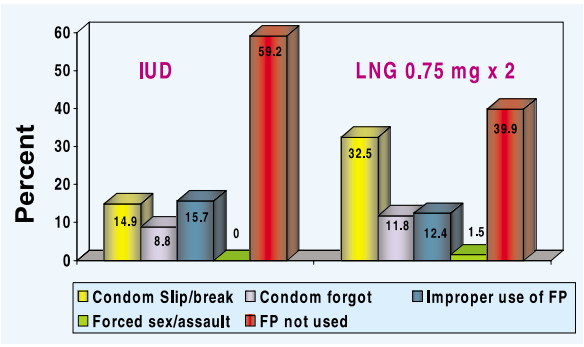


Fig. 12. Reasons for women seeking EC.

Side effects with LNG were nausea, headache and dizziness (10-14%) and with IUD low abdominal pain (49.5%) and irregular bleeding (15.2%).

Seven pregnancies were reported in the levonorgestrel group (3 user failure and 3 method failure) giving a typical use failure rate of 1.73%

and the per cent pregnancies averted with LNG were 78.7. No pregnancy was reported with IUCD CuT 200B.

Return of menstruation within 7 days of expected period was observed in 92-95% women while in 3-6% the cycles occurred earlier than one week and in 2% they were prolonged beyond 8 days.

Women's perceptions indicated that majority (93.2%) would like to consult a doctor and preferred to avail the method either from clinics/ hospitals (58.9%) or on the prescription of a doctor (46.6%). Only 7.0% women preferred to avail from the chemist directly. Majority (77.8%) indicated that they would like to avail the method as and when they need it.

Clinical Trial with Once a Month Combined Injectable Contraceptive-Cyclofem (Medroxy progesterone Acetate MPA 25 mg + Oestradiol Cypionate 5 mg)

In this study, till date a total of 1330 women have been enrolled at 16 HRRCs and observed for 11387 women months of use. Of them 574 have completed one year of use. No method failure has been reported till date.

The continuation rates at 6 and 12 months were 74.2 and 68.6 per 100 users. Women discontinued the method due to various reasons which include pain at injection site, menstrual disturbances, medical reasons, planning pregnancy, use of permanent method/other FP methods and personal reasons.

Analysis of menstrual pattern for a reference period of 3 months (90 days) each indicated that 29.2% women had acceptable menstrual pattern in the first reference period which improved to 37.8% by the fourth reference period *i.e.* one year of use (Fig. 13).

Clinical Trial with SMA, an Intravasal Injectable Male Contraceptive

A novel male contraceptive approach, reversible inhibition of sperm under guidance (RISUG), was developed at IIT, New Delhi. RISUG was injected in 141 subjects at three centres in Delhi out of which two could not

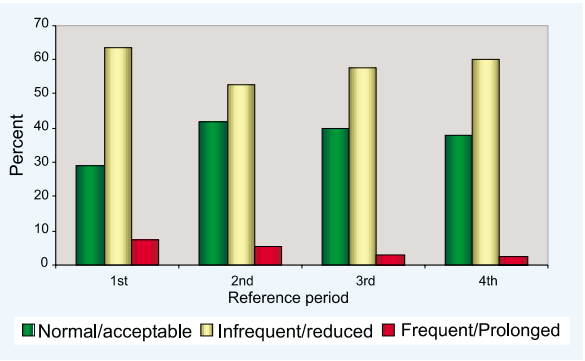


Fig. 13. Analysis of menstrual pattern of women.

complete the protocol. Therefore, 7139 subjects who completed six months of follow up were included in the analysis. Scrotal swelling was seen in 84.1% subjects at one week follow up which continued in 52.2% subjects up to one month. Around 36% subjects felt persistent pain in scrotal region, which persisted in 25.2% subjects for one month. Scrotal nodules were observed in 23.4% subjects at one week and 33.3% subjects after one months of injection. Scrotal abscess, fluid collection around scrotum and inflammatory pathology were seen in one case each after one month of treatment. Albumin and sugar were noticed in urine of 14 and one subjects respectively after six months of injection.

Outcome of the treatment was considered successful if, a) azoospermia manifested within two months of the treatment, b) three monthly semen analysis thereafter showed azoospermia and c) no pregnancy was attributable to a period following the onset of azoospermia. The data indicated that 79.1% subjects achieved azoospermia after two months of injection while rest of them achieved it between 3 to 6 months (Fig. 14). Six subjects could not achieve

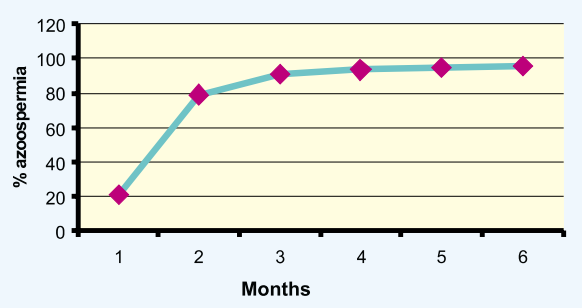


Fig. 14. Contraceptive efficacy of RISUG.

azoospermia, out of which in one subject it resulted in pregnancy.

INFERTILITY

FEMALE INFERTILITY

Studies on Genetic Aspects of Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is a well-recognized inherited disorder. Its genetic basis has been postulated on the basis of evidences from familial clustering and reports of concordance in monozygotic twins. However, factors involved in its genetic predisposition and the mode of inheritance are still not clear. Evidence regarding diversities in its phenotypes and multiple organ involvement suggests a complex multi-genetic basis. Using a candidate gene approach, attempts to elucidate the genetic markers for determining pre-disposition to the disorder and determine the genotype-phenotype association were undertaken. Candidate genes selected were: CYP11A1, leptin, CYP17, follistatin and insulin receptor with emphasis on two genes *viz*. CYP11A1 and leptin, associated with PCOS - hyperandrogenicity and obesity.

Subjects included in the study were those with documented evidence of PCOS in association with hyperandrogenicity with or without obesity. Those with evidence of thyroid, adrenal or pituitary disease were excluded. First degree relatives of index cases along with healthy controls were also screened. The entire coding sequence of both the genes *viz*. CYP11A1 and leptin were analyzed for reported as well as novel mutations by PCR-SSCP/RFLP for each of the exons followed by DNA sequencing to confirm the detected mutations. Fig. 15 shows PCR amplification of the coding sequences of CYP11A1. Some of the PCR amplified fragments were further subjected to SSCP analysis for detection of mutations / polymorphisms. Fig.16 shows the SSCP analysis of exon 9 in 3 PCOS families along with 2 obese control families and 4 controls. Screening revealed variations in exon 9 of CYP11A1 in two of the index cases and in the family members. Variations are being confirmed by DNA sequencing.

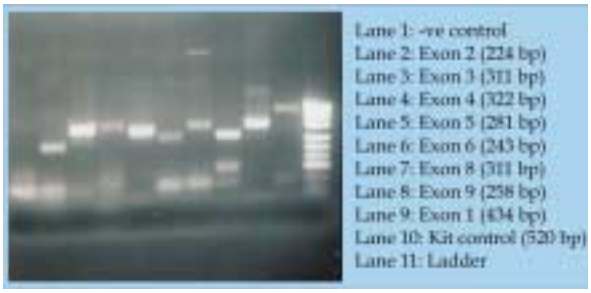


Fig. 15. PCR amplification of coding regions of CYP11A1.

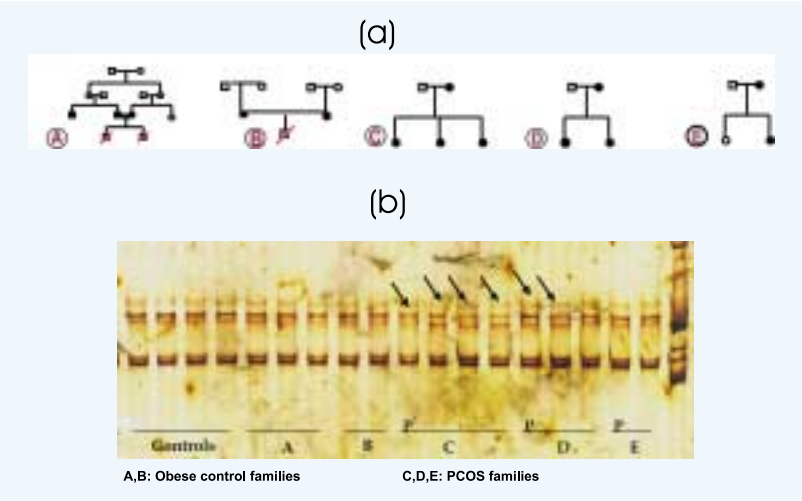


Fig. 16. (a) Pedigree charts of obese and PCOS families. (b) SSCP analysis of exon 9 of CYP11A1 gene.

Genomic Studies in Women with Premature Ovarian Failure

Premature ovarian failure (POF) defined as ovarian failure occurring in women under the age of 40 yr is being increasingly diagnosed. Several etiological factors have been postulated for early depletion of oocytes. Candidate genes or loci that have been suggested to cause familial or sporadic POF include genes on the X chromosome (POF1, POF2, FMR1), inhibin and FOX L2. Data available so far are based on Western population and there is a need to investigate this aspect in the Indian context. Study was initiated to determine the mutations/ premutations in the FMR1, inhibin and FOX L2 genes in women with idiopathic POF and their families and to select the best candidate gene for determining predisposition to POF. Studies in 30 patients revealed that FOX L2 gene mutations could be one of the factors associated with early ovarian failure.

Identification and Expression of Endometrial Functional Markers in Fertile and Infertile Primates

In an attempt to identify novel endometrial factors that may play a potential role in endometrial receptivity and implantation, differential display RT-PCR (DD-RTPCR) approach was used to screen endometria from fertile, infertile and mated bonnet monkeys. Three cDNA fragments have been cloned that show differential pattern of expression in onapristone-treated infertile animals as compared to control animals. One of these fragments, (DD2A) was found to be over-expressed in the endometria of onapristone treated infertile bonnet monkeys and was identified to be a Rab coupling protein (RCP) by *in silico* analysis. This is the first report demonstrating existence of RCP in the endometrium and its possible regulation by progesterone.

MALE INFERTILITY

Microdeletion of Y-Chromosome in Non Obstructive Azoospermic and Severe Oligoasthenozoospermic Males

Microdeletions of Y-chromosome are associated with disruption of spermatogenesis. Chromosomal abnormalities and microdeletions of Y-chromosome contribute towards poor embryo quality and early pregnancy loss.

A study has been initiated to assess the frequency and type of microdeletions associated with non-obstructive azoospermia and severe asthenozoospermia.

Sixty-nine infertile men (age 32 yr) have been recruited from the Institute's Male Infertility Clinic. Using 6 STS primers to amplify the PCR products, microdeletions of mixed type were seen in 6 subjects showing, a frequency rate of 8.6%. Further studies are ongoing.

Molecular Characterization of Human Sperm Progesterone Receptor

Classical steroid hormone receptors are transcription factors that act via genomic mode of action. However, progesterone receptors (PR) on the human spermatozoa act through a non-genomic mode of action. Study was conducted for identifying and characterizing the membrane bound sperm PR and understanding its mechanism of action.

The results reveal that both PR transcripts and protein are expressed in the human testis and spermatogenic cells. The membrane bound PR appears to be translationally modified form of the conventional PR.

Identification and Characterization of Sperm Membrane Protein Profiles of Fertile and Subfertile Men

A human sperm membrane protein specific to fertile men and absent or poorly expressed in subfertile subjects has been identified. Monoclonal antibodies were raised against this 57 kDa fertility associated sperm antigen (FASA) and of the 18 hybrids, 3 were selected for limiting dilution based on their reactivity with sperm. Two clones $3H_4B7$ and $3H_4A7$ were characterized and these antibodies inhibited sperm-egg binding in a dose-dependent manner.

On screening a human epididymal cDNA library with a 57kDa antibody, a 1.8 kb cDNA clone was identified. The sequence of this clone showed 98% homology with human chromosome

11 and 87% homology with Huntington protein (HP), which is known to be involved in microtubule formation, vesicle-mediated transport and cell-cell signalling.

REPRODUCTIVE TRACT INFECTIONS

Chlamydia trachomatis Infection: Diagnosis, Prevalence and Immuno-pathogenesis

Sexually transmitted infections (STIs) continue to represent a major public health concern worldwide, despite aggressive STI control efforts undertaken during the last several decades. A PCR has been standardized at the NIRRH to screen *C. trachomatis* infection and study the immunopathogens associated with this infection in 91 subjects enrolled and tested for RTI's/STI infections. The results revealed that the infection rate of *C. trachomatis* has decreased amongst women attending the gynecology clinic. Molecular HLA typing has been standardized to study the host factor. Of the infected pregnant women who were treated and followed up during the year, 4 had normal delivery and 1 had a cesarean section. All the babies were healthy and free of infection.

Transport of HIV through Spermatozoa: Identification and Characterization of CD4 Independent HIV Receptors on Spermatozoa

An HIV receptor/binding 160 kDa sperm protein on spermatozoa, that is bound specifically by gp120 HIV envelop glycoprotein as well as cell free HIV has been identified by Western blot analysis. To identify and isolate cDNA encoding the 160 kDa sperm protein, human testicular λZAP cDNA library is being immuno-screened using gp120 and its antibody. The positive clones will be further screened to isolate a full length cDNA clone for 160kDa sperm protein.

Reproductive Tract Infections: A Clinical and Microbiological Study in Women

Asymptomatic disease is responsible for frequent and severe long term morbidity of RTIs in women and for the persistence and spread of STIs in the community.

Study was initiated to evaluate the relationship between clinical manifestations and microbiological diagnosis of common RTIs (bacterial vaginosis, candidiasis, trichomoniasis and *C. trachomatis*) in women at low risk for RTIs and to assess the therapeutic response using clinical and microbiological diagnosis. A total of 560 women attending the NIRRH Family Welfare clinics have been screened and enrolled for participation in this study.

Eighty percent of the women came for their scheduled follow up and completed the study. Women (34) who were positive for *C. trachomatis* by DFA at the initial examination were given necessary treatment. Male partners were treated for *C. trachomatis* and *Trichomonas* infections identified in the women. Standard therapy was administered as defined in the WHO guidelines. Observations suggest that RTI infections, single or multiple, do occur in asymptomatic women and simple, easy methods for their detection need to be incorporated into the primary health care system. Also, the women and community need to be sensitized to distinguish between normal physiological, cyclical changes and abnormal symptoms which definitely need medical intervention. The other important aspect is the need to ensure compliance of therapy and recommend preventive measures to reduce transmission between partners.

MATERNAL HEALTH

Contraceptive Knowledge and Practices of Women Requesting Medical Termination of Pregnancy

A study to assess contraceptive knowledge, attitude and practices among abortion seekers in an urban hospital set up and to identify the determinants of unwanted or mistimed pregnancies in these women was undertaken.

Of the 700 women interviewed, 72% were in the age group of 21 – 30 yrs, 2.4% were unmarried and over 21% had an induced abortion in the past. Majority of the women (94.5%) were in the first trimester of pregnancy while only 5.5% had pregnancy of more than 12 weeks of gestation. Sixty six per cent of

women reported the use of some contraceptive method to prevent the current pregnancy. Majority of the women never mentioned withdrawal as a family planning (F.P.) method but on in depth questioning the details of the method used were obtained.

Women reported the use of methods like withdrawal (36.5%), condom (34.4%), oral contraceptive pill (8%), rhythm (5.4%), Copper T (3.5%), tubal ligation (0.4%), spermicide (0.2%), a combination of more than one method like condom and withdrawal or rhythm (5.4%) or vaginal cleaning (5.1%). Among the women using some F. P. methods, 35% had experienced condom break, leak, slip or withdrawal failure and hence were candidates for emergency contraception (EC). None of the women were aware of EC or the lactational amenorrhoea method.

Irregular use was more frequently observed with condom followed by oral contraceptive pill and withdrawal. Young child, infrequent coitus, if conceived then would opt for medical termination of pregnancy (MTP), past history of treatment taken for infertility were some of the main reasons for irregular use or non use of F. P. methods. No stock of oral contraceptive pill or condom, no suitable method for self, fear of side effects, family members against were some of the reasons wherein the women felt the need but could not use any method. Awareness of MTP related side effects was poor among women requesting an abortion for the first time (~10 %) as compared to repeat abortion (~35%). Incomplete / incorrect knowledge and myths about the various F.P. methods prevailed among these subjects.

The study results strongly stress the need for increased and sustained use of effective methods together with counselling regarding correct use, clearing myths, treatable side effects and failure rate of each method, so as to help clients decide and choose a suitable F.P. method.

Induced Abortion and Concurrent Adoption of Contraception in the Rural Areas of India

To obtain information from rural married women regarding their attitude, behaviour, practices and utilization of services for induced abortion and concurrent acceptance of contraception, a total of 1851 women who had an induced abortion during the previous 3 years were interviewed in detail during a cross sectional survey carried out in 13 states. The main reason for seeking abortion was "don't need any more children" (42%) and "don't need any more daughters" (12.4%) (Fig. 17). Around 46% women accessed abortion services from private clinics as compared to government hospital (37%) and primary health centre/community health centre (PHC/CHC) (14.0%) (Fig. 18). The decision to terminate pregnancy and place of abortion was made by the husband in 42.8% and 52.5% respectively. Regret for abortion was expressed by 29.6% women. However, only 7.2% said they would not advise others for induced abortion. Nearly one half of the women undergoing abortion accepted a family planning method

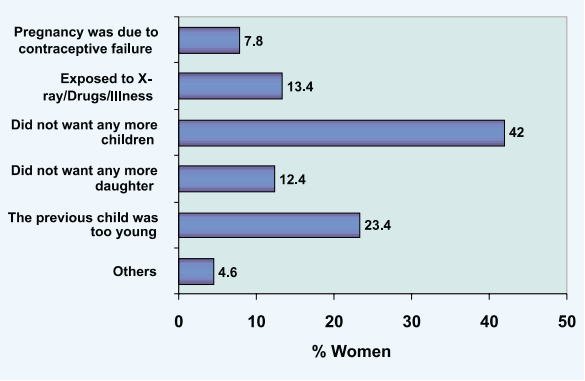


Fig. 17. Reasons for induced abortion.

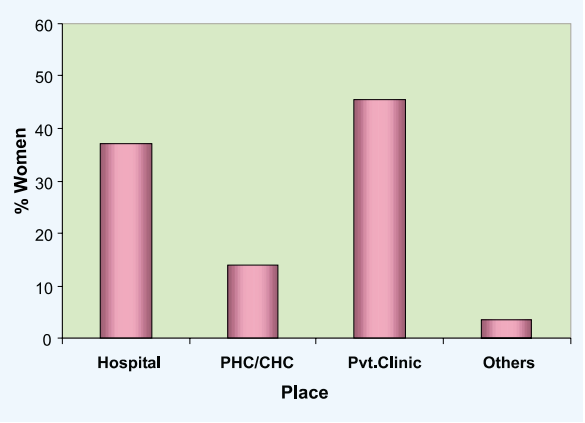


Fig. 18. Place of induced abortion.

concurrently; of these uterine device/oral contraceptives and a permanent method was adopted by 37.2% and 49.1% respectively. Acceptance of vasectomy by male partner was found to be low (1.3%). "Husband objected" (32.3%) was the main reason for not accepting post abortal contraception. Majority of the acceptors said they would recommend to others the same place where they had undergone abortion, thus indicating their satisfaction with the source and services received. There is need to strengthen and introduce safer methods of abortion services at PHC/CHC level to meet the demand in rural areas. In addition, counselling for post abortal contraceptives should be provided to the couple so that they can make an informed choice.

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

Active management of the third stage of labor, a known evidence based intervention that includes administration of a uterotonic, can prevent PPH due to uterine atony. Misoprostol (oral prostaglandin) has a tremendous advantage over other currently available uterotonics as it is inexpensive, stable at room temperature and is given orally. It has minor side effects that are self-limiting and usually do not require any medication.

A community-based task force study is ongoing at Pune, Cuttack, Jaipur, Baroda and Madurai to study the feasibility of administration of oral misoprostol for prevention of PPH by the paramedical worker at PHC level. this project would serve as a model applicable to rural settings throughout India and in other developing countries. The project is being carried out through ICMRs network of HRRCs and the DHO/CMO of the selected district. A total of 30 PHCs have been selected and randomly allocated as intervention or non intervention areas. In the intervention areas the active management of third stage of labor included administration of 600 mcg of misoprostol tablet after delivery of baby, early clamping and cutting of cord, and removal of placenta by controlled cord traction whereas in the non-intervention PHC the existing practice for prevention of PPH under the RCH programme is being provided. Blood loss after delivery is being measured using a calibrated blood collection drape.

Interim analysis of 467 and 373 women who received and did not receive the intervention respectively indicated that they were similar in respect to age, parity, education and occupation. Majority (79%) of the women were in the active phase of labor, about 2/3rd of women in both the groups had haemoglobin less than 10.0 g%. The IIIrd stage of labor was managed by the peripheral health workers in the intervention areas according to the guideline in almost all the deliveries (99%). There was significant reduction in the duration of IIIrd stage of labor in the intervention group as compared to comparison group (Fig. 19).

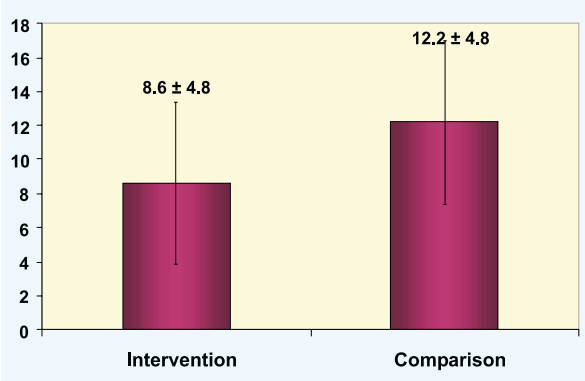


Fig. 19. Duration of third stage of labor.

The incidence of PPH was low (<1%) in both intervention and comparison areas. Only 0.9% cases in intervention area and 0.8% in comparison area had PPH (blood loss >500 ml) and one woman in intervention area was given blood transfusion at the medical college. However, average blood loss was significantly lower in intervention area compared to control area (Fig. 20).

Side effects like nausea and vomiting were comparable in both groups. An increased number of women had moderate to severe shivering in the intervention area. Similarly, rise in temperature >38^0 C was observed in intervention and comparison group in 4.5% and 1.3% women respectively. However, these side effects were self-limiting and did not require any treatment.

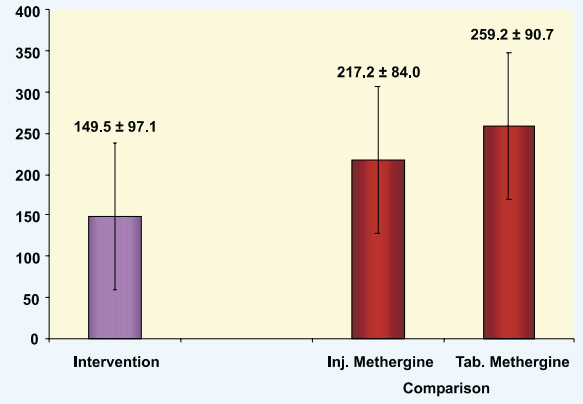


Fig. 20. Mean blood loss at 1 hr.

Management Practices of Meconium Stained Amniotic Fluid and Meconium Aspiration Syndrome

An exploratory study was carried out at 30 HRRCs with the objective to assess the management practices of obstetric cases with meconium stained amniotic fluid (MSAF) and to study morbidity and mortality in newborn babies with meconium aspiration syndrome (MAS), a major complication during delivery and childbirth. From among deliveries conducted at HRRCs during the study period, 7619 women with MSAF were enrolled in the study. Of these, 644 (8.5%) babies born to these mothers developed MAS. There was wide variation between centres at KMC, Chennai (2.7%) and medical college, Madurai (35.8%) reporting the lowest and the highest number of MAS babies respectively. The mean age of women with MSAF was 24.3±4.0 and in 52.1% it was their first pregnancy. The character of the meconium was thick in 33.7% and 18.3% of these babies developed MAS. Forty six percent women in labor were managed by low segment cesarean section, whereas 8.6% were managed by vacuum extraction and forceps delivery. Forty five percent women who were in established labor delivered normally. Amnio infusion was done in around 14.9% of the MSAF cases. Babies born to mothers who were not given oxygen inhalation (71.0%) were at higher risk of developing MAS. No such association was found in respect to oxytocin drip amnio infusion, which were used for management of labor. The babies born to mothers with fetal distress (44%), non-progress of labor (12.2%) and prolonged rupture of membrane during labor (4.3%) were at very high risk of developing MAS. Of total deliveries, 3.4% neonatal deaths, 0.5% still births and 0.3% intrapartum deaths amounting to 4.2% deaths were reported. In 91.5% babies who did not develop MAS, there were 0.3% intrapartum deaths, 0.6% still births and 1.6% deaths during neonatal period. Out of 8.5% MAS babies, 23.1% died during neonatal period and 0.3% were intrapartum deaths. The main cause of neonatal deaths was birth asphyxia accounting for 53.9% of the total 4.2% deaths of newborns in the study.

Diagnostic Markers for Osteoporosis

Osteoporosis is considered as one of the significant and growing health issues amongst elderly population. Its etiology is multifunctional and several factors including hormonal, environmental and genetic have been linked with bone loss in men and women.

Biochemical markers of bone turnover were estimated in serum samples from 206 women in the age group 20-60 yr. The preliminary data indicate a distinct change in the biochemical markers of bone turnover, reflecting the age related changes in bone metabolism. The level of markers in 60 menopausal women who had hormone replacement therapy showed a significant drop (9-12%) within 3 months of therapy.

A study has been initiated to develop an in-house ELISA for osteocalcin, extracted and isolated from bovine bones. Antisera have been raised.

For studying mechanism of action of accelerated bone resorption during menopause, immunoassays have been standardized for interleukin 1, interleukin 6 and tumour necrosis factor alpha.

CHILD HEALTH

Home Based Management of Young Infants

Current neonatal mortality rate in India is 45/1000 live births accounting for almost two thirds of the infant deaths. In view of developing a model for reduction of neonatal mortality a project on home based management of newborn is being carried out in rural areas of five states in the country as more than 60% deliveries take

place at home setting in rural India. There are two models of intervention—in one arm a community based worker chosen by the community and in the other an Anganwadi Worker (AWW) at the ground level are the provider of intervention. The proposed package of home based intervention comprises care of the infant at birth, care of normal and low birth weight babies, treatment of local infections, referral of sick infants, health education, provider partnership and community participation. The workers (SR/AWW) under the project receive extensive training spread over a period of 6-9 months. A careful post training evaluation is done to judge necessary skills transfer. The impact of intervention is to be assessed by doing baseline and endline survey.

Baseline survey included mortality survey, facility survey and survey of practitioners. Major activities of formative phase included ethical clearance, interphasing with health system, baseline survey, randomization and training/ skill building of SRs/AWWs for providing services and training of ANM/LHVs who supervise the activities of SRs/AWWs.

Baseline survey was carried out in 9 PHCs from which 6 PHCs similar in terms of neonatal mortality rate were finally randomized into different intervention arms. The results of the mortality survey reveal that neonatal mortality rate was 48.5, 45.8, 41.1, 77.9 and 48.3 per 1000 livebirths and infant mortality rate 90.9, 62.2, 56.7, 113.9 and 59.8 per 1000 live births in Lucknow (U.P.), Cuttack (Orissa), Patna (Bihar), Udaipur (Rajasthan) and Wardha (Maharashtra) respectively. Fig. 21 shows the percent neonatal deaths in first four weeks of life in these areas.

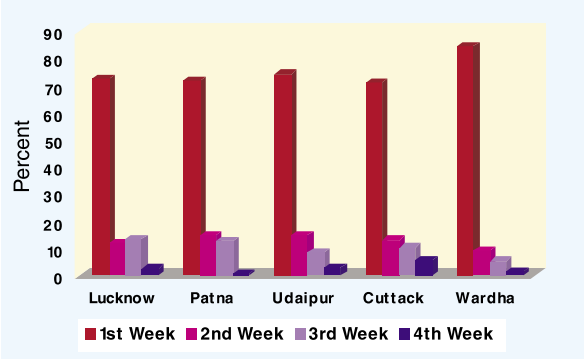


Fig. 21. Percent neonatal deaths in first four weeks of life.

Training of master trainers and SRs/ AWWs in step ladder fashion *i.e.* class room training followed by field practice is ongoing. Four master trainers from each centre have been trained at Gadchiroli. These master trainers are providing training to SRs at the respective sites.

National Neonatal Perinatal Database

A fundamental prerequisite for planning, implemention and montioring the health care programmes is to ensure an accurate ongoing assessment of morbidity and mortality derived from a reliable database. National neonatal-perinatal database network established at the tertiary hospitals collects data on neonatal-perinatal morbidity and mortality on a standardized protocol developed for this purpose. There is paucity of information on morbidity and mortality of neonates admitted at district/ subdistrict hospitals. Eight HRRCs (KEM Hospital, Mumbai, K.G. Medical College, Lucknow, JIPMER, Pondicherry, Baroda Medical College, Baroda, PGIMER, Chandigarh, Kasturba Hospital, Delhi, AIIMS, N. Delhi and KEM Hospital, Pune) collected information on intramural deliveries, extramural births and maternal parameters from the district hospitals on structured format.

Data received on 18,074 neonates have been analysed. Three quarter of women who delivered at district hospitals had at least 3 antenatal contacts. Around 80% were normal deliveries and 16% were delivered by LSCS. Mean birth weight was 2741±660 gm, 22.5% were low birth weight while 7.2% were preterm. Around 96% babies cried after birth within 1 min, 2.2% between 1-5 min and 1% after 5 min. Resuscitation at birth was required in the form of oxygen in 4.4%, bag and mask ventilation in 2.1%, chest compression in 0.6% and medications in 2.1% babies delivered.

Common morbidities in these neonates included septicemia (0.7%), hyperbilirubinemia (1%) hypothermia (0.8%), hypoglycemia (0.8%), seizures (0.4%) and apnoea (0.3%), antibiotics (6.5%), oxygen (4.5%), blood/plasma transfusion 0.1% and phototherapy (0.5%). There were 1.0% neonatal deaths, while 0.3% left the hospital against medical advice and 1.9% were referred

to higher centres. Single most important cause of death included perinatal asphyxia (45%), prematurity (30%), infections (3.9%), malformations (2.3%) and others (9.4%) and cause was not established in 10.3% of cases. (Fig. 22). Age at death is shown in Fig. 23.

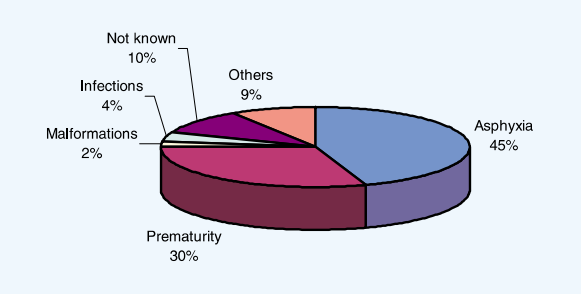


Fig. 22. Primary causes of death (inborn babies)

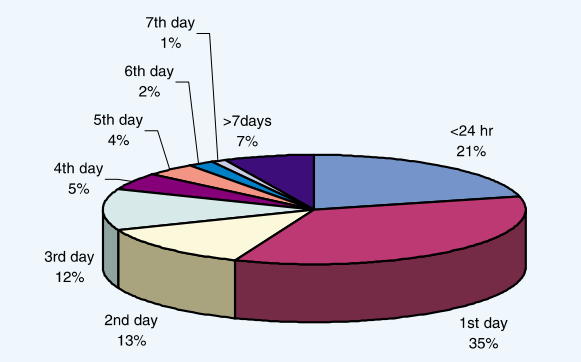


Fig. 23. Age at death

Morbidity and Mortality Details of Outborn Babies

A total of six participating ICMR HRRCs collected data for a cumulative 42 months on 681 outborn babies. Fifty six percent babies were born in hospitals while 29% were born in home settings; 45% babies were low birth weight while 30% were preterm. At admission the mean weight of babies was 2323 gm (±618) and mean age was 5.4 (±7.0) days. The morbidities included respiratory distress (38.7%), septicaemia (25.6%), hyperbilirubinaemia (9.8%), seizures (4.5%) and hypothermia (4.5%). Overall mortality was 16.7% while 3.5% babies left the hospital against medical advice and 9.5% were referred to higher centres. Mean age at death was 1.1 (±4.1) days. Single most important cause of death included perinatal asphyxia (50.2%), sepsis (36.1%),

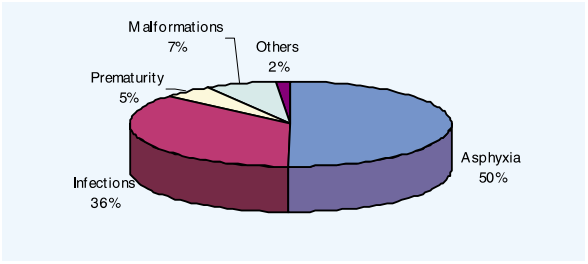


Fig. 24. Primary causes of death (outborn babies)

prematurity (5.2%), and malformations (7.0%). (Fig. 24).

Cognitive Problems in Low Birth Weight Children

Due to paucity of Indian data an in-depth longitudinal study of cognitive and learning problems in low birth weight neonates (followed upto the age of 12 yr.) was carried out at KEM Hospital, Pune to assess their potential for learning (intelligence quotients) and actual achievements in learning.

A total of 180 children (73 girls, 107 boys) with birth weight <2000 gm were prospectively followed up since birth for a period of 12 yr. Full term children comprised 81.2% while rest were preterm. Out of 147 preterm children, half were appropriate for gestational age (AGA) and the other half were small for gestational age (SGA). Amongst all the SGA children 31% were full term and 69% preterm.

Low birth weight, especially the very low birth weight (VLBW) (birth weight <1500gm) and the preterm small for gestational age children have lower IQs compared to normal controls (Fig. 25). Writing and mathematical

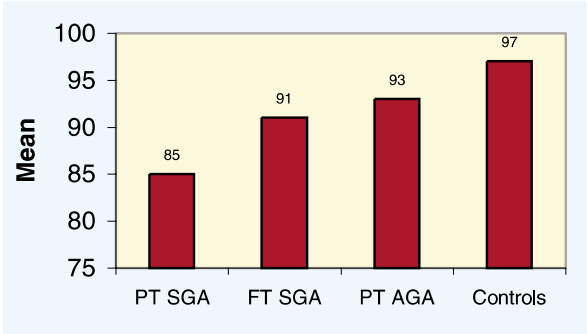


Fig. 25. Mean IQ at 12 yr.

skills of VLBW and preterm children with gestation less than 32 wks were particularly poor. All children from the study group performed poorly on the ABC Movement test. Girls performed poorly compared to boys in body balance and ball skills, but were somewhat better in manual dexterity. The academic performance of the low birth weight children was also poor. There were more failures with poor academic performance. The IQs correlated well with marks in the examination. Environmental factors like socio-economic status and spaciousness of the house and parental education greatly influenced the IQ. The only biological risk factor influencing IQ at 12 yr. was the birth weight.

ADOLESCENT REPRODUCTIVE HEALTH

Knowledge, Attitude and Felt Need of Emergency Contraception amongst Adolescents and Youth. Health Care Providers and Family Planning Counsellors in and around Mumbai

Emergency contraceptives (ECs) have an important role in preventing unwanted pregnancies, induced abortions and abortion related mortality and morbidity. In view of this it is essential that the potential users as well as providers are aware of such methods and their timely correct use. In this study the knowledge, attitude and felt need of EC among adolescents and youth, health care providers, parents and teachers, woman's health advocates and chemists in and around Mumbai were assessed. Qualitative and quantitative information was collected from adolescents and youth, service providers and family welfare counsellors, parents, teachers, women health advocates (WHA) and non-governmental organizations (NGOs), and drug store (chemist shop) owners/employees.

The overall awareness among adolescents and youth regarding EC was 4.2%, parents - 8% teachers - 12.2% and service providers - 48% (i.e., 75% among Obstetricians and Gynecologists, 46.7% among other medical practitioners, 40% among family planning counsellors and 31% among nurses). Among WHAs and NGOs, 18.5% reported being aware of ECs. The awareness among chemists and drug store owners was 60% (68% among medical and fancy store personnel and 40% among medical stores personnel). However, even among those who were aware of EC, most of them did not have correct knowledge.

To prevent unwanted pregnancies, majority of the WHAs and NGOs opined that it was necessary to promote safer sex. Majority (37%) of WHAs and NGOs and more than one-third of the parents felt that EC methods should be provided through doctor's prescription. About 90% parents were of the opinion that sex education should be provided to prevent unwanted pregnancies. Six of every 10 parents and more than half of WHAs and NGOs (55.6%) and chemists feared that EC may be misused and may affect women's health adversely.

Equal proportion (46%) of adolescents and youth, and parents, one-fifth of teachers and three-fourth of service providers felt that EC should be made available to both married and unmarried persons. More than one-third of service providers and 15% chemists and drug store owners reported that they had suggested the use of EC pills to those who had unprotected intercourse or contraceptive failure or had missed the use of contraceptive pills.

About 71% of adolescents and youth, two-thirds of service providers, 70.9% teachers, 50.3% parents, and 88.9% of WHAs and NGOs opined that EC should be included in the National Family Welfare Programme. Seven in 10 teachers and 71.7% of parents viewed that easy accessibility and availability of EC would increase the use among married and unmarried people.

Majority (85%) of adolescents and youth felt that EC information should be provided in their schools and colleges. About half of the service providers felt that various media should be utilized for disseminating information regarding EC. One-third of teachers and two-third of parents viewed that EC services should be provided through medical and paramedical personnel and information should be disseminated through media.

The study indicated that awareness of EC among various groups is low, attitude towards

EC is positive and felt need of contraception is observed among various groups. All the respondents expressed their desire to know more about contraception and EC. The study underscores the pressing need to increase awareness and knowledge of EC through effective intervention programmes such as audiovisuals (television and radio), print media (posters, pamphlets, brochures and flipcharts), help-line, hotline and internet services, so that unwanted pregnancies could be prevented.

Improving Reproductive Health of Adolescents: An Urban School Based Approach

A study was launched in two schools and two colleges to assess the knowledge, attitude and practices about reproductive health among 300 adolescents aged 11-19 yr from different socio-economic groups and to operationalise Adolescent Friendly Centres in those settings and to assess the uptake of these services.

Focus group discussions revealed that pornographic ljterature and films were accessed by these adolescents. Blue films were watched at home through CD's procured from special outlets using code words which represented Blue Print (BP - Bhaji Pala, Bharat pakistan, Bharat Petroleum etc.). These were available at rates which adolescents could manage with pocket money. They were aware of websites which displayed blue films which they viewed in cyber cafes.

Knowledge on various aspects of reproductive health including HIV/AIDS was greater among boys than girls. Adolescents from the lower socio-econimic class reported more reproductive health problems as compared to those from middle socio-economic class. Problems reported by girls were mainly dysmenorrhoea, irregular bleeding, excessive vaginal discharge with foul smell and pruritis vulvae (Fig. 26). Boys reported itching of genitals, painful micturition and discharge from urethra (Fig. 27).

Majority of adolescents from the lower socio-economic class sought household remedies for their problems, while some did go to municipal dispensaries. More boys than girls visited

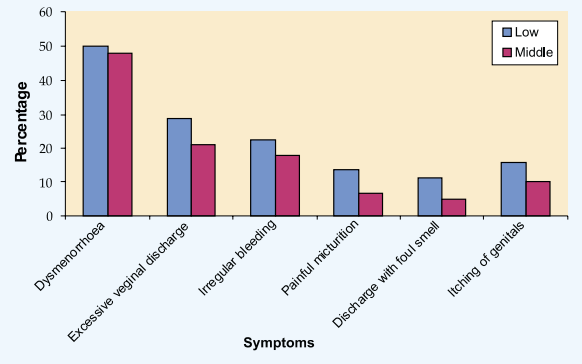


Fig. 26. Reproductive health problems of girls aged 11-14 yr.

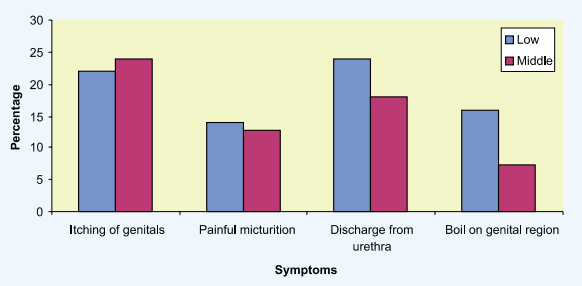


Fig. 27. Reproductive health problems of boys aged 11-14 yr.

quacks. Adolescents from the middle socio-economic class went mainly to private practitioners.

About 13% of unmarried girls in the 11-19 yr age group in low socio-economic class as against 7% from the middle socio-economic class reported having had sexual intercourse. However, more girls from the middle socio-economic class reported non-coital sex.

Adolescent Friendly Centres were organized in one school and one college, and held twice a week for 2 hours each and evinced a positive response. Around 150 adolescents visited these centres during the working months of the school. A letter box was provided to maintain anonymity at each centre so that the adolescents drop their questions. The answers to these questions were displayed on the notice board of the centre. This intervention elicited an advice on good response and adolescents regularly visited the centre for various medical problems, information and counselling.

Reproductive health check up and counselling was carried out for boys and their

parents. Preliminary analysis and experiences from these studies suggest that adolescents have a quest for information on reproductive and sexual health issues. They are willing to approach adolescent friendly centres for various reproductive health problems, however, their health seeking behaviour is poor. Many of the reproductive health problems like anaemia, genital anomalies remain undiagnosed due to ignorance on the part of adolescents themselves and their parents. School health checkups which are part of our system lack reproductive health focus which needs to be incorporated in order to reduce the disease burden of adolescents in adult life and hence a comprehensive approach with medical/health check up is very essential in addition to providing IEC.

Nutrition

In the field of nutrition, major thrust of the Council was on providing technical support and guidance to strengthen the ongoing national nutrition programmes. Community surveys were undertaken besides studies on women's nutritional status, diet related cancers, micronutrient deficiencies, non-communicable diseases due to nutritional deficiencies such as diabetes, cataract *etc*. Surveys were also conducted for finding out nutritional status of tribals in various states of the country. The Council's National Institute of Nutrition (NIN), Hyderabad undertakes most of the studies in nutrition.

Another community-based study to assess diet and nutritional status in drought-affected areas in the country during May-June 2003 has shown that the mean intakes of all foodstuffs were below the suggested levels in almost all the states surveyed. Also, the recommended levels of cereal and millet intake were not met. Though drought relief programmes like 'Food for Work' could ensure steady supply of certain cereals and millets, there was insufficiency of other foodstuffs among the affected people. Prevalence of underweight and stunting in preschool-aged children and chronic energy deficiency in adults was found to be significantly high.

COMMUNITY STUDIES

Community Survey to Study Prevalence of Micronutrient Deficiency Disorders

A large scale, eight-state community based survey was carried out to study the prevalence of micronutrient deficiency disorders involving both clinical and biochemical forms of vitamin A deficiency (Bitot spots), iodine deficiency disorders (IDD) and iron deficiency anaemia during the year. The overall prevalence of Bitot spots was 0.8% and that of goiter was 4%. About 42% of the households were using non-iodized salt. Mostly lactating and pregnant women, adolescent girls and pre-school children were found to be affected by anaemia. While IDD registered a decline well below the epidemic level, vitamin A deficiency continued to be a matter of public health concern in many states. The results underscore the need to strengthen the existing national nutrition programmes as well as nutrition education component embedded in them.

A country-wide survey carried out to assess the changes in the prevalence of IDD particularly in the districts with higher levels of endemicity revealed that the overall prevalence of total goiter registered a significant decline from 14-69% in 1984 to 3-40% in 1994 especially in the north-eastern region of the country.

Nutritional Studies in Tribals of Madhya Pradesh

Evaluation of effect of intervention (safe drinking water) on endemic fluorosis in Mandla by RMRC, Jabalpur revealed that supply of water with less than 1-ppm fluoride reduced genu valgum in children from 51.2% in 1996 to 2.6% in 2003. Urinary fluoride reduced to 9.8% (2003) from 40.8% (1996), though dietary intake pattern did not change much. Other biochemical parameters like serum alkaline phosphatase, calcium and inorganic phosphorus remained similar to pre-intervention period *i.e.* within normal range. Thus safe drinking water and nutrition supplementation resulted in reversal of bone deformities due to fluorosis (Fig. 1).

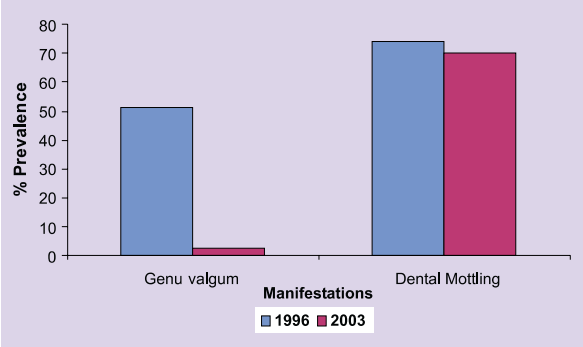


Fig. 1. Clinical manifestations before and after intervention.

Nutritional Status of Raika Community in Jodhpur

Raika community (OBC) in Jodhpur district commonly consumes camel milk which reduces diabetes and may be helpful in reducing nutritional deficiencies and morbidities in adult community. A nutritional survey revealed that *Raika* adults suffered from chronic energy deficiency (44.1%), vitamin A and B complex deficiencies (3.4 % & 2.4%) and anaemia (87.7%). Main morbidities reported at the time of survey were aches (56.6 %), gastric complaints such as abdominal pain (26.1%) and respiratory problems (8.8%). Morbidity showed negative association with personal cleanliness, housing conditions, education and haemoglobin estimation. Diet analysis also revealed that *Raika* adults suffered from calorie deficit (50.5%), but intake of proteins met the allowances recommended by ICMR.

Nutritional Habits and Cancer in Mizoram Community

Confirmed cases of stomach cancer (274) belonging to Christian community of Mizoram were enrolled in a study conducted by RMRC, Dibrugarh for finding risk factors for stomach cancer in relation to their practices and food habits. Consumption of smoked salted fish and meat was found to be the risk factor. However, consumption of fresh fish and chicken was a protective factor. Among the peculiar food habits of Mizoram, consumption of fermented pork fat, fermented soybean and Soda were found to be the risk factors. A local cigarette (*meiziol*) was high risk factor for stomach cancer.

CLINICAL STUDIES

Osteoporosis in Indian Women

Indian data show early onset of osteoporosis among Indian women compared to women from West. Most of these women belonging to the underprivileged sections of the society subsist on a diet low in calories, proteins as well as calcium. These women breastfeed their infants for prolonged period of time (> 1 year). Studies are being carried out to establish peak bone mineral density (BMD) reference values for both men and women and also to assess the prevalence of osteopenia and osteoporosis in Indian population groups in a multicentric task force study. Results have indicated that conservation of calcium occurs either through increased absorption or reduced excretion, or both. These compensatory mechanisms were observed to offset the breast milk calcium loss only in women who enjoyed better nutritional status (body weights and BMI). The link between body weight and BMI with peak bone mass is being explored in further studies.

Effect of Egg Intake on Serum Lipid Profile

In a study conducted by AIIMS, New Delhi, 34 healthy young (22 men, 12 women; age 25.7±5.8 yr) vegetarian normolipidaemic volunteers were given one boiled egg per day for eight weeks. Out of them only 45% had greater than 15% rise in LDL cholesterol level and significant rise in total cholesterol, LDL cholesterol and total HDL cholesterol ratio after egg consumption. This indicates that knowing the cholesterolaemic response of an individual to eggs may be important before including the eggs regularly in the daily diet.

Effect of Ghee (Clarifed Butter) on Serum Lipid Profile

The study on 63 healty physically active adult volunteers (52 men and 11 women) was conducted at AIIMS, New Delhi following a randomized controlled parallel design. The experimental group was provided *ghee* and mustard oil in diet for 8 weeks. Their serum total cholesterol and HDL cholesterol level increased while LDL cholesterol level did not show any change. The study did not indicate any adverse effect of *ghee* on lipoprotein profile.

Lipid Profile, Blood Glucose and Insulin Levels in Adolescents belonging to Affluent Families

In a study conducted by Institute of Home Economics, New Delhi, 773 adolescents (boys-351; girls-422; age, 13-19 yr.) from affluent families were enrolled from five South Delhi

public schools. The data revealed that snacking in between meals and bingeing, eating out at restaurants and fast food joints was quite popular among the subjects. Most of the adolescents were engaged in sedentary activites in their leisure time like reading/listening to music/watching TV, talking to frients on the telephone, playing video games and working on computers/surfing the net. As per Garrow's classification, 11.4% of the adolescents were in grade I, 3.2% in grade II and 0.3% in grade III obesity (Fig. 2). Nearly 30% subjects had systolic blood pressure (SBP)>120 mm Hg and 16.7% had diastolic blood pressure (DBP)>80 mm Hg. A total of 27.8% of the subjects could be at risk of developing hypercholesterolemia and coronary artery disease (CAD) later in life. Of these, 5.8% subjects had cholesterol levels >200mg/dl and 22% between 170-200mg/dl. The data also revealed that 8.1% of the subjects were at risk of diabetes having fasting blood sugar levels > 100 mg/dl.

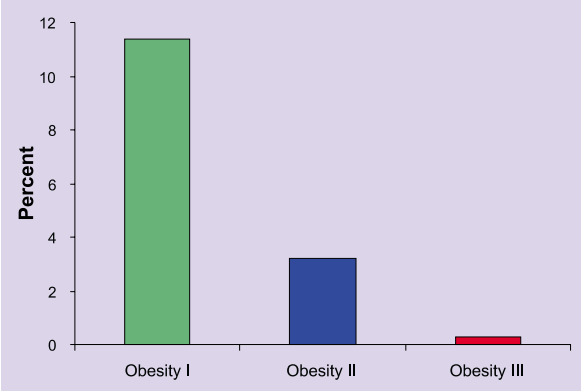


Fig. 2. Type of obesity in adolescents.

STUDIES ON MICRONUTRIENT DEFICIENCY

Vitamin A Deficiency

Assessment of vitamin A status in the population groups is a prerequisite for successful prevention and control of vitamin A deficiency disorders. A technology for collecting dried blood spot (DBS) on filter paper and later analyzing it for vitamin A using HPLC has been developed with the support from Micronutrient Initiative and MOST, New Delhi.

Prevalence of Multiple Micronutrient Deficiencies amongst Pregnant and Non-pregnant Women

In a study conducted by AIIMS, New Delhi, 225 pregnant mothers and 225 newly married non-pregnant women in a rural block of Haryana State were enrolled to determine the prevalence of various micronutrient deficiencies.

Around 88% pregnant women were found deficient in zinc concentration, while 62% pregnant women and 68% newly married women had folic acid deficiency. Around 8.3 and 10% pregnant and newly married non-pregnant women respectively had iodine deficiency (Fig. 3&4)

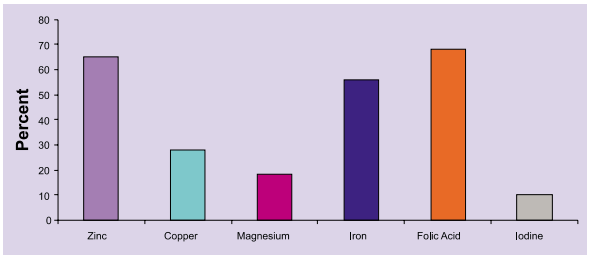


Fig. 3. Micronutrient deficiencies in newly-married non-pregnant women.

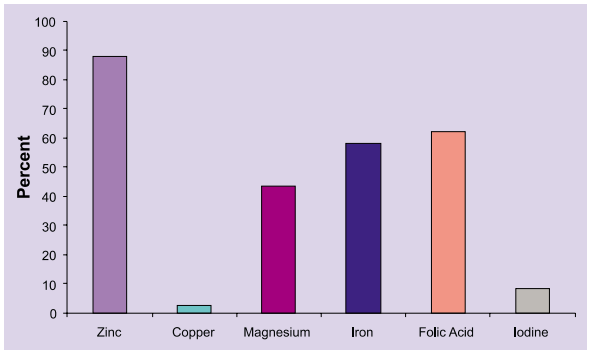
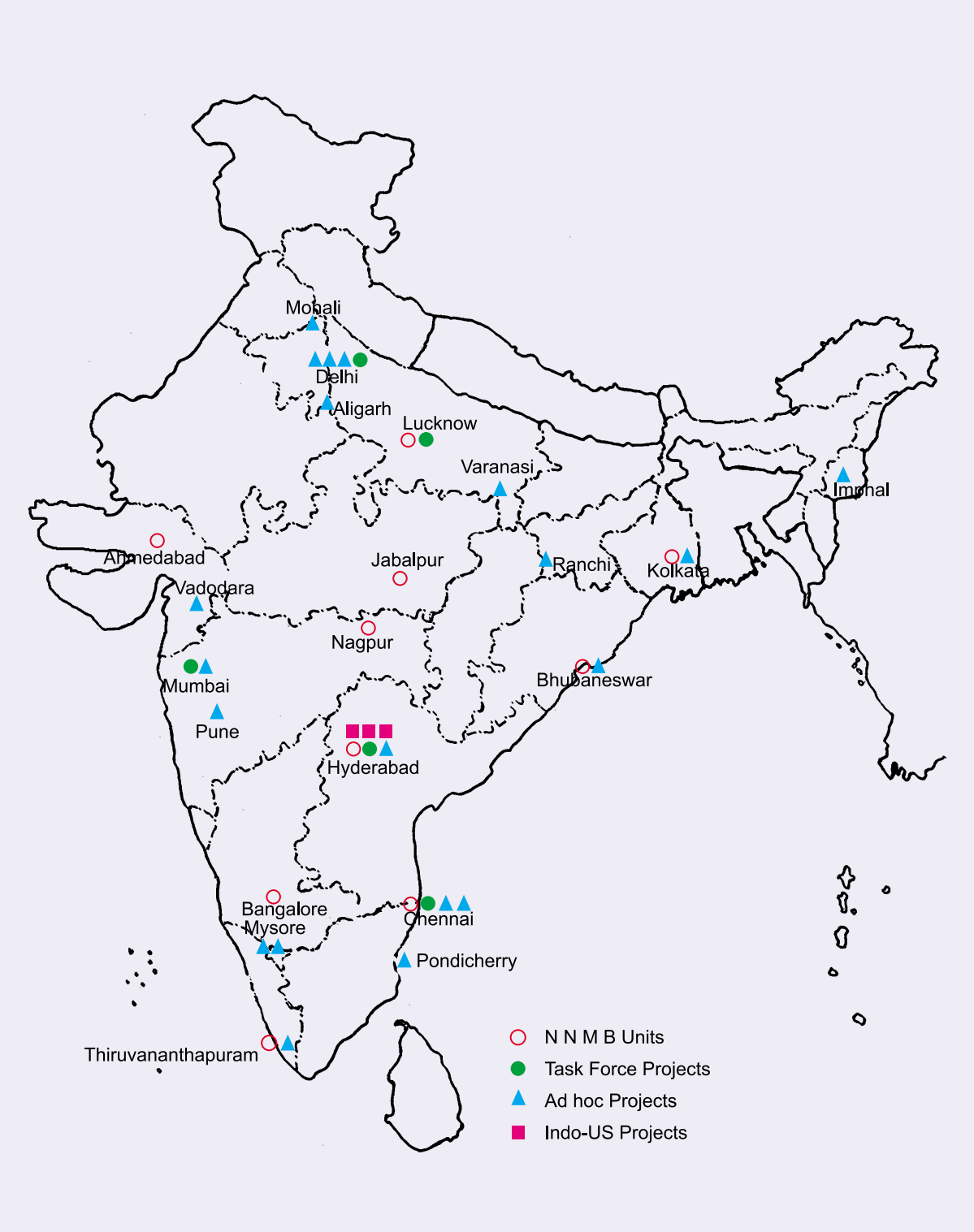


Fig. 4. Micronutrient deficiencies in pregnant women.

DIET AND NON-COMMUNICABLE DISEASES

AR Inhibitory Activity in Foods and Cataract

The enzyme, aldose reductase (AR) in lens has been a drug target because of its involvement in the development of secondary complications



MAJOR ICMR RESEARCH PROJECTS IN NUTRITION

of diabetes including cataract. A study carried out to assess the inhibition of AR by *Emblica officinalis in vitro* and in lens organ culture revealed that its aqueous extract inhibited rat lens AR and recombinant human AR. The hydrolysable tannoids of *E. officinalis* were found to be responsible for AR inhibition. In an alternative approach, antiglycating agents (MAB1) have been worked out for delaying the onset of opacification of lens.

Resistin as a Molecular Link between Diabetes and Obesity

Resistin, a cysteine rich secretory protein, which is downregulated by anti-diabetic drugs like thiazolidinediones (TZDs), has been implicated as the link between type 2 diabetes and obesity in mouse.

In an attempt to understand its role, the human resistin was cloned, expressed and purified to homogeneity from *E. coli*. The biophysical characterization of this recombinant protein revealed its unusually stable nature, which was possible due to intermolecular disulfide linkages. Resistin showed a tendency to aggregate at higher concentration where it undergoes dynamic structural changes as a function of concentration and time. While a link between insulin resistance and inflammation has been established, the exact mechanism has still not been worked out. However, it is seen that the recombinant resistin protein activates monocytic/macrophage cells (both murine and human) leading to enhanced secretion of pro-inflammatory cytokines, tumour necrosis factor (TNF-α) and interleukin (IL-12).

Dietary Fatty Acids and Insulin Resistance

Studies were carried out to investigate the effect of increasing dietary long chain n-3 polyunsaturated fatty acids (PUFA) from fish oil on membrane lipid composition and insulin sensitivity in skeletal muscle and adipose tissue of sucrose induced insulin-resistant rats. The results showed that replacement of 0.5en% long chain n-3 PUFA (n-6/n-3 ratio = 10) prevented sucrose induced insulin resistance by increasing peripheral insulin sensitivity.

Effect of Calorie Restriction on Aging

A study was carried out to assess the effect of calorie restriction with/without micronutrient deficiency on oxidative stress and aging. The findings of the study established the beneficial effect of calorie restriction *per se* in protecting animals against oxidative stress and hyperinsulinemia.

FOOD TOXICITY

An immuno-diagnostic kit has been developed based on latex agglutination test for rapid detection of *Staphylococcus aureus* in food samples. The sensitivity of this kit was found to be over 90%, while specificity was 88% with an efficiency of 90%. This kit can be used in the quality control of foods and as a substitute to imported kits.

NUTRITION AND CANCER

Antimutagenicity of Ginger

Antimutagenic and antigenotoxic potential of ginger was clearly established in a study. Another study was conducted on patients suffering from upper gastrointestinal tract cancers. Estimation of *in vivo* nitrosation potential after administering proline was carried out. The metabolites of nitroproline were found to be significantly higher.

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

A study was carried out to determine the effect of vitamin A restriction and supplementation on drug induced apoptosis of rat intestinal mucosal cells. It was observed that riboflavin and folic acid supplementation helps in preventing DNA damage, mutations and the occurrence of cancer as well as chemotherapy restricted adverse effects.

Antioxidant Properties and Hypocholesterolemic Effects of Sesame Oil

Sesame oil (SO) is known to be stable against oxidative deterioration and its keeping quality

is mainly attributed to the presence of endogenous unsaponifiable components such as sesamolin, sesamol and sesamin (absent in other vegetable oils). A study conducted by Central Food Technological Research Institute (CFTRI), Mysore showed that sesame oil is very stable against oxidative deterioration compared to sunflower (SFO) and groundnut oils (GNO) at room temperature over a period of time. When SO was heated at 60 and 180ºC, various oxidative parameters were lower than in SFO and GNO. Blending of SO with GNO and SFO increased the shelf life of blended oils at room temperature and heated oils and the oxidative stability of blended oils increased as the content of SO in blended oils increased. Nutritional studies showed that SO reduced the cholesterol and triglyceride levels in both normal and cholesterol fed rats. SO was effective in reducing increased peroxidation induced by iron and in preventing triglyceride accumulation in liver induced by administration of carbon tetrachloride and ethanol. SO also helped in maintaining erythrocyte membrane integrity in cholesterol fed rats.

OTHER STUDIES

Molecular Analysis of WNIN/Ob Rats

Research carried out on obese rat model included identification of some obesity-related genes like steroyl COA desaturase, uncoupling protein, leptin and lipoprotein lipase.

PCR based DNA Fingerprinting in Obese Rats

DNA fingerprinting of the obese mutant rats using random primers yielded a fairly constant DNA fingerprint for the GR-Ob strain. Similar pattern was not found in WNIN/Ob strain and hence alternative techniques to obtain results are being explored. Also, genetic typing of obese mutant rats using microsatellite markers was carried out. Out of 100 markers, 60 primers spanning majority of the chromosomes have been screened.

Toxicity of Khesari Dal

A rapid community survey carried out in the villages of Bhandara district of Maharashtra revealed that several people were affected with toxicity-related illness on consuming *Khesari dal* (*Lathyrus sativus*).

Fluoride Toxicity in Drinking Water

In another study carried out in some villages of Nawada district of Bihar, high fluoride concentration in drinking water lead to vitamin D deficiency causing bone deformities in young children. Appropriate strategies to combat the problem were suggested.

Environmental and Occupational Health

Research in the field of environmental and occupational health is being carried out through the Council's National Institute of Occupational Health (NIOH) at Ahmedabad and its regional centres (ROHC) located at Bangalore and Kolkata.

During the year under report priority was given to the occupational health problems of the vulnerable groups like women, children and the workers of unorganized sector of industries such as farmers, salt workers and workers engaged in quartz crushing units in Gujarat.

Health Problems of Women in Fish Processing Industry

Fish processing industry employs nearly 2 lac women workers in the coastal regions of India. Due to the nature of the job, women in fish processing work are exposed to cold environment, chlorinated water and other fish protein related bioagents. Use of improper hand tools and implements and awkward working postures are the contributory factors for musculo-skeletal pain and discomfort of the body parts. A study was initiated in coastal Gujarat to explore the work related problems of such workers. These women (67%) had high prevalence of musculo-skeletal pain and discomfort. The lower back is the most affected area, followed by shoulder and upper back. The cold induced blanching and numbness of hands and Raynaud's like phenomena were observed among these women workers.

Suitable ergonomic interventions were introduced in order to mitigate the work-related hazards. Data indicated that the wearing of gloves substantially improved the skin temperature profile of the hand (Fig. 1). As large as 84% women did not show any blanching of fingers and Raynaud's phenomena with the wearing of gloves. With the continuing use of the gloves for the rest of the workday all the women including those who had developed cold-induced symptoms expressed satisfaction in their voting in comfort scale.

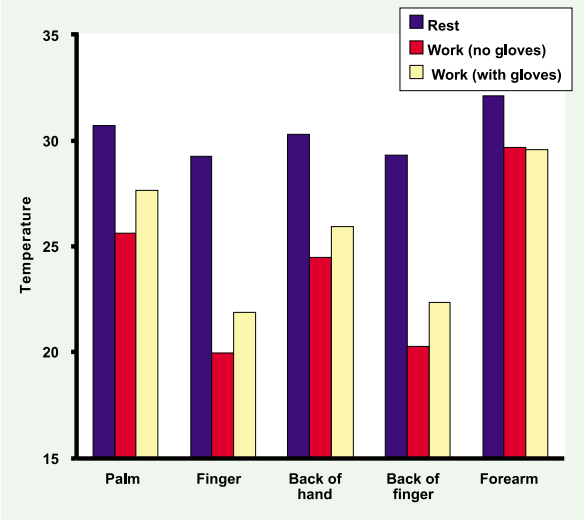


Fig. 1. Temperature of different areas of hand before and after using the gloves.

Occupational Health Problems of Child Labour-A study in Gem Polishing Industries

Child labour is an important social, economical and occupational problem. A study of 586 child labourers of gem polishing industry was carried out. Among the exposed group the common symptoms included respiratory problems, eye strain, headache and repeated finger injuries (Fig. 2 & 3). Around 75% child labourers had one or the other complaint. Chest radiography revealed tuberculosis in 4% children.

The environmental monitoring suggested that in few places the noise levels were above threshold limit values (TLV) while in most of the places the illumination levels were below TLV (Fig. 4).

Fig. 2. Drilling processes may result in piercing finger injuries.

Fig. 3. Polishing process being carried out using chromium powder.

Fig. 4. Child labourers at work in poor illumination.

Assessment of Persistent Pollutants (PCDDs and PCDFs) in Biological Media

Polychlorinated dibenzo-p-dioxins (PCDDs) and furans (PCDFs) are byproducts of incineration, uncontrolled burning and industrial processes. They are persistent in nature and bio-accumulate through food chain. Residues of these toxicants have been detected in human adipose tissue, blood and milk. They are known endocrine disruptors, induce stillbirths, cancer and skin disorders. Biological and food samples collected from Ahmedabad, Vadodara and Surat cities were analyzed for PCDD/F residues. The total equivalent quotient for *desi* and farm eggs and *desi* and broiler chicken and human milk were determined. High correlation was observed between lipid and residues of dioxin in human milk samples (Fig.5).

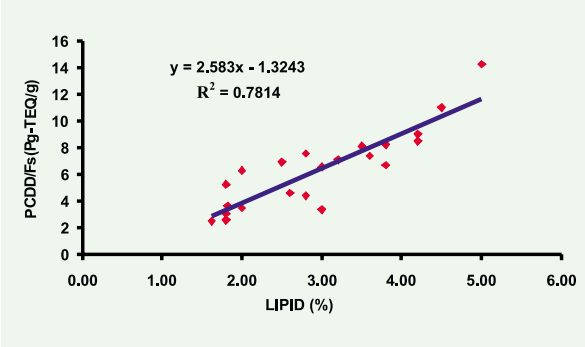


Fig. 5. Relationship between total PCDD/Fs and lipid in human milk.

Health Risk Assessment and Development of Intervention Programme in Quartz Crushing Units

Quartz stones are mined and crushed to powder which is used as a raw meterial in the manufacture of glass. Of the 28 crushing units in Godhra (Gujarat) 20 are in operation. Study was undertaken to evaluate the efficacy of control devices in three units. The exposure occurs mainly at three locations *viz*, crusher, screening/bagging and disintegrator. Dust control systems have been installed in about 15 units except crushers which are usually outside the factory shed and require separate control system.

The mean reduction in total dust concentration at different locations like disintegrator and screening/bagging processes was 85-86% (Fig. 6) whereas reduction in

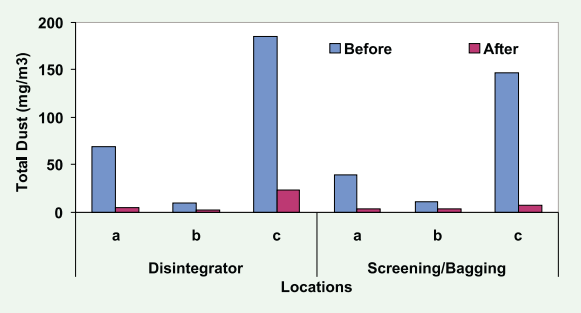


Fig. 6. Total dust concentrations before and after the installation of engineering control.

respirable dust levels was around 69-75% (Fig. 7). The dust levels, however, are still higher than the permissible level of exposure for quartz, which is 0.3 mg/m^3 for total dust and 0.1 mg/m^3 for respirable dust. Therefore, workers were advised to wear disposable masks. Management of the quartz crushing units has been advised to use these measures compulsorily. Dust control system on crushers is under installation.

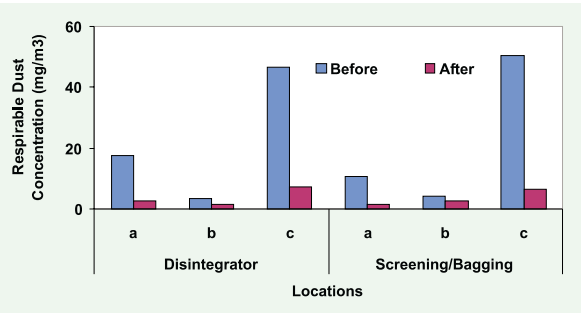


Fig. 7. Respirable dust concentrations before and after installation of engineering control.

Health Risk among Spray Painters

Twenty-five spray painters exposed to paint (Fig. 8) were examined to evaluate its effect specially on reproduction and thyroid. Results indicated some notable neurological (tingling and numbness, irritation in eyes, fatigue, asthenia, and headache) and psychological symptoms (loss of temper, lack of memory, worrying and disliking and insomnia) and clinical findings

Fig. 8. Spray painters exposed to solvents and chemicals.

(tremor, hypertension and vision defects—myopia, hypermetropia, presbyopia). Thyroid stimulating hormone levels were high (Fig. 9) while T_4 levels were low in spray painters. Impairment in the levels of LH and FSH was also observed in some individuals.

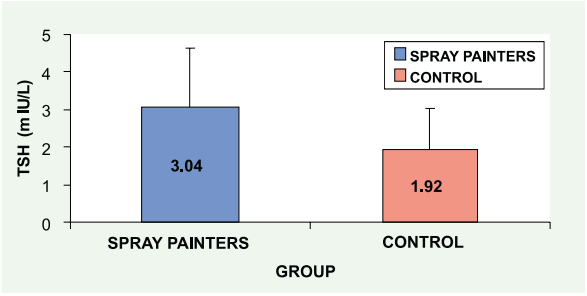


Fig. 9. Levels of TSH in spray painters.

Pesticide Exposure in Chilli Cultivators of Gujarat

Pesticide related-illness forms one of the major health hazards in the developing countries including India. Maximum amounts of pesticides are being used on vegetables and cotton crop in

Fig. 10. Chilli farm workers.

India. A study of pesticide exposure in 256 chilli cultivators (Fig. 10) showed that 73% of them had 11-20 rounds and 15% had 21-30 rounds of pesticide spray during the season which resulted in high pesticide exposure (Fig. 11). Majority of the pesticides belonged to organophosphate group. Plasma and RBC cholinesterase activity was found to be significantly inhibited after exposure to pesticides. Eight workers gave history of severe pesticide poisoning and hospitalization in the past.

Fig. 11. Pesticide spraying on chilli crop.

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

Health risk assessment due to indoor air pollution was carried out in rural population. The result showed that the geometrical mean of benzene exposure for cooks during cooking hours in indoor kitchen using mixed fuel was 69.5 mg/m^3, while the exposure was 114.1 mg/m^3 for cooks in indoor kitchen using dung fuel. Similarly the benzene exposure was 36.5 mg/m^3 for cooks using wood fuel. This study revealed that wood used as cooking fuel had significant impact on the occurrence of age dependent cataracts.

Occupational Health Problems of Cycle Rickshaw Pullers and Redesign of Cycle Rickshaw on Ergonomic Principles

The study of occupational health problems of cycle rickshaw pullers showed high prevalence of musculo-skeletal and respiratory diseases. The new design of cycle rickshaw is being made at ROHC, Kolkata, based on ergonomic principles and three models have been developed (Fig.12). The initial results are very encouraging. The comparative assessment of energy cost of the various models (M1, M2 and M3) of cycle rickshaw pulling showed that the energy cost of model M3 is significantly lower than the existing old model (Fig.13). Research work to assess the efficacy of the new model is in progress.

Assessment of Health Hazards of Arsenic Exposed Population of West Bengal

A pilot study on environmental-cum-biological monitoring of arsenic exposed population of West Bengal was carried out. The result showed that about 15% of the tube-wells had arsenic level above 50µg/l. Most important observation in exposed population was skin pigmentation. The level of arsenic in hair and nail samples was also high. Higher prevalence of anaemia, angular stomatitis, glossitis and cough was present in exposed group. Clinical examination revealed liver enlargement and rise in serum SGOT/SGPT and alkaline phosphatase in exposed population.

Health Problems in Workers Exposed to Toxic Metals from Electroplating Process

A pilot study of 50 workers engaged in electroplating process was carried out by ROHC, Bangalore. They were examined for liver

Fig. 12. Various models of cycle rickshaw.

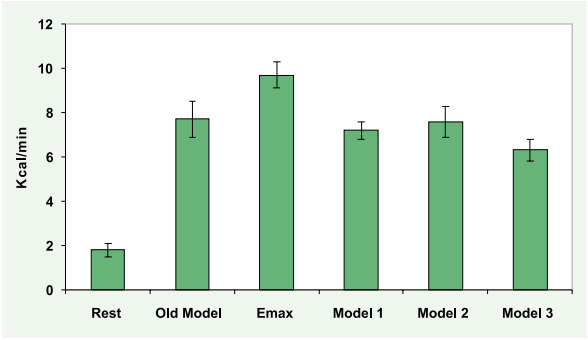


Fig. 13. Comparison of energy cost of rickshaw pulling with existing old model and redesigned model.

function, renal tubular dysfunction and level of nickel and chromium in urinary samples.

The levels of nickel and N-acetyl -β-d-glucosaminidase were significantly higher in workers exposed to toxic metals. Synthetic and cellular functional integrity of liver was found to have decreased in exposed subjects.

National Environmental Health Profile and Health Risk Assessment

The volume and variety of toxic agents in air, water and food have shown an increasing trend particularly in urban areas. Exposure to such agents on long-term basis even at very low level has been found to cause variety of health effects.The results of the study suggest that the average annual level of suspended particulate matter (SPM) in the selected commercial areas in Bangalore has decreased in recent years and is within the prescribed national ambient air quality standards (NAAQS). The level of SO_2 increased in industrial zone due to rapid increase in vehicular traffic. However, level of CO in the commercial and industrial areas is significantly higher compared to residential areas.

Further, proportion of subjects whose COHb exceeded the limit was 2.5% more for the smokers in industrial areas. The water quality parameters measured were well within the prescribed limits. Higher levels of oxidants were recorded among firewood and kerosene users compared to LPG users.

The morbidity conditions *viz*. cough in the morning was significantly higher among the smokers in all the areas. The other morbidity conditions identified in all these areas were non significant. However, more number of individuals residing in slum and residential areas complained of sputum. Further study is in progress.

Morbidity among Workers of Textile Industry of Rajasthan

Study was conducted among the workers of textile industry in Pali and Jodhpur districts. Around 53% workers were found to suffer from various kinds of sickness. Main morbidities reported included aches, respiratory and gastric complaints such as abdominal pain and fever. Chronic energy malnutrition, protein calorie malnutrition vitamin A, B complex and C deficiencies and anemia were reported by many workers.

Non-Communicable Diseases

India is facing progressive onslaught of non-communicable diseases like cancer, cardiovascular diseases, psychiatric disorders, disability and accident related injuries with increase in developmental activities and industrialization. Changes in life-style resulting from improvement in socio-economic status is another factor leading to higher prevalence of non-communicable diseases. Average life-expectancy has increased thereby resulting in rise in ageing population and health problems in these people. The Council is carrying out research projects in major non-communicable diseases like cancer of the cervix, breast and stomach, hypertension, rheumatic heart disease, ophthalmic disorders and mental illnesses.

The Council's Institute of Cytology and Preventive Oncology (ICPO) at New Delhi continued its research and human resource developmental activities in the field of cancer of the uterine cervix, breast and stomach.

ONCOLOGY

In the field of oncology Cancer Registries continued to provide valuable data on cancer occurrence which has its utility in development of hypothesis as well as for evaluation of intervention projects. Project on cancer atlas tried to assess the magnitude of problem through 99 pathology laboratories in India. An operational research project on screening for common cancers has been initiated. Besides this studies are being conducted on various aspects of cervical and breast cancer.

NATIONAL CANCER REGISTRY PROGRAMME

The National Cancer Registry Programme (NCRP), initiated in 1981-82, continues to collect authentic data on cancer occurrence in the country. The report providing data till the year 1998 has been printed. The network of NCRP has been expanded by initiation of six population based cancer registries in North-East India and one rural population based cancer registry at Ahmedabad district. These new registries are one each at Dibrugarh and Kamrup (Assam), West Imphal district (Manipur), Mizoram and Sikkim. The new registry at Silchar covers urban area only, while other five registries cover urban as well as rural areas under the district/state. Other existing population based cancer registries are located at Bangalore, Bhopal, rural Barshi, Chennai, Delhi, and Mumbai. Hospital based cancer registries are functioning at Bangalore, Chennai, Dibrugarh, Mumbai and Thiruvananthapuram. These registries aim at generation of reliable data on cancer occurrence, conducting epidemiological studies and developing human resource in the field of cancer epidemiology and registration. Monitoring and evaluation of the programme is being undertaken by a coordinating unit (Bangalore) under the guidance of a Steering Committee.

The crude incidence rate of cancer for 1999 in different urban population based cancer registry areas varied between 55.7 and 92.5 per 100,000 males and between 61.4 and 103.0 per 100,000 females. The crude incidence rate in the rural registry at Barshi (Maharashtra) was 46.1 per 100,000 males and 56.5 per 100,000 females. Hospital based cancer registries at Chennai, Thiruvananthapuram and Mumbai have initiated a project to study the patterns of care and survival in cancers of cervix, breast, and head and neck. Currently investigation is being done in patients diagnosed during 1997 and 1998.

The project on development of an atlas of cancer in India is collecting data from the departments of pathology of medical colleges and major cancer hospitals. About 99 centres are actively providing the data. So far, information on about 100,000 cases has been received. The minimum crude incidence rates for different districts have also been calculated.

CERVICAL CANCER

Multidisciplinary Study on Cervical Cancer

A multidisciplinary study on cervical cancer is ongoing at ICPO. The study involves cytomorphological, HPV, genetic and molecular approaches. During the year under report 5063 new smears were screened cytologically, thus bringing the total cumulative to 24,163. Of these smears a total of 5.6% epithelial abnormalities were observed. Atypical squamous cells of undetermined significance (ASCUS) were reported in 3.3%, low grade squamous epithelial lesions (LSIL) in 1.2%, high grade SIL in 0.4%, atypical glandular cells of undetermined significance (AGUS) in 0.2% and 0.5% were malignant/suspicious. Rest of the smears were inflammatory or negative. Cytologically detected and biopsy proven lesions form the basis of cohort recruitment for various studies on cervical cancer and its precursors.

Early Detection of Cervical Cancer

Research projects are ongoing for developing alternate methodologies for early detection of cervical cancer and its precursors since 1988. A programme involving magnivisualizer was launched to study the efficacy and feasibility of its use by para-medical workers and its delivery to gynaecologists for their suggestions on improving its suitability and specificity. It further envisages training of paramedical personnel for use in the peripheral sectors.

Further, a technical manual and a pictorial calendar has been prepared for use of visual inspection aids (VIA). These have already been circulated widely to the medical colleges and cancer hospitals. This manual is expected to go a long way in developing human resources for early detection of cancerous and precancerous lesions of the cervix.

Precancerous Lesions of Cervix

The ICPO continued its efforts for developing treatment modalities for precancerous lesions of cervix. ICPO has been recognized by International Agency for Research in Cancer as one of the centres for initiating a multinational randomized trial to study the comparative efficacy of single *vs* double freeze technique of cryotherapy in controlling carcinoma-*in-situ* (CIN) lesions.

Biological Behaviour of HPV Infection

Various studies have been initiated at ICPO involving different aspects of human papilloma virus (HPV). One of these is the study of biological behaviour of HPV infection. During the year under report 580 women attending gynecologic OPD of a teaching hospital were tested for HPV DNA by PCR using L1 primer and 20.5% of them tested positive. Further typing for HPV high risk types (16 and 18) revealed rather low positivity, the reasons for which are being investigated.

Efforts are ongoing at ICPO for development of low cost easy HPV detection tests. Earlier it was shown by the Institute that HPV screening using hybrid capture technology has 75% sensitivity for detection of CIN 1 lesions and nearly 100% sensitivity for detection of high grade (CIN II+) lesions with a specificity of about 83%. Though the positive predictive value was rather low (6.7%), a very high negative predictive value of 99.2% makes it an ideal tool for Indian situation where frequent screening, as is being done in the western countries, is not possible. Once in a life time screening using HPV (high risk types) detection at 35 yr of age would confer an immunity for life in over 99% of the subjects. The only negative aspect of HPV screening is the prohibitive cost of more than Rs.500-700 per test. In order to resolve this issue, ICPO has initiated research for development of indigenous early detection tools involving multiplex PCR so that a single test can detect women harbouring high risk types of HPV. Another important aspect of HPV screening is the transport and storage of HPV samples from periphery to central PCR-based laboratories. A breakthrough made in developing a paper smear technology, wherein a dry smear can be stored and transported to the centralized laboratories without any risk of loss of DNA material is under patenting.

The ICPO is also engaged in molecular control of HPV infection by using synthetic and

herbal oxidants. In addition, phase III clinical trial of microbicidal polyherbal neem creams/ tablets against HPV infection continued during the year.

The ICPO has been recognized by WHO for participating in the multinational programme for developing vaccine against HPV.

DNA Methylation Pattern and Differential Gene Expression in Cervical Cancer

Studies have been initiated to investigate DNA methylation pattern and expression level of methylase enzyme and differential gene expression in cervical and breast cancer. This study along with genetic instability in precancerous and cancerous lesions would increase the understanding of the molecular mechanism in the development of these cancers.

Telomerase Activity in Cancerous Lesions

In another study on cervical cancer, telomerase activity has been assessed in 150 samples comprising cancerous and precancerous lesions. In all the tumours and majority of dysplastic lesions around 68% were positive for telomerase activity which showed a positive correlation with hTERT expression. However, hTR expression was observed in all tumour lesions. This study further revealed that hTR and hTERT both are upregulated in the presence of HPV infection.

Genomic Instability and Genomic Deletion

Study on genetic instability, loss of heterozygosity (LOH) and β-catenin gene mutation continued during the year. Microsatellite instability was found to be an early event in the process of cervical carcinogenesis. Microsatellite instability (MSI) along with HPV infection appears to be a potential marker for detecting the disease in its early stage.

BREAST CANCER

Multidisciplinary Study

The ICPO has initiated a cohort study on breast cancer to study the clinical profile, epidemiological risk factors, treatment patterns and survival of breast cancer patients. In addition, the prognostic factors including the role of sex hormones will be elucidated. One of the important parameters of the study would be identification of the disease susceptibility gene including genetical instability. A data bank and a bio-bank for storing biological samples from familial cases of breast cancer will be developed.

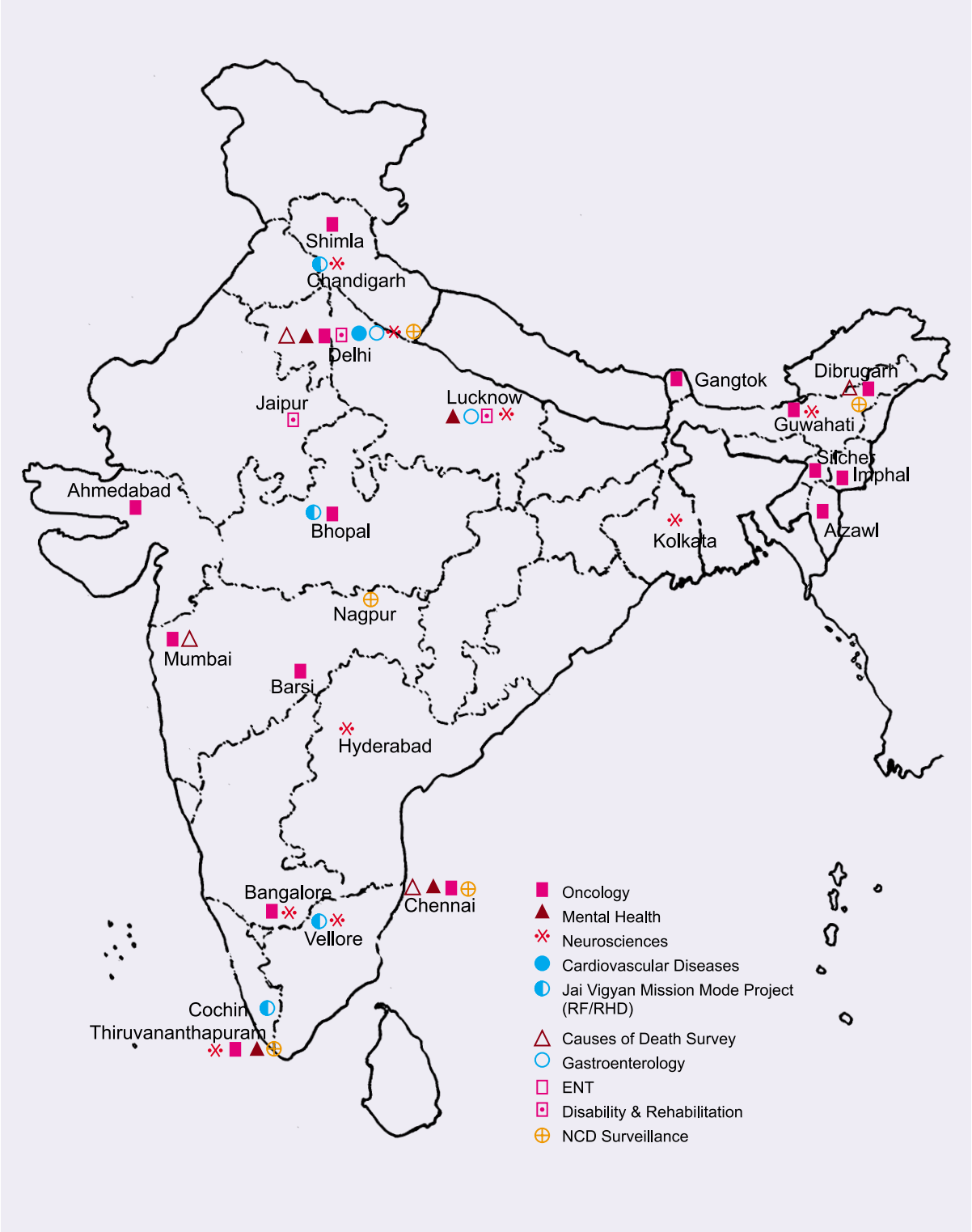
Other Studies in Breast Cancer

A study has been initiated to determine mutation of BRCA1, BRCA2 and P53 genes from tumour biopsies from 105 sporadic cases and blood samples from 28 familial breast cancer patients. All exons of BRCA1 and specific exons 2, 9, 11, 11a, 18 and 20 of BRCA2 which are frequently mutated in BRCA2 were analysed.

In sporadic breast cancer biopsy samples, only 4.8% mutations comprising 2% in exon 2 and 1% in exon 11 of BRCA1 and 2% in exon 2 of BRCA2 were detected by PCR-SSCP assay. Other exons of BRCA1 and BRCA2 showed no mutation. Out of 28 familial breast cancer samples analyzed, only 7% mutations could be detected in exon 2 of BRCA1 genes and no mutation in BRCA2 gene. In addition, 2.8% mutations were detected in exon 5 of p53 gene. Among 105 sporadic cases, no mutation was found in other exons. Out of 28 familial breast cancers analysed only one mutation could be detected in exon 4 of the p53 genes. In 60 samples expression of BRCA1 gene was found to be down-regulated and that of p53 gene was over-expressed. In almost all breast cancer cases, preliminary studies on levels of transcription factors, AP1 and NFKB suggest possible downregulation.

CARDIOVASCULAR DISEASES

The entire Southeast Asian region is threatened by the hidden epidemic of cardiovascular diseases (CVD). The number of deaths due to ischaemic diseases in this region is second to deaths caused by HIV in the younger age group of 5 to 59 yr; in the older age group of ≥ 60 yr ischaemic diseases accounted for maximum number of deaths. Identification of



MAJOR ICMR RESEARCH PROJECTS IN NON-COMMUNICABLE DISEASES

Non-Communicable Diseases

novel risk factors in Indian population using modern research tools will help in developing preventive strategies.

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

The study is ongoing at New Delhi, Bangalore, Lucknow and Hyderabad and so far 2310 subjects have been enrolled.

Jai Vigyan Mission Mode Project

Community Control of Rheumatic Fever (RF)/Rheumatic Heart Disease (RHD)

This project was initiated under the Prime Minister's initiative as a mission mode project. Various components of the project-(i) to study the epidemiology of streptococcal sore throat; (ii) to establish registries for RF/RHD; (iii) vaccine development for streptococcal infections and (iv) conducting advanced studies on pathological aspects of RF/RHD - are interrelated and are providing a large data on disease prevalence in the northern and southern regions of the country, the types of group A streptococci (GAS) strains circulating in the community and the effectiveness of the secondary preventive measures in control of RF/RHD. The study is paving a way towards an indigenous vaccine against GAS. The epidemiology component undertaken at Chandigarh and Vellore has been completed. The *emm* typing data from both these centres show that the strains from Vellore are more heterogeneous than those from Chandigarh. The *emm* typing of 78 GAS strains from Chandigarh showed that 78% strains were homologous to M77, 81, 11, 71 and 69 *emm* types, rest were 18, 44, 65, 68, 75, 85, 87, 88, 92, 118, ST854 (Fig.1)

Under the Registry component, the three centres (Chandigarh, Vellore and Cochin) have registered 314, 274 and 142 confirmed cases of RF/RHD respectively after a thorough screening of suspected cases. Under the active surveillance component, screening of 23336, 26551 and 26341 school children by Chandigarh, Vellore and Cochin centres showed RF/RHD prevalence of 1.02, 1.46 and 0.228 per 1000 respectively. The

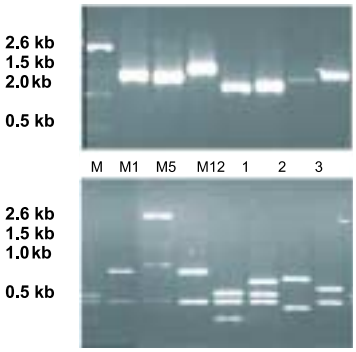


Fig. 1. (a) PCR amplification of *emm* gene and (b) RFLP pattern of the amplified product of *emm* gene. (lane 1-2 pharyngitis strains; lane 3-4 RF/RHD strains; M, M1, M5, M12 lanes show corresponding *emm* types).

three centres are also conducting training workshops for medical and para-medical staff for identifying and referring suspected cased of RF/RHD as well as community education programme in the selected districts.

Under the vaccine component 12 peptides corresponding to 20 amino acid of amino terminal of M protein have been synthesized. The tetanus toxoid conjugated peptides showed adequate protection of the immunized mice. Except for antipeptide sera against N terminal peptides of one strain, all other 10 antipeptide sera showed opsonic activity ranging from 43-95% against homologous strains. The results indicate that anti N terminal peptide sera mainly opsonize homologous strains with some exceptions. The cross protection is minimal.

OPHTHALMOLOGY

Prevalence of Glaucoma

Glaucoma has been identified as one of the main causes of preventable blindness all over the world. In India there is a lack of data on prevalence of glaucoma in the population. The ICMR has conducted a population based study to determine the glaucoma prevalence in Angamaly district of Kerala. A total of 17706 individuals aged > 35 yr were screened of which 358 had confirmed glaucoma and 223 were glaucoma suspects. Out of the 358 cases 231 had primary open angle glaucoma, 74 primary angle closure glaucoma, 31 secondary glaucoma and the rest had other types of glaucoma. Prevalence

of glaucoma was the highest (2.91%) in the 55-64 yr age group. The age-specific rates showed a different trend in males and females. In males the highest rate was in the 65-74 yr age group (3.46%) while in females 55-64 yr age group had the highest prevalence (31.4%). The overall prevalence of glaucoma was 2.0% in individuals aged>35 yr. Primary open angle glaucoma had a prevalence of 1.3% while primary angle closure glaucoma had a prevalence of 0.42%.

The prevalence of blindness in the study area was 1.52%. The blindness figures have shown a decline as compared to the earlier multicentric study conducted by ICMR in the 1970. The decline is even more prominent when the figures are compared to one of the centres (Madurai) which was similarly located geographically. (Fig. 2)

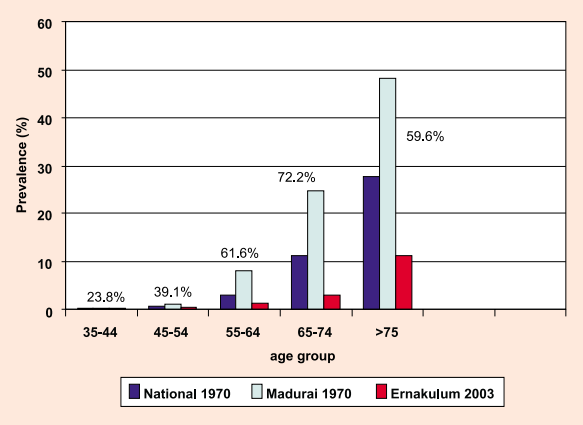


Fig. 2. Prevalence of blindness in Angamaly.

Figures in red indicate the quantum of decline from the national average.

MENTAL HEALTH

According to World Bank study, mental health problems (including self inflicted injuries) are one of the largest causes of lost years of Quality of Life accounting for 8.1% of all such lost years. In adult population (15-44 yr), the neuropsychiatric disorders account for 12% of global burden of diseases. According to a World Bank report, psychiatric conditions measured in disability adjusted life years (DALYs) are five of the 10 leading causes of disability world wide. National and International statistics do not reflect the enormous toll of misery from mental disorders because these conditions are not the immediate cause of death. The burden of DALYs due to mental health problems is projected to increase to 15% by the year 2020.

Urban Mental Health Problems and their Services Needs

Rapidly growing population in urban areas in India is causing various problems related to mental health. The rapid growth, without proper health services (especially those related to mental health aspects), stress, pollution, noise and overcrowding have a direct correlation with mental health.

The ICMR initiated a study on urban mental health problems at three centres *viz*. Delhi, Lucknow and Chennai with support from WHO. The study aims to collect and collate data related to existing mental health services-government, private and NGOs, in urban areas, through mapping of these services in the selected cities. The pilot phase of the project has been completed. The work was carried out as mapping of specialized mental health services, the assessment of diagnostic profile and pattern of utilization of services at five treatment centres, and the assessment of needs and services in community. Instruments were developed and pre-tested. Mapping of the specialized mental health services and NGOs was undertaken. In-depth interviews were held with patients, informants and service providers. Key informant interviews, free listing and focus group discussions were also undertaken with general practitioners and faith healers. As per the community perception, mental health problems were reported due to stress in majority and to medico-religious causes in a few patients. Interestingly most of the faith healers reported that mental health problems were due to illness of brain. The burden of psychological and psychiatric problems in community was reported to be 30% by general practitioners, 50% of whom felt that mental health services were satisfactory.

Suicide Behaviour

Suicide is a major public health problem and is among the top ten causes of death in most countries. Looking at the sociocultural diversity

of Indian population there is a need for well designed prospective study. A task force project on suicide behaviour was initiated at Delhi and Thiruvananthapuram with the objectives to adapt/develop and pretest study instruments, to work out field work logistics and referral system for community settings, to establish project work logistics for hospital based study and prepare guidelines for intervention and manuals for training of research staff. The study instruments have been translated, tested and adapted. Community surveys were conducted in metropolitan areas at both centres. Individual data from the families was collected. The qualitative study has indicated wide acceptability without any negative effect of the project in the community. Hospital arms of the project were also undertaken in both the cities. Preliminary results indicated that mean scores on all the instruments had increasing trend with the grade of suicidal ideation.

Mental Health Service Needs and Service Delivery Models in the Disaster (Earthquake) affected Population in Gujarat

Pilot study of the task force on mental health service needs and service delivery models in the disaster (earthquake) affected population in Gujarat was completed. The study highlighted the definitive need to focus on emotional and psychological needs of the disaster affected populations. It was observed that communities and populations can and do take care of their emotional and psychological needs with their own resources. Qualitative research methods have been finalized. The main study ongoing at 3 centres in Gujarat would focus on the long term psychological effects, psychiatric disorders, coping mechanisms and response pattern in disaster affected population.

NEUROLOGICAL DISORDERS

Epilepsy in Pregnant Women

Epilepsy is one of the most common neurological disorders and its prevalence in pregnant women is estimated to be around 0.5%-2%. A longitudinal prospective study was initiated to assess the risk of malformations in newborn children of women with epilepsy at Safdarjung Hospital, New Delhi. So far, 170 women have been enrolled. The incidence of major malformations was found to be 6.8% in epileptic women compared to 2.87% in controls. The malformations were 12.1% in women with duration of epilepsy more than five years. Another project on Registry of Epilepsy in Pregnancy has been initiated in Thiruvananthapuram.

Other Studies

Studies have been initiated to detect Parkene gene mutations in Parkinson's disease and on prevalence of neurocysticercosis in Indian population.

GASTROENTEROLOGY

Interferon has been used as treatment for hepatitis C, either alone or in combination with other anti-viral agents. As this therapy is expensive and has to be taken for a very long duration, there is a need to identify some marker to predict the non-response and outcome. Though high baseline viral load and HCV genotype 1b has been reported to be influenced by therapy, there is scarcity of data to substantiate this claim in India.

A task force study to determine host and viral factors responsible for non-response to interferon therapy in patients with hepatitis C virus infection is ongoing at GB Pant Hospital, New Delhi. This project is also studying the genetic factors influencing the outcome of the therapy. The study population includes HCV RNA positive patients with histologically proven chronic hepatitis C with raised ALT. A total of 59 patients have completed 12 month follow up. Non-1 HCV genotype was detected in 43 patients, while standardization of the protocols for genotypes 2 and 3 are being undertaken. HLA typing has been completed in 16 patients. The CCR5 gene has been also studied and significant difference was found between the responders and non-responders of the therapy. Genotyping of 136 HCV patients has so far been completed. None of the CCR5 and TNF alpha allelic variants correlated with the disease severity and hepatic

inflammation. Based on univariate analysis, TNF-β A/A allele correlated significantly with hapatic inflammation. Amongst the VDR alleles, BB and tt were significantly associated with hepatic inflammation. VDR Aa were associated significantly with hepatic inflammation. TNF-β G/G and A/A, but not CCR5 δ 32 mutation, correlated with severity of hepatic fibrosis and liver disease. Among the VDR alleles, Bsm 1BB, bb Taq 1:TT and tt correlated significantly with the severity of liver disease.

CAUSES OF DEATH BY VERBAL AUTOPSY

A task force project on developing and testing the feasibility of utilizing the verbal autopsy technique to identify the underlying cause/s of death is ongoing since January 2001. The initial two years were utilized for developing and testing the study instruments and a pilot survey in two districts of Rajasthan and Chennai. Realizing the utility of this method to act as an adjunct to the existing system of death data collection in the country, the study was expanded to cover 5 representative states in the central, south, east, west and northeast regions of the country *viz*. Rajasthan, Tamil Nadu, Bihar, Maharashtra and Assam. Training programmes for the field staff were organized and the participating centres were Institute for Research in Medical Statistics (IRMS), Delhi, National Institute of Epidemiology (NIE), Chennai, NIRRH, Mumbai and RMRC, Dibrugarh. In each of these states the main study has taken off during the years 2003-2004. The first round of data collection has yielded information on more than 5000 deaths for a recall period of 6 months. More than 70% of these deaths constitute adult deaths. The preliminary data analysis shows that CVD is the leading cause of death in all the centres comprising 20-30% of all deaths. Cancer is ranked as the second major killer followed by accidents. Pulmonary tuberculosis has also resulted in a substantial number of deaths in some centres. The second round is in progress and the data entry has begun.

ASSESSMENT OF BURDEN OF NON-COMMUNICABLE DISEASES

An ICMR-WHO project for assessment of burden of non-communicable diseases and related risk factors was initiated during 2003-04. Till date a systematic review of all the available studies on ischaemic heart disease, stroke, diabetes and cancer and their risk factors *viz*. tobacco and hypertension has been done. The data on mortality and population have been collected combined with the prevalence/incidence data from available studies using diseases modelling.

NON-COMMUNICABLE DISEASE SURVEILLANCE

The initiative for development of NCD surveillance was started in December 2001. Two major studies were initiated, one on development of sentinel health monitoring centres in India and another on health behaviour surveillance for risk factors of NCDs.

Development of Sentinel Health Monitoring Centres in India

The study was undertaken at Ballabhgarh (Haryana), Chennai (Tamil Nadu), Dibrugarh (Assam), Nagpur (Maharashtra) and Thiruvananthapuram (Kerala), using the adapted WHO STEP wise modules. The risk factors for NCDs which were studied included consumption patterns of alcohol and tobacco, fruits and vegetables, levels of physical activity, weight, height, blood pressure and waist circumference.

The study population was divided into 5 age cohorts (15-24, 25-34, 35-44, 45-54, 55-64 yr) in urban, slum and rural areas, and both the sexes were studied. In the urban areas and slums, census block was the sampling unit whereas village was the sampling unit in rural areas. Overall, 39,437 subjects were studied at all centres, of which 49.2% were males and 50.8% females. Around 6500 men and women were in rural, urban and town areas. Complete analysis of data is ongoing.

The study on health behaviour surveillance for NCD risk factors is also ongoing.

Basic Medical Sciences

Basic medical research under the aegis of the ICMR is being carried out at Institute of Pathology (IOP), New Delhi, Institute of Immunohaematology (IIH), Mumbai and through extramural research in various research institutes, medical colleges and universities in the country. Major areas of research include pathology, haematology traditional medicine, pharmacology, biochemistry, immunology, toxicology, physiology, genetics and geriatrics. The Council also handles the Toxicology Review Panel for investigation on new drugs and assists the drug controller General of India in taking decisions on clinical trials/marketing of new drugs in the country.

PATHOLOGY

TUMOUR BIOLOGY

BREAST CANCER

Genetics of Breast Cancer in Indian Population

Studies have been undertaken at IOP, Delhi to elucidate the role of genetic factors in development of breast cancer in Indian population. A Total of 204 breast cancer cases (196 female and 8 male) were screened for mutations in BRCA 1 / 2 genes; 23.5% of them had family history of breast/ovarian cancer and 5.39% had multiple malignancies. Sequence variation in BRCA 1 gene was noticed in 24% patients, 18.36% of whom had family history of breast/ovarian cancer and 73.4% had early onset cancer. Fifty sequence variations were noticed in BRCA2 gene of 19.6% patients, around 5% patients showed variants/ polymorphism in multiple exons, 22.5% had early onset. Sequence analysis of DNA fragments showed eight protein truncating mutations including four splice site variants, three recurrent frame shift mutations and one nonsense mutation. Three missense mutations including three polymorphisms novel to north Indian population were also identified.

To study the role of p53 gene in imparting susceptibility to breast cancer and its correlation with other breast cancer susceptibility genes (BRCA1 and BRCA2), screening of genomic and tumour DNA has been initiated.

Study on E- Cadherin Expression in Breast Cancer

E-cadherin (E-CD) is an important cell adhesion molecule shown to be an invasion tumour suppressor gene. Study was undertaken to analyze the expression of E-CD in different morphologic variants of breast cancer as well as to study its prognostic value by comparing its expression with various clinical, histopathological and biological markers. A total of 40 cases of varying histomorphological types were included *viz*. (23 pure infiltrating ductal carcinoma (IDC); 7 pure infiltrating lobular carcinoma (ILC); 7 mixed ductal and lobular type; and 1 each of ductal carcinoma-in-situ (DCIS), infiltrating cribiform and sweat gland carcinoma). The expression of E-Cad antibody was found to be significantly high in cases of pure IDC (60.8%) than in pure ILC (39.2%) cases. Out of 7 mixed cases, 71.4% revealed aberrant expression in both ductal and lobular areas, while in remaining cases positivity was seen in ductal areas only. Invasive cribiform carcinoma case revealed a stronger expression, while negative staining was observed in sweat gland carcinoma. Increased number of high-grade tumour cases (70%) showed aberrant expression. In infiltrating carcinomas, stronger staining was observed in lymph node tumour deposits. Among the other immuno markers employed, a direct correlation of E-cadherin positive staining was observed with ER expression (72.5% cases). Thus, the study revealed that E-cadherin expression has limited value in differentiating high grade IDCs from ILCs, as the expression is lost in all high grade tumours. The expression is stronger in the metastatic deposits as comapred to primary tumour.

PROSTATIC NEOPLASIA

Apoptotic and Anti-apoptotic Genes in Neoplastic and Preneoplastic Conditions of Prostate Gland

Study was done to evaluate the role of apoptotic and antiapoptotic genes in neoplastic and preneoplastic conditions of prostate. Total 100 cases of prostatic neoplasia including 55 prostate cancer, 11 atypical adenomatous hyperplasia (AAH) and 34 prostatic intraepithelial neoplasia cases (PIN) were studied for expression of p53, bcl-2, bax and caspase-3 gene and correlation was done with androgen receptor expression. p53 immunoreactivity was found increased as the disease progressed from PIN (26.6%) to cancer (40%). In cases of cancer statistically significant correlation was found with the grade and stage but not with hormone response. In cases of bcl-2 family gene, immunoreactivity for bax gene was found higher in preneoplastic cases (66.6%) as compared to bcl-2 (33%). In cases of cancer bax positivity was 29% (more in localized cancers) while bcl-2 positivity was 18.8%, (more in high grade tumours). A significantly high immunopositivity for bax gene was found in hormone sensitive prostate cancer. Caspase-3 immunoreactivity was found increased in cancer (63.5%) as compared to PIN (44.4%) cases and it also showed significant correlation with hormone sensitive cases. Immunoreactivity for androgen receptors was 60% in cancer prostate and showed no correlation with clinical hormone response.

BLADDER CANCER

Role of In vitro Cytotoxicity Assessment and Immunologic Enhancement in the Management of Superficial Bladder Cancer

Patients having superficial transitional cell carcinoma (TCC) were given intravesical adjuvant chemotherapy and immunotherapy after *in vitro* cytotoxicity assessment on patients' own cultured tumour cells.

A total of 48 cases of superficial TCC were included in the study in whom *in vitro* cytotoxicity assessment had been done followed by intravesical administration of drugs. All these patients were followed up for evidence of recurrence or metastasis. Among 21 new cases studied majority of cases (60%) responded to single drug. In three cases showing recurrence, repeat cytotoxicity assesment was done.

Study of Host Immune Response in Superficial Bladder Cancer

Study has been undertaken to elucidate the immune mechanism responsible for antineoplastic activity of immunomodulating / chemotoxic agents as well as immunological factors associated with recurrence of superficial TCC of bladder.

Flowcytometric immunophenotyping of PBMC in patients of superficial TCC was done for cell surface markers *viz*. CD3, CD4, CD8, CD25 and CD56 using fluorochrome conjugated monoclonal antibodies. Significant decrease in CD3 and CD4 surface antigens and increase in CD8 and CD25 was noted in cancer patients. No significant difference was noticed in CD56 expression in these patients.

NEURO-ONCOLOGY

Immune Expression of p53 and Vascular Endothelial Growth Factor (VEGF) in Human Gliomas and their Correlation with Proliferation Marker Ki67

At IOP, 50 cases of different histological types of gliomas were studied and graded according to revised WHO classfication. Clinical data with reference to age, sex, location were tabulated. Immunoexpression for p53 and VEGF will be correlated with the histological grade and the proliferation marker Ki-67. P53 staining has been completed in all cases while VEGF and Ki-67 are being standardized.

HAEMATOPOIETIC – LYMPHOID MALIGNANCIES

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

Study was carried out to assess the spontaneous ability of acute leukemic cells to

undergo cell death by flow cytometry and to correlate spontaneous apoptosis with clinical response of patients following induction chemotherapy. Thirty one samples were analyzed. Childhood acute lymphoblastic leukaemia (ALL) patients had higher mean apoptotic cell counts while adult ALL patients had higher mean live cell count. Mean live cells were higher than mean apoptotic cells in patients with AML. The mean apoptotic cell count was higher in patients who achieved complete remission (CR) as compared to those who did not achieve CR. Multivariate analysis will be done to see if low apoptosis and high cell viability may be an independent predictor of a poor chemotherapeutic response in patients with acute leukemia.

Expression Pattern of Proliferative and Apoptotic related Proteins in Lympho-proliferative Disorders

Sixty biopsies of lymphoproliferative disorders (35 of non Hodgkin's lymphoma (NHL), 12 of Hodgkin's lymphoma (HD), 11 of reactive lymphadenopathy and 2 of metastatic carcinoma) were included in the study. Of the NHL indolent lymphomas comprised 26%, aggressive 71% and highly aggressive 3%. In NHL, 66% were B-cell and 34 % T- cell type. Primary nodal lymphoma comprised 77% and primary extranodal lymphoma 23%.

The expression of apoptotic associated proteins (Bcl-2 and Bax) and their ratio (Bcl-2 : Bax protein ratio, BBPR) were correlated with immunophenotyping and the histological grade of the tumours. Bcl-2 expression was higher in indolent lymphomas while Bax expression was higher in aggressive lymphomas. The mean BBPR was significantly higher for indolent lymphomas as compared to aggressive lymphomas. Cells with high BBPR tend to survive and those with low BBPR undergo apoptosis readily. The mean proliferative labelling index was significantly lower in indolent as compared to aggressive lymphomas. P53 expression was found to be strongly expressed in 29% of high grade lymphomas. Weak or no expression was seen in low grade lymphomas. Thus, a significant correlation has been found between BBPR and the predicted biological behaviour of indolent and aggressive lymphomas indicating important role of Bcl-2 and Bax in biological behavior of lymphomas.

PATHOLOGY OF INFECTIOUS DISEASES

CHLAMYDIA TRACHOMATIS INFECTION

Development of Diagnostic Assay for C. trachomatis

A serovar specific monoclonal antibody (Mab) to *C. trachomatis* has been developed which showed greater sensitivity and specificity as compared to existing diagnostic methods. 32.5% symptomatic and 5.6% asymptomatic cervical specimens were found positive by EIA using D serovar specific Mab as compared to DFA (Fig.1). Epitope specificity was done for the developed D serovar specific Mab by EIA using peptides from variable sequences (VS1, VS2, VS3 and VS4) of MOMP for serovar D. The reactivity of core epitope for D serovar specific Mab in VS4 region was high.

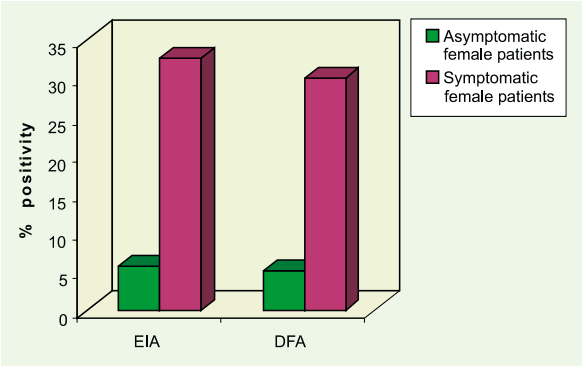
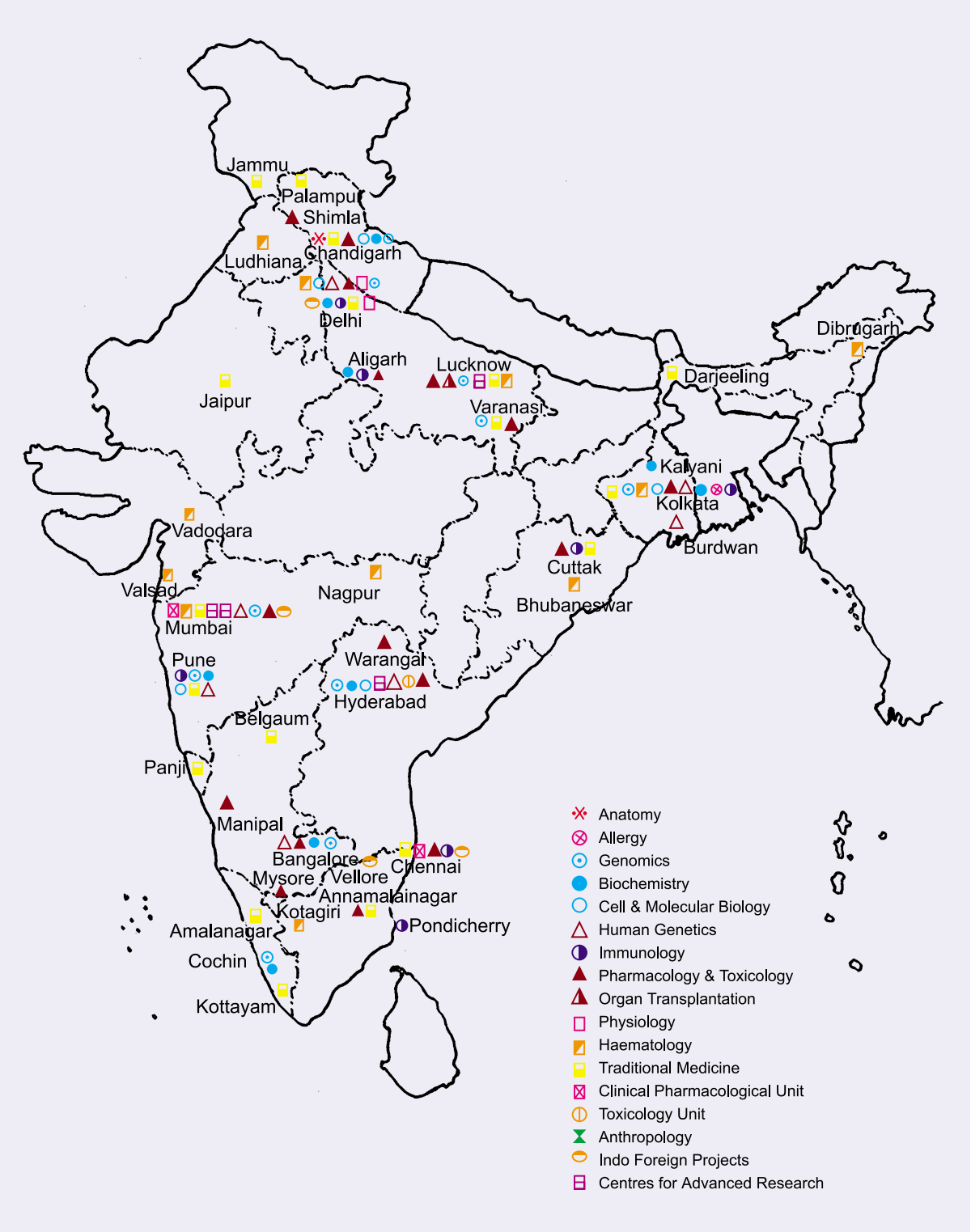


Fig. 1. Prevalence of *C. trachomatis* infection in cervical specimens.

Cytokine Regulation in the Immunopathogenesis of Salpingitis/ Infertility due to C. trachomatis Infection in Women

The production of various Th1/Th2 cytokines in the genital tract (*viz.* cervical secretions and laparoscopic specimens from the fallopian tube) was estimated by ELISA and flow cytometry in *C. trachomatis* positive infertile women after ruling out the presence of few other STD pathogens in the cervix.



MAJOR ICMR RESEARCH PROJECTS IN BASIC MEDICAL SCIENCES

By ELISA: Statistically significant decrease in IL-2, IL-6 and IL-12 cytokines was observed in the fallopian tube while the levels of IFN-γ, IL-10 and IL-12 cytokines were significantly upregulated in the cervical secretions of *C. trachomatis* positive infertile women (Figs. 2, 3).

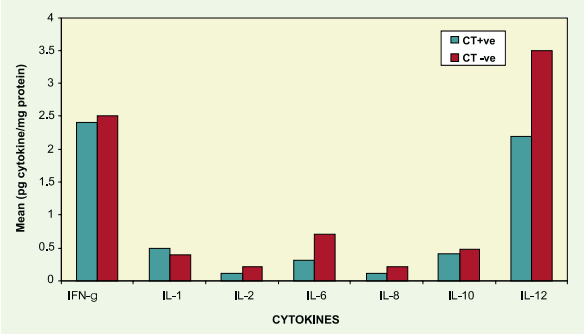


Fig. 2. Cytokine profile in the fallopian tube of *C. trachomatis* positive *vs* negative infertile women (by ELISA).

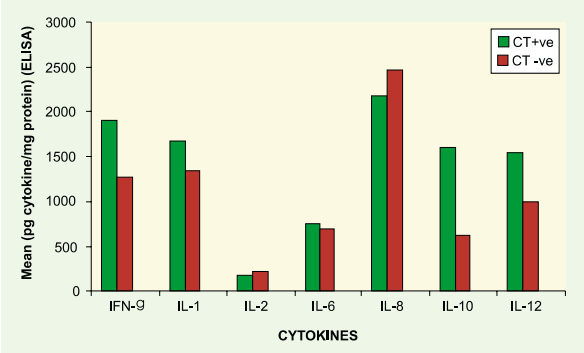


Fig. 3. Cytokine profile in the cervix of *C. trachomatis* positive *vs* negative infertile women (by ELISA).

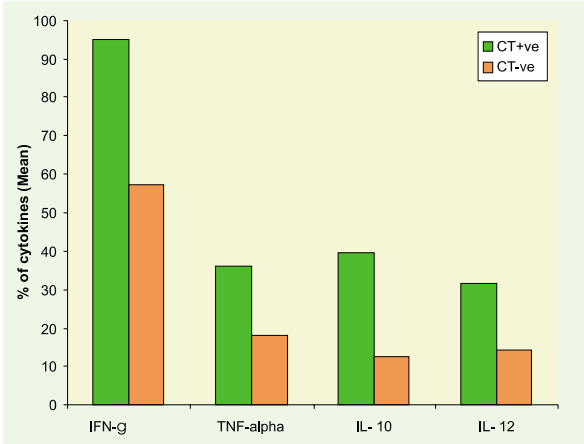


Fig. 4. Pattern of cytokines (IFN-γ, TNF-α, IL-12) in cervix of *C. trachomatis* positive *vs* negative infertile women (by flow cytometry).

By Flow Cytometry: IFN-γ, TNF-α, IL-10 and IL-12 cytokines were significantly more often detected in the cervix of *C. trachomatis* positive infertile women (Fig. 4).

PATHOLOGY OF LEISHMANIASIS

Parasite Detection in Patients with PKDL in India

Evaluation of the sensitivity and specificity of serological, immunohistochemical, and molecular methods in the diagnosis of PKDL was undertaken in 25 confirmed PKDL patients. The diagnostic usefulness of immunohistochemical staining was compared with ELISA with a recombinant (rk39) antigen, and a species specific PCR assay. IHC significantly enhanced the sensitivity of detection (88%) of PKDL over routine H & E staining. ELISA with a recombinant antigen provided an economical and practical assay with 96% sensitivity. PCR was found to be the most sensitive and specific diagnostic method. The tests would facilitate diagnosis of patients with PKDL enabling their timely treatment.

Nested PCR Assay for Detection of L. donovani in Slit Aspirates from PKDL Lesions

A nested PCR assay to detect parasite DNA in slit aspirates from skin lesions of patients with PKDL was developed. PCR results were positive in 93% samples by nested PCR assay, while only 69% were positive in a primary PCR assay. The nested PCR assay allows reliable diagnosis of PKDL in a noninvasive manner.

Centrin Knockout Mutants

Centrin is a calcium binding cytoskeletal protein involved in duplication of centrosomes in higher eukaryotes. In order to explore its role in this protozoan parasite, *Leishmania* deficient in the centrin gene (*LdCEN*) was created at IOP, Delhi. These centrin null mutants (*LdCEN*-/-) showed selective growth arrest as axenic

amastigotes but not as promastigotes. Flow cytometry analysis confirmed that the mutant axenic amastigotes have a cell cycle arrest at the G2/M stage. The axenic amastigotes also showed failure of basal body duplication and failure of cytokinesis resulting in multinucleated 'large' cells. Growth of *LdCEN*-/- amastigotes in infected macrophages *in vitro* was inhibited and also resulted in large multinucleated parasites. This is the first report where disruption of a centrin gene displays stage specific/cell type specific failure in cell division in a eukaryote.

Genomic Microarray based Identification of Differentially Expressed Parasite Genes in PKDL

Studies were undertaken to identify genes differentially expressed in *Leishmania* parasites isolated from PKDL patients in comparison with those from kala-azar patients, using the highly sensitive microarray technology. These gene products are most likely candidates responsible for the different clinical manifestations in case of PKDL. Overexpression of gp63, gp46 and calpain like protease was established in PKDL. Such differentially expressed genes may hold the key to understanding of the parasite genetic factors that regulate the persistence after clinical cure of VL.

OTHER STUDIES

Monitoring of Organic Chemical Pollutants in Placental Tissue

Study was conducted at IOP, Delhi with the aim to establish the utility of human placenta as a tool for comprehensive bio-monitoring for organic pollutants. Samples collected from a total of 45 women (30 random and 15 exposed to agricultural chemicals during pregnancy) were analyzed.

The results revealed presence of pyrethroid, an active ingredient of commonly used mosquito repellent in significantly large number of samples. Some other organo-chlorine and organo-phosphorus compounds were also detected. Further extraction, analysis and reconfirmation of observed compounds is being carried out.

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

The method to culture multi-layered differentiated epidermis was standardized using Rheinwald and Green culture conditions. The cultured epidermis was applied on limited areas (less than 500 cm^2) in two patients. In one patient the take was about 70% of the grafted 65 cm^2 area and in the other it was 100% of the total grafted 400 cm^2 area. Grafting in larger than 500 cm^2 area is being attempted.

Flowcytometric Evaluation of Estrogen Receptors in the Ejaculated Human Spermatozoa and Germ Cells of Rats

Earlier studies undertaken at IOP demonstrated the immunohistochemical localization of estrogen receptors (ER) and a number of estrogen modulated proteins in the ejaculated human spermatozoa.

During the year studies were undertaken to investigate the localization of ER in spermatozoa using flow cytometry. Preliminary studies have indicated that the ER can be evaluated flowcytometrically. (Fig. 5).

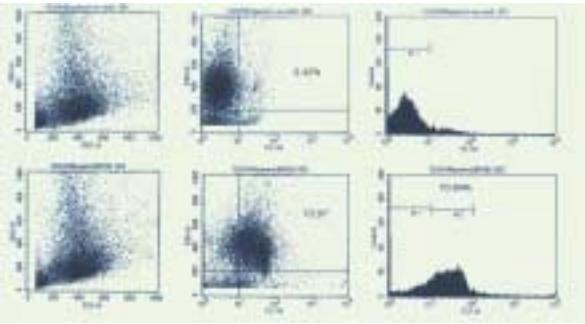


Fig. 5. Flow cytometric separation of ER α labeled human ejaculated spermatozoa. The top panels show the control and the lower two ER α labeled with FITC. The % of unlabeled/labeled sperms are represented as M1 and M2.

Studies have also been undertaken to evaluate the presence of splice variant of ER and PR, if any, in human spermatozoa from fertile subjects and to investigate correlation of the same with male infertility.

Preliminary results show localization of ER α in different germ cell populations of rat testes (Fig.6)

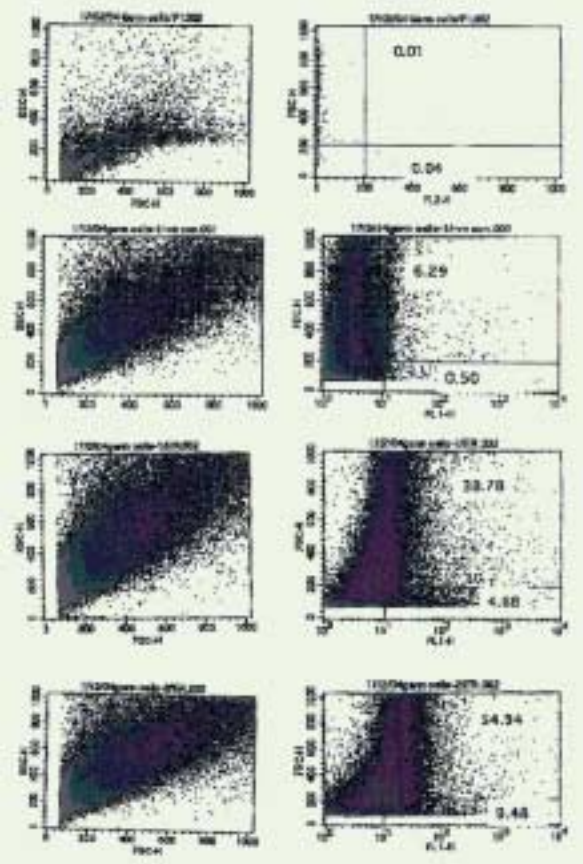


Fig. 6. Flow cytometric separation of ER α labeled rat testicular germ cells. The top two panels indicate the controls and the lower two FITC labeled ER α samples.

BIOCHEMISTRY

A study on the transcriptional regulation of human LDL-receptor gene by cholesterol has been concluded at PGIMER, Chandigarh. The study revealed that transmembrane signalling through cholesterol specific 69 kDa receptor (Ck) was involved in transcription regulation of 160 kDa apoprotein B specific LDL receptor gene.

In another project, effect of prenatal exposure of ethanol on the functional development of intestine in rats was studied at Punjab University, Chandigarh. The litter size was reduced, gestation period delayed and pups born to ethanol fed mothers exhibited low body and intestinal weight and intestinal length during postnatal period. Aldolase dehydrogenase activity after 3-4 weeks of birth and transport of glucose, glycine and leucine in intestine was reduced in ethanol exposed pups. Absorption and binding of IgG and activities of brush border sucrase, lactase and leucine aminopeptidase were also reduced in intestine of pups born to rat mothers fed ethanol during gestation. The findings suggest that prenatal ethanol exposure modifies intestinal development after birth in rats.

Study of protective efficacy of *M. tuberculosis* complex specific protein antigens against experimental tuberculosis was carried out at PGIMER, Chandigarh. Preliminary results suggest that supplementation of BCG with immunodominant antigens (*i.e. M. tuberculosis* complex specific proteins) enhances the immunogenicity of BCG and hence may potentially increase its protective efficacy.

Other ongoing studies include development of antigen detection based diagnostic technique for tuberculosis, understanding molecular basis of pathogenesis of tuberculosis and development of peptide based immunogens from different stages of *P. vivax*.

IMMUNOLOGY

Immunological and molecular studies on the mosquito humoral factors involved in the susceptibility/regulation of *W. bancrofti* infection and development in *C. quinquefasciatus* is ongoing at VCRC, Pondicherry. Analysis of haemolymph samples from infected, normal and naïve mosquitoes indicated six proteins (two new proteins of 40 and 22 kDa, three proteins of 7, 14 and 70 kDa and one protein of 110 kDa).

Study to understand the role of sialoglycoconjugates in host-parasite interactions in visceral leishmaniasis is ongoing at IICB. Kolkata. During the year 13 clinical isolates procured from the Kala-azar Research Centre, Varanasi have been preserved in Leishmania Bank and their *in vitro* anti-leishmanial drug responsive profile has been studied. Identification of different derivatives of sialoglycans on *L. donovani* has also been done.

PHYSIOLOGY

A simultaneous electroencephalography (EEG) and MRI study of sleep-wakefulness in

rat brain has been concluded at AIIMS, New Delhi. Under the study a stereotaxic restraining assembly was designed and developed for simultaneous electrophysiological recordings and functional MRI (fMRI) data acquisition from a conscious rat. Non-magnetic stereotaxic apparatus thus designed facilitated the restraining of head and body of the unanesthetized conscious animal during MRI experiments.

The apparatus was used for carrying out simultaneous electrophysiological and fMRI acquisitions during sleep-wakefulness in a 24-hr sleep deprived rat. Functional data shows activation of preoptic area (POA) and deactivation of fronto parietal cortex during sleep as compared to wake state. Such experiments are useful in characterizing the functional state of different brain regions with good temporal and spatial resolution and are useful in studying different neurophysiological mechanisms like sleep and seizure activity. This study demonstrates the feasibility of carrying out simultaneous electrophysiology and fMRI experiments from conscious animals.

Another study on physiological and behavioural aspects of human circadian rhythm under prolonged socio-temporal isolation was accomplished at Madurai Kamaraj University, Madurai. Sleep, wake and rectal temperature rhythms of eights subjects (age 20-22 yr) under societal conditions showed 24h periodicity.

In two separate experiments a newly married couple (32 and 23 yr old) and a mother (41 yr), son (14 yr) and daughter (12 yr) lived together inside the Human Isolation Chamber (HIC), where all facilities except information on time were available. The couple stayed in the HIC for 29 days and showed circadian periodicity of more than 24h in their sleep - wake and temperature rhythms including a week during which they had their wristwatches indicating that mere knowledge of time is an inadequate zeitgeber. Similarly family members (stayed 14 days) also showed circadian patterns in their sleep, wake and temperature rhythms with more than 24h periods. All the five subjects showed close to 24h periods under societal conditions, recorded both during pre-and post isolation. Their 2h estimations positively correlated with the duration of wakefulness during isolation indicating that short and long time estimates are based on different mechanisms. The timings of sleep and wakefulness for three infant (two boys and one girl) subjects were noted unobtrusively by their parents, from birth to 5-6 months of age. At early ages there were several bouts of sleep and wake components and the infants exhibited circadian rhythm in their sleep-wakefulness. After 14-15 weeks of age the rhythm became apparent circadian. The numbers of bouts of sleep and wakefulness decreased with increasing ages. However, the duration of sleep was still greater than that of wakefulness at the age of six months. Thus a clear circadian pattern of sleep and wakefulness was not yet evident at the age of six months.

GENETICS

Genetic causes of Male Infertility

In a study for establishing genetic causes of male infertility in India at Centre for Cellular and Molecular Biology (CCMB), Hyderabad a total of 209 infertile males (age 26-42 yr) were included. Analysis of cytogenetic and hormone profile, Y-chromosome, Southern hybridization, POLG gene, DAZ gene cluster and DAZL gene was undertaken. Y chromosome microdeletion and rearrangement was seen in 11.5% men. Deletion of AZF regions and AZFb and AZEc regions was detected in 12 azoospermic samples and in 4 of them the deletions were very large involving also the heterochromatin region. CAG repeats in the mtDNA polymerase gene (POLG) were found to be involved in male infetility. Around 83% azoospermic men had homozygous wild type allele. Deletion of one or more copies of DAZ gene was seen in 63 men, 14.52% of whom were azoospermic, 25% were oligospermic and 12.5% were oligoteratozoospermic. Novel mutations in DAZL gene were observed in 5 azoospermic men.

Single Nucleotide Polymorphisms (SNP) in ICAM1 & TNFα among the Jarawa in A & N Islands

A survey of DNA sequence variation in two functionally coding regions *i.e.* genes coding

for tumor necrosis factor α (TNFα) and intercellular adhesion molecule 1 (ICAM1) was conducted among *Jarawas*, a negrito tribe of Andaman & Nicobar Islands by the RMRC, Port Blair. Both these genes play important roles in a variety of human diseases. Genomic DNA was isolated from blood samples of 35 *Jarawas* and amplified and sequenced. A total of six polymorphic sites were detected in the TNF-α gene, of which two single nucleotide and one insertion/deletion (indel) polymorphisms present in gene have already been reported. Three new polymorphisms have been detected in *Jarawas*.

The only exonic (exon4 and 3' UTR) SNP found in TNF-α harbours an A to C transversion while the remaining five changes lie either in upstream regions of the gene or in intron.

Four SNPs were detected in genomic region coding ICAM1. Like the SNPs present in TNF-α, the frequencies of ICAM1 SNPs are also moderate to high. A total of eight haplotypes were observed, of which HT-1 and 2 are equally frequent. Except for one haplotye (HT-8), all haplotypes occur more than once in *Jarawa* gene pool. All ICAM1 haplotypes can be joined sequentially by single site mutational difference, though the possibility of recombination in this gene cannot be ruled out. The major observations emerging from the pattern of sequence variability of TNF-α and ICAM1 genes in *Jarawas* are: (1) there is low DNA sequence variability, (2) rare SNPs are absent, (3) the group harbours new SNPs, and (4) there is restricted variation in haplotypes.

Mobile Workshops in Genetics

Mobile workshops were organized in Maharashtra for students in human genetics.

HANDIGODU SYNDROME

Handigodu syndrome is a peculiar disease of the osteoarticular system found in Shimoga and Chikmaglur districts of Karnataka amongst the *Chennagi* and *Chaluvadi* Scheduled Caste communities. Earlier studies could not attribute the disease to toxicity or nutritional deficiency and stressed need for identification of the gene responsible for the disease. The localisation and characterisation of the gene may provide insight into its pathophysiology and role of calcium nutrition on the course and progression of the disease. Study is being carried out at Bangalore and Mumbai for identifying families with Handigodu disease for mapping and localizing putative gene and for evaluating suitable intervention programme for management of the disease.

The pedigree charts of all the families have been studied and in many of them all 3 generations were found to be affected. Age of onset of disease symptoms was found to be 20-60 yr and atleast one affected parent was identified. The prevalence amongst males and females was found to be equal and almost 50% family members were affected confirming the autosomal dominant pattern of inheritance. The radiological changes were predominantly present in hip joints and spine. The primary change is dysplasia of femoral head epiphyses, usually bilateral. Spinal changes also occur along with changes in knees and wrist joints.

ANTHROPOLOGY

Study on determinants of genetic and socio-cultural aspects of health (*vis-a-vis* role of health providers) among the tribes of coastal, desert and Himalayan regions was carried out at University of Delhi, Delhi. *Dhodias* of Valsad, *Bhils* of Barmer and *Kinnauras* of Kinnaur were found to be in different stages of demographic transition gradually progressing for a better future. *Dhodias* can be considered as most progressive followed by *Kinnauras* and *Bhils*. Morbidity trends were not very clearly defined amongst them. Malaria was not recorded among *Kinnauras* at all but was rampant among *Dhodias* and was seasonal among the *Bhils*. The HbS had a high frequency among *Dhodias* but was not found in *Bhils* and *Kinnauras*. *Dhodias* and *Bhils* also revealed high frequency of problems related with oral cavities, while *Kinnauras* showed comparatively high frequency of fracture and problems related with vertebral column

because of heavy load lifting on back due to steep terrain. Few cases of fluorosis were recorded among *Bhils*. Tuberculosis was more prevalent among *Bhils* and *Dhodias*. Other morbid conditions (water borne and communicable diseases, skin diseases, infections *etc.*) were common among all with varying frequencies.

All the three tribal populations had very strong preference for utilizing the services of traditional healers. These were "*Bhagat-Bhua*" in *Dhodias*, "*Bhope*" in *Bhils* and "*Amchi/Lama*" in *Kinnauras*. As far as providers were concerned, the best situation was observed among *Dhodias* — large number of private practitioners with recognized medical degree were practicing among them. No private practitioners were there in *Kinnauras* and very few in *Bhils*. Government health providers were doing stupendous job in all the three districts. However, scattered populations in Kinnaur and Barmer due to hilly terrains and desert conditions, poor transportation/connectivity and vacant position at various levels hampers effective health care delivery. *Dhodias* also had the highest female literacy but were economically not affluent whereas *Kinnauras* are economically affluent as well as literate. *Bhils* in comparison are neither literate nor economically affluent. Road transport leading to connectivity with the providers is most efficient in *Dhodias* but the *Kinnauras* and *Bhils* have poor connectivity. It can be concluded that health providers are the most important factors in improving the health status of the tribal groups in India.

GERIATRICS

Advanced Centre for Studies on Biochemical Correlates of Aging

Studies were undertaken at University of Hyderabad, Hyderabad to understand the molecular mechanisms of aging process in brain, establish molecular markers for aging process and to take up interventions to retard the progress of aging and certain age associated diseases.

TRADITIONAL MEDICINE

The Centre on Pharmacological Research for Drug Development from Plant Sources in Selected Traditional Remedies at CDRI, Lucknow is focussing on hepato-protective effect of *Picroliv*, wound healing activity of *Centella asiatica* and adaptogenic activity of *Terminalia chebula* as well as its chemical fingerprinting.

Clinical trials and pharmacokinetic studies with Picroliv revealed that response to picroliv therapy is good with no side effects. Phase III double blind multicentric clinical trials in patients with alcoholic cirrhoris and tuberculosis receiving MDT have been initiated at KEM Hospital, Seth GS Medical College, Mumbai. Chemical fingerprinting of *Picroliv* has identified seven compounds *viz*. Catalpol, Piccin, Androcin, Minecoside, 6-O-Feruloyl Catolpol, Cucurbitacin Glucoside-13 and Cucurbitacin Glucoside-21.

Studies on the effect of *T. chebula, Panax ginseng* and its active compound K022 on acute and chronic stress reveled that all these compounds possess potent adaptogenic activity but K022 is more effective than standard *P. ginseng.*

Studies on effect of *C. asiatica* fresh extract on learning and memory and anti-stress activity revealed its potential as memory enhancer. Chemical fingerprinting and stability studies with marker compounds asiaticoside -C and madicassodide revealed that the former was stable for more than two years.

At the Centre for Clinical Pharmacology of Traditional Medicine at BYL Nair Hospital, Mumbai studies are continuing on *Pterocarpus marsupium*, medicated oral rehydration solution (ORS) and Neem oil.

Study is being carried out to elucidate the mechanism of action of *P. marsupium* using experimental aspects such as protection against beta cell damage, effect on angiogenesis, immunomodulatory effects and insulin mimetic activity.

Evaluation of medicated ORS, an *Ayurvedic* formulation containing *Cyperus rotundus* (*Nagarmotha*-whole red kidney beans), *Zinziber officinale* (*Sunthi*) and *Cuminum cyminum* (*Jeerak*) (Fig. 7), was done experimentally and

Cyperus rotundus - root

Zingiber officinalis – rhizome

Cuminum cyminum - seed

Fig. 7. Constituents of medicated oral rehydration solution.

clinically in diarrhoea. The activity of medicated ORS was studied *in vitro* and *in vivo*. Effect of crude extract of *C. rotundus* reduced bacterial translocation in intestine. Only hot extract of *Zinziber officinale* showed dose dependent anti-bacterial activity. It is planned to isolate and identify the most common organisms from stool samples and test the effect of plant extracts on them.

Clinical and *in vitro* studies were conducted with in-house prepared *Neem* formulation, *Neem-b-heal* (commercial) and glycerine-acriflavin (conventional) preparation for its wound healing effect.

Composite wound score and wound area decreased more with in-house *Neem* oil preparation. The best effect of *Neem* was seen on the granulation tissue formation, rate of formation and collagen deposition (Fig. 8). A herbal formulation containing *Neem*, *Aloe vera* and *Calendula officinalis* showed significant increase in angiogenesis.

Studies carried out at AIIMS, New Delhi in experimental models of Alzhiemer's disease in rats suggested that aqueous extracts of *C. asiatica* and *Celastrus paniculatus* can be used as cognitive enhancers in diseases associated with dementia and oxidative stress like Alzheimer's, Parkinson's, Huntington's, Pick's diseases *etc. C. asiatica* and *C. paniculatus* significantly prevented the cognitive impairment, cholinergic deficit and oxidative stress induced by brain glucose

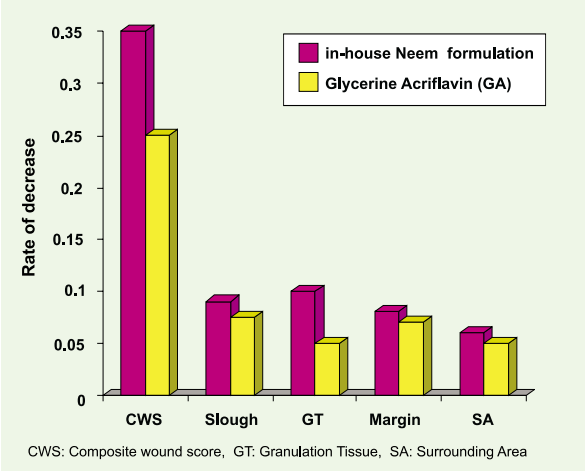


Fig. 8. Rate of decrease in wound score with neem oil formulation.

metabolism impairment in ICV streptozotocin treated rats. The results are in accordance with previous reports that *C. paniculatus* enhances learning and memory.

At the ICMR unit on standardisation, quality control and formulation of traditional medicines at National Institute of Pharmaceutical Education and Research (NIPER), Mohali studies were done on *Streblus asper*, *Crataeva nurvala* and *P. marsupium*. Isolation and purification of alkaloid (cadabacine) from *C. nurvala*, strebloside, mansonin , cannodimethoside and asperoside from *S. asper* and pterostilbene, liquiritigenin, marsupin and propterol from *P. marsupium* (Fig. 9) has been done so far.

Fig. 9. *Pterocarpus marsupium* tree.

CLINICAL PHARMACOLOGY

The Clinical Pharmacology Unit at TRC Chennai carried out studies on malabsorption of rifampicin and isoniazid in HIV infected patients with and without tuberculosis; bio-availability of rifampicin and other anti-tuberculosis drugs in patients with advanced HIV; analysis of generic antiretroviral formulations manufactured in India; vitamin A levels in sputum positive pulmonary tuberculosis patients in comparison with household contacts and healthy 'normals'; standardization of the method for the estimation of ethambutol in pharmaceutical preparations and biological fluids and antibacterial and antimycobacterial activities of compounds from fruits of *Piper longum*.

The study on rifampicin and isoniazid absorption in HIV infected patients with and without tuberculosis revealed malabsorption of these drugs in them. Significant correlation between CD4 counts and urinary level of rifampicin was seen. The results of the study further suggested that D-xylose absorption test in urine can be used to screen HIV infected patients who may not be absorbing rifampicn and isoniazid adequately.

Analysis of generic antiretroviral formulations manufactured in India by Aurobindo Pharma, Ranbaxy and Cipla indicated that the amount of active drug is very similar to medications manufactured in the USA.

Study of vitamin A levels in sputum positive pulmonary tuberculosis patients revealed that vitamin A deficiency is common among them. The study further showed that levels returned to normal following anti-TB treatment (Fig. 10) suggesting that vitamin A supplementation may not be necessary. An association was seen between serum vitamin A levels and sputum smear gradation in patients at the start of treatment.

A simple and accurate method has been developed for determination of ethambutol in urine and in pharmaceutical preparations containing ethambutol alone and in combination. Sensitivity, reproducibility, recovery and stability of the method were found to be very good.

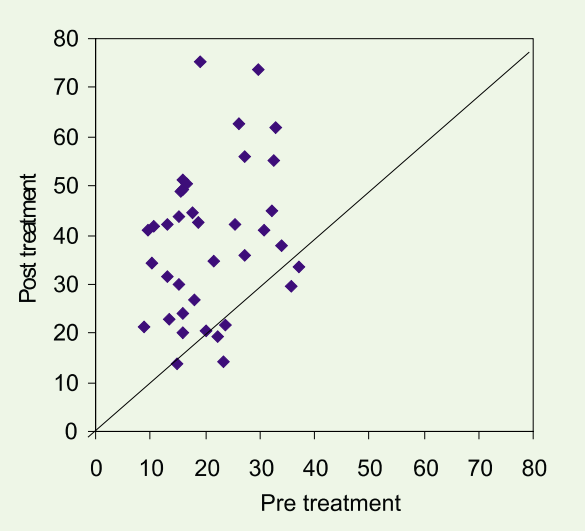


Fig. 10. Serum vitamin A levels at start and end of treatment in pulmonary TB patients.

Studies were continued at Clinical Pharmacology Unit at Seth G.S. Medical College and KEM Hospital, Mumbai for assessing the safety and efficacy of primaquine *vs* bulaquine as gametocidal agents in *P. faciparum* malaria in adults. It was found that at higher doses (60 to 240 mg) bulaquine was more effective than primaquine.

Studies on therapeutic drug monitoring of lamotrigine in epileptic patients was completed to evaluate the relationship between plasma concentration of lamotrigine and its efficacy and toxicity and to identify the therapeutic range of lamotrigine in Indian population.

Studies on menstrual cycle and hormonal changes in women receiving antiepileptic therapy and evaluation of effect of anti- epileptic drugs on bone mineral density and biochemical markers in young Indian epileptic patients are ongoing.

PHARMACOLOGY

Evaluation of the effect of exposure of rats to a pyrethroid based mosquito repellent (containing allethrin) during development was carried out at Industrial Toxicology Research Centre, Lucknow. Neurochemical and neurobehavioural studies indicated that inhalation during early life may lead to significant abnormalities in infants by affecting the CNS. Damage to the brain was long lasting. Further oxidative stress levels in different regions of the brain in pups after prenatal, postnatal and perinatal exposure resulted in significant alterations.

Drug Development through Genomics

In a project completed at CDRI, Lucknow cloning of DNA ligase gene from *Mycobacterium* using PCR technique was done using host strain of *E. coli*.

PRECLINICAL TOXICOLOGY

The Pre-clinical Toxicology Unit at NIN, Hyderabad continued pre-clinical safety assessment of pharmaceuticals having potential therapeutic efficacy; safety assessment of pharmaceuticals having toxic actions on specific organs; pharmacokinetic/pharmacodynamic profile of drugs and regulatory pharmacology.

ORGAN TRANSPLANTATION

Fetal neural cells remain the most widely used graft source for transplantation in rat model of Parkinson's disease. However, low survival and less availability of the fetal tissue as well as the ethical issues associated with use of fetal grafts hinder this approach. These limitations led to development of newer techniques using paraneural cells as substitutes for dopamine and to provide trophic support. Study on cellular and functional recovery of Parkinsonian rats after intrastriatal transplantation of paraneural cells [carotid body (CB) and olfactory ensheating cells (OEC)] was conducted at ITRC, Lucknow.

Paraneural cell aggregates were co-transplanted with fetal ventral mesencephalic cells (VMC). Significant functional restoration in co-transplanted group was seen compared to individual VMC or OEC transplanted group. The results suggest that OECs are rich in various neurotrophic factors while CB cells release large amount of dopamine in hypoxic conditions due to which they can be used as alternate to fetal VMC. Moreover, these cells are also rich in various neurotrophic factors thereby helping in increased survival of transplanted VMCs as well as host dopaminergic neurons.

HAEMATOLOGY

BLEEDING DISORDERS

Risk Factors for Coronary Artery Disease

The project ongoing at IIH, Mumbai brought out a very important association of hyperhomocysteinaemia with coronary artery disease leading to myocardial infarction. Of the total patients studied, 55% were found to have hyperhomocysteinaemia. In 60% of them folic acid therapy lowered the homocysteine levels significantly. It remains to be seen whether folic acid therapy on long term basis can prevent myocardial infarction in these patients.

von Willebrand Disease (VWD)

VWD is an autosomally inherited bleeding disorder. Studies undertaken at IIH revealed that in ~12% of the patients idiopathic menorrhagia occurs due to VWD and in 8% it occurs due to an ancillary coagulation disorder. Antenatal diagnosis of severe VWD by using DNA based technology has been established at this institute.(Fig.11)

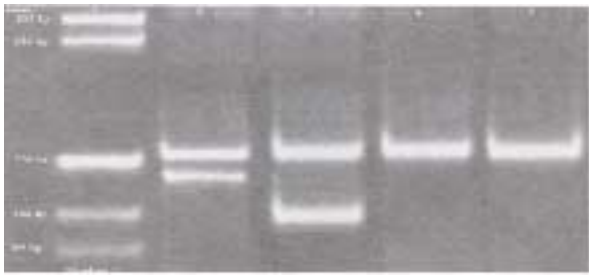


Fig. 11. Prenatal diagnosis in type 3 VWD family.

Hemophilia

Establishment of Prenatal Diagnosis in Hemophilia A and B

Till date prenatal diagnosis has been offered at IIH, Mumbai in 300 pregnancies to patients coming either in first or second trimester from all over India. Affected families were counselled and all of them opted for medical termination of pregnancy. It is an important achievement of IIH as in developing countries it is one of the main approaches of controlling this serious heritable bleeding disorder.

PCR Technique for Detection of Factor IX Gene Mutations

A multiplex PCR technique has been established at IIH to detect mutation for factor IX deficiency. Of the tested patients 10.5% showed the presence of a deletion. This technique will be useful for prenatal diagnosis in families of sporadic cases of hemophilia B.

Human Leucocyte Antigen (HLA) in Chronic Hemophilic Synovitis

Studies were undertaken in 400 hemophilia patients to see whether chronic synovitis in these patients was linked to any particular HLA antigen. Sixty four percent hemophilia patient with chronic synovitis were found to possess HLA – B27 antigen indicating that the risk of getting chronic synovitis in patients having HLA-B-27 is >12.

Molecular Basis of G6PD Deficiency in India

In studies undertaken at IIH, it was found that besides G6PD Mediterranean there are other variants like G6PD Orissa and G6PD Kerala - Kalyan in our country responsible for drug induced hemolysis and neonatal jaundice.

Platelet Antigen Polymorphism in Newborns in India

Molecular technique to detect human platelet alloantigen system (HPA 1 – HPA 8) was standardized at IIH. The population distribution of these antigens in Western India has been worked out. Several neonatal alloimmune thrombocytopenic purpura (NAITP) patients were detected and helped by proper intervention.

HAEMOGLOBINOPATHIES

Jai Vigyan Mission Mode Project on Community Control of Thalassemia

The multicentric project on community control of thalassemia syndromes aims at education, screening, counselling and identifying

couples at risk of having thalassemic children so as to prevent birth of these children and to develop a national referral centre for control of thalassemia major in the country. Study is being carried out on college students and pregnant women in Maharashtra, Gujarat, Assam, West Bengal, Punjab and Karnataka.

A total of 21645 cases (10673 college students and 10972 antenatal cases) have been screened till date. The results showed that majority of students had no knowledge about the disease. In Kolkata and Vadodara centres 40-50% students knew only the name of the disease. The maximum percentage of iron deficiency was seen in females from Dibrugarh (40%) and Kolkata (27%). The prevalence of β-thalassemia trait varied from 2 to 4%, Hb E was predominantly seen in Dibrugarh and Kolkata whereas HbD was found in Ludhiana. The prevalence of anemia varied from 78% to 93%. Iron deficiency based on FEP levels ranged from 29 to 41%. The prevalence of iron deficiency varied from 17-69% in β–thalassemia carriers.

Molecular Characterization of δβ Thalassemia and Herediatary Persistence of Foetal Haemoglobin (HPFH)

A gap PCR approach was used for molecular characterization of patients who were phenotypically characterized for thalassemia. Eight out of 30 cases were heterozygous for 48.5 Kb Indian deletion (HPFH-3), 11 were heterozygous for Asian Indian inversion deletion Gγ (Arδβ) thalassemia and 4 were found to be heterozygous for Vietnamese deletion (12.5Kb). Seven cases still remain uncharacterized.

POPULATION GENETICS

Molecular Characterization of Bombay Phenotype

Thirty eight serologically confirmed Bombay phenotype samples were investigated for detecting the T 725 G mutation in the H (FUT 1) gene. All samples except two showed T 725 G mutation.

STEM CELL BIOLOGY

Umbilical Cord Blood Stem Cells and their Expansion ex vivo

Different conditioning media (PCM, GF 1, GF 2 and stromal cells +GF2) were used for *ex vivo* expansion of CD 34 +ve umbilical cord cells at IIH. It was found that GF 2+ stromal cells provided the maximum expansion (10 fold) over 14 days (Fig. 12). Besides this cryopreservation of stem cells with different agents was tried and an optimum cryoprotectant xixture for this purpose has developed.

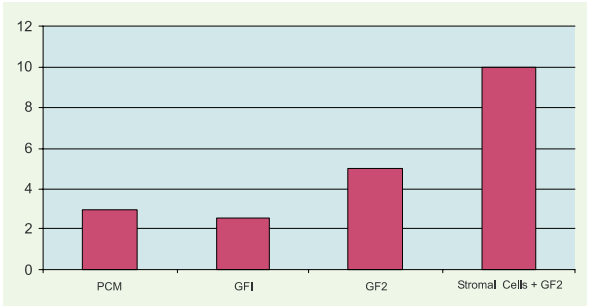


Fig. 12. Total expansion of CD34 in umbilical cord stem cells with different media.

OTHER STUDIES

Cytogenetic Factors in Myelodysplastic Syndrome (MDS)

In India most of the patients of MDS present as young adults (20-40 yr). Cytogenetic studies and mitomycin C test (for chromosomal fragility) was conducted on 27 MDS patients. Atypical cytogenetic abnormalities were seen in 40% (Fig.13 & 14) and increased chromosomal breakages in 45% of these patients.

HLA Association with HIV-1 Infection

HLA class I allele frequency was tested in 38 HIV-1 positive patients and compared with 120 matched controls. HLA B*3520, B*1801 and Cw*1507 alleles were found to be uniquely associated with HIV.

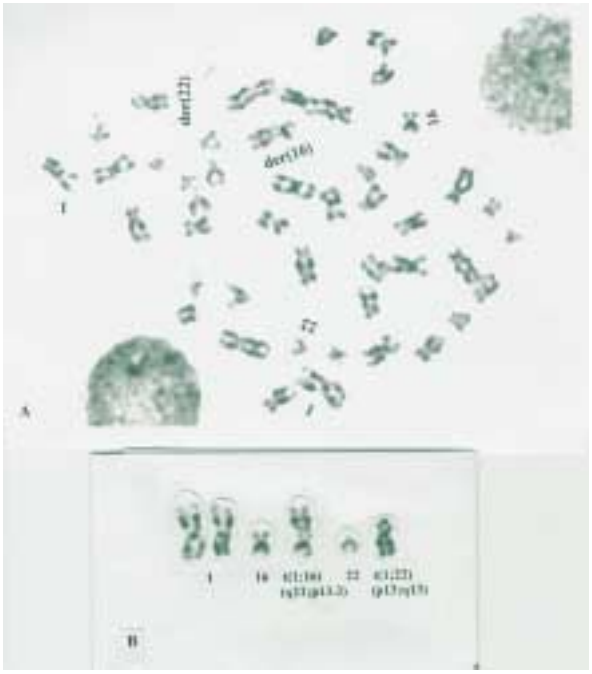


Fig. 13. Atypical cytogenetic abnormalities in MDS patients.

Fig. 14. Chromosomal breakage seen in MDS patients.

HAEMOGLOBINOPATHIES/BLOOD DISORDERS AMONG TRIBALS

Nutritional Anaemia and Haemoglobinopathies amongst Tribal Populations of India

A multicentric intervention programme on nutritional anaemia and hemoglobinopathies amongst some primitive tribal populations of India is ongoing in four states (Maharashtra, Gujarat, Orissa and Tamil Nadu).

A total of 11511 individuals from the primitive tribal groups of *Katkaris, Madias, Kotvadias, Kolchas, Irulas, Kurumbas, Molukurumbas, Paniyas, Bondos and Didayis* were clinically examined. Mild to moderate anaemia was found to be more common in all the tribes and the females were more anaemic than males. Iron deficiency anaemia was found to be very high among *Juangas* followed by *Didayis, Bondos, Irulas, Madias, Kurumbas, Katkaris, Paniyas, Kolchas Kolams, Kotvadias, Moolu kurumbas* and *Kathodis* (Fig.15) A higher percentage of sickle cell trait and homozygotes was found among the *Madias, Paniyas, Irulas, Kurumbas and Moolu Kurumba* tribal groups, whereas β-thalassemia trait was more common among the *Kolchas, Katkaris, Juangas, Didayis, Bondos* and *Kolams* (Fig. 16). G6PD deficiency was found in all the tribals. Iron deficiency anaemia was also found to be very common among the sickle cell anaemia, sickle cell trait and β-thalassemia trait cases. Prevalence of malaria was found to be high in cases with sickle cell trait, sickle homozygotes, β-thalassemia trait and G6PD deficiency. Hepatosplenomegaly was found to be common in AS, SS and β-thalassemia cases.

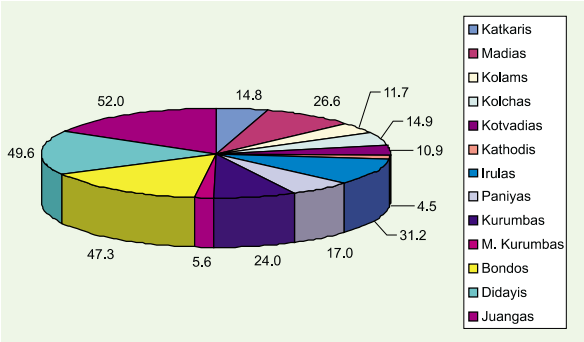


Fig. 15. Prevalence of iron deficiency anaemia in different tribal groups.

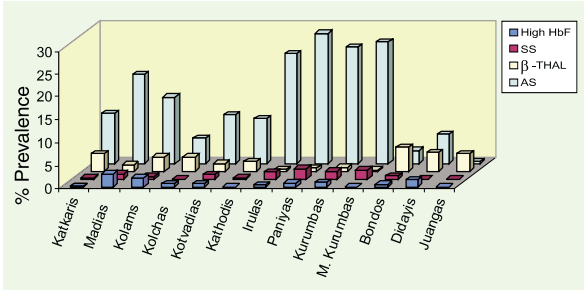


Fig. 16. Haemoglobinopathies in different tribal groups.

Intervention and follow up is continuing in nutritional anaemia and sickle cell anaemia cases. Folic acid and Fersolate tablets have been given to cases of nutritional anaemia and sickle cell disease without iron deficiency. Sickle cell anaemia patients were advised to take electral powder and plenty of fluid during vaso-occlusive crisis. An improvement in Hb and reduction in FEP levels was observed in cases taking tablets regularly. Hepatitis, *H. influenzae* and pneumococcus vaccines were given to sickle cell anaemia cases. Report Cards were distributed to all the individuals whose blood was tested. Genetic counselling was given to the unmarried young individuals to avoid marriage between carriers of haemoglobinopathies particularly Hbs and β-thalassemia and young carrier couples have been advised to come for prenatal diagnosis.

Haemoglobinopahies among Scheduled Castes and Scheduled Tribes of Madhya Pradesh

Genetic mapping of the haemoglobinopathies was done among the scheduled tribes (ST) and scheduled castes (SC) of Shahdol district by the RMRC, Jabalpur. Studies revealed that sickle haemoglobin is the main form of haemoglobinopathy in them with very high prevalence in *Panika* tribe (28.6%) (Fig.17). Most of the sickle cell disease patients have mild to moderate anaemia and high level (10-15%) of fetal haemoglobin. Prevalence of anaemia is very high in *Gond* and *Baiga* tribes (70-80%) as compared to *Panikas* and *Chaudharys* (55%).

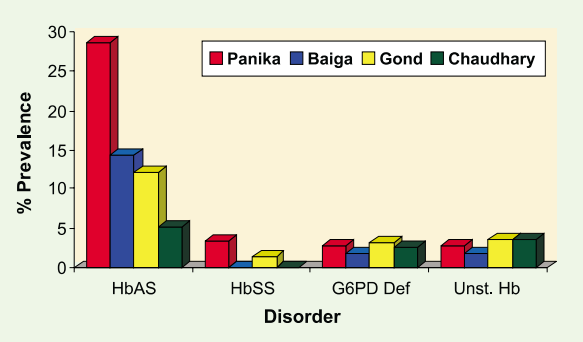


Fig. 17. Genetic disorders among STs and SCs in Shahdol district.

A semi-longitudinal study on sickle cell disease patients revealed that painful crisis, fever and abdominal/splenic pain are the common clinical manifestations. About 10% of patients had massive spleen (>9 cm), requiring multiple blood transfusions. Most (70-80%) of these patients *i.e.* aged upto 15 yr showed moderate to severe growth retardation.

Supporting Facilities

Biostatistical and epidemiological studies were conducted at Council's National Institute of Epidemiology (NIE), Chennai and Institute for Research in Medical Statistics (IRMS), New Delhi as during the past.

The Council co-ordinates collaboration in biomedical research between India and other countries/international agencies. During 2003-04 various international meetings were organized and visits of scientists were arranged under joint projects and bilateral programmes.

Advice and assistance on intellectual property rights issues is being provided to ICMR's scientists by an IPR Cell in the Council. Besides this, training programmes/workshops are conducted by all the ICMR institutes in diverse areas for the benefit of biomedical scientists, doctors, technicians and students.

NATIONAL INSTITUTE OF EPIDEMIOLOGY (NIE), CHENNAI

Field Epidemiology Training

At the Institute two-year field Epidemiology Training Programme (FETP) leading to Master of Applied Epidemiology (MAE) is ongoing since 2001. Four batches are currently attending the programme. Training on basic concepts of epidemiology and biostatistics was imparted to them during the first contact session of three months from January 2004. All the scholars of the 3rd cohort successfully completed the second contact session at NIE and are on field assignments. All the six scholars of the 2nd cohort completed their course requirements and submitted their bound volumes and dissertations. Two scholars from the first cohort have completed all the course requirements including viva-voce examination for the MAE-FETP course.

Outbreak Investigations

The NIE was involved in the investigation of an outbreak of cholera among inmates of a care Centre in Thirumullaivayil, Chennai in September 2003.

Clinical Trial for Diabetes Mellitus

A multicentric flexible dose open trial is ongoing at Chennai, Cuttack, Kottayam and New Delhi to assess the effect of *Vijayasar* on patients with type 2 diabetes uncontrolled by allopathic oral hypoglycemic drugs and in those who opted for *Vijayasar* treatment.

Clinical Trial for Chronic Hepatitis C

Study is ongoing to assess the effect of combination therapies of interferon-glycyrrhizin and interferon-ribavirin on chronic hepatitis C in Indian patients.

Other objectives of the study include evaluation of side-effects / toxicity of the trial drugs, cost effectiveness of therapies and role of factors like genotype, viral load, cost factor *etc*. in deciding the outcome of therapy.

The study is continuing at nine centres-Chandigarh, New Delhi (3 centres), NOIDA, Lucknow, Kolkata, Mumbai and Hyderabad. Total duration of the trial is three years. The intake to the trial is expected to be completed in 1½ years. The follow up of all patients is ongoing.

Leprosy Vaccine Trial

The NIE is the international co-ordinating centre for the multicentric trial to assess the efficacy and effectiveness of 6 month MDT for all types of leprosy. The trial is being conducted at four centres in India and one centre in China with the objective of closely monitoring response in terms of an acceptable cumulative level of 5% relapse rate at the end of five years.

Psycho-social Challenges faced by HIV Positive Persons

Study is ongoing at NIE to understand the impact of HIV positive status, personally, emotionally and socially on the HIV infected

individuals. Data collection has been completed for 460 HIV infected persons through in-depth interviews and further work is going on.

Epidemiological Profile of Acute Lower Respiratory Tract Infection (ALRI) among Pre-School Children in South India

Study was carried out in 787 children (>5 yr) from seven *panchayat* blocks of Sriperumbudur taluk near Chennai to find out the epidemiological profile of ALRI in rural childern, to identify etiological agents of ALRI and to understand the risk factors for ALRI in rural community.

All the children were followed up twice a week through door-to door visits by trained para medical workers for symptoms of ARI. All the children with one / more symptoms of ALRI were followed up daily to detect and treat pneumonia at eary stage. During 8 weeks surveillance 656 / 787 children had one episode of ARI. Only one child had two episodes. Out of 656 ARI episodes 23 progressed to ALRI. All ALRI cases except one was given home care. One child with bilateral broncho-pneumonia was referred to hospital for treatment.

Modified Life-tables for India and Tamil Nadu using Decennial Censuses (1961-2001)

The life tables for India during each decadal census from 1961 till 2001 by age, sex, rural and urban were constructed. The results suggest that for India there is definite improvement in expectation of life over every decadal census. The increase in expectation of life is more in the younger ages. Similar results were found for Tamil Nadu. However, the expectation of life at birth for both the sexes is higher for Tamil Nadu when compared to rest of India.

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

End Line Evaluation of India Population Project VIII

The IRMS was entrusted with the evaluation of India Population Project VIII by the Ministry of Health and Family Welfare. The Institute was the nodal agency for providing technical expertise for conducting the study, supervising the work of the field agencies and conducting 5% sample checks. The Institute organized a series of Workshops for capacity building of state level agencies. The project aimed to provide integrated health and family welfare services to urban slum populations and strengthen linkages between family welfare services and other interventions in slums of four metropolitan cities *viz.* Bangalore, Kolkata, Delhi and Hyderabad. The aim of the end line survey was to evaluate the inputs/ strengths used for implementation of the project. A stratified multi-stage sampling design was used to select the households and for the assessment of health infrastructure. All the health facilities constructed were found to be located at the appropriate place serving the community as well as the staff managing the health facilities. The facilities were well equipped though the survey showed the need for necessary equipments. Use of inventory list by health facility was suggested for providing and allocating equipments.

It was found that the project resulted in capacity building of the staff such as medical officers, para-medical staff, link volunteers, *Anganwadi* workers *etc.* Besides, the project made efforts to create demand for family welfare services through the area specific IEC activities in collaboration with local NGOs, private medical practitioners and medical colleges. The study found that IEC activities led to incease in utilization of the services. Interpersonal communication was found to be the best channel for conveying the messages. The project has established a monitoring mechanism. All the cities adopted innovative schemes as per the demand of the community.

There was decline in total fertility rate (TFR) and infant mortality rate (IMR) in four cities. Though the knowledge of family planning methods was high, the contraceptive prevalence varied in these cities. Knowledge regarding RTI/ STD was low. Morbidity due to vaginal discharge and post abortion problems was also reported. Overall the end line evaluation found that the project was able to reach its objectives, though there was scope for strengthening the services created by the project.

Usage and Acceptability of Indian Systems of Medicine and Homoeopathy

The Department of Indian Systems of Medicine and Homoeopathy of MOHFW entrusted the study on usage and acceptability of Indian systems of medicine and homoeopathy to IRMS. The study covered 35 districts spread over 19 states consisting of high and low utilization areas. From 16 major states, two districts have been selected whereas one district each was covered from two states *viz*. Manipur and Tripura. It was observed that 33% sick persons availed ISM & H in normal ailments whereas only 14% availed it for serious ailments. The major reason for the non preference was slow progress of the treatment and non availability of the practitioners. Traditional healers were consulted mainly for bone setting, dogbite, snakebite and jaundice. Most of the households suggested opening new government dispensaries.

ICMR LIBRARY NETWORK

The facilities and infrastructure of the Council's library and information network are being modernized/ upgraded. For optimal utilization of journals subscribed by all ICMR libraries, the Council has subscribed the JCCC (J- Gate Custom Content for Consortia), an e-journal gateway-cum-database. The Union Catalogue of Journals in ICMR libraries has been compiled by the Council for the better utilization of journal resources available in ICMR libraries for the benefit of scientists. Manual of procedures for management of libraries and information centres has been prepared to streamline the procedures in ICMR library and information centres.

INDO-FOREIGN COLLABORATION

The ICMR coordinates international collaboration in biomedical research between India and other countries/international agencies. During the year 2003-04, many international meetings between scientists from India and France, Germany, USA and Russia were facilitated (with financial support). A total of 36 exchange visits of scientists to and from India were arranged by the Council under various joint collaborative projects / programmes.

During the year, a number of meetings of Health Ministry's Screening Committee (HMSC) were organized, wherein 55 projects for international collaboration / assistance were approved by the Indian side.

Under new initiatives undertaken by the Council during the year 2003-2004 ICMR International Fellowships were established for young and senior biomedical Indian scientists as well as for scientists from developing countries. With the view of interaction and exchange of scientific information between Indians and persons of Indian Origin (PIOs) from various countries, a Scientific Advisory Committee (SAC-Overseas) was constituted.

The activities relating to the WHO biennium programme under country budget for the biennium 2002-2003 were coordinated and processed.

INTELLECTUAL PROPERTY RIGHTS

A total of nine patents have been filed at the Indian Patent Office and one patent was filed at the United States Patent and Trademark Office (USPTO) during the period under report. One patent on anti-malarial drug, titled, "A new tissue schizontocidal and gametocidal drug in the treatment of malaria" is likely to be granted by the Indian Patent Office. With the assistance of WHO the IPR Unit organised an Expert Consultation on IPR & WTO Issues and discussed the proposed negotiations at Cancun (Mexico) Ministerial meeting of the WTO. The final reports of three WHO supported projects on IPR and WTO issues are being compiled.

Steps have been initiated to establish the Regulatory Authority for Medical Devices (IMDRA) in the country.

BIOMEDICAL ETHICS

Attempts are being made to develop an accreditation system for ethical review in different

medical institutions of the country. Curriculum is being developed in medical bioethics for medical schools and universities and prepration of teaching material for training programmes is ongoing. During the year under report training workshops were conducted for researchers, sponsors and policymakers in the field of biomedical ethics.

TRAINING PROGRAMMES

Various institutes of the Council continued to provide referral services in their field of speciality such as viral diseases, nutrition, occupational health, haematology, pathology, *etc.* Training programmes and workshops were also organized by them in their areas of expertise during the year under report.

ICMR Awards and Prizes 2001

The Indian Council of Medical Research awarded the following prizes to Indian scientists for outstanding research in various fields of biomedical sciences:

DR. B.R. AMBEDKAR CENTENARY AWARD FOR EXCELLENCE IN BIOMEDICAL RESEARCH

Prof. T. Jacob John
Former Head
Department of Virology
Christian Medical College
Vellore

Life time achievement award
(Pulse Polio Immunization)

BASANTI DEVI AMIR CHAND PRIZE, 2002

Prof. S. Majumdar
Professor and Head
Department of Experimental
Medicine and Biotechnology
Postgraduate Institute of Medical Education
and Research
Chandigarh

Molecular Biology
(Molecular basis of pathogenesis
of disease process)

CHATURVEDI KALAWATI JAGMOHAN DAS MEMORIAL AWARD

Dr K. Shivakumar
Scientist 'E'
Division of Cellular and Molecular Cardiology
Sree Chitra Tirunal Institute for
Medical Sciences and Technology
Thiruvananthapuram

Cardiovascular Diseases
(Myocardial fibrosis in response to
cerium and magnesium deficiency)

DR. KAMALA MENON MEDICAL RESARCH AWARD

Dr Amita Aggarwal
Associate Professor
Department of Clinical Immunology
Sanjay Gandhi Postgraduate Institute of
Medical Sciences
Lucknow

Paediatrics
(Juvenile idiopathic arthritis)

KSHANIKA ORATION AWARD

Dr Ashima Anand
Principal Scientific Officer
DST Centre for Visceral Mechanisms
V.P. Chest Institute
Delhi University Campus
New Delhi

Physiology
(Cardio-respiratory control mechanisms)

JALMA TRUST FUND ORATION AWARD

Dr E. Daniel
Head
Department of Ophthalmology
Schieffelin Leprosy Research and Training Centre, Karigiri
Vellore

Leprosy
(Ocular leprosy)

AMRUT MODY UNICHEM PRIZE

Prof. S.K. Sarin
Professor and Head
Department of Gastroenterology
G.B. Pant Hospital New Delhi

Gastroenterology
(Management of chronic hepatitis and cirrhosis)

Prof. (Brig) Sunder Lal
Professor and Head
Department of Social and Preventive Medicine
Postgraduate Institute of Medical Sciences
Rohtak

Maternal & Child Health
(Integrated Child Development Services in rural areas)

CHATURVEDI GHANSHYAM DAS JAIGOPAL MEMORIAL AWARD

Prof. Rakesh Bhatnagar
Chairman
Centre for Biotechnology
Jawaharlal Nehru University
New Delhi

Immunology
(Development of recombinant anthrax vaccine)

DR. PREM NATH WAHI AWARD

Dr Ravindran Ankathil
Associate Professor
Division of Cancer Research
Regional Cancer Centre
Medical College Campus
Thiruvananthapuram

Cytology and Preventive Oncology
(Cytogenetic studies in cancer)

DR D.N. PRASAD MEMORIAL ORATION AWARD

Prof. Y.K. Gupta
Professor in Pharmacology
All India Institute of Medical Sciences
New Delhi

Pharmacology
(Evaluation of drug action in various neurodegenerative diseases)

SHAKUNTALA AMIR CHAND PRIZES

Dr Sanjay Jain
Associate Professor
Department of Internal Medicine
Postgraduate Institute of Medical Education and Research Chandigarh

Internal Medicine
(Takayasu's arteritis- an enigmatic disease)

Dr Ravinder Goswami
Assistant Professor
Department of Endocrinology and Metabolism
All India Institute of Medical Sciences
New Delhi

Endocrinology
(Studies on autoimmune endocrine disorders)

Dr U.C. Ghoshal
Assistant Professor
Department of Gastroenterology
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Lucknow

Gastroenterology
(Studies on portal hypertension)

Dr Harpreet Kaur
Senior Research Officer
Indian Council of Medical Research
New Delhi

Parasitology
(Giardiasis)

MAJOR GENERAL SAHEB SINGH SOKHEY AWARD

Dr M.V. Murhekar
Deputy Director
Regional Medical Research Centre
Port Blair

Tribal Health
(Viral Hepatitis among tribes of Andaman & Nicobar Islands)

ICMR Permanent Institutes/Centres

1. Central JALMA Institute for Leprosy
   Taj Ganj
   Agra 282001

2. National Institute of
   Occupational Health
   Meghani Nagar
   Ahmedabad 380016

3. National Institute of
   Epidemiology
   1, Sathyamurthi Road
   Chetput
   Chennai 600031

4. Tuberculosis Research Centre
   Mayor V.R. Ramanathan Road
   (Spurtank Road)
   Chetput
   Chennai 600031

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

6. National Institute of Nutrition
   Jamai Osmania
   Hyderabad 500007

7. Food and Drug Toxicology
   Research Centre
   National Institute of Nutrition
   Jamai Osmania
   Hyderabad 500007

8. National Centre for
   Laboratory Animal Science
   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

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

11. Enterovirus Research Centre
Haffkine Institute Campus
Acharya Donde Marg, Parel
Mumbai 400012

12. National Institute for Research in
Reproductive Health
Jehangir Merwanji Street
Parel
Mumbai 400012

13. ICMR Genetic Research Centre
B.J. Wadia Hospital for Children
Acharya Donde Marg
Parel
Mumbai 400012

14. Institute of Immunohaematology
13th Floor, New Multistoreyed Building,
K.E.M. Hospital Campus,
Parel
Mumbai 400012

15. Institute for Research in
Medical Statistics
ICMR Head Quarters Campus
Ansari Nagar
New Delhi 110029

16. Institute of Cytology and
Preventive Oncology
Maulana Azad Medical College
Campus,
Bahadur Shah Zafar Marg
New Delhi 110002

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

18. Rajendra Memorial Research
Institute of Medical Sciences
Agamkuan
Patna 800007

19. Vector Control Research Centre
Medical Complex
Indira Nagar
Gorimedu
Pondicherry 605006

20. 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
Post Box No.11
Pune 411001

Regional Medical Research Centres

1. Regional Medical Research Centre
   Nandankanan Road
   P.O. Chandrasekharpur
   Bhubaneswar 751016

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

3. Regional Medical Research
   Centre for Tribals
   Medical College Campus
   Nagpur Road
   P.O. Garha
   Jabalpur 482003

4. Desert Medicine Research Centre
   P.O.Box No. 122
   New Pali Road
   Jodhpur 342005

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

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

ICMR Centres for Advanced Research

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

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

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

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

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

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

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

8. Advanced Centre for Liver Diseases
   G.B. Pant Hospital
   New Delhi 110002

Training Programmes Conducted by ICMR Institutes during 2003-2004

Diarrhoeal Diseases

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

- Domestic Training Programme on Molecular Epidemiology of Diarrhoeal Diseases with Special reference to Cholera (November 3-12, 2003)
- Third Country Training Programme on Molecular Epidemiology of Diarrhoeal Diseases with Special reference to Cholera (January 13-26, 2004)

Immunization

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

- Training Prgrammes on Immunization Strengthening Project (July 21-26; August 4-9; August 18-23; September 8-13 and September 22-27, 2003)

Leptospirosis

At the Regional Medical Research Centre, Port Blair:

- Hands-on Training Workshop on Laboratory Diagnosis of Leptospirosis (September 17-30, 2003)

Leishmaniasis

At the Rajendra Memorial Research Institute of Medical Sciences, Patna:

- Advanced Training Course on Immunology of Leishmaniasis (January 23-February 13, 2004).
- Advanced Training Course on Microbiology and Molecular Biology of Leishmaniasis (February 16 - March 15, 2004).

Medical Entomology

At the Vector Control Research Centre, Pondicherry:

- Postgraduate Diploma in Medical Entomology (from August 6, 2003)

HIV/AIDS

At National AIDS Research Institute, Pune:

- Regional Workshop on Quality Assurance in Laboratory Methods in HIV (WHO sponsored) (November 24-28, 2003)

Reproductive Health

At the National Institute for Research in Reproductive Health, Mumbai:

- Workshop on Insertion and Management of Complications with IUCDs (April 21-April 30, 2003)
- Training Course on Gynaecological Cytology and Colposcopy (April 21-May 2, 2003)
- Workshop on Obstetrics and Gynaecological Ultrasonography (August 25-29, 2003)

Nutrition

At the National Institute of Nutrition, Hyderabad:

- M.Sc. in Applied Nutrition (June 16, 2003-March 15, 2004)
- Training Course on Techniques for Assessment of Nutrition Anaemias (December 1-12, 2003)
- Postgraduate Certificate Course in Nutrition (January 1-March 12, 2004)

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Certificate Course on Endocrinological Techniques and their Application (August 11-September 19, 2003)

Occupational Health

At the National Institute of Occupational Health, Ahmedabad:

- Workshop on Environmental and Occupational Epidemiology (January 13-16, 2004)

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Blood Group Serology and Blood Bank Methodology for Blood Bank Technicians (February 17-March 17, 2004)
- Training Course in Transfusion Medicine for Blood Bank Medical Officers (February 17-March 31, 2004)
- Training Course in Advanced Haematology and Immunohaematology (April 19-30, 2004)

Research Methodology/Biotechnology

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

- Hands on Training in Biotechnology for Graduate Students (July 2003)

Genetics

At Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow:

- Short-term Course in Genetic Counselling (February 9-21, 2004)

Biomedical Statistics/Epidemiology

At the National Institute of Epidemiology, Chennai:

- Basic Course in Statistics for Medical Doctors (September 2003)
- Training Course on Controlled Clinical Trials (September 2003)
- Training Course in Field Epidemiology (January 2004; for 2 years)

At the Institute for Research in Medical Statistics, New Delhi:

- Training Course in Research Methodology - Clinical Trials (July 21-25, 2003)
- Training Course in Statistical Methods in Epidemiology (March 15-20, 2004)

Laboratory Animal Technology

At the National Centre for Laboratory Animal Science, National Institute of Nutrition, Hyderabad:

- Training Course for Laboratory Animal Technicians (June 14 - July 31, 2003).

- Training Course for Laboratory Animal Supervisors (September 1 - November 28, 2003).

Biomedical Communication

- Training Programmes in Biomedical Communication at (i) Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow (August 30-31, 2003); (ii) Mahatama Gandhi Institute of Medical Sciences, Sevagram (September 29-October 1, 2003); (iii) Karnataka Institute of Medical Sciences, Hubli (February 25-26, 2004) and (iv) Dayanand Medical College, Ludhiana (March 27-28, 2004).

- Training Workshop for ICMR Librarians and Scientists on full text e-databases acquired by the Council for ICMR Libraries at NIN, Hyderabad (July 26, 2003) and ICMR Hqrs., New Delhi (December 4, 2003).

Intellectual Property Rights

- Workshop on IPR and WTO Issues at NIN, Hyderabad (October 16-17, 2003); CJIL, Agra (November 22-23, 2003); Regional Occupational Health Centre(s), Bangalore (December 18-19, 2003); and RMRC, Jabalpur (February 16-17, 2004).

Seminars/Symposia/Conferences/Workshops

The following ICMR aided Symposia/Seminars/Workshops/Conferences were held during 2003-04

Title	Dates	Organisers
III Biennial Conference on Indian Association of Hyperthermic Oncology and Medicine	April 5-6, 2003	Smt. Sarojben Centre for Hyperthermic Oncology & Medicine Dr. Balabhai Nanavati Hospital & Medical Research Centre Mumbai
CSIR Diamond Jubilee Symposium on Rasayana Drugs	August 7-8, 2003	Central Drug Research Institute Lucknow
Symposium on Molecular Maneuverings in Biological Defense Systems	August 8-10, 2003	Sri Sathya Sai Institute of Higher Learning Prasantinilayam Anantapur
National Seminar on Medicinal Plants and Health Care	August 27-28, 2003	PSGR Krishnammal College for Women Coimbatore
National Seminar on Modern Biology	August 28-30, 2003	Nagarjuna University Guntur
Conference of Medical Microbiologists (Maharashtra Chapter)	September 6-7, 2003	Armed Forces Medical College and Command Hospital Pune
International Symposium on Current Trends in Cancer	September 21-28, 2003	Maulana Azad Medical College and Associated Hospitals New Delhi
Annual Conference of the International Medical Science Academy	September 26-28, 2003	K.J. Hospital Chennai
II National Conference of Indian Academy of Pediatrics	September 27-28, 2003	Indian Academy of Paediatrics (West Bengal Branch) Kolkata
CME and I Annual Meeting of North India Anatomists Federation	October 4-5, 2003	Postgraduate Institute of Medical Education & Research Chandigarh
CME-cum-Workshop on an Update on Diagnostic Techniques for Parasitic Diseases	October 6-9, 2003	Postgraduate Institute of Medical Education & Research Chandigarh
Seminar on I Nutraceutical Summit	October 8-10, 2003	Central Food Technological Research Institute Mysore

Title	Dates	Organisers
V National Congress on Pediatric Critical Care	October 10-12, 2003	Amruta Hospital Surat
Workshop on Research Methodology in Health / Medical Sciences	October 11-12, 2003	Rural Medical College of Pravara Medical Trust Ahmednagar
Workshop on Medicinal Plants - Perspectives, Prospects and Challenges	October 11-12, 2003	Gandhigram Rural Institute (Deemed University) Gandhigram
IV Annual National Conference of Leptospirosis Society	October 13-15, 2003	Sher-I-Kashmir Institute of Medical Sciences Srinagar
National Symposium on Biotechnology Expanding Horizons	October 17-18, 2003	Acharya Narendra Dev College University of Delhi Delhi
Workshop on Diagnosis and Management of Leprosy in the Context of Integration of Leprosy Programme with General Health Services	October 19, 2003	Central JALMA Institute for Leprosy Agra
XV National Symposium on Chronobiology	October 20-21, 2003	Pt. Ravishankar Shukla University Raipur
XII National Conference of Indian Association of Oral and Maxillofacial Pathologists	October 31-November 2, 2003	Dental College Maulana Azad Medical College New Delhi
XVIII National Conference of Federation of Operative Dentistry of India and XI National Conference of India Endodontic Society	November 1-3, 2003	Institute of Medical Sciences Banaras Hindu University Varanasi
XXIV Annual Conference of Indian Association of Biomedical Scientists	November 1-4, 2003	Institute of Nuclear Medicine & Allied Sciences Delhi
XVII Carbohydrate Conference	November 5-7, 2003	Indian Association for the Cultivation of Science Jadavpur University Kolkata
International Symposiumm on Molecular Toxicology and Environmental Health	November 5-8, 2003	Industrial Toxicology Research Centre Lucknow
National Seminar on New Millennium Strategies on Quality, Safety and GMPs of Herbal Drugs/ Products	November 11-13, 2003	National Botanical Research Institute Lucknow
Symposium on Molecular Modulation by Oxidative Stress and Cell Function	November 20-22, 2003	Panjab University Chandigarh

Title	Dates	Organisers
25th Annual Conference of Association of Radiation Oncologists of India	November 20-23, 2003	Government Medical College Thrissur
69th Annual Meeting of the Indian Academy of Sciences	November 21-23, 2003	Indian Institute of Technology Guwahati
XXX Annual Conference of Indian Immunology Society and Symposium on Immunology from Laboratory to Clinic	November 23-25, 2003	Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
VII Conference of International Biometric Society	November 23-27, 2003	Banaras Hindu University Varanasi
Workshop on Cellular and Molecular Physiology	November 24-29, 2003	All India Institute of Medical Sciences New Delhi
World Congress on Prosthodontics and 31st Indian Prosthodontic Society Congress	November 26-29, 2003	Maulana Azad Medical College and Associated Hospitals New Delhi
Workshop on Adjunct Techniques in Cytology	November 27, 2003	Armed Forces Medical College and Command Hospital Pune
National Seminar on Recent Advances in Stress Physiology, Toxicology and Immunology	November 27-28, 2003	University of Kalyani Kalyani
National Symposium on Current Trends in Comparative Endocrinology : Impact of Biology and Biotechnology	November 27-29, 2003	Nagpur University Nagpur
XXI Annual Conference of Indian Society for Medical Statistics	November 28-30, 2003	Desert Medicine Research Centre Jodhpur
Asia Pacific Conference on Breastfeeding and National Convention of BPNI	November 30- December 3, 2003	Breastfeeding Promotion Network of India BP-33, Pitampura Delhi
XVI Annual Conference of ISAR and International Seminar on Recent Developments in Atherosclerosis Research	December 1-3, 2003	Banaras Hindu University Varanasi
International Conference on Cancer Research, Prevention and Treatment	December 2-4, 2003	The Cachar Cancer Hospital Society Silchar
Satellite Symposium on Molecular Aspects of Cellular Signalling	December 3-4, 2003	University of Hyderabad Hyderabad
National Convention of Medical Library Association of India	December 3-5, 2003	National Institute of Virology Pune

Title	Dates	Organisers
Silver Jubilee Congress of Indian Association of Sports Medicine	December 3-7, 2003	Guru Nanak Dev University Amritsar
Conference on Pharmaco-Vigilance	December 4-6, 2003	Seth G.S. Medical College and K.E.M. Municipal Hospital Mumbai
Workshop on Advanced Techniques in Reproduction Endocrinology and Fertility Management	December 4-18, 2003	Banaras Hindu University Varanasi
XXXVI Annual Conference of the Indian Pharmacological Society and International Symposium on Pharmacovigilance	December 5-7, 2003	Vallabhbhai Patel Chest Institute Delhi
National Live (hands on) Workshop on Stem Cell Harvesting and Blood Component Manufacture	December 5-7, 2003	Armed Forces Medical College and Command Hospital Pune
III National Conference on Siddha Medicine for all Ages	December 6-7, 2003	Friends of Siddha Medicine Palayamkottai
Symposium on Expanding Contraceptive Choices: International and Indian Experiences and their Implications for Policies and Programmes	December 7-10, 2003	National Institute for Research in Reproductive Health Mumbai
10th Congress of Federation of Asian and Oceanian Biochemists and Molecular Biologists	December 7-11, 2003	Indian Institute of Science Bangalore
III Annual Conference of Indian Society of Cerebro-Vascular Surgery	December 11, 2003	Postgraduate Institute of Medical Education & Research Chandigarh
International Symposium on Clinical Data Management	December 11-13, 2003	University of Poona Pune
35th Annual Conference Society of Nuclear Medicine-India and Symposium by the Indo-American Society of Nuclear Medicine	December 11-14, 2003	Jawaharlal Nehru Cancer Hospital and Research Centre Bhopal
35th Annual Conference of Nutrition Society of India	December 12-13, 2003	National Institute of Nutrition Hyderabad
V SASS International Conference on Emerging Concepts in Leukemia and Lymphoma	December 13-16, 2003	All India Institute of Medical Sciences New Delhi

Title	Dates	Organisers
Annual Conference of Physiologists and Pharmacologists of India	December 14-17, 2003	Gauhati Medical College Guwahati
International Conference on Recent Advances in Brain Research	December 15-18, 2003	National Brain Research Centre Manesar Gurgaon
CME Programme on Medicine Update-2003	December 16-18, 2003	Maulana Azad Medical College and Associated Hospitals New Delhi
Research Methodology Workshop for Senior Medical Teachers	December 19-20, 2003	Topiwala National Medical College and BYLN Charitable Hospital Mumbai
Joint AAPI-CSMMY Conclave : Newer Trends and Strategies in Progress of Modern Medicine	December 23-24, 2003	Chhatrapati Shahuji Maharaj Medical University Lucknow
40th Annual Convention of Chemists	December 23-27, 2003	Bundelkhand University Jhansi
Guha Research Conference- 2003	December 25-29, 2003	Guha Research Conference Bose Institute Kolkata
National Conference on Trends in Biological Chemistry	December 26-28, 2003	Sri Venkateswara University Tirupati
International Conference on Recent Statistical Techniques in Life Testing Reliability, Sampling Theory and Quality Control	December 29-31, 2003	Banaras Hindu University Varanasi
Symposium on Current Trends in Vaccination, Surveillance and Treatment of HIV/AIDS	December 31, 2003	Sumananjali Educational and Research Channel (SEARCH) Aurangabad
91st Session of the Indian Science Congress	January 3-7, 2004	Panjab University Chandigarh
XXVII All India Cell Biology Conference and International Symposium	January 7-10, 2004	University of Poona Pune
57th Annual Congress of Indian Radiological and Imaging Association	January 8-11, 2004	Indian Radiological and Imaging Association Somasiguda Hyderabad
29th Annual Conference of Indian Society of Human Genetics	January 8-11, 2004	National Institute of Mental Health and Neurosciences Bangalore
I Biological Congress on Biome and Bioresources	January 9-10, 2004	Muthayammal College of Arts and Science Rasipuram Nammakkal

Title	Dates	Organisers
Joint International Conference of International Society for Heart Research -Indian Section and International Academy of Cardiovascular Science	January 9-11, 2004	Chhatrapati Shahuji Maharaj Medical University Lucknow
III Global Meeting on Parasitic Diseases	January 12-16, 2004	Bangalore University Bangalore
International Conference on Recent Advances in Biomedical and Therapeutic Sciences	January 13-15, 2004	Bundelkhand University Jhansi
International Workshop on ICT for Sustainable Development	January 14-16, 2004	Indian Institute of Science Bangalore
National Symposium on Cellular and Molecular Biophysics	January 14-17, 2004	National Institute of Mental Health and Neurosciences Bangalore
IV International Seminar of Asian Network of Research on Antidiabetic Plants	January 16-18, 2004	University College of Medicine Kolkata
International Conference on Natural Products, Free Radicals and Radioprotectors in Health	January 17-19, 2004	Annamalai University Annamalai Nagar
International Symposium on Recent Trends in Macromolecular Structure and Function	January 19-23, 2004	University of Madras Chennai
Seminar on IX International CME in Surgical Pathology and Cytology	January 22-24, 2004	Sri Ramachandra Medical College and Research Institute Chennai
III National Symposium on Venoms and Toxins	January 23-24, 2004	University of Mysore Mysore
XIV Annual Meeting of the Indian Society for Study of Reproduction and Fertility	January 23-25, 2004	Indian Institute of Science Bangalore
VII National Conference and Workshop on Prenatal Diagnosis and Therapy	January 23-25, 2004	Genetics Centre, Bima Nagar Ahmedabad
XXII Symposium on Reproductive Biology & Comparative Endocrinology	January 25-27, 2004	Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences Chennai
International Conference on the Frontiers of Research and Development in Medicinal Plants	January 28-30, 2004	St. Xavier's College Palayamkottai

Title	Dates	Organisers
Symposium on Creating Scientific Temperament Towards Research among Medical Students	January 29, 2004	Acharya Shri Chander College of Medical Sciences & Hospital Jammu
International Conference on Schizophrenia	January 29 - February 2, 2004	Schizophrenia Research Foundation (India) Anna Nagar Chennai
23rd Annual Convention of the Indian Association for Cancer Research	January 29-31, 2004	Tata Memorial Centre Navi Mumbai
CME Programme in Surgical Gastroenterology	January 30-31, 2004	Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
National Symposium on Management of Aquatic Resources for Biodiversity Maintenance and Conservation	February 2-4, 2004	Jai Narain Vyas University Jodhpur
32nd Annual National Conference of Indian Association of Physical Medicine and Rehabilitation	February 6-8, 2004	Medical College and Hospital Kozhikode
V Annual Conference of Indian Society of Neuroanaesthesiology and Critical Case	February 6-8, 2004	National Institute of Mental Health and Neurosciences Bangalore
National Conference on Environment Health and Sustainable Development	February 12-13, 2004	International Development Centre Bhikaji Cama Place New Delhi
Symposium on Immunology of Infectious Diseases	February 13-15, 2004	Jawaharlal Nehru University New Delhi
I Interdisciplinary Conference on Nutrition in Health and Disease	February 13-15, 2004	Government Medical College and New Civil Hospital Surat
III Convention of Society for Immunology and Immunopathology and National Symposium on Cytokines and Signal Transduction	February 13-15, 2004	Central JALMA Institute for Leprosy Agra
Symposium on NMR Drug Design and Bioinformatics International Symposium on Current Trends in Drug Discovery Research	February 17-20, 2004 February 17-20, 2004	Bose Institute Kolkata Central Drug Research Institute Lucknow
International Conference on Mathematical Biology	February 19-21, 2004	Indian Institute of Technology Kanpur
Conference on Medical Record towards the New Millennium - Need for Technological Development	February 20-21, 2004	National Institute of Mental Health and Neurosciences Bangalore

Title	Dates	Organisers
Workshop cum Symposium on Microwave Applications in Medicine, Remote Sensing Industry	February 20-21, 2004	School of Environmental Sciences Jawaharlal Nehru University New Delhi
National Conference on Hospital Administration Recent Trends - 2004	February 21-22, 2004	Postgraduate Institute of Medical Education & Research Chandigarh
Workshop on Drug Delivery and Development in New Millennium Interfacing with Pharmacological and Toxicological Experimentation	February 26-29, 2004	National Institute of Pharmaceutical Education and Research Mohali
31st Annual National Conference of Indian Association of Preventive and Social Medicine	February 27-29, 2004	Postgraduate Institute of Medical Education & Research Chandigarh
4th Indian Veterinary Congress and IX Annual Conference of Indian Association for the Advancement of Veterinary Research	February 27-29, 2004	Indian Veterinary Research Institute Izatnagar
29th Annual Conference of Environmental Mutagen Society of India and Symposium on Environmental Pollution	March 3-5, 2004	CCS Haryana Agricultural University Hissar
Symposium on Current Trends in Human Genetics, Health and Society	March 8-9, 2004	Sri Venkateswara University Tirupati
Seminar on Role of Chemistry in Emerging Areas of Applied Sciences	March 15-17, 2004	Sri Venkateswara University Tirupati
International Update on Heart Failure	March 19-20, 2004	Sri Ramachandra Medical College and Research Institute Chennai
ISECON-2004 Meeting	March 19-21, 2004	All India Institute of Medical Sciences New Delhi
Workshop on Bioinformatics	March 25-27, 2004	Dibrugarh University Dibrugarh
Workshop on Emerging Issues in Tribal Health and Medicine	March 29-30, 2004	University of Delhi Delhi
International Workshop on Genetics of Complex Diseases with an emphasis on type 2 Diabetes	March 30- April 1, 2004	Andhra University Visakhapatnam

Research Schemes Funded during 2003-2004

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
EPIDEMIOLOGY AND COMMUNICABLE DISEASES			
1.	Field programme for the epidemiological studies in leprosy at Ghatampur	Dr. Kiran Katoch Central JALMA Institute for Leprosy Agra	16.04
2.	Diagnosis and molecular epidemiology of tuberculosis in the North-East	Dr. V.M. Katoch Central JALMA Institute for Leprosy Agra	11.00
3.	Characterization of the human B and T cell immune response to the membrane capsid, NS1, NS2β and NS5 proteins of Japanese encephalitis virus	Dr. S. Vijaya Indian Institute of Science Bangalore	6.94
4.	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	3.08
5.	Evaluation of ovarian function in female patients with multibacillary leprosy	Dr. Neena Khanna National Tuberculosis Institute Bangalore	1.46
6.	Virulence markers in *Helicobacter pylori* isolated in Bangalore and its association with disease	Dr. Regini Macaden St. John's Academy of Health Sciences Bangalore	1.29
7.	Intervention for hereditary common haemolytic disorders among the major tribals of Sundargarh district of Orissa	Dr. R.S. Balgir Regional Medical Research Centre Bhubaneswar	3.80
8.	Intervention programme for cholera, intestinal parasitism, vitamin - A deficiency disorders and scabies amongst some primitive tribal populations of Orissa - A pilot study	Dr. G.P. Chhotray Regional Medical Research Centre Bhubaneswar	17.74
9.	Virulence of *P.aeruginosa* in relation to catheter-associated urinary tract infections	Dr. Kusum Harjai Panjab University Chandigarh	0.71
10.	Effect of outer membrane proteins from *Salmonella typhi* grown under different stress conditions on macrophages	Dr. Praveen Rishi Panjab University Chandigarh	2.39

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
11.	Studies on mutation of TGFβ and IFNγ genes in the pathogenesis of pulmonary fibrosis	Dr. Digambar Behera Postgraduate Institute of Medical Education and Research Chandigarh	3.53
12.	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	1.44
13.	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	1.33
14.	Identification and characterization of a toxin from enteroaggregative *Escherichia coli*	Dr. Sujata Ghosh Postgraduate Institute of Medical Education and Research Chandigarh	2.32
15.	Study on the pathophysiology of *V.cholera* induced diarrhoea : At transcriptional level and at translational level	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.28
16.	Study on the cellular responses by a galactose specific adhesin of enteroaggregative *Escherichia coli*	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	2.68
17.	Role of parasite and host factors in the pathogenesis of trichomoniasis	Dr. Nancy Malla Postgraduate Institute of Medical Education and Research Chandigarh	1.44
18.	Developing a verbal autopsy instrument and using it to measure cause - specific mortality in adults	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	0.25
19.	Association of genital mycoplasma and *Chlamydia trachomatis* in neonatal infections	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	2.37
20.	Intestinal antimicrobial peptides : isolation, purification and characterisation	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	3.34
21.	Identification of novel mutation pattern in the ParC and GyrA genes of ciprofloxacin resistant clinical isolates of *Neisseria gonorrhoeae*	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	1.09

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
22.	Immunity to group A 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	1.05
23.	Study of clinical utility and effect of a tumour necrosis factor inhibitor (pentoxyphylline) on immune profile in patients with HIV infection	Dr. Ajay Wanchu Postgraduate Institute of Medical Education and Research Chandigarh	0.99
24.	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	2.83
25.	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	1.35
26.	Tracking financial flows for health research in India	Dr. Sumathi Sundram National Institute of Epidemiology Chennai	0.50
27.	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	0.92
28.	High resolution genotyping of *Mycobacterium tuberculosis* IS 6110 low-copy number strains combining novel approaches for global detection of tuberculosis epidemics	Dr. Sujatha Narayanan Tuberculosis Research Centre Chennai	1.00
29.	Human leucocyte antigen (HLA) and non-HLA gene polymorhism studies in HIV and HIV-TB patients	Dr. P. Selvaraj Tuberculosis Research Centre Chennai	6.34
30.	Detection and molecular characterisation of mycobacteria by polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP) and DNA sequencing technique from ocular and other clinical specimens	Dr. K. Lily Therese Vision Research Foundation Sankara Nethralaya Chennai	5.06
31.	Multicentric feasibility study on the use of intradermal administration of tissue antirabies vaccines in India	Dr. Jeeva Kalai Selvan Pasteur Institute Conoor (Nilgiris)	1.26

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
32.	Integrated vector control of malaria, filaria and other vector-borne diseases	Dr. Sarala K. Subbarao Malaria Research Centre Delhi	171.00
33.	Studies on estimation of disease burden of infectious diseases	Dr. M.A. Ansari Malaria Research Centre Delhi	171.00
34.	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	0.92
35.	Prevalence of *M.pneumoniae* infection in patients of acute exacerbation of chronic obstructive pulmonary disease	Dr. Mandira Varma Basil Vallabhbhai Patel Chest Institute Delhi	3.38
36.	Analysis of isoniazid and rifampicin resistance mutations in the clinical isolates of *M.tuberculosis* by sequencing and DOT-BLOT hybridization	Dr. Mridula Bose Vallabhbhai Patel Chest Institute Delhi	2.01
37.	Studies on epidemiology and aspects of immunodiagnosis of penicillosis marneffei	Dr. H.C. Gugani Vallabhbhai Patel Chest Institute Delhi	1.76
38.	*In vitro* biointeractions between *Candida* species, *Aspergillus fumigatus* and some other human pathogenic fungi	Dr. H.S. Randhawa Vallabhbhai Patel Chest Institute Delhi	0.87
39.	Studies on HIV/AIDS and drug abuse in Dimapur, Nagaland	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	12.56
40.	Studies on HIV/AIDS and drug abuse in Aizwal, Mizoram	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	12.56
41.	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	18.58
42.	Diagnosis and molecular epidemiology of tuberculosis in the North-East	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	37.50
43.	Health aspects among the primitive tribals of *Chenchus* in the Nallamala Hills of Andhra Pradesh	Dr. G. Eswaraiah Centre for Social Development Hyderabad	1.35

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
44.	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 Hyderabad	2.90
45.	Application of heuristic engine : A novel forecasting software tool to predict the outbreak of JE in Andhra Pradesh	Dr. U. Suryanarayana Murty Indian Institute of Chemical Technology Hyderabad	2.87
46.	Multicentric feasibility study on the use of intradermal administration of tissue culture antirabies vaccines in India	Dr. G. Sampath Institute of Preventive Medicine Hyderabad	0.88
47.	Concomitant infection of intestinal parasites with filariasis	Dr. Dasarathi Das Regional Medical Research Centre for Tribals Jabalpur	0.25
48.	Generation of peptide mimics against the immunodominant lipoglycan/lipopolysaccharide antigens of *Mycobacterium tuberculosis* & *Vibrio cholerae* using phage display libraries & their evaluation as diagnostic and prophylactic agents	Dr. Sujoy K. Das Gupta Bose Institute (New Campus) Kolkata	2.30
49.	Optimization of dendritic cell-based vaccination/therapy against murine visceral leishmaniasis induced by antimony-resistant and - sensitive strains of *Leishmania donovani*	Dr. Santu Bandyopadhyay Indian Institute of Chemical Biology Kolkata	3.87
50.	An approach to develop DNA vaccine against experimental visceral leishmaniasis	Dr. Syamal Roy Indian Institute of Chemical Biology Kolkata	3.38
51.	Genetic predisposition to antituberculosis drug-induced hepatotoxicity	Dr. Bidyut Roy Indian Statistical Institute Kolkata	4.24
52.	Natural history of *Helicobacter pylori* infection and its outcome in India	Dr. Abhijit Chowdhury Institute of Postgraduate Medical Education and Research and S.S.K.M. Hospital Kolkata	4.42
53.	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 S.S.K.M. Hospital Kolkata	2.52

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
54.	Setting up a clinical management unit at ID and BG Hospital, Kolkata	Dr. S.K.Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	39.00
55.	Studies on estimation of diseases burden of identified infectious disesaes	Dr. S.K. Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	39.00
56.	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	2.24
57.	Monitoring of multiple antibiotic resistance among clinical strains of enteric pathogens	Dr. T. Ramamurthy National Institute of Cholera and Enteric Diseases Kolkata	3.16
58.	Multicentric feasibility study on the use of intradermal administration of tissue culture antirabies vaccines in India	Dr. S.S. Dutta Pasteur Institute Kolkata	0.92
59.	A correlative study of the prevalence of IgM immunoglobulins against torch infections in pregnancy, with congenital malformations	Dr. Zuhara K.F. University of Calicut Kozhikode	1.16
60.	Assessment of determinants of intravenous device associated nosocomial infections in pediatric wards	Dr. Amita Jain Chhatrapati Shahuji Maharaj Medical University Lucknow	1.00
61.	Role of bacteria in the pathogenesis of juvenile idiopathic arthritis	Dr. Amita Aggarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	4.27
62.	Development of an animal model for Indian strains of *Helicobacter pylori*	Dr. Archana Ayyagari Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.99
63.	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis-C	Dr. G. Choudhuri Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.38
64.	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	1.67

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
65.	*Campylobacter* infection and Guillain - Barre syndrome	Dr. K.N. Prasad Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	2.32
66.	Magnitude of intestinal taeniasis and systemic cysticercosis in pig farming community of north India	Dr. K.N. Prasad Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.94
67.	Host parasite relationship : a study on host immunity to survival of *Mycobacterium tuberculosis* isolates	Dr. R.M. Pitchappan Centre for Advanced Research in Health & Behaviour Madurai	4.81
68.	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	28.43
69.	Shiga toxigenic *Escherichia coli* (STEC) in foods of animal origin and clinical samples	Dr. B. Dhanashree Kasturba Medical College and Hospital Mangalore	1.41
70.	Acute-phase proteins during *Mycobacterium smegmatis* 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	3.84
71.	To study the potential of Buddemeyer type radirespirometric assay based on CO2 evolution from (1-14C) palmitic acid by *M.leprae* as a rapid index of viability	Dr. Vanaja P. Shetty The Foundation for Medical Research Mumbai	1.90
72.	Study on impact of health programmes in Bihar state	Dr. Chakradhar Sinha B.R. Ambedkar Bihar University Muzaffarpur	1.11
73.	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	0.64
74.	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	4.59

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
75.	Natural history of *Helicobacter pylori* infection in a birth cohort in an urban slum setting : Risk factors, rates of clearance and re-infection, immune response to first infection, impact of infection on physical growth	Dr. Rajiv Bahl All India Institute of Medical Sciences New Delhi	9.51
76.	*Helicobacter pylori* infection in early childhood : Characterization of isolates and determination of their ability to exert pathogenic effect in *in vitro* models	Dr. Shinjini Bhatnagar All India Institute of Medical Sciences New Delhi	6.15
77.	Etiological significance of microscopic colitis in chronic diarrhoea in children and its pathogenesis	Dr. Shinjini Bhatnagar All India Institute of Medical Sciences New Delhi	5.00
78.	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	2.44
79.	A study of *clostridium difficile* - an emerging nosocomical pathogen with special reference to epidemiological typing	Dr. Rama Chaudhry All India Institute of Medical Sciences New Delhi	4.76
80.	Aerobic and anaerobic bacteriological profile of diabetic foot ulcers with special reference to methicillin resistant *Staphylococcus aureus*	Dr. Benu Dhawan All India Institute of Medical Sciences New Delhi	1.23
81.	Typing of extended spectrum beta - lactamases (ESBLS) produced by *Klebsiella pneumoniae* isolated from AIIMS Hospital, New Delhi	Dr. Arti Kapil All India Institute of Medical Sciences New Delhi	2.13
82.	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	2.39
83.	Molecular analysis of cytokine gene polymorhism in leprosy	Dr. N.K. Mehra All India Institute of Medical Sciences New Delhi	3.90
84.	T cell signalling pathways using *M.leprae* derived antigens in leprosy patients	Dr. D. Nageswara Rao All India Institute of Medical Sciences New Delhi	4.42
85.	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	2.23

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
86.	Molecular characterisation of *Streptococcus pneumoniae* isolates causing various infections in human beings	Dr. Gita Satpathy All India Institute of Medical Sciences New Delhi	4.95
87.	Comparison of diagnostic efficacy of histochemistry with histology and urease based tests before and after eradication therapy for *H.pylori* in peptic ulcer disease	Dr. M.P. Sharma All India Institute of Medical Sciences New Delhi	1.39
88.	Identification of target genes of the devR-devS two-component system of *M.tuberculosis* and development of rapid assays to measure its activity	Dr. Jaya Sivaswami Tyagi All India Institute of Medical Sciences New Delhi	7.05
89.	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	1.72
90.	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	13.05
91.	Detection analysis of food - borne parasites using molecular approaches	Dr. Jaishree Paul Jawaharlal Nehru University New Delhi	0.86
92.	Molecular biotyping, epidemiological and fungal susceptibilities of oppurtunistic human pathogenic fungi	Dr. Rajendra Prasad Jawaharlal Nehru University New Delhi	9.26
93.	Rapid diagnosis of dengue virus serotypes from clinical samples by reverse transcription polymerase chain reaction	Dr. Anita Chakravarti Maulana Azad Medical College and Associated Hospitals New Delhi	1.26
94.	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	5.91
95.	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	3.45

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
96.	Intracellular trafficking of *Salmonella* in macrophages to understand the mechanism of bacterial survival	Dr. Amitava Mukhopadhyay National Institute of Immunology New Delhi	2.49
97.	Mechanistic studies on the defensive mechanisms of *Leishmania donovani* against oxidative stress : Role of phase I and phase II defensive enzymes of the parasite	Dr. Chandrima Shaha National Institute of Immunology New Delhi	1.89
98.	Development of probiotic strains of lactobacilli of desirable characteristics for reproductive health	Dr. G.P. Talwar Talwar Research Foundation New Delhi	1.47
99.	Protein tyrosine phosphatases from *Mycobacterium tuberculosis* and their role in pathogenesis	Dr. Anil K. Tyagi University of Delhi South Campus New Delhi	6.65
100.	Studies on the role of virS gene in the pathogenesis of *M.tuberculosis*	Dr. Anil K. Tyagi University of Delhi South Campus New Delhi	2.08
101.	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	0.92
102.	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	2.45
103.	Studies on estimation of diseases burden of identified infectious diseseas	Dr. P.K. Das Vector Control Research Centre Pondicherry	2.45
104.	Operational feasibility and impact of co-administration of albendazole and DEC in controlling lymphatic filariasis	Dr. S.P. Pani Vector Control Research Centre Pondicherry	3.83
105.	Prevention and control of hepatitis B infection among the primitive tribes of Andaman and Nicobar Islands	Dr. S.C.Sehgal Regional Medical Research Centre Port Blair	3.52
106.	Further strengthening of the National Leptospirosis Reference Centre	Dr. S.C. Sehgal Regional Medical Research Centre Port Blair	5.53

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
107.	Surveillance for drug resistance to anti-TB drug in HIV seronegative tuberculosis patients in Pune	Dr. A.R. Risbud National AIDS Research Institute Pune	1.12
108.	Microbial enzyme inhibitors : A novel define against secondary fungal infection	Dr. Mala Rao National Chemical Laboratory Pune	0.40
109.	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	14.18
110.	Kala-azar diagnostic kit and commitment of ICMR in kala-azar elimination programme for BHU, Varanasi	Dr. Shyam Sundar Banaras Hindu University Varanasi	2.50
111.	Establishing laboratory based surveillance network to monitor anti - microbial resistance	Dr. M.K. Lalitha Christian Medical College and Hospital Vellore	9.86
Reproductive Health and Nutrition			
112.	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	1.85
113.	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	1.58
114.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. Binod C. Agrawal Taleem Research Foundation Ahmedabad	2.38
115.	Human Reproduction Research Centre	Dr. Gauri Ganguli Moti Lal Nehru Medical College Allahabad	9.50
116.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. Gauri Ganguli Moti Lal Nehru Medical College Allahabad	0.80
117.	National Nutrition Monitoring Bureau	Dr. M.B. Rudrappa Directorate of Health and Family Welfare Services Bangalore	13.94

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
118.	Genomics of male infertility	Dr. Arun Kumar Indian Institute of Science Bangalore	10.75
119.	Genomics of male infertility	Dr. T.C. Anand Kumar Inter Academy Bio-Medical Science Forum Bangalore	1.88
120.	Genomics of male infertility	Dr. K.M. Prasanna Kumar M.S. Ramaiah Medical College and Teaching Hospital Bangalore	1.49
121.	National Neonatal Perinatal Database	Dr. Swarna Rekha Bhatt St. John's Academy of Health Sciences Bangalore	0.84
122.	Human Reproduction Research Centre	Dr. B.S. Kodkany Jawaharlal Nehru Medical College Belgaum	7.86
123.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. B.S. Kodkany Jawaharlal Nehru Medical College Belgaum	0.80
124.	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	1.58
125.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. Uday Jain Mahila Chetna Manch Bhopal	2.38
126.	National Nutrition Monitoring Bureau	Dr. S.K. Kar Regional Medical Research Centre Bhubaneswar	13.94
127.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. S.K. Kar Regional Medical Research Centre Bhubaneswar	2.38
128.	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	2.73

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
129.	Human Reproduction Research Centre	Dr. Vijay Shree Mahasani S.P. Medical College and Associated Group of Hospitals Bikaner	10.15
130.	Assessment of antioxidant status in pregnancy induced hypertension	Dr. Gurjit Kaur Government Medical College and Hospital Chandigarh	1.13
131.	Influence of oxidative stress on cyclin dependent kinase and heat shock proteins in meiotic mouse spermatocytes	Dr. M.P. Bansal Panjab University Chandigarh	2.73
132.	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	1.76
133.	Human Reproduction Research Centre	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	14.28
134.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	0.80
135.	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	2.50
136.	Reactive oxygen intermediates and reactive nitrogen intermediates with microbiological studies in copper intrauterine device users	Dr. Indu Gupta Postgraduate Institute of Medical Education and Research Chandigarh	0.29
137.	Birth asphyxia, hypoxic ischaemic encephalopathy : Aetiology, management and outcome	Dr. Anil Narang Postgraduate Institute of Medical Education and Research Chandigarh	2.00
138.	National Neonatal Perinatal Database	Dr. Anil Narang Postgraduate Institute of Medical Education and Research Chandigarh	0.91
139.	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	0.49

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
140.	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	1.58
141.	National Nutrition Monitoring Bureau	Dr. V. Vasanthi Directorate of Public Health and Preventive Medicine Government of Tamil Nadu Chennai	13.94
142.	Human Reproduction Research Centre	Dr. M. Sakunthala Bharathi Government Kasturba Gandhi Hospital for Women & Children Chennai	14.30
143.	Human Reproduction Research Centre	Dr. V. Madhini Government Kilpauk Medical College and Hospital Chennai	10.83
144.	Human Reproduction Research Centre	Dr. R. Thirupurasundari Government R.S.R.M. Hospital Chennai	14.95
145.	National Neonatal Perinatal Database	Dr. N. Saraswathi Institute of Obstetrics and Gynaecology and Government Hospital for Women and Children Chennai	0.91
146.	Human Reproduction Research Centre - Regional Centre for Clinical Research	Dr. A. Sundaravalli Institute of Obstetrics and Gynaecology and Government Hospital for Women and Children Chennai	12.40
147.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. A. Sundaravalli Institute of Obstetrics and Gynaecology and Government Hospital for Women and Children Chennai	0.80
148.	Novel cardiovascular risk factors and preclinical atherosclerotic markers in subjects with glucose intolerance	Dr. Deepa Raj Madras Diabetes Research Foundation Chennai	5.71
149.	Studies of the genetic variation in hepatocyte nuclear factor genes and glucokinase gene in relation to maturity onset diabetes of the young (MODY) and early onset diabetes in South Indians	Dr. Radha Venkatesan Madras Diabetes Research Foundation Chennai	2.89

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
150.	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. Catherine Barnard Service & Research Foundation of Asia on Family & Culture Chennai	0.52
151.	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	0.67
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. G. Srinivasan The Tamil Nadu Dr. M.G.R. Medical University Chennai	1.58
153.	Human Reproduction Research Centre	Dr. Sabita Patnaik S.C.B. Medical College Cuttack	5.00
154.	Promoting male involvement under RCH strategy - An action research on adolescents in rural Orissa	Dr. Saraswati Swain The National Institute of Applied Human Research and Development Cuttack	3.30
155.	Human Reproduction Research Centre	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	15.34
156.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	0.80
157.	Study of health consequences of domestic violence with special reference to reproductive health	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	2.38
158.	National Nutrition Monitoring Bureau	Dr. W.R. Hegan Directorate of Health, Medical Services and Medical Education Gandhinagar	13.94
159.	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. M.C. Das Gauhati Medical College Guwahati	11.50
160.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. M.C. Das Gauhati Medical College Guwahati	0.80
161.	Genetic and molecular studies in diabetic nephropathy	Dr. Q. Hasan Bhagvan Mahavir Hospital Medical Research Centre Hyderabad	7.91

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
162.	Detection of lead toxicity, functional consequences and prevention	Dr. B. Dinesh Kumar National Institute of Nutrition Hyderabad	16.05
163.	Bioavailability of iron and zinc in representative Indian and US diets	Dr. K. Madhavan Nair National Institute of Nutrition Hyderabad	24.27
164.	Assessment of the prevalence of osteoporosis in the adult population of India	Dr. Veena Shatrugna National Institute of Nutrition Hyderabad	3.14
165.	Central Reference Laboratory of the National Nutrition Monitoring Bureau	Dr. B. Sivakumar National Institute of Nutrition Hyderabad	13.94
166.	National Nutrition Monitoring Bureau	Dr. B. Sivakumar National Institute of Nutrition Hyderabad	13.94
167.	The effectiveness of integrated feeding and care intervention among 3-15 month old infants in Andhra Pradesh, India	Dr. Shahnaz Vazir National Institute of Nutrition Hyderabad	12.10
168.	Genetic and molecular factors in the aetiology of endometriosis	Dr. Vijaya Lakshmi Kodati Vasavi Medical and Research Centre, Vasavi Hospital Hyderabad	5.19
169.	Studies on the nutritional and microbiological quality of sundried, semifermented and salt cured fishes of Manipur	Dr. W. Vishwanath Singh Manipur University Imphal	1.17
170.	National Nutrition Monitoring Bureau	Dr. Tapas Chakma Regional Medical Research Centre for Tribals Jabalpur	13.94
171.	A study of reproductive and sexual health education of adolescents	Dr. R.S. Goel Indian Institute of Health Management Research Jaipur	2.58
172.	Human Reproduction Research Centre	Dr. Adarsh Bhargava S.M.S.Medical College and Hospital Jaipur	14.44

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
173.	Human Reproduction Research Centre	Dr. Sadhna Sharma Government Medical College and S.M.G.S. Hospital Jammu	9.00
174.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. Sadhna Sharma Government Medical College and S.M.G.S. Hospital Jammu	0.80
175.	Human Reproduction Research Centre	Dr. V.K. Singh G.S.V.M.Medical College Kanpur	5.50
176.	Spatial dimensions of reproductive health status and services : An analysis of RCH/RHS/RFHS	Dr. B.N. Bhattacharya Indian Statistical Institute Kolkata	1.61
177.	Human Reproduction Research Centre - Regional Centre for Clinical Research	Dr. B.K. Saumondal Institute of Postgraduate Medical Education and Research and S.S.K.M. Hospital Kolkata	19.19
178.	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	1.58
179.	Human Reproduction Research Centre	Dr. M. Sangthamita Medical College and Eden Hospital Kolkata	12.28
180.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. M. Sangthamita Medical College and Eden Hospital Kolkata	0.80
181.	Human Reproduction Research Centre	Dr. A.K. Mondal R.G.Kar Medical College and Hospital Kolkata	9.09
182.	National Nutrition Monitoring Bureau	Dr. A. Roy Chowdhury Regional Occupational Health Centre (Eastern) Kolkata	13.94
183.	Human proacrosin-acrosin system and sperm-egg interaction	Dr. A.K. Bhattacharya University College of Science Kolkata	1.21
184.	Prediction of ovulation in women and evaluation of saliva and urine	Dr. A.K. Bhattacharya University College of Science Kolkata	3.00

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
185.	A study of reproductive and sexual health education of adolescents	Dr. Sibnath Deb University College of Science and Technology, University of Calcutta Kolkata	2.58
186.	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 Chhatrapati Shahuji Maharaj Medical University Lucknow	1.58
187.	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 Chhatrapati Shahuji Maharaj Medical University Lucknow	1.79
188.	Human Reproduction Research Centre	Dr. Vinita Das Chhatrapati Shahuji Maharaj Medical University Lucknow	17.68
189.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. Vinita Das Chhatrapati Shahuji Maharaj Medical University Lucknow	0.80
190.	National Neonatal Perinatal Database	Dr. G.K.Malik Chhatrapati Shahuji Maharaj Medical University Lucknow	0.45
191.	Screening for prevalence of breast pain and nodularity	Dr. Sandeep Kumar Chhatrapati Shahuji Maharaj Medical University Lucknow	1.69
192.	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	5.17
193.	Assessment of the prevalence of osteoporosis in the adult population of India	Dr. Eesh Bhatia Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	2.57
194.	National Neonatal Perinatal Database	Dr. Manorama Verma Christian Medical College and Brown Memorial Hospital Ludhiana	0.45

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
195.	Human Reproduction Research Centre	Dr. P. Meenambal Madurai Medical College and Government Rajaji Hospital Madurai	17.33
196.	National Neonatal Perinatal Database	Dr. K.K. Diwakar Kasturba Medical College and Hospital Manipal	0.87
197.	Human Reproduction Research Centre	Dr. Rukma Idnani L.L.R.M. Medical College Meerut	11.75
198.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. Rukma Idnani L.L.R.M. Medical College Meerut	0.80
199.	Chracterization of angiotensin receptors in diabetic rats	Dr. P. Ramarao National Institute of Pharmaceutical Education and Research Mohali	0.80
200.	Human Reproduction Research Centre	Dr. Rekha G. Dever Grant Medical College and Sir J.J.Group of Hospitals Mumbai	2.27
201.	Clinical trial with once a month combined injectable contraceptive “lunelle” through cafeteria approach	Dr. Rekha G. Dever Grant Medical College and Sir J.J.Group of Hospitals Mumbai	0.80
202.	A study of psychosocial, cultural and service factors affecting reproductivemorbidity amongst rural women in India	Dr. Ravi Verma International Institute for Population Sciences Mumbai	0.74
203.	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	1.58
204.	Assessment of the prevalence of osteoporosis in the adult population of India	Dr. Rashmi S. Shah National Institute for Research in Reproductive Health Mumbai	1.56
205.	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. Vinita Salvi Seth G.S. Medical College and K.E.M. Municipal Hospital Mumbai	15.60

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
206.	Biological efficacy of antihypertensive peptides from cereals and pulses common to Indian diet	Dr. P.S. Rajini Central Food Technological Research Institute Mysore	1.52
207.	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 Hospital Nagpur	1.58
208.	National Neonatal Perinatal Database	Dr. D.N.Palpande Indira Gandhi Medical College and Mayo General Hospital Nagpur	0.91
209.	National Nutrition Monitoring Bureau	Dr. D.J. Dhande Public Health Institute Building Nagpur	13.94
210.	Assessment of the prevalence of osteoporosis in the adult population of India	Dr. A.C. Ammini All India Institute of Medical Sciences New Delhi	3.97
211.	Congenital CMV infection in offsprings of immune mothers	Dr. Lalit Dar All India Institute of Medical Sciences New Delhi	15.21
212.	Trophoblast biology : intracellular signaling mechanisms	Dr. Chandana Das All India Institute of Medical Sciences New Delhi	3.05
213.	National Neonatal Perinatal Database	Dr. A.K. Deorari All India Institute of Medical Sciences New Delhi	0.45
214.	Effect of (Ala 8,13,18)-magainin II amide on human trophoblast cells *in vitro*	Dr. Debabrata Ghosh All India Institute of Medical Sciences New Delhi	3.00
215.	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	1.58
216.	Genomics of male infertility	Dr. Kiran Kucheria All India Institute of Medical Sciences New Delhi	4.87

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
217.	Immunogenetic and humoral profile of diabetes mellitus in Asian Indians	Dr. N.K. Mehra All India Institute of Medical Sciences New Delhi	3.70
218.	Human Reproduction Research Centre	Dr. Suneeta Mittal All India Institute of Medical Sciences New Delhi	19.64
219.	National Neonatal Perinatal Database	Dr. Suneeta Mittal All India Institute of Medical Sciences New Delhi	0.08
220.	A randomized controlled trial on the efficacy of yogic intervention in premenstrual syndrome	Dr. Ratna Sharma All India Institute of Medical Sciences New Delhi	8.42
221.	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	1.33
222.	A study of reproductive and sexual health education of adolescents - Coordinating Centre	Dr. R.N. Gupta Indian Council of Medical Research New Delhi	0.89
223.	Home based management of young infants - Coordinating Unit	Sh. N.C. Saxena Indian Council of Medical Research New Delhi	3.81
224.	Women's work and child survival	Dr. Padam Singh Indian Council of Medical Research New Delhi	2.37
225.	National Nutrition Monitoring Bureau	Dr. Arvind Pandey Institute for Research in Medical Statistics New Delhi	13.94
226.	Long term management of retinal and renal complications in experimental diabetes by vanadate and antidiabetic compounds	Dr. Najma Zaheer Baquer Jawaharlal Nehru University New Delhi	2.43
227.	Urogynaecological complaints in postmenopausal women with particular reference to stress incontinence (evaluation and management)	Dr. Uma Goyal Lady Hardinge Medical College and Associated Hospitals New Delhi	1.88

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
228.	Evaluation of nitric oxide as a marker of severity and prognosis of asthma in children	Dr. Virendra Kumar Lady Hardinge Medical College and Associated Hospitals New Delhi	0.97
229.	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	8.24
230.	Identification and characterization of spermatozoa surface proteins involved in binding to zona pellucida glycoproteins	Dr. Satish K. Gupta National Institute of Immunology New Delhi	0.20
231.	Genomics of male infertility	Dr. Satish K. Gupta National Institute of Immunology New Delhi	5.19
232.	Study to identify factors involved in paracrine modulation of testicular cells to increase our understanding about cellular regulation of spermatogenesis	Dr. S.S. Majumdar National Institute of Immunology New Delhi	2.20
233.	Estimation of spread of HIV/AIDS	Dr. M. Kapilashrami National Institute of Health and Family Welfare New Delhi	3.76
234.	A study of reproductive and sexual health education of adolescents	Dr. Shashi Prateek Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	2.58
235.	Human Reproduction Research Centre	Dr. Sudha Salhan Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	15.89
236.	Study of health consequences of domestic violence with special reference to reproductve health	Dr. Prabha Ramalingaswami Vulimiri Ramlingaswami Foundation New Delhi	2.38
237.	Development of recombinant protein, insulin like polypeptide-P from *Momordica charantia* and docking and dynamics study with insulin receptors	Dr. R. Latha Indian Institute of Environment Management New Mumbai	4.49
238.	Human Reproduction Research Centre	Dr. Prasad Neurencar Goa Medical College Panaji	8.83

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
239.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Prasad Neurencar Goa Medical College Panaji	0.80
240.	Human Reproduction Research Centre	Dr. Sushma Pandey Patna Medical College and Hospital Patna	13.79
241.	Stimulatory effects of antioxidants in pollutant - induced male sterlity of mammal	Dr. Akhileshwari Nath Patna University Patna	5.76
242.	National Neonatal Perinatal Database	Dr. B. Vishnu Bhatt Jawaharlal Institute of Postgraduate Medical Education & Research Pondicherry	0.68
243.	Human Reproduction Research Centre	Dr. Syed Habeebullah Jawaharlal Institute of Postgraduate Medical Education & Research Pondicherry	9.49
244.	Clinical trial with once a month combined injectable contraceptive "lunelle" through cafeteria approach	Dr. Syed Habeebullah Jawaharlal Institute of Postgraduate Medical Education & Research Pondicherry	0.80
245.	Reproductive and child health care problems among the six primitive tribes of Tamil Nadu	Dr. T. Subramanyam Naidu University of Pondicherry Pondicherry	2.64
246.	Growth during early infancy and its relation with risk factors for adult diseases	Dr. Shobha S. Rao Agharkar Research Institute Pune	1.95
247.	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	0.80
248.	Human Reproduction Research Centre	Dr. Aparna Shrotri B.J. Medical College and Sasoon General Hospital Pune	6.00
249.	Human Reproduction Research Centre	Dr. K.Coyaji King Edward Memorial Hospital Research Centre Pune	7.25

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
250.	A study of reproductive and sexual health education of adolescents	Dr. Seema Sahay National AIDS Research Institute Pune	5.17
251.	Social and cultural aspects of women suffering from pulmonary tuberculosis: Issues for social and national programme	Dr. Aarti Nagarkar University of Poona Pune	1.58
252.	Impact of dietary counselling and food supplementation on the lipid profile status of population in Thiruvananthapuram	Dr. S. Chellammal Kerala Agricultural University Thiruvananthapuram	1.37
253.	A study of reproductive and sexual health education of adolescents	Dr. M.K.C. Nair Medical College and SAT Hospital for Women & Children Thiruvananthapuram	2.58
254.	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. K. Rajamohan Medical College and SAT Hospital for Women & Children Thiruvananthapuram	1.58
255.	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	1.58
256.	Human Reproduction Research Centre	Dr. P.B. Sulekha Devi Medical College and SAT Hospital for Women & Children Thiruvananthapuram	14.46
257.	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	0.80
258.	National Nutrition Monitoring Bureau	Mrs. Rasheeda Bai State Nutrition Bureau Nutrition Research Centre Thiruvananthapuram	13.94
259.	Obesity in school going children	Dr. Uma Mahadevan Iyer M.S. University of Baroda Vadodara	1.63
260.	Human Reproduction Research Centre	Dr. L.N. Chauhan Medical College and S.S.G. Hospital Vadodara	16.10

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
261.	National Neonatal Perinatal Database	Dr. Dulari J.Gandhi Medical College and S.S.G. Hospital Vadodara	0.50
262.	Poverty, under-nutrition and fertility nexus in rural eastern Uttar Pradesh	Dr. R.C. Yadav Banaras Hindu University Varanasi	5.01
263.	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. P. Raghupathy Christian Medical College and Hospital Vellore	1.58
264.	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. S.K. Mishra Child In Need Trust 24-Parganas	0.79
Non-Communicable Diseases			
265.	Mental health service needs and service delivery models in the disaster affected population, Ahmedabad Centre	Dr. A.P.S. Chouhan Hospital for Mental Health Ahmedabad	2.91
266.	Cholinesterase and paraoxonase patterns in organophosphate (op) poisoning	Sh. Ashwin B. Patel National Institute of Occupational Health Ahmedabad	0.81
267.	Rural Cancer Registry	Dr. D.V. Bala The Gujarat Cancer and Research Institute (M.P. Shah Cancer Hospital) Ahmedabad	4.34
268.	Study of TGF beta system in advanced human breast tumors	Dr. Sunil Trivedi The Gujarat Cancer and Research Institute (M.P. Shah Cancer Hospital) Ahmedabad	12.00
269.	Population based cancer registry	Dr. Eric Zomawig Civil Hospital Aizwal	12.00
270.	Development of sentinel health monitoring centres in India	Dr. B. Krishnan Anand Comprehensive Rural Health Centre Ballabhgarh	5.44
271.	National Cancer Registry Coordinating Unit (Technical wing)	Dr. A. Nandakumar Kidwai Memorial Institute of Oncology Bangalore	40.00

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
272.	Hemicraniectomy with duroplasty for treatment of acute ischemic stroke : A prospective randomized study	Dr. D. Nagaraja National Institute of Mental Health and Neurosciences Bangalore	0.79
273.	A prospective serial correlative study of neurocysticercosis by clinical and imaging methods	Dr. A. Nalini National Institute of Mental Health and Neurosciences Bangalore	4.38
274.	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	1.67
275.	A multicentric study on prevalence of asthma	Dr. George D'souza St.John's Academy of Health Sciences Bangalore	2.22
276.	Urban hospital-based case-control study to identify risk factors for acute myocardial infarction - Control Data Unit	Dr. Prem Pais St.John's Academy of Health Sciences Bangalore	2.60
277.	Mental health service needs and service delivery models in the disaster affected population in Gujrat, Bhuj Centre	Dr. Sanjeev Gupta Hospital for Mental Health Bhuj	5.73
278.	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	9.10
279.	Orbital blood flow studies in glaucoma	Dr. V.P. Munjal Government Medical College and Hospital Chandigarh	0.81
280.	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	6.81
281.	Endothelin - 2 gene polmorphism in patients with essential hypertension and in patients with target end organ damage	Dr. Veena Dhawan Postgraduate Institute of Medical Education and Research Chandigarh	2.14
282.	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	6.69

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
283.	To develop a model for the primary immunological inter-vention for the management of rheumatic fever and RHD in a rural community with the available primary health care with intervention in the form of secondary prophylaxis	Dr. Anil Grover Postgraduate Institute of Medical Education and Research Chandigarh	2.26
284.	HLA typing in vogt Koyanagi Harada (VKH) syndrome in Indian population	Dr. Amod Gupta Postgraduate Institute of Medical Education and Research Chandigarh	3.12
285.	Cervical carcinoma : Analysis of HLA polymorphism and its relationship to human papilloma virus type 16	Dr. Babita Jindal Postgraduate Institute of Medical Education and Research Chandigarh	2.00
286.	A multicentric study on prevalence of asthma	Dr. S.K. Jindal Postgraduate Institute of Medical Education and Research Chandigarh	1.69
287.	Homocysteine and essential hypertension in Indian subjects : Relation with folate, vitamin B12 and methylene tetrahydrofolate reductase (MTHFR) gene mutation	Dr. Madhu Khullar Postgraduate Institute of Medical Education and Research Chandigarh	3.17
288.	Relationship between BCG vaccination and prevalence of atopic diseases specially asthma in school children	Dr. Lata Kumar Postgraduate Institute of Medical Education and Research Chandigarh	1.78
289.	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	2.92
290.	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	7.85
291.	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	19.35
292.	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	3.37

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
293.	*Jai Vigyan* mission mode project on RF/RHD (Registry Protocol)	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	7.36
294.	To study the effect of predominant methanogenic flore 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	0.65
295.	*Jai Vigyan* mission mode project on community control of RF/RHD in India	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	13.42
296.	Assessment of severity of acute pancreatitis : Role of inflammatory mediators and cytokines	Dr. J.D. Wig Postgraduate Institute of Medical Education and Research Chandigarh	4.69
297.	A comprehensive retrospective immunohistochemical evaluation of axillary nodal status for micrometastasis and prognostic marker status in primary tumour in breast cancer patients	Dr. K.R. Rajalakshmy Cancer Institute (W.I.A.) Chennai	1.57
298.	Study of epidemiological and molecular cytogenetic aspects of patients with congenital heart disease	Dr. K.M. Cherian Institute of Cardiovascular Diseases Chennai	1.78
299.	Urban mental health problems and their service needs	Dr. S. Nambi Institute of Mental Health Chennai	3.33
300.	Development of sentinel health monitoring centres in India	Dr. V. Mohan Madras Diabetes Research Foundation Chennai	5.44
301.	Role of tetraspanin proteins, p53 family proteins, rac 1-tiam 1 signal transduction, cadherine, catenins and proteases and its inhibitors in retinoblastoma and correlation with aggression	Dr. S. Krishnakumar Vision Research Foundation Sankara Nethralaya Chennai	2.32
302.	To study the expression of oxidative stress in human corneal diseases by immunohistochemistry	Dr. S. Krishnakumar Vision Research Foundation Sankara Nethralaya Chennai	1.86

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
303.	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 Sankara Nethralaya Chennai	2.82
304.	Molecular biological and virological study of intraocular fluids from patients with viral retinitis and choroiditis-correlation with clinical features and visual outcome	Dr. H.N. Madhavan Vision Research Foundation Sankara Nethralaya Chennai	5.23
305.	Role of metalloporphyrins in therapeutics of cardiovascular complications during hypoxic stress	Dr. Ramesh Chandra Dr.B.R.Ambedkar Centre for Biomedical Research Delhi	8.18
306.	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	1.07
307.	Studies on suicide behaviour	Dr. N.G. Desai Institute of Human Behaviour and Allied Sciences Delhi	12.27
308.	Urban mental health problems and their service needs	Dr. N.G. Desai Institute of Human Behaviour and Allied Sciences Delhi	6.68
309.	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	2.96
310.	Development of a disposable vaginal speculum for gynaecological application	Dr. R.K. Diwan Shriram Institute for Industrial Research Delhi	2.91
311.	Predictors of physical function among the old	Dr. N.K. Chadha University of Delhi Delhi	3.62
312.	To study the mechanism of exertional breathlessness (*i.e.* development of practical applications arising from advances in visceral mechanisms *i.e.* J. receptors, chemoreceptors *etc.*	Dr. Ashima Anand Vallabhbhai Patel Chest Institute Delhi	26.00

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
313.	Potentiation of allergic asthma by air pollution : The ozone - allergen interaction and its modulation by dietary antioxidants, alpha - tocopherol and ascorbic acid	Dr. S.K. Chhabra Vallabhbhai Patel Chest Institute Delhi	1.50
314.	Studies on foods as sensitizing and inducing factors of allergy disorders with special reference to bronchial asthma	Dr. Raj Kumar Vallabhbhai Patel Chest Institute Delhi	2.79
315.	A multicentric study on prevalence of asthma	Dr. V.K. Vijayan Vallabhbhai Patel Chest Institute Delhi	2.53
316.	A study on treatment seeking behaviour and reporting pattern of patients to health service centres especially with fever symptom	Sh. Himanshu Kumar Chaturvedi Regional Medical Research Centre Dibrugarh	2.55
317.	Epidemiological evaluation of the impact of insecticide treated mosquito nets on occurence of Japanese encephalitis cases in two selected endemic PHC areas of Assam, India	Dr. Prafulla Dutta Regional Medical Research Centre Dibrugarh	4.55
318.	Malaria control in a forest fringe village of Assam : A pilot study	Dr. Prafulla Dutta Regional Medical Research Centre Dibrugarh	4.60
319.	Morbidity surveillance in Sikkim	Dr. N.C. Hazarika Regional Medical Research Centre Dibrugarh	6.83
320.	Molecular epidemiological analysis of methicillin resistant *Stapylococcus aureus* in Assam, India	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	5.54
321.	Development of Sentinel Health Monitoring Centres in India	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	5.44
322.	Causes of death by verbal autopsy	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	15.94

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
323.	Population Based Cancer Registry	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	47.5
324.	Studies on paragonimiasis in hill tribes of Arunachal Pradesh	Dr. Kanwar Narain Regional Medical Research Centre Dibrugarh	5.01
325.	Population Based Cancer Registry	Dr. Yogesh Verma Sir Thutob Namgyal Memorial Hospital Gangtok	5.01
326.	Population Based Cancer Registry	Dr. Jagannath Sharma Dr. B. Borooah Cancer Institute Guwahati	5.01
327.	Cancer chemopreventive potential of certain vegetables, fruits and medicinal plants of the North Eastern region of India	Dr. Rupjyoti Bharali Gauhati University Guwahati	1.81
328.	Homocysteine and stroke	Dr. N.C. Borah Institute of Neurological Sciences Guwahati	7.25
329.	Role of growth factors and receptors in cataract	Dr. Yogendra Sharma Centre for Cellular and Molecular Biology Hyderabad	5.42
330.	Differentiation of embryonal carcinoma cells with curcumin and identification of differentially expressed genes that trigger differentiation	Dr. Usha K. Srinivas Centre for Cellular and Molecular Biology Hyderabad	1.54
331.	Role of apoptosis in tissue damage and wound healing in corneal infections	Dr. Geeta K.V. L.V. Prasad Eye Institute Hyderabad	1.45
332.	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	2.76
333.	Population Based Cancer Registry	Dr. Y.M. Singh Regional Institute of Medical Sciences Imphal	2.76

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
334.	Prevention of disability among pre - school children	Dr. M.K. Mathur S.M.S. Medical College and Hospital Jaipur	4.19
335.	Mental health service needs and service delivery models in the disaster affected population in Gujrat	Dr. Chitra Somasundaram Shri M.P. Shah Medical College Jamnagar	5.48
336.	*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	9.20
337.	A cross-sectional study on the prevalence of behavioural risk factors of chronic diseases among Kerala population	Dr. T.N. Sugathan Centre for Survey Research and Management Services Kochi	9.27
338.	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	2.76
339.	Epidemiology of major neurological disorders - a random sample survey in the city of Calcutta	Dr. Shyamal K. Das Bangur Institute of Neurology Kolkata	7.86
340.	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	0.28
341.	Evaluation of purified glutaminase as a potential inhibitor of tumoural angiogenesis	Dr. Putul Maity Chittaranjan National Cancer Institute Kolkata	2.17
342.	Kit formulation of thiolate complexes of technetium - 99 using S - thiomethyl as a novel protecting group for SH - containing ligands	Dr. Mita Chatterjee Debnath Indian Institute of Chemical Biology Kolkata	0.99
343.	Prevalence of *H.pylori* 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 S.S.K.M. Hospital Kolkata	2.14

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
344.	To study the epidemiology of rheumatic diseases in rural and urban population of Lucknow (North India)	Dr. S.K. Das Chhatrapati Shahuji Maharaj Medical University Lucknow	9.40
345.	Assessment of Agnor technique as tumour marker in cervical carcinogenesis	Dr. Vinita Das Chhatrapati Shahuji Maharaj Medical University Lucknow	0.86
346.	Prevention of disability among pre - school children	Dr. J.V. Singh Chhatrapati Shahuji Maharaj Medical University Lucknow	7.83
347.	Urban mental health problems and their service needs	Dr. S.C. Tiwari Chhatrapati Shahuji Maharaj Medical University Lucknow	6.68
348.	Molecular approaches for early detection of gall bladder cancer	Dr. G. Choudhuri Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	4.30
349.	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	2.86
350.	Comparative study of periodontal health of people living in submountaneous and plain areas of Punjab	Dr. N.C. Mann Christian Medical College and Brown Memorial Hospital Ludhiana	1.68
351.	Seroepidemiology of *Taenia solium* cysticercosis in India : A multi - population study	Dr. Daljit Singh Dayanand Medical College and Hospital Ludhiana	1.96
352.	Studies on the genetics of inherited Aniridia in Indian population	Dr. P. Sundaresan Aravind Eye Hospital and Postgraduate Institute of Ophthalmology Madurai	2.44
353.	Genetic and structural analysis of myocilin protein involved in juvenile onset primary open angle glaucoma	Dr. P. Sundaresan Aravind Eye Hospital and Postgraduate Institute of Ophthalmology Madurai	3.21
354.	Investigations on hydroxyapatite coatings of TI and TI - 6A1 - 4V for dental implants	Dr. V. Surendra Shetty College of Dental Surgery Manipal	0.50

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
355.	Lipoprotein(a) level and other lipid profiles in myocardial infarction	Dr. P. Gopalakrishna Bhat Kasturba Medical College and Hospital Manipal	0.93
356.	Comparative evaluation of *Triphala* and chlorhexidine as a mouthwash : A controlled clinical trial	Dr. Shobha Tandon Kasturba Medical College and Hospital Manipal	1.76
357.	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	1.67
358.	Causes of death by verbal autopsy	Dr. C.P. Puri National Institute for Research in Reproductive Mumbai	12.72
359.	Development of MUC1 - single chain - MET - ETA recombinant antibody (SCFV) for *in vivo* imaging and targetted therapy in breast cancer	Dr. Dilip Bandyopadhyay Tata Memorial Hospital Mumbai	3.20
360.	Development of sentinel health monitoring centres in India	Dr. Prashant Joshi Government Medical College and Hospital Nagpur	5.44
361.	Development and synthesis of UV lamp phosphors for phototherapy	Dr. C.P. Joshi Shri Ramdeobaba Kamla Nehru Engineering College Nagpur	4.82
362.	Molecular cytogenetic studies in oral cancer	Dr. Manoj B. Mahimkar Advanced Centre for Treatment, Research & Education in Cancer (ACTREC) Navi Mumbai	3.00
363.	Studies on the molecular mechanism of tamoxifen - induced apoptosis of astrocutoma cells	Dr. Neelam V. Shirsat Advanced Centre for Treatment, Research & Education in Cancer (ACTREC) Navi Mumbai	1.52
364.	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	2.26

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
365.	Study of risk factors in adult onset focal dystonia	Dr. Madhuri Behari All India Institute of Medical Sciences New Delhi	1.30
366.	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	4.98
367.	Molecular genetic analysis of parkin gene among Indians with autosomal recessive juvenile Parkinsonism (ARJP)	Dr. Madhuri Behari All India Institute of Medical Sciences New Delhi	3.64
368.	Evaluation of iatrogenic nerve injuries following orthopedic procedures and role of nerve stimulation in their management	Dr. Surya Bhan All India Institute of Medical Sciences New Delhi	1.21
369.	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	4.45
370.	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	0.52
371.	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	3.33
372.	Role of genetic factors in tropical pancreatitis	Dr. P.K. Garg All India Institute of Medical Sciences New Delhi	2.04
373.	The development and standardization of a comprehensive dementia assessment scale	Sh. Surya Gupta All India Institute of Medical Sciences New Delhi	2.28
374.	Urban hospital-based case-control study to identify risk factors for acute myocardial infarction	Dr. B.L. Jailkhani All India Institute of Medical Sciences New Delhi	2.56

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
375.	Feasibility of transporting blood dried on filter paper for the measurement of lipids, lipoproteins and markers of glycaemic index, glucose, glycosylated haemoglobin and insulin for cardiovascular diseases	Dr. B.L. Jailkhani All India Institute of Medical Sciences New Delhi	1.89
376.	Presynaptic membrane receptor autoantibodies in myasthenia gravis	Dr. B.L. Jailkhani All India Institute of Medical Sciences New Delhi	1.98
377.	Reactivity of muscle nicotinicavetyl choline receptors and nonreceptor antigens from different animals with myasthenic antibodies	Dr. B.L. Jailkhani All India Institute of Medical Sciences New Delhi	4.05
378.	Estimation of serum sialic acid - glycosaminoglycans in patients of ankylosing spondylitis - development of a possible new laboratory test for diagnosis early ankylosing spondylitis	Dr. Arvind Jayaswal All India Institute of Medical Sciences New Delhi	2.20
379.	Effect of glutamine supplementation on clinical outcome and nutritional status in patients of acute myeloid leukaemia (AML)	Dr. Y.K. Joshi All India Institute of Medical Sciences New Delhi	2.15
380.	Emerging biochemical markers of mycardial injury following cornary artery bypass grafting (CABG) with or without cardiopulmonary bypass (CPB)	Dr. Shailaja C. Kale All India Institute of Medical Sciences New Delhi	1.57
381.	Assessment of nutritional factors in breast cancer : A case control study	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	5.81
382.	Human paraoxonase GLN-ARG (q/r) polymorphism in Indians with acute myocardial infarction	Dr. R. Lakshmy All India Institute of Medical Sciences New Delhi	1.40
383.	Comparison of recovery, and complications and recurrence rate after endoscopic versus open carpal tunnel release	Dr. Rajesh Malhotra All India Institute of Medical Sciences New Delhi	13.64
384.	Development and dissemination of intervention strategies for specific learning disability	Dr. Manju Mehta All India Institute of Medical Sciences New Delhi	0.19

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
385.	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	1.95
386.	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	2.37
387.	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	16.11
388.	Medulloblastoma in children and adults : A comparative study with special reference to clinicopathological features as well as cell proliferation, apoptosis and their regulatory proteins	Dr. Chitra Sarkar All India Institute of Medical Sciences New Delhi	2.95
389.	Ultrasound biomicroscopic study in primary angle closure glaucoma families	Dr. Ramanjit Sihota All India Institute of Medical Sciences New Delhi	1.39
390.	Incremental predictive accuracy of transcranial magnetic stimulation (TMS) as prognostic indicators for motor recovery in patients with acute stroke	Dr. Sumit Singh All India Institute of Medical Sciences New Delhi	0.91
391.	Amniotic membrane transplantation in acute ocular burns : A randomised controlled clinical trial	Dr. Radhika Tandon All India Institute of Medical Sciences New Delhi	1.05
392.	Prognostic markers in retinoblastoma : An immunohistochemical study	Dr. H.K. Tewari All India Institute of Medical Sciences New Delhi	1.34
393.	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	0.56
394.	Molecular study on mitochondral dysfunction in Parkinson's disease	Sh. S. Vivekanandhan All India Institute of Medical Sciences New Delhi	1.41

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
395.	Non-response to interferon therapy in patients with chronic hepatitis C in India : Evaluation of mechanisms, viral and host factors	Dr. S.K. Sarin G.B. Pant Hospital New Delhi	13.71
396.	Plasma modification of polypropylene monofilament for biomedical application	Dr. Bhuvanesh Gupta Indian Institute of Technology New Delhi	1.13
397.	Pathophysiological, biomechanical and metallurgical study of orthopaedic implants	Dr. R.K. Saxena Indian Institute of Technology New Delhi	4.69
398.	The role of pentanucleotide repeat (PNR) and kringle IV polymorphism in atherosclerosis	Dr. Uttam Pati Jawaharlal Nehru University New Delhi	6.35
399.	Investigation into androgen - independent activation of androgen receptor in prostrate cancer	Dr. Rakesh Kumar Tyagi Jawaharlal Nehru University New Delhi	2.21
400.	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	2.07
401.	Studies on the association of chronic infection with coronary artery disease (CAD) with special reference to *Chlamydia pneumoniae*	Dr. S. Padmavati National Heart Institute New Delhi	4.57
402.	Role of IGF - 1 and TNF alpha in progress and treatment of neurodegenerative diseases	Dr. Kakoli Ghoshal National Institute of Immunology New Delhi	3.98
403.	Comparison of arhroscopically assisted anterior crucate ligiament reconstructions using bone graft and senitendinasus graft for the management of symptomatic anterior cruciate ligament deficient knees: A clinical study	Dr. Deepak Choudhary Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	2.26
404.	Prevention of disability among pre - school children	Dr. H.C. Goyal Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	5.78
405.	Risk of malformations in children of women with epilepsy - A prospective, controlled study	Dr. D.C. Jain Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	4.72

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
406.	*In vitro* cultivation of differentiated epidermis from human keratinocytes suitable for autologous grafting in burns patients	Dr. R.P. Narayan Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	6.49
407.	Prevalence of STI in rural and urban community in Delhi	Dr. Krishna Ray Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi	14.51
408.	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	2.54
409.	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	2.85
410.	Relevance and significance of proteins S100 - A2, A4, A6 and B in CNS neoplasms and development of cell lines from clinical specimens	Dr. Anjali S. Shiras National Centre for Cell Sciences (NCCS) Pune	0.57
411.	Mental health service needs and service delivery models in the disaster affected population, Rajkot Centre	Dr. M.J. Somani Government Medical College Rajkot	4.01
412.	Control of cancer through multi-organ approach - A district level operational research project	Dr. H.L. Kapoor Indira Gandhi Medical College Shimla	10.21
413.	Population Based Cancer Registry	Dr. Sekhar Chakravarty Silchar Medical College Silchar	10.21
414.	Recent trends in role of diet and drinking water in urolithiasis	Dr. Y.M. Fazil Marickar Medical College and Sat Hospital for Women & Children Thiruvananthapuram	3.61
415.	Chemotherapy response in osteosarcoma : Role of intrinsic cellular factors	Dr. N. Geetha Regional Cancer Centre Thiruvananthapuram	1.15
416.	Trivandrum quality of life study : A study on quality of life in breast cancer patients undergoing treatment with curative intent	Dr. Manoj Pandey Regional Cancer Centre Thiruvananthapuram	0.12

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
417.	Human papillomavirus E6, E7 and p53 gene polymorphism in Indian cervical carcinoma	Dr. M. Radhakrishna Pillai Regional Cancer Centre Thiruvananthapuram	2.50
418.	Prognostic evaluation of karyotypic changes and telomerase activity in preleukemic and leukemic conditions	Dr. A. Ravindran Regional Cancer Centre Thiruvananthapuram	1.28
419.	Angiotensin II in the pathogenesis of myocardial lesions in magnesium deficiency	Dr. K. Shivakumar Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram	1.49
420.	Development of sentinel health monitoring centres in India	Dr. K.R. Thankappan Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram	5.43
421.	Registry of pregnancy in women with epilepsy	Dr. Sanjeev V. Thomas Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram	2.85
422.	Evaluation of intraoperative SSEP and MEP changes in patients undergoing spinal cord surgery in order to predict the outcome	Dr. K. Srinivasa Babu Christian Medical College and Hospital Vellore	0.68
423.	Studies on energy deficiency in an animal model of hepatic microvesicular steatosis produced by inhibition of fatty acid oxidation	Dr. K.A. Balasubramanian Christian Medical College and Hospital Vellore	2.47
424.	*Jai Vigyan* mission mode project on RF/RHD (Registry Protocol)	Dr. Vinohar Balraj Christian Medical College and Hospital Vellore	15.88
425.	*Jai Vigyan* mission mode project on community control of RF/RHD in India	Dr. K.N. Brahmadathan Christian Medical College and Hospital Vellore	7.78
426.	Quantifying the contribution of neurocysticercosis to the causation of seizures and study the seroprevalence of cysticercosis in rural and urban communities in Vellore district of Tamil Nadu	Dr. Vedantam Rajshekhar Christian Medical College and Hospital Vellore	5.08
427.	Organophosphate poisoning : The relationship of oxidative stress to the occurrence of intermediate syndrome	Dr. Anand Zachariah Christian Medical College and Hospital Vellore	0.52

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
Basic Medical Sciences			
428.	Leprosy genomics : The genomic diversity of leprosy bacillus and expression of its genes in human host	Dr. V.M. Katoch Central Jalma Institute for Leprosy Agra	5.49
429.	Immunogenecity of DNA damaged by singlet oxygen: Implications for anti-DNA antibodies in autoimmune disorders	Dr. Rashid Ali Jawaharlal Nehru Medical College, Aligarh Muslim Universtiy Aligarh	2.88
430.	Studies on the reactive oxygen species damaged DNA : Implications in the etiopathogenesis of SLE	Sh. Moinuddin Jawaharlal Nehru Medical College, Aligarh Muslim Universtiy Aligarh	0.63
431.	Development of new erythromycin derivatives	Dr. P.K. Manna Annamalai University Annamalai Nagar	0.81
432.	Functional genomics of the proteins interacting with the bacterial cell division protein FTSZ in the proliferating and dormant *Mycobacterium tuberculosis* H37RV	Dr. P. Ajit Kumar Indian Institute of Science Bangalore	3.00
433.	Gene-expression profiling of normal and malignant human ratina and eyelids	Dr. Arun Kumar Indian Institute of Science Bangalore	3.14
434.	Molecular basis of rotavirus pathogenesis : Comparative structural and biological functional studies on the rotaviral enterotoxigenic protein NSP4	Dr. C. Durga Rao Indian Institute of Science Bangalore	2.66
435.	Redox reactivities of metal oxides and peroxides	Dr. M.S. Hegde Indian Institute of Science Bangalore	2.08
436.	Functional and structural genomics of RECA intein of *Mycobacterium tuberculosis* and *M.leprae*	Dr. K. Muniyappa Indian Institute of Science Bangalore	4.53
437.	Mechanism of transcription termination in mycobacteria	Dr. V. Nagaraja Indian Institute of Science Bangalore	5.29
438.	Identification and functional characterization of genes modulated by bacterial components and/or proinflammatory cytokines in a hepatoma cell line, H6	Dr. Dipankar Nandi Indian Institute of Science Bangalore	3.15

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439.	Immunogenomics and pathogenomics of *M.tuberculosis* and *M.bovis* (BCG)	Dr. R. Nayak Indian Institute of Science Bangalore	5.61
440.	DNA repair and susceptibility to cancer	Dr. M.R.S. Rao Indian Institute of Science Bangalore	2.50
441.	Proposal for support for an ICMR programme of advanced research and training in human molecular cytogenetics	Dr. H. Sharat Chandra Indian Institute of Science Bangalore	17.62
442.	Gene expression profiling of cisplatin sensitive and resistant cells using cDNA microarrays	Dr. K. Somasundaram Indian Institute of Science Bangalore	3.03
443.	A functional genomics approach to understanding diarrhoeas mediated by the heat-stable enterotoxin	Dr. Sandhya S. Visweswariah Indian Institute of Science Bangalore	5.77
444.	Molecular genetic basis of hot water epilepsy	Dr. Anuranjan Anand Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	15.50
445.	Purification of anti-malarial compounds from Indian herbs and elucidation of their mode of action in *Plasmodium falciparum*	Dr. Namita Surolia Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	2.53
446.	Molecular diagnosis of common opportunistic infections in cancer	Dr. R.S. Jayshree Kidwai Memorial Institute of Oncology Bangalore	2.26
447.	A molecular genetic study of special sub-groups of psychoses	Dr. Sanjeev Jain National Institute of Mental Health and Neurosciences Bangalore	1.50
448.	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	2.02
449.	Puerperal cerebral venous thrombosis: A genetic approach to etiology	Dr. D. Nagaraja National Institute of Mental Health and Neurosciences Bangalore	3.58
450.	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	1.89

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451.	Handigodu diseases - Phase II	Dr. K. Taranath Shetty National Institute of Mental Health and Neurosciences Bangalore	2.50
452.	Molecular genetics of neuro-muscular disorders	Dr. Anisya Vasanth National Institute of Mental Health and Neurosciences Bangalore	1.50
453.	*Jai Vigyan* mission project on community control of thalassaemia syndromes - Awareness, screening, genetic counselling and prevention	Dr. Cecil R. Ross St. John's Academy of Health Sciences Bangalore	13.15
454.	Survey and designing of monograph on medicinal plants of Western Ghat situated in Karnataka state	Dr. F.V. Manvi K.L.E. Society's College of Pharmacy Belgaum	0.33
455.	A survey of the medicinal plants of Western Ghat	Dr. S.D. Kholkute Regional Medical Research Centre Belgaum	7.15
456.	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. G.P. Chhotray Regional Medical Research Centre Bhubaneswar	3.67
457.	Characterization of serine/ threonine kinases of *Mycobacterium tuberculosis*	Dr. P.K. Chakraborti Institute of Microbial Technology Chandigarh	4.78
458.	Effect of prenatal exposure of ethanol on the functional development of intestine in rats	Dr. Akhtar Mahmood Panjab University Chandigarh	0.66
459.	Detection and identification of fungal pathogens in blood using molecular probes	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	2.07
460.	Characterization of IgA protease gene of *H. influenzae* from children of different age groups by DNA based techniques	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	2.68
461.	Characterization of virulent genes of enteroaggregative *E.coli* to correlate their role in disease progression	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	3.41
462.	Genomics of glucose-6-phosphate dehydrogenase deficiency in North Indian population	Dr. Gurjeevan Garewal Postgraduate Institute of Medical Education and Research Chandigarh	4.21

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463.	Study on the effect of the disease specific sialo glycoconjugate specific lectin in lung carcinoma	Dr. Sujata Ghosh Postgraduate Institute of Medical Education and Research Chandigarh	2.91
464.	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	2.53
465.	Studies on the effect of chronic ethanol feeding on transport of folate and expression of its transporter in rat intestine	Dr. Jyotdeep Kaur Postgraduate Institute of Medical Education and Research Chandigarh	2.30
466.	Analysis of genomic variation in population with kidney stone disease	Dr. Madhu Khullar Postgraduate Institute of Medical Education and Research Chandigarh	3.16
467.	Genetic risk factors in adolescents and young adults for coronary artery disease : Genetic polymorphism in apoA, apoB, apoE gene loci and its influence on blood lipid levels	Dr. Madhu Khullar Postgraduate Institute of Medical Education and Research Chandigarh	4.82
468.	Chemotherapeutic potential of poly (lactide -co-glycolide) micro-particles as controlled release delivery systems for antitubercular drugs against experimental tuberculosis	Dr. G.K. Khuller Postgraduate Institute of Medical Education and Research Chandigarh	3.08
469.	Immunoprophylactic properties of 30kDa secretory protein of *M.tuberculosis* H37RA in different adjuvant systems and immunophenotyping during immunization/infection	Dr. G.K. Khuller Postgraduate Institute of Medical Education and Research Chandigarh	1.43
470.	Protective efficacy of *M. tuberculosis* complex specific protein antigens against experimental tuberculosis	Dr. G.K. Khuller Postgraduate Institute of Medical Education and Research Chandigarh	4.16
471.	Role of vitamin E in the regulation of surfactant synthesis, secretion and protection of the lung alveolar type II cells following hyperoxic injury	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	4.74

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
472.	Alterations in the phospholipid transfer protein (PLTP) gene expression in neonates with respiratory distress syndrome	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	5.29
473.	Alteration in interleukin-6 (IL-6) and tumour necrosis factor alpha (TNF alpha) gene expression in neonatal sepsis	Dr. Anil Narang Postgraduate Institute of Medical Education and Research Chandigarh	5.70
474.	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	7.61
475.	Facial reconstruction of skulls	Dr. Daisy Sahni Postgraduate Institute of Medical Education and Research Chandigarh	1.96
476.	Antimycobacterial activity of human neutrophil peptide -1 (HNP-1)against drug resistant strains of mycbacteria and its role as antiresistance peptide	Dr. Indu Verma Postgraduate Institute of Medical Education and Research Chandigarh	2.81
477.	Immunoprophylactic studies in filariasis using recombinant parasitic enzymes : Transglutaminase and thioredoxin peroxidase	Dr. Perumal Kaliraj Centre for Biotechnology Chennai	3.67
478.	Flexible dose open trial on *Vijayasar* for known diabetes	Dr. R.S. Hariharan Chennai Medical College and Government General Hospital Deemed University Chennai	9.56
479.	A study on the efficacy of alcohol oxidase loaded erythrocytes in combating methanol toxicity	Dr. A. Namasivayam Dr.A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai	1.50
480.	A survey of the medicinal plants of Western Ghats	Dr. S. Ignacimuthu Entomology Research Institute Chennai	2.43
481.	Antimycobacterial activity of *Solanum trilobatum, Adhatoda vesica* and *Garcinia pictoria*	Dr. S. Ignacimuthu Entomology Research Institute Chennai	2.04

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
482.	Central Biostatistical Monitoring Unit for Traditional Medicine Research	Dr. M.D. Gupte National Institute of Epidemiology Chennai	9.86
483.	Clinical Pharmacology Unit	Dr. V. Kumaraswami Tuberculosis Research Centre Chennai	5.78
484.	Flexible dose open trial on *Vijayasar* for known diabetes	Dr. P.K. Mishra S.C.B. Medical College Cuttack	5.7
485.	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	Col. Arvind Gupta Base Hospital Delhi	1.22
486.	Analysis of polymorphism and expression profile of genes of mammalian cell entry (MCE) operons in clinical isolates of *M.tuberculosis*	Dr. Vani Brahmachari Dr. B.R. Ambedkar Centre for Biomedical Research University of Delhi Delhi	2.78
487.	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	5.46
488.	Genetic markers: Vulnerability to common neuro-psychiatric diseases	Dr. Suman Kapur Institute of Human Behaviour and Allied Sciences Delhi	4.36
489.	Genetic diversity of *Plasmodium falciparum* and *P.vivax* in India using molecular markers	Dr. Hema Joshi Malaria Research Centre Delhi	3.81
490.	Determinants of genetic and sociocultural aspects of health *vis-a-vis* the role of health providers among the tribes of coastal, desert and Himalayan regions	Dr. G.K. Kshatriya University of Delhi Delhi	5.70
491.	Studies on mechanism of signal transduction during release of proinflammatory cytokines IL-1beta and TNF-alpha by alveolar macrophages in asthma	Dr. S.K.Bansal Vallabhbhai Patel Chest Institute University of Delhi Delhi	6.96

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
492.	Investigation of antihepatotoxic activity of certain traditionally used plant species of Assam	Dr. J.C. Gogoi Assam Medical College Dibrugarh	6.13
493.	*Jai Vigyan* mission project on community control of thalassaemia syndromes - Awareness, screening, genetic counselling and prevention	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	8.55
494.	Genetic analysis of pancreatitis in Indian population	Dr. G.R. Chandak Centre for Cellular and Molecular Biology Hyderabad	6.06
495.	Handigodu diseases - phase II	Dr. G.R. Chandak Centre for Cellular and Molecular Biology Hyderabad	22.00
496.	Gene expression profiling of skeletal muscle stem cells using DNA microarrays	Dr. Jyotsna Dhawan Centre for Cellular and Molecular Biology Hyderabad	10.68
497.	Genetics of reproductive dysfunction in women	Dr. A.P. Singh Centre for Cellular and Molecular Biology Hyderabad	2.25
498.	Immunotherapy against intracellular infections, using TLTF cDNA delivered as naked DNA	Dr. Tushar Vaidya Centre for Cellular and Molecular Biology Hyderabad	3.25
499.	Computational analysis and functional characterization of mycobacterial protein(s) interacting with macrophage effector-APC functions - An approach to understand the molecular basis of pathogenesis of *M.tuberculosis*	Dr. Sangita Mukhopadhyay Centre for DNA Fingerprinting and Diagnostics Hyderabad	2.29
500.	Molecular genetic analysis of some forms of inherited childhood blindness, and genetic counselling of the affected families	Dr. Chitra Kannabiran L.V. Prasad Eye Institute Hyderabad	3.91
501.	PPAR mediated regulation of glucose metabolism and coronary heart diseases: Understanding the mechanism of action	Dr. Nasreen Z. Ehtesham National Institute of Nutrition Hyderabad	2.50

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
502.	Centre for Advanced Research for Pre-clinical Toxicology	Dr. B. Sivakumar National Institute of Nutrition Hyderabad	7.21
503.	Preclinical investigations on the molecular mechanism of testicular/post-testicular contraceptive effects of the seed products of *Carica papaya*	Dr. N.K. Lohiya University of Rajasthan Jaipur	1.30
504.	Application of primary monolayer cultures of rat hepatocytes in the development of hepatoprotectives from medicinal plants	Dr. R.K. Johri Regional Research Laboratory Jammu Tawi	1.56
505.	Development of a synergistic hepatoprotective formulation	Dr. O.P. Suri Regional Research Laboratory Jammu Tawi	1.55
506.	Development of DNA fingerprints as molecular marker in selected medicinal plants	Dr. V. Verma Regional Research Laboratory Jammu Tawi	3.30
507.	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	3.74
508.	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	2.81
509.	Adrenergic, gabaergic and serotonergic gene expression, their interaction on insulin secretion and pancreatic β-cell proliferation	Dr. C.S. Paulose Cochin University of Science and Technology Kochi	4.50
510.	Functional genomics of *E.histolytica* to identify genes controlling growth and proliferation	Dr. Anuradha Lohia Bose Institute (New Campus) Kolkata	10.14
511.	Genomics, proteomics and bioinformatics of some target genes of *M.tuberculosis* for drug development	Dr. Joyoti Basu Bose Institute (Main Campus) Kolkata	7.85

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
512.	Antigens and immune response in tuberculous infections	Dr. Parul Chakrabarti Bose Institute (Main Campus) Kolkata	4.03
513.	Experimental determination of suitability of cholesteryl oleyl carbonate in fluidizing cholesteryl oleate in atherosclerotic plaque	Dr. Pradip Das Bose Institute (Main Campus) Kolkata	2.84
514.	Host cell signalling in relation to *Helicobacter pylori* pathogenesis	Dr. Manikuntala Kundu Bose Institute (Main Campus) Kolkata	3.24
515.	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	3.16
516.	Potential plant as antileishmanial drug	Dr. Sharmila Chattopadhyay Indian Institute of Chemical Biology Kolkata	2.83
517.	Molecular mechanisms of virulence loss associated with laboratory maintenance of the enteric pathogen *Vibrio cholerae*	Dr. Rukhsana Chowdhury Indian Institute of Chemical Biology Kolkata	4.29
518.	Role of sialoglycoconjugates in host-parasite interactions in visceral leishmaniasis	Dr. Chitra Mandal Indian Institute of Chemical Biology Kolkata	1.98
519.	Study of protein histidine kinase in *L.donovani*: A potential new chemotherapeutic target against kala azar	Dr. Sucheta Mukherji Indian Institute of Chemical Biology Kolkata	2.23
520.	Molecular characterization of Wilson's disease in Indian population	Dr. Kunal Ray Indian Institute of Chemical Biology Kolkata	4.38
521.	Characterization of cytokine gene polymorphism in *H.pylori* infected Indian population	Dr. Susanta Roychoudhury Indian Institute of Chemical Biology Kolkata	6.48

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
522.	Effect of alu insertion / deletion polymorphism at the DCP1 locus on blood pressures among individuals belonging to defined haplogroups drawn from two tribal populations of India	Dr. P.P. Majumder Indian Statistical Institute Kolkata	2.97
523.	Studies on the antileishmanial properties of novel naphthoquinonoid derivatives and their therapeutic applications	Dr. Banarasi Hazra Jadavpur University Kolkata	1.69
524.	Production of a functional antimicrobial peptide in order to study the potential bacterial resistance it may encounter	Dr. S.K. Pal Jadavpur University Kolkata	3.08
525.	*Jai Vigyan* mission project on community control of thalassaemia syndromes - Awareness, screening, genetic counselling and prevention	Dr. M.K. Ghosh N.R.S. Medical College and Hospital Kolkata	16.87
526.	Rotavirus genomics	Dr. T.N. Naik National Institute of Cholera and Enteric Diseases Kolkata	5.49
527.	Studies on the mechanism of oxidative damage to anaemic red blood cells and protection by anti-oxidants	Dr. A.G. Datta The Society for Research on Haematology and Blood Kolkata	1.04
528.	Isolation, purification and characterization of antibacterial activity against *Vibrio cholerae* from medicinal plants	Dr. P.K. Bag University College of Science Kolkata	9.42
529.	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. K.S. Asokan Nilgiris Adivasi Welfare Association Kotagiri	4.08
530.	Flexible dose open trial on *Vijayasar* for known diabetes	Dr. R.V. Jayakumar Medical College and Hospital Kottayam	7.07
531.	Identification and functional studies on potential drug targets from *M.tuberculosis*, *P.falciparum* and *L.donovani*	Dr. C.M. Gupta Central Drug Research Institute Lucknow	10.04

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
532.	Search for potent antifungal peptides using knowledge based combinatorial libraries of peptides	Dr. Bijoy Kundu Central Drug Research Institute Lucknow	1.71
533.	Design and development of new class of antimycobacterial agents	Dr. R.P. Tripathi Central Drug Research Institute Lucknow	0.29
534.	Neurochemical, reproductive and immunotoxicological evaluation of the pyrethroid based mosquito repellents exposed during developmental period	Dr. P.K. Seth Industrial Toxicology Research Centre Lucknow	0.29
535.	Chemopreventive effects of black tea and its constituents	Dr. Yogeshwer Shukla Industrial Toxicology Research Centre Lucknow	0.72
536.	Microsatellite variation in North Indian subpopulations	Dr. Suraksha Devi Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	3.50
537.	Molecular epidemiology of human and animal hepatitis E viruses (HEV) in India	Dr. Rakesh Aggarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	5.97
538.	Role of alpha, beta and gamma delta T - cells in Takayasu's arteritis	Dr. Soniya Nityanand Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	4.39
539.	*Jai Vigyan* mission project on community control of thalassaemia syndromes - Awareness, screening, genetic counselling and prevention	Dr. Sheila Das Christian Medical College and Brown Memorial Hospital Ludhiana	16.61
540.	Physiological and behavioural aspects of human circadian rhythms under prolonged socio-temporal isolation	Dr. G. Marimuthu Madurai Kamaraj University Madurai	0.48
541.	Evaluation of the effect of potecan in combination with radiation in cultured human fibroblasts	Dr. G.C. Jagetia Kasturba Medical College and Hospital, Mahe (Deemed University) Manipal	1.02
542.	ICMR Unit on Standardisation and Quality Control and Formulation of Traditional Medicine	Dr. K.K. Bhutani National Institute of Pharmaceutical Education and Research Mohali	3.67

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
543.	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	2.77
544.	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India - Technical Coordinating Centre	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	10.96
545.	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	4.54
546.	*Jai Vigyan* mission project on community control of thalassaemia syndromes - Awareness, screening, genetic counselling and prevention	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	16.86
547.	Catalytic antibodies against factor VIII : Structure, function and implications for therapy	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	1.21
548.	Incidence and molecular characterization of G6PD deficiency in North East India	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	9.64
549.	Molecular pathology of some haematological disorders	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	5.11
550.	Study of some genetic aspects of essential hypertension in North-East region	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	5.11
551.	Genomic imprinting: A paternal contribution to embryogenesis	Dr. Nafisha Huseni Balasinor National Institute for Research in Reproductive Health Mumbai	2.24
552.	Genomic studies related to micro-deletion of Y-chromosome in severe oligospermic and non-obstructive azoospermic males	Dr. Jyotsna S. Gokral National Institute for Research in Reproductive Health Mumbai	6.08
553.	Mutational analysis of human gonadotropin receptor genes and its implications in physiology and pathophysiology of pituitary-gonadal function	Dr. Smita Dilip Mahale National Institute for Research in Reproductive Health Mumbai	3.00

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
554.	Genomic studies in polycystic ovaries and congenital adrenal hyperplasia	Dr. Anurupa Maitra National Institute for Research in Reproductive Health Mumbai	3.54
555.	Genomic studies in premature ovarian failure (POF) : Its association with fragile X permutation	Dr. P.K. Meherji National Institute for Research in Reproductive Health Mumbai	2.83
556.	Cryptic chromosomal rearrangements amongst couples with recurrent abortions - Molecular analysis	Dr. Zareen M. Patel National Institute for Research in Reproductive Health Mumbai	0.39
557.	Role of a novel androgen regulated hoxβ-2 containing gene expressed in the epididymis	Dr. Vijaya Raghavan National Institute for Research in Reproductive Health Mumbai	4.38
558.	Endometrial maps of receptive and non-receptive uterus in primates	Dr. Geetanjali Sachdeva National Institute for Research in Reproductive Health Mumbai	4.93
559.	Survey on medicinal plants of Western Ghat	Dr. Usha Mukundan Ramnirajan Jhunjhunwala College Mumbai	1.57
560.	Towards the development of therapeutic agents using information from malaria immune persons from endemic areas of Orissa	Dr. Shobhona Sharma Tata Institute of Fundamental Research Mumbai	3.41
561.	Development of enriched / cocktail antivenin to the toxic principles of *Vipera russelli* venom of different regions of India	Dr. T. Veerabasappa Gowda University of Mysore Mysore	0.61
562.	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. D.L. Jain Government Medical College and Hospital Nagpur	4.55
563.	Handigodu disease - Phase II	Dr. S.S. Agarwal Advanced Centre for Treatment, Research & Education in Cancer (ACTREC) Navi Mumbai	5.00
564.	Flexible dose open trial on *Vijayasar* for known diabetes	Dr. A.C. Ammini All India Institute of Medical Sciences New Delhi	6.89

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
565.	Ophthalmic drug formulations using polymeric nanoparticles as carriers	Dr. N.R. Biswas All India Institute of Medical Sciences New Delhi	2.71
566.	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	5.98
567.	Immunogenetics of mycobacterial diseases : A 13IHWC international study	Dr. N.K. Mehra All India Institute of Medical Sciences New Delhi	4.00
568.	Developing epitope based immunogen using different stages of *P.vivax* using inbuilt immuno adjuvants and delivery in microspheres	Dr. D. Nageswara Rao All India Institute of Medical Sciences New Delhi	2.25
569.	Effect of alternations in intracellular cacium ion concentration on ORLI (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	1.00
570.	A study of the expression and targeting of inhibitor(s) of apoptosis - an *in vitro* and *in vivo* study	Dr. Neeta Singh All India Institute of Medical Sciences New Delhi	2.73
571.	Evaluation of topical cyclosporin A in prevention of corneal graft rejection	Dr. R.B. Vajpayee All India Institute of Medical Sciences New Delhi	2.83
572.	Cellular and molecular mechanism of alcohol related organ damage : Biochemical, immunological and genetic studies	Dr. Suman Vasisht All India Institute of Medical Sciences New Delhi	2.93
573.	Azathioprine *versus* coticosteroids for the treatment of *Parthenium* dermatitis - A double blind randomized controlled trial	Dr. K.K. Verma All India Institute of Medical Sciences New Delhi	1.84
574.	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India - Coordinating Unit	Dr. Vasantha Muthuswamy Indian Council of Medical Research New Delhi	2.79

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
575.	*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	3.41
576.	Construction and screening of *L.donovani* genomic DNA microarray for identification of differentially expressed genes in parasite isolates from kala-azar and PKDL patients	Dr. Poonam Salotra Institute of Pathology New Delhi	4.98
577.	Molecular analysis of refractoriness of mosquito *Anopheles culicifacies* to malaria parasite	Dr. R.K. Bhatnagar International Centre for Genetic Engineering and Biotechnology New Delhi	5.59
578.	Development of high throughput screen system based on heme detoxification of malaria parasite	Dr. V.S. Chauhan International Centre for Genetic Engineering and Biotechnology New Delhi	0.50
579.	Antigen-dependent lymphocyte activation thresholds in adaptive immunity	Dr. K.V.S. Rao International Centre for Genetic Engineering and Biotechnology New Delhi	13.91
580.	Hypoperfusion / reperfusion - induced brain ischaemia : Search for protective agents from herbo-mineral sources	Dr. Fakhrul Islam Jamia Hamdard (Hamdard University) New Delhi	2.76
581.	Herbal constituents as metabolic interceptors of chemical carcinogenesis	Dr. Sarwat Sultana Jamia Hamdard (Hamdard University) New Delhi	1.82
582.	Comparative genomics approach to identify pathogenesis - Related genes in *Entamoeba Histolytica*	Dr. Sudha Bhattacharya Jawaharlal Nehru University New Delhi	3.49
583.	To investigate neurochemical regulation of REM sleep and cellular changes after REM sleep deprivation	Dr. B.N. Mallick Jawaharlal Nehru University New Delhi	2.36
584.	Genetic engineering of edible crop plants with oxalate decarboxylase for removal of oxalic acid, an antinutritional stress factor for better human nutrition	Dr. Subhra Chakraborty National Centre for Plant Genome Research New Delhi	9.23

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
585.	Innate immune recognition of filarial parasites by phagocytes	Dr. Vineeta Bal National Institute of Immunology New Delhi	2.54
586.	Domestication and cultivation of characterized population of *Picrorrhiza kurrooa* royle ex.benth. in Indian Western Himalaya	Dr. Virendra Singh Institute of Himalayan Bioresource Technology Palampur	3.33
587.	Survey of medicinal plants of Western Ghats of Goa state	Dr. B.F. Rodrigues Goa University Panaji	0.33
588.	Genetic polymorphism of drug metabolising enzymes in South Indian population	Dr. C. Adithan Jawaharlal Institute of Postgraduate Medical Education & Research Pondicherry	2.78
589.	Immunological and molecular studies on the mosquito humoral factors involved in the susceptibility/ regulation of *Wuchereria bancrofti* infection and development in *Culex quinquefasciatus*	Dr. K.P. Paily Vector Control Research Centre Pondicherry	2.33
590.	HIV-1 subtyping and detection of HIV-1 recombinants in India	Dr S.P. Tripathy National AIDS Research Institute Pune	2.97
591.	Multi cellular spheroids (MCS) - A 3D *in vitro* model for studies on cellular and molecular aspects of tumour progression and metastasis	Dr. Padma R. Shastry National Centre for Cell Sciences (NCCS) Pune	4.51
592.	Antioxidant vitamin supplements as palliative treatment of bone disorders	Dr. A.N. Sontakke Padmashree Dr. D.Y. Patil Medical College for Women Pune	2.94
593.	Handigodu disease - Phase II	Dr. Natraj Sagar General Hospital Sagar	7.03
594.	Survey of medicinal plants of Western Ghats of Kerala	Dr. A. Banerji Regional Research Laboratory Thiruvananthapuram	1.17
595.	Inhibition of tumour specific angiogenesis of endothelial cells by curcuminoid derivatives	Dr. Girija Kuttan Amala Cancer Hospital and Research Centre Thrissur	2.32

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
596.	*Jai Vigyan* mission project on community control of thalassaemia syndromes - Awareness, screening, genetic counselling and prevention	Dr. R.Z. Patel Medical College and S.S.G. Hospital Vadodara	16.70
597.	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Y.M. Italia Valsad Raktadan Kendra Valsad	3.03
598.	Studies on the status of gastric mucosal defensive factors *per se* and on physical and chemical factors-induced gastric ulceration in experimental diabetic rats *vis a vis* some Indian medicinal plants	Dr. R.K. Goel Institute of Medical Sciences Banaras Hindu University Varanasi	1.31
599.	Role of minor histocompatiblity system in the clinical outcome of familial marrow transplanation	Dr. Alok Srivastava Christian Medical College and Hospital Vellore	2.03
600.	Pharmacokinetics of enantiomers of profens in women during different phases of menstrual cycle	Dr. V. Venkateswarlu University College of Pharmaceutical Sciences Warangal	2.93
Medicinal Plants Unit			
601.	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. M. Rajani BV Patel Pharmaceutical Education and Research Development Centre Ahmedabad	1.13
602.	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	8.30
603.	Quality standards of Indian medicinal plants and preparation of monographs thereof	Dr. M. Rajani BV Patel Pharmaceutical Education and Research Development Centre Ahmedabad	8.30
604.	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	9.87

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
605.	Medicinal plant monographs on diseases of public health importance - Filaria	Dr. R.K. Shenoy T.D.Medical College and Hospital Alappuzha	0.05
606.	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. Karan Vasisht Panjab University Chandigarh	6.33
607.	Quality standards of Indian medicinal plants	Dr. A. Saraswathy Captain Srinivasamurthy Drug Research Institute for Ayurveda Chennai	3.72
608.	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	8.01
609.	Heavy metals and persistent pesticide analysis for quality assurance of selected therapeutically important medicinal plants	Dr. Poonam Kakkar Industrial Toxicology Research Centre Lucknow	4.40
610.	Quality standards of Indian medicinal plants and preparation of monographs thereof	Dr. A.K.S. Rawat National Botanical Research Institute Lucknow	3.44
611.	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. R.T. Sane Ram Narain Ruia College Mumbai	7.10
612.	Monographs on Medicinal Plants of India	Dr. Ashok Gupta Indian Council of Medical Research New Delhi	7.49
613.	Medicinal plant monographs on diseases of public health importance - Coordinating Unit	Dr. Ashok Gupta Indian Council of Medical Research New Delhi	5.42
614.	Review monographs on Indian medicinal plants	Dr. Ashok Gupta Indian Council of Medical Research New Delhi	25.29
615.	Quality standards of Indian medicinal plants and preparation of monographs thereof	Dr. A.M. Majumdar Agharkar Research Institute Pune	3.44

Sl. No.	Title of the Project	Investigator/Institute	Grant Released during the year (Rs. in lakhs)
616.	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. V. George Tropical Botanic Garden and Research Institute Thiruvananthapuram	2.62
617.	Medicinal plant monographs on diseases of public health importance - Anti-inflammatory Drugs	Dr. R.H. Singh Institute of Medical Sciences Banaras Hindu University Varanasi	2.62
Publication and Information			
618.	Scientometric studies - An ICMR sponsored study	Dr. K. Satyanarayana Indian Council of Medical Research New Delhi	3.01
Intellectual Property Rights			
619.	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	1.93
620.	WISTA: Vaccines/diagnostics	Dr. K.V. Swaminathan Waterfalls Institute of Technology Transfer New Delhi	1.50

Research Fellowships Funded during 2003-2004

Sl. No.	Title of the Project	Name of the Fellow/Institute
Epidemiology and Communicable Diseases		
1.	Role of apoptosis in the pathogenesis of rabies. correlation of virological, pathological and immunological parameters - A study in human, canine and rodent nervous system	Km. M.S. Suja National Institute of Mental Health and Neurosciences Bangalore
2.	Molecular and cellular approach to the pathogenesis of neurotuberculosis: A preliminary study on characterization of *M. tuberculosis* isolates from CSF and sputum	Sh. M.V. Manjunath National Institute of Mental Health and Neurosciences Bangalore
3.	Development of an immunodiagnostic assay using recombinant p1 protein of *Mycoplasma pneumoniae*	Smt. Irum Tabassum National Tuberculosis Institute Bangalore
4.	A study of polymorphic regions of the genes encoding protective antigens of *P. vivax* and *P. falciparum* strains prevalent in North - Western regions of India	Sh. Umar Farooq Gaur Postgraduate Institute of Medical Education and Research Chandigarh
5.	Cytokine responses in symptomatic *vs* asymptoimatic amoebiasis patients	Sh. Devendra Bansal Postgraduate Institute of Medical Education and Research Chandigarh
6.	To study the expression of major virulence factor: Streptococcal 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
7.	Rapid detection and identification of dengue virus by molecular methods	Km. Jayashri Mahalingam King Institute of Preventive Medicine Chennai
8.	A study of the clinical presentation of tuberculosis in HIV positive patients and its correlation with CD4 and CD8 counts	Dr. Amit Mann Base Hospital Delhi
9.	Dermatological manifestations in HIV infection and its correlation with CD4 count	Dr. Gulhima Chawla Base Hospital Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
10.	Role of apoptosis in the pathogenesis of influenza A virus, correlation of virological and immunological parameters : A study in human and murine model	Sh. Vikram Srivastava Vallabhbhai Patel Chest Institute University of Delhi Delhi
11.	Identification and pathogenesis of influenza virus in acute exacerbation of asthma	Sh. Pankaj Kumar Vallabhbhai Patel Chest Institute University of Delhi Delhi
12.	Analysis of molecular basis of pyrazinamide resistance in mycobacteria	Smt. E. Ezhilkatharine Vallabhbhai Patel Chest Institute University of Delhi Delhi
13.	Study of extracellular proteinase and phospholipase activities of clinical and environmental isolates of *Cryptococcus neoformans*, *Candida albicans* and *non-albicans*	Sh. S.R. Nawange Rani Durgawati Vishwavidyalaya Jabalpur
14.	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	Sh. Arup Banerjee ICMR Virus Unit Kolkata
15.	Characterization of extended spectrum beta lactamase producing *Klebsiella* spp. isolated from Intensive Care Unit	Sh. Rajesh Kumar Mondal Chhatrapati Shahuji Maharaj Medical University Lucknow
16.	Effect of chromium on dengue virus infection in mice	Km. Richa Shrivastava Industrial Toxicology Research Centre Lucknow
17.	A prospective study to evaluate the role of *Clostridium perfringens* in diarrhoea versus controls and their phenotypic and genotypic characterization	Km. Lovely Joshy All India Institute of Medical Sciences New Delhi
18.	Development of a conjugate vaccine for enteric fevers	Km. Sanyukta Sengupta All India Institute of Medical Sciences New Delhi
19.	Revalidation of syndromic approach for the management of genital ulcer disease in Northern India	Dr. Manjula Singh All India Institute of Medical Sciences New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
20.	Characterization of devR - devS and devS homologue (Rv2027C gene product) of *Mycobacterium tuberculosis* with special reference to their phosphorylation	Sh. S. Chakravorty All India Institute of Medical Sciences New Delhi
21.	Study of chronic hepatitis B and C in patients co-infected with human immuno deficiency virus	Dr. A.K. Garg Army Hospital (Research & Referral) New Delhi
22.	Adrenocortical function in human immunodeficiency virus (HIV) infection	Dr. Amitava Mitra Army Hospital (Research & Referral) New Delhi
23.	Study of mutation in the HBV genome in fulminant hepatitis patients and its clinical significance	Sh. Abdul Malik Jamia Milia Islamia New Delhi
24.	Cytoadherence and receptor - ligand interactions of *Plasmodium falciparum* field isolates with different receptor specificities	Sh. Anup Kumar Biswas Jawaharlal Nehru University New Delhi
25.	Epidemiology, molecular typing, strain characterization and drug resistance profiling of candidial infections in burn patients	Dr. Nivedita Gupta Jawaharlal Nehru University New Delhi
26.	Genital infection with human papilloma virus : Correlation with pregnancy and neonatal outcome	Dr. Garima Chauhan Maulana Azad Medical College and Associated Hospitals New Delhi
27.	Role of hepatitis E virus (HEV) infection in acute viral hepatitis and fulminant hepatitis during pregnancy	Km. Nishat Jilani Maulana Azad Medical College and Associated Hospitals New Delhi
28.	Study of hepatitis B virus (HBV) genotypes and their clinical significance in patients with HBV - related liver diseases	Sh. Saket Chattopadhyay Maulana Azad Medical College and Associated Hospitals New Delhi
29.	Study of non structural protein encoding gene of hepatitis C virus	Sh. Deepak Kumar Maulana Azad Medical College and Associated Hospitals New Delhi
30.	Seroefficacy of hepatitis B vaccine administered in the expanded programme of immunization at 0,6 wks and 9 months (along with DPT and measles)	Dr. Ajay Kumar Jain Maulana Azad Medical College and Associated Hospitals New Delhi
31.	Characterization of extended spectrum β-lactamases (ESBL) and β-lactmases of clinical strains of *Yersinia enterocolitica* isolated from India	Sh. Sachin Sharma University of Delhi South Campus New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
32.	Epidemiology and pathogenesis of fungal infections of nose and paranasal sinuses	Dr. Gurparamjit Singh Gill Government Medical College and Rajendra Hospital Patiala
	Reproductive Health and Nutrition	
33.	Clinico-biochemical profile of the referred sick newborns at admission and its relationship to outcome in terms of morbidity and mortality	Dr. Ruchi Rai Moti Lal Nehru Medical College Allahabad
34.	Role of oxidative stress on reproductive activity in mice	Km. Parminder Kaur Panjab University Chandigarh
35.	Evaluation of hepatoprotective role of zinc in conditions of nickel toxicity induced in protein deficient rats	Sh. P.S. Sidhu Panjab University Chandigarh
36.	Impact of maternal hypothyroidism on androgen receptor gene expression in the ventral prostate during pre-pubertal and pubertal period in rats	Km. P.J. Arokya Mary Sashi Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai
37.	Clinical effectiveness of co-trimoxazole - *versus* - amoxycillin for pneumonia in children - A randomized controlled trial	Dr. S.M. Rajesh Base Hospital Delhi
38.	Nutritional and hypoglycemic effect of fruit pulp and leaves of *Annona squamosa* (custard apple)	Sh. R.K. Gupta Dr. B.R. Ambedkar Centre for Biomedical Research Delhi
39.	First trimester uterine artery doppler velocimetry and pregnancy outcome	Dr. Arifa Anwar Elahi University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
40.	A randomised comparative trial of two different dose regimens of misoprostol for medical termination of pregnancy up to 8 weeks of gestation	Dr. Ritu Goyal University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
41.	Evaluation of doppler ultrasonography and correlation with perinatal outcome in intrauterine growth restriction	Dr. Tuleeka Sethi University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
42.	Longitudinal assessment of resistance, pulsatility and amniotic fluid index by ultrasonography in post term pregnancy and their correlation with fetal outcome	Dr. Aneesha Minocha University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
43.	An anthropological study on current prevalence, nature and etiology of childhood and adolescent obesity in Delhi	Dr. Sonali Walia University of Delhi Delhi
44.	Long-term (2 year) effects of a reduced-fat diet intervention in type 2 diabetes mellitus	Km. Neelima Gundupallee The Nizam's Institute of Medical Sciences Hyderabad
45.	Investigating activation of NAD(p)H oxidase and characterization of its components in the implanting embryos	Sh. Rajesh Kumar Jha Devi Ahilya Vishwavidyalaya Indore
46.	Hormonal control of male fertility using testosterone buciclate (TB) and 7-alpha methyl-19-nor testosterone (MENT)	Sh. S. Panneerdoss University of Rajasthan Jaipur
47.	Studies on further development of progesterone releasing intrauterine device (IUD) to enhance its duration of release	Dr. A.K. Ghosh Jadavpur University Kolkata
48.	Studies on the effect of supplementation of variable dietary components (protein and carbohydrate) in the diet on excitatory neurotransmitter in relation to brain regions and immune response in young and aged mammals	Km. Sudipta Pal University College of Science Kolkata
49.	Studies on structural and functional properties of nonglycosylated and glycosylated haemoglobins in diabetes mellitus	Sh. Subhrojit Sen University College of Science and Technology Kolkata
50.	Studies on the antioxidative effects of sesame lignans in diabetes induced rats	Dr. Krishna Chattopadhyay University College of Science and Technology Kolkata
51.	Studies on the mechanism of action of CDRI-84/35 (1-formyl-4-dichloroacetyl piperazine), a potent antispermatogenic agent in rat	Km. Priti Ojha Central Drug Research Institute Lucknow
52.	Role of enzyme adenosine deaminase (ADA) in early pregnancy/threatened abortion in women	Dr. Savita Srivastava Chhatrapati Shahuji Maharaj Medical University Lucknow
53.	A study on the effect of various herbal hypoglycemic agents on oxidative stress and antioxidant status in diabetics	Km. Anu Chandra Chhatrapati Shahuji Maharaj Medical University Lucknow
54.	Cellular and molecular mechanism of endometrial receptivity in women	Dr. Annu Makker Chhatrapati Shahuji Maharaj Medical University Lucknow

Sl. No.	Title of the Project	Name of the Fellow/Institute
55.	Role of testosterone in spermatogenesis: Regulation of nuclear chromatin condensation in adult male rat	Sh. M.A. Ansari National Institute for Research in Reproductive Health Mumbai
56.	Idenitfication and characterization of sperm specific antigen/s by using vasectomy induced antisperm antibodies	Km. Monali Shashikant Wakle National Institute for Research in Reproductive Health Mumbai
57.	Gene reguation of endometrial apoptosis	Smt. Mathura Yatin Narkar National Institute for Research in Reproductive Health Mumbai
58.	Diabetes associated male reproductive dysfunction: Role of oxidative stress and its nutritional amelioration	Km. Shrilatha Balakrishnan Central Food Technological Research Institute Mysore
59.	Studies on influence of raw and heat processed garlic and onion on bile metabolism	Sh. S.K. Vidyashankar Central Food Technological Research Institute Mysore
60.	Studies on the bioavailability of micronutrients from selected Indian foods	Smt. S. Hemalatha Central Food Technological Research Institute Mysore
61.	A computer application to analyse trace element inter- relationships in serum of normal, Alzheimer's and Parkinson's disorder : a relevance to diagnostic approach	Sh. M.B. Sanjay Pande University of Mysore Mysore
62.	Determination of the efficacy of reflexology therapy in the management of mastalgia and nodularity of the female breast by estimating the physio-chemical parameters	Km. Charulata Jindal All India Institute of Medical Sciences New Delhi
63.	Measurment of peak systolic velocity in the fetal middle cerebral artery for monitoring pregnancies complicated by Rh isoimmmunization and to time the invasive procedures	Dr. Neema Sharma All India Institute of Medical Sciences New Delhi
64.	An investigation on chromosome mosaicism and aneuploidy on early embryos through preimplantation genetic diagnosis	Sh. Ashish Kumar Fauzdar All India Institute of Medical Sciences New Delhi
65.	Nutritional status of diabetics	Dr. Sneh Arora All India Institute of Medical Sciences New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
66.	Efficacy of daily and weekly iron folic acid supplementation in correction of iron deficiency anemia amongst 3-5 year old children	Smt. Shoba Suri All India Institute of Medical Sciences New Delhi
67.	Efficacy and safety of tranaexamic acid for dysfunctional uterine bleeding and its comparison with cyclical progesterone therapy	Dr. Vidushi Kulshreshtha All India Institute of Medical Sciences New Delhi
68.	Role of uterine artery embolisation in management of symptomatic uterine fibroids	Dr. Kanupriya Army Hospital (Research & Referral) New Delhi
69.	Study of hepatic enzymes in neonates with perinatal asphyxia	Dr. Naveen Rana Army Hospital (Research & Referral) New Delhi
70.	Role of conventional radiography, computerized tomography, magnetic resonance imaging in the evaluation of pituitary gland and its abnormalities	Dr. Nilu Mehrotra Army Hospital (Research & Referral) New Delhi
71.	Clinical predictors of sickness in young infants (age 0-2 months)	Dr. Anuj Jain Deen Dyal Upadhyay Hospital New Delhi
72.	Study of placental histopathology and foeto-placental ratio in intrauterine growth retardation	Dr. Meenal Sharma Deen Dyal Upadhyay Hospital New Delhi
73.	Lactational performance of the nursing mothers in Delhi	Km. Kajali Paintal Institute of Home Economics New Delhi
74.	Development of card based kit for rapid detection of aflatoxin in food stuff	Sh. Faraz Rashid Jamia Hamdard (Hamdard University) New Delhi
75.	Analysis of mutation in *sry* gene and chromosomal anomalies in infertile patients and its clinical importance	Sh. Mohammad Shahid Jamia Milia Islamia New Delhi
76.	Endometrial evaluation in Indian postmenopausal women	Dr. Saira Zafar Maulana Azad Medical College and Associated Hospitals New Delhi
77.	The effect of ethinyl estradiol in clomiphene induced cycles on endometrial thickness and pregnancy outcome	Dr. Shalini Pal Maulana Azad Medical College and Associated Hospitals New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
78.	Antioxidative effects of melatonin to counter damage induced by lipid peroxidation during pregnancy and post delivery : Studies in rats	Dr. Kanchan Upreti National Institute of Health and Family Welfare New Delhi
79.	Estimation of serum magnesium in normal pregnancy as a predictor of gestational hypertension	Smt. Usha Kumari Patna Medical College and Hospital Patna
80.	Potential of antioxidants in fruits and vegetables in prevention of oxidation stress related disorders prevalent in Indians with special reference to cataract	Smt Kirtan Vilas Tarwadi Agharkar Research Institute Pune
81.	Potential of antioxidants and micronutrients from foods and herbal materials for treatment of type II diabetes	Km. Sangeeta Shashikant Mengal Agharkar Research Institute Pune
82.	Role of micronutrients (vitamins and W-3 fatty acids) in foetal adaptations to undernutrition and implications for adult health using rat model	Dr. Sadhana Ramachandra Joshi Agharkar Research Institute Pune
83.	Dietary antioxidants in habitual foods of different population groups and the prevalence of coronary heart disease risk factors	Dr. K. Kodanda Reddy Sri Venkateswara University Tirupati
84.	Glycemic index of the cereal based traditional recipes of Rajasthan	Km. Nikita Bordia College of Home Science Udaipur
85.	*In vitro* studies of the embryos of *scotophilus heathi* and *Cynopterus sphinx*	Km. Anjana Tiwari Banaras Hindu University Varanasi
86.	Effect of short and long-term feeding of some common Indian spices on male reproductive performance	Sh. R.K. Mishra Banaras Hindu University Varanasi
Non-Communicable Diseases		
87.	Electromyographic and biomechanical analysis of VDU operators in relation to postdural stress and musculoskeletal discomfort	Km. Era Poddar National Institute of Occupational Health Ahmedabad
88.	Role of environmental chemicals in human male reproductive system	Sh. Minal Devendra Mankad National Institute of Occupational Health Ahmedabad

Sl. No.	Title of the Project	Name of the Fellow/Institute
89.	Carcinoma of the breast : Evaluation of risk factors and biomarkers	Sh. R. Kumuraguruparan Annamalai University Annamalai Nagar
90.	Clinical trial assessing efficacy of single agent (cisplatin) chemoradiation protocol *versus* conventional primary surgery and post-operative radiotherapy in advanced resectable pyriform fossa cancer	Dr. Abhey Sood Kidwai Memorial Institute of Oncology Bangalore
91.	A hospital based study on progressive and regressive changes in oral precancerous lesions	Dr. Binti A. Jhuraney National Tuberculosis Institute Bangalore
92.	Evaluation of the radiosensitizing effect of withaferin A and hyperthermia on a radioresistant mouse melanoma - cellular and subcellular studies	Sh. Guruprasad K. Jawaharlal Nehru Cancer Hospital and Research Centre Bhopal
93.	Effect of polychlorinated biphenyal (aroclor 1254) on Leydig cell steoridogenesis and beneficial effects of vitamin supplementation	Sh. Murugesan Palaniappan Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences Univerity of Madras Chennai
94.	Etiological and clinical profile of seizure disorder in children (01 month - 05 years)	Dr. Pradipta K. Acharya Base Hospital Delhi
95.	Clinical study of operative conditions and hemodynamic response in cholecystectomy in general anesthesia *versus* combined spinal epidural anesthesia technique	Dr. Pallavi Kwatra Hindu Rao Hospital Delhi
96.	Role of *Chlamydia pneumoniae* infection in acute ischemic stroke	Dr. Meghna Nathani University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
97.	Role of hypertonic saline in initial resuscitation of patients with acute pancreatitis	Dr. Himanshu Arora University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
98.	Role of facial nerve monitoring in lowering of facial ridge in tympanomastoid surgery	Dr. Medha Mehta University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
99.	Studies on oxidative DNA damage induced by organophosphate pesticides, chlorpyrifos and parathion in rats and search of a suitable biomarker	Sh. Radhey Shyam Verma Jiwaji University Gwalior

Sl. No.	Title of the Project	Name of the Fellow/Institute
100.	Studies on ceramide in relevance to synovial cell and fluid of rheumatoid arthritis to find a basis for recovery	Dr. Aditi Banerjee Indian Institute of Chemical Biology Kolkata
101.	Oxidative injury in cerebral diseases	Dr. Sibani Sarkar Indian Institute of Chemical Biology Kolkata
102.	Chromosomal aberrations and sister chromatid exchanges in the symptomatic individuals exposed to Arsenic through drinking water in West Bengal	Km. Julie Mahata Indian Institute of Chemical Biology Kolkata
103.	MIB-1 immunocytochemical expression in normal and neoplastic epithelium of human uterine cervix	Dr. Anju Mehrotra Chhatrapati Shahuji Maharaj Medical University Lucknow
104.	Immunomodulatory role of *Aswagandha* (*Withania somnifera*) in patients of lung cancer	Dr. Neelu Gupta Chhatrapati Shahuji Maharaj Medical University Lucknow
105.	Studies on correlation of chlorinated pesticide and heavy metal lead and cadmium residues with human semen quality	Km. Niraj Pant Industrial Toxicology Research Centre Lucknow
106.	Evaluation of the antineoplastic and radiosensitizing activities agents in cultured Hela cells	Sh. Shrinath M. Baliga Kasturba Medical College and Hospital Manipal
107.	Influence of curcumin on the wound healing properties of artificially wounded mouse exposed to different doses of gamma radiation	Sh. G.K. Rajanikanth Kasturba Medical College and Hospital Manipal
108.	Study on optical fibre evanescent wave immunosensor	Sh. G. Biju Kumar All India Institute of Medical Sciences New Delhi
109.	Studies on the interaction of endosulfan and malathion with serum complement and macrophages	Km. Sadia Ayub All India Institute of Medical Sciences New Delhi
110.	Cytokine profiles of peripheral blood lymphocytes in patients with oral cancer	Km. Abhilasha Agarwal All India Institute of Medical Sciences New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
111.	Study of angiogenesis in renal cell carcinoma and its correlation with biological and clinical behaviour	Sh. M.K. Govindan All India Institute of Medical Sciences New Delhi
112.	Correlation of polymorphism of apolipoprotein E gene with dyslipidemia and body composition in Northern Indian subjects : A case-control study	Km. Manjari Dwivedi All India Institute of Medical Sciences New Delhi
113.	To assess the response of chemotherapy and radiotherapy in high grade malignant glioma and estimation of micronuclei in these radio-chemo exposed human populations	Dr. Dilip Kumar Parida All India Institute of Medical Sciences New Delhi
114.	Concomitant *versus* sequential chemoradiation in locally advanced stage carcinoma of the oesophagus : A comparative study	Dr. Siddhartha Nanda All India Institute of Medical Sciences New Delhi
115.	Assessment of alcohol and tobacco abuse in adolescent children in government schools in the National Capital Territory of Delhi	Km. Vinita Singh All India Institute of Medical Sciences New Delhi
116.	C667T and A1298C mutations in methylene tetra hydrofolate reductase gene in patients with mycocardial infarction in comparison with healthy controls	Dr. Mukta Sharma All India Institute of Medical Sciences New Delhi
117.	Effect of antioxidant supplementation on pain, antioxidant profile and oxidative stress in chronic pancreatitis	Smt. Payal Bhardwaj All India Institute of Medical Sciences New Delhi
118.	Retinal effects of chloroquine: Evaluation by electroretinogram and computerized automated perimetry	Dr. Pankaj Kataria Army Hospital (Research & Referral) New Delhi
119.	A study on foveal avascular zone in patients with diabetic retinopathy	Dr. Keerti Mundey Army Hospital (Research & Referral) New Delhi
120.	Study of low - dose bupivacaine with fentanyl in spinal anaesthesia for urologic surgeries	Dr. Pramod Patra Army Hospital (Research & Referral) New Delhi
121.	To evaluate and compare the efficacy between laryngeal mask airway-classic, laryngeal mask airway-proseal and the endotracheal tube in patients undergoing diagnostic gynaecologic laparosopic surgery	Dr. Pratyush Gupta Army Hospital (Research & Referral) New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
122.	Evaluation of intraoperative acute normvolemic hemodilution (ANH) in open heart surgeries	Dr. Tasskin Rehman Hazarika Army Hospital (Research & Referral) New Delhi
123.	A study of efficacy of ND : YAG laser (1064 nm) in thermal mode (free-running) for laser trabeculoplasty in controlling intra - ocular pressure in primary open angle glaucoma in three different situations	Dr. Pradip Kumar Army Hospital (Research & Referral) New Delhi
124.	The comparative effects of propofol *versus* seroflurane in induction, maintenance and recovery in day care surgery	Dr. B.M. Nayyar Army Hospital (Research & Referral) New Delhi
125.	A comparative study of bupivacaine and bupivacaine with fentanyl for post - op analgesia in oncosurgical patients through continuous thoracic epidural technique	Dr. Subrata Chakravarty Army Hospital (Research & Referral) New Delhi
126.	A comparative study of different doses of propofol with fentanyl on tracheal intubating conditions, without muscle relaxants in children	Dr. Sushil Garg Army Hospital (Research & Referral) New Delhi
127.	Evaluation of endoscopic sinus surgery with and without partial middle turbinate resection in patients of chronic sinusitis	Dr. Meena Chaudhari Dr.Ram Manohar Lohia Hospital New Delhi
128.	Molecular studies on the BRCA2 gene and the p53 gene mutation in breast cancer	Sh. Neeraj D. Jain Jamia Milia Islamia New Delhi
129.	Comparison of early and late pulmonary changes in inhalation burn injuries - A prospective study	Dr. Swaroop Singh Gambhir Lok Nayak Jai Prakash Narayan Hospital New Delhi
130.	Role of caspases, Bax, k ras and apoptosis in malignant and premalignant lesions of oral cavity	Sh. Navneet Saini Maulana Azad Medical College and Associated Hospitals New Delhi
131.	Telomerase activity as tumor marker in cervical cancers	Km. Alpana Sharma Maulana Azad Medical College and Associated Hospitals New Delhi
132.	Evaluation of single stage ossicular chain reconstruction in patients operated for chronic suppurative otitis media	Dr. Anita Taparwal Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
133.	Effect of topical anti - glaucomatous medication on human conjunctiva - An evaluation by conjunctival impression cytology	Dr. Simaljit Kaur Sethi Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi
134.	To study the role of mitomycin C in preventing adhesion formation following endoscopic sinus surgery	Dr. Manish Gupta Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi
135.	Evaluation of results of obliterating mastoid cavity using vascularized temporalismyofascial flap with open cavity mastoid operations	Dr. Sunita Sanehi Vardhman Mahavir Medical College & Safdarjung Hospital New Delhi
136.	Pharmacogenomics of selected genes in upper serodigestive tract cancers in a South Indian population	Km. Soya Sisy Sam Jawaharlal Institute of Postgraduate Medical Education & Research Pondicherry
137.	Enhancement of memory in the aged : An intervention study	Dr. K. Lalitha Sri Venkateswara University Tirupati
Basic Medical Sciences		
138.	Hepatoprotective effect of andrographolide on liver cancer	Smt. Neha Pravinbhai Trivedi Gujarat University Ahmedabad
139.	Regulatory mechanisms of insulin action by taurine in high fructose-fed rats	Km. A.T. Anitha Nandhini Annamalai University Annamalai Nagar
140.	The antihyperglycaemic activity of *Casearia ovata* (lam.) willd.root extracts in streptozotocin-induced diabetic rats	Sh. A. Prakasam Annamalai University Annamalai Nagar
141.	Effect of ursolic acid on chronic-ethanol induced toxicity in rats	Sh. R. Saravanan Annamalai University Annamalai Nagar
142.	Neuro & psychopharmacological studies of *Enhydrina schistosa* venom, its photooxidised venom product and screening of herbal drugs for antivenom property	Sh. S.R. Fattepur Al-Ameen College of Pharmacy Bangalore
143.	Role of neurofilament phosphorylation in chronic aluminium neurotoxicity in rat	Km. Amarpreet Kaur Postgraduate Institute of Medical Education and Research Chandigarh

Sl. No.	Title of the Project	Name of the Fellow/Institute
144.	Effect of garlic and carotenoids on oxidative stress due to isoniazid and rifampicin in rat liver	Sh. Ravinder Pal Postgraduate Institute of Medical Education and Research Chandigarh
145.	Investigation of the role of beta-amyloid peptide on nitric oxide release in Alzheimer's disease	Dr. K. Samuel Jesudoss Central Leather Research Institute Chennai
146.	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	Sh. M. Ravishankar Ram Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai
147.	Mutational analysis of alpha-l iduronidase gene (IDUA) in South Indian population	Sh. K. Mahalingam Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai
148.	Therapeutic efficacy of *Tinospora cordifolia* stem extract along with paclitaxel on 7, 12-dimethyl benz(a) anthracene induced breast cancer in albino rats	Km. M.Sarumathi Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai
149.	A study on the expression of TAMM-horsfall glycoprotein under oxalate stress	Km. Sumitra Kamalanathan Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai
150.	A study on the imbalance between the expression and activity of inducible and endothelial nitric oxide.	Sh. Pragasam Viswanathan Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences University of Madras Chennai
151.	Construction of a novel shuttle vector system for enhanced expression of *Mycobacterium tuberculosis* antigens	Km. C. Mani Tuberculosis Research Centre Chennai
152.	Design and development of iron (iii) hexacyanoferrate based amperometric sensor electrode for estimation of reduced glutathione in clinical samples	Sh. S.M. Senthil Kumar University of Madras Chennai
153.	Putative antioxidant properties of HMG CoA reductase inhibitors	Sh. K. Gauthaman University of Madras Chennai

Sl. No.	Title of the Project	Name of the Fellow/Institute
154.	Molecular mechanism of action of *Holarrhena antidysenterica* against enteropathogenic *Escherichia coli*	Km. D. Kavitha University of Madras Chennai
155.	To study the effect of dietary fat and endotoxin on immune responses and pathogenesis of experimental alcoholic liver disease	Km. Charu Mehra Kamal Dr. B.R. Ambedkar Centre for Biomedical Research Delhi
156.	Study of lipoprotein(a) levels and apolipoprotein(a) polymorphism in patients with premature coronary artery disease	Smt. Harsimrut Kaur Kalsey University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
157.	Detailed studies on mechanism of action of the hypoglycemic compounds obtained from the bark of *Ficus bengalensis*	Km. Shweta Gupta University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
158.	Role of oxidative stress in the induction of bronchial hyper responsiveness and its modulation by dietary antioxidant vitamin C and E in guinea pigs	Km. Sujata Upadhyay Vallabhbhai Patel Chest Institute University of Delhi Delhi
159.	Therapeutic effectiveness of *Propolis* extract and its active principle against carbon tetrachloride induced liver damage in rats	Km. Monika Bhadauria Jiwaji University Gwalior
160.	Adhesion mediated cell survival signals in normal and cancerous cells	Dr. Rajeswari Jinka Centre for Cellular and Molecular Biology Hyderabad
161.	Studies on activation of neutrophils by galectin-1	Sh. R.K. Gupta Devi Ahilya Vishwavidyalaya Indore
162.	Anti-thyroid action of phenylhydrazine : Studies on the hypothalamopituitary - thyroid axis in juvenile and adult male rats	Dr. Mitali Pramanik Bose Institute (New Campus) Kolkata
163.	Studies on the synthesis of diphenylamine derivatives, benzanilide derivatives and 2-phenylbenzo-4-pyrone derivatives as antileishmanial agents in relation to their mode of action	Km. Ramesh Kumari Jadavpur University Kolkata
164.	Molecular basis of inhibition of experimental hepatocarcinogenesis by *Trianthema portulacastrum* Linn	Km. Mitali Basu Jadavpur University Kolkata
165.	Study of the potential of antisense insulin like growth factor (IGF2) phosphorothioate oligomers as a future drug for liver cancer	Smt. Shampa Ghosh Jadavpur University Kolkata

Sl. No.	Title of the Project	Name of the Fellow/Institute
166.	Screening, characterization and production of novel antibiotics from marine actinomycetes isolated from the deltaic Sundarbans	Sh. Malay Saha Jadavpur University Kolkata
167.	Studies on the biochemical effects of food additive (erythrosine B) in relation to brain serotonergic system and immune response	Sh. Arindam Dalal University College of Science Kolkata
168.	Pharmacological and structural evaluation of toxins from the skin extract of snake head fish *Channa striatus*	Sh. Surajit Karmakar University College of Science and Technology Kolkata
169.	Study of longitudinal growth and bone radiography in relation to oral iron chelator deferiprone (Kelfer)	Dr. Anita Saxena Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
170.	The evaluation of the chemopreventive, chemoprotective and radioprotective properties of naringin in mice	Sh. T. Koti Reddy Kasturba Medical College and Hospital Manipal
171.	Design and evaluation of novel drug delivery systems of anti-malarial drugs	Sh. N.K.Tayade Bombay College of Pharmacy Mumbai
172.	Investigation of purinergic neurotransmission in smooth muscle : Effect of ATPase inhibition on synaptic potentials in the mammalian vas deferens	Km. Parakashtha Ghildyal Indian Institute of Technology Mumbai
173.	Molecular role of steroid acute regulatory (STAR) gene in steroidogenesis	Km. Heena U.Shirwalkar National Institute for Research in Reproductive Health Mumbai
174.	Studies on immunoexpression of anti-apoptotic and transcription marker molecules in ovariectomized rat hippocampus	Sh. Kanhaiya Sharma All India Institute of Medical Sciences New Delhi
175.	Physico-chemical characterization of *Plasmodium vivax* heat shock metalloprotease	Sh. Asim Anees Siddiqui All India Institute of Medical Sciences New Delhi
176.	Outcome of HBsAg positive renal transplant recipients	Dr. Durga Shankar Army Hospital (Research & Referral) New Delhi

Sl. No.	Title of the Project	Name of the Fellow/Institute
177.	Interplay of the coronary risk agents in pediatric group of young parents affected with coronary artery disease (CAD)	Smt. Vibha Pagare G.B. Pant Hospital New Delhi
178.	Production of bioactive gonadotropin by insect cell using baculovirus expression vector system	Km. V. Pooja Jamia Hamdard (Hamdard University) New Delhi
179.	Formulation and evaluation of novel drug delivery systems for anti-acne products using tea tree oil	Sh. S.S. Biju Jamia Hamdard (Hamdard University) New Delhi
180.	Development of new drug delivery system with sodium- hydrogen exchanger modulators and evaluation of their role in epilepsy	Sh. Atif Ali Jamia Hamdard (Hamdard University) New Delhi
181.	Effect of low level 2.45 and 16.5 gHz radiation on developing rats brain	Sh. R. Paulraj Jawaharlal Nehru University New Delhi
182.	Effects of arsenic on cell growth and development of *Dictyostelium discoideum*	Dr. Sampati Mukhopadhyay Jawaharlal Nehru University New Delhi
183.	Elucidation of the role of neuropeptide, neurokinin B and its analogues on molecular and biochemical correlates in aging brain functions	Sh. M. Anil Kumar Jawaharlal Nehru University New Delhi
184.	Evaluation of the modulatory effects of some common dietary constituents on radiation induced damage	Dr. Ashu Bhan Tiku Jawaharlal Nehru University New Delhi
185.	The role of oxidative stress and cellular transcription factor ap-1 in pre and post operative cases of breast carcinomas	Km. Priyanka Verma Lady Hardinge Medical College and Associated Hospitals New Delhi
186.	Neural repair by glial cell line derived neurotrophic factor (GDNF) in experimental model of Parkinson's disease	Km. Shalini Singh Maulana Azad Medical College and Associated Hospitals New Delhi
187.	Assessment of the probiotic potential of pediocin producing natural isolates of *Pediococcus* Sps	Smt. Baljinder Kaur Punjabi University Patiala
188.	Biochemical variation among hill peoples of Lahaul-Spiti and Kulu districts of North Himachal Pradesh	Km. Rupinder Kaur Bansal Punjabi University Patiala

Sl. No.	Title of the Project	Name of the Fellow/Institute
189.	Molecular diagnosis of chronic myeloid leukemia and its relevance to clinical management	Dr. Anshuman Chaturvedi Armed Forces Medical College and Command Hospital Pune
190.	Development of floating drug delivery systems in the effective management of *Helicobacter pylori*	Km. R.B. Umamaheswari Dr.Hari Singh Gour Vishwavidyalaya Sagar
191.	Osmotically regulated multi-drug oral delivery systems development and characterization	Sh. D. Prabakaran Dr.Hari Singh Gour Vishwavidyalaya Sagar
192.	Leucocyte and platelet deposition in atherosclerotic plaques: Role of sugar specific adhesion to endothelial lectin galectin 1 and prospect of its inhibition by human erythrocyte membrane oligosaccharides	Km. S.R. Sangeetha Sree Chitra Tirunal Institute for Medical Sciences and Technology Thiruvananthapuram
193.	Effect of coadministration of cyanoglycosides isolated from Cassava and alcohol on experimental animals	Km. R.G. Boby University of Kerala Thiruvananthapuram
194.	Studies on monocyte-macrophage differentiation	Km. A. Radhika University of Kerala Thiruvananthapuram
195.	Biodemography and longevity among tribal populations of Kerala	Dr. T. Parvathi Kumara Reddy Sri Venkateswara University Tirupati
196.	Evaluation of biochemical changes of bile juice under the influence of a compound indigenous drug in biliary stone diseases	Dr. Pankaj Srivastava Institute of Medical Sciences Banaras Hindu University Varanasi
197.	Studies on the cardioprotective actions of bradykinin and its signal cascade mechanism in rats with experimental myocardial infarction	Sh. V. Krishna Kumar Andhra University Visakhapatnam
198.	Investigations on biosynthesis, continuous production and kinetics of urokinase (UK) employing immobilized mesangio proliferative glomerulo nephritis (MPGN) kidney cells	Km. Bhavani Devi Ravuri Andhra University Visakhapatnam

Expenditure on Fellowships during the year Rs. 206.00 Lakhs

Research Publications of ICMR Institutes

Allred, M., Campolucci, S., Falk, H., Ganguly, N.K., Saiyed, H.N. and Shah, B. Bilateral environmental and occupational health program with India. *Int J Hyg Environ Health* 206 (2003) 323.

Aggarwal, B.B., Kumar, A. and Bharti, A.C. Anticancer potential of Curcumin: Pre clinical and clinical studies. *Anticancer Res* 23 (2003) 363.

Ali, R., Bhunia, B., Chhotray, G.P., Reddy, M.V.R. and Harinath, B.C. Microscopic haematuria as an occult filarial infection in Bhubaneswar,an endemic area for bancroftian filariasis. *Indian J Clin Biochem* 18 (2003) 61.

Ansari, M.A. and Razdan, R.K. Bio-efficacy and operational feasibility of alphacypermethrin (Fendona) impregnated mosquito nets to control rural malaria in Northern India. *J Vect Borne Dis* 40 (2003) 33.

Aralappa, N., Balakrishna, N., Kumar, S., Brahmam, G.N.V. and Vijayaraghavan, K. Diet and nutritional status of rural elderly in India. *J Nutr* 22(2003) 35.

Arankalle, V.A. and Chadha, M.S. Who should receive hepatitis A vaccine? *J Viral Hep* 10 (2003) 157.

Arankalle, V.A., Murhekar, K.M. and Murhekar, M.V. Predominance of genotype D in primitive tribes of Andaman and Nicobar Islands, India (1989-1999). *J Gen Virol* 84 (2003) 1915.

Arora, N.K., Mathur, P., Anjali, A. and Patwari, A. Upper gastrointestinal bleeding in children: Etiology and management. *Indian J Pediatr* 70 (2003) 73.

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