Overview

The Indian Council of Medical Research is the national apex body which develops strategies for biomedical research by identifying priority areas, formulating research programmes and operationalizing these research programmes through grant of financial aid to research institutes, medical colleges and universities. Intramural research is conducted through its network of 21 research institutes/centres and 6 regional centres whereas for extramural research, grants in the form of Centres for Advanced Research, task force and *ad hoc* research projects and fellowships is provided to individual scientists/students. The Council has instituted several awards/prizes also for recognizing excellent research carried out in India by Indian biomedical scientists. Financial support is provided to research institutes/medical colleges for conducting seminars/symposia/workshops *etc.* The Council also brings out several publications in the biomedical field including a journal, the Indian Journal of Medical Research.

Communicable Diseases

In the field of tuberculosis, basic, clinical and operational studies are being undertaken at the Council's Tuberculosis Research Centre (TRC), Chennai. During the year, studies were conducted for surveillance of drug resistance in tuberculosis. Immunological studies to understand the potential role of natural killer cells in tuberculosis was carried out at TRC. A model centre for directly observed treatment short-course (DOTS) implementation, tuberculosis control, training and research has been established by the TRC in collaboration with the Tamil Nadu State TB Programme. During the year, studies were carried out to identify the mode of involvement of private medical practitioners in the revised National Tuberculosis Control Programme and to assess the feasibility of the programme.

The Council's Central JALMA Institute for Leprosy (CJIL), Agra is carrying out therapeutic trials on multidrug therapy for multibacillary leprosy. In a field study conducted by the National Institute of Epidemiology, Chennai, the WHO design for leprosy elimination monitoring was tested. Immunological studies are also being undertaken at CJIL to study the immune status of leprosy patients.

The National Institute of Cholera and Enteric Diseases, Calcutta is collaborating with Japanese International Co-operative Agency for surveillance of emerging diarrhoeal pathogens and management of diarrhoea. Studies have been undertaken to understand the molecular biology of *Vibrio cholerae* and *V.parahaemolyticus.* Investigation of the diarrhoeal outbreak in the cyclone affected areas of Orissa state and molecular epidemiological studies were undertaken.

New technologies are being introduced by the Council for malaria control under the National Anti-Malaria Programme. Under the integrated vector control project research activities were carried out for evaluation of new antimalarial drugs, diagnostic kits, insecticides and repellents, and for epidemic investigations and bio-environmental methods for malaria control. Geographical information system has been used to map the distribution of *Anopheles dirus* in India. Studies are ongoing on artemisinin, an antimalarial principle isolated from *Artemisia annua*. Rapid methods for estimation of prevalence of bancroftian filariasis and its mapping by grid sampling technique is being validated by the Council's Vector Control Research Centre at Pondicherry. Molecular probes are being developed for detection and diagnosis of the disease.

The ICMR's National AIDS Research Institute at Pune is involved in high level research on various aspects of human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS). Priority has been

given to immunological and virological studies for development of vaccine and diagnostic tests, drug development and generation of reagents and virus repositories for use in HIV research. Socio-behavioural studies on women's education, awareness, reproductive health and treatment seeking behaviour were also conducted in different parts of the country besides epidemiological surveys for finding out the prevalence of HIV/AIDS.

Other viral diseases which received high priority under the Council's research programmes include Japanese encephalitis, poliomyelitis and hepatitis.

ICMR Institutional Network

Reproductive Health

The ICMR continued to place significant emphasis on research in the field of reproductive health. Several new initiatives have been launched in the areas of family planning/contraception, safe motherhood, abortions, reproductive tract infections/sexually transmitted diseases, adolescent health and operationalising the available technologies. Studies are ongoing for developing antifertility vaccines for the male and female and on intranasal male contraceptive at the Council's Institute for Research in Reproduction (IRR) at Mumbai. At the request of the Ministry of Health & Family Welfare, the Council initiated two studies – one to evaluate the sensitivity and specificity of a pregnancy detection kit and the feasibility of using it in rural/urban slum areas and the other for assessment of vaccine wastage during pulse polio immunization programme. A study has been undertaken for involving the practitioners of Indian systems of medicine in the delivery of reproductive and child health services

in rural areas.

It is proposed to initiate a programme on neonatal mortality and home-based management of sick neonates in the near future.

Nutrition

Nutrition related problems continue to be widely prevalent in the country despite many programmes being implemented by the Government of India. The Council has identified priority areas for research such as development of nutrition surveillance system, biochemical tests for detection of micronutrient deficiencies, identification of foods rich in micronutrients *etc*. Besides these, surveys were conducted by the Council's National Nutrition Monitoring Bureau on the nutrition status of tribal populations living in various backward areas and on adolescents and the aged. A hospital-based study in preschool children showed that serum transferrin receptor level is a better indicator than haemoglobin level for assessing iron status in anaemia. Studies were also conducted for investigation of antimutagenic properties of some medicinal plants. A study undertaken to establish the efficacy of the obese rat model has shown that it can be effectively used to study xenobiotic metabolism.

Environmental and Occupational Health

Studies in the field of environmental and occupational health were conducted at the Council's National Institute of Occupational Health at Ahmedabad and its regional centres at Bangalore and Calcutta. Air pollution due to vehicular traffic was studied in various cities of Gujarat state and in Bangalore whereas a method for testing the toxicity of industrial effluents is being developed. Assessment of adverse health effects on workers engaged in various industries such as chemical, automobile, tobacco, news-paper, dyes and pesticides is being done.

Non-communicable Diseases

The aim of research in the field of non-communicable diseases ongoing at the Council is to identify risk factors, their prevention and control. In the field of oncology studies continued to provide data on occurrence of various types of cancers such as cervical, oral and breast cancers. The National Cancer Registry Programme continued to collect, analyse and interpret data and conduct epidemiological studies on cancers.

Streptococcal infections and rheumatic heart disease has been identified as a nationally relevant area under the *Jai Vigyan Mission* mode. Studies have been initiated on the epidemiology and management of glaucoma.

At the ICMR's Regional Medical Research Centre at Dibrugarh, survey of tobacco and other substance abuse in the north-east region was undertaken. Another study was conducted on the socio-demographic and behavioural aspects of drug addicts in Assam and Arunachal Pradesh.

In the field of haematology, basic, clinical and epidemiological studies were continued on various types of haemoglobinopathies, bleeding and thrombotic disorders, blood transfusion, bone marrow transplantation and blood disorders among tribal populations in Maharashtra, Gujarat, Orissa and Tamil Nadu.

Basic Medical Sciences

Studies were carried out on breast cancer, oncogenes in premalignant and malignant prostate enlargement,

experimental model of Indian childhood cirrhosis and guinea pig model for vitiligo at the Council's Institute of Pathology at New Delhi.

A study was supported at the Industrial Toxicology Research Centre, Lucknow on toxicological and immunotoxicological potential of commonly used plastics. Another study was conducted for synthesizing antiasthmatic/antiallergic agents at the Central Drug Research Institute, Lucknow. Role of lipoproteins as risk factors in coronary, peripheral and cerebral atherosclerosis was studied at the All India Institute of Medical Sciences at New Delhi.

The Council continued studies on various plants/plant products such as (*Pterocarpus marsupium (Vijaysar), Picrorrhiza kurroa, Terminalia chebula, Centella asiatica, Azadirachta indica etc.* Two Centres for Advanced Research have been initiated for clinical pharmacology and drug development at Mumbai and Lucknow respectively.

Publication, Information and Communication

The Council continued to publish its periodicals, the Indian Journal of Medical Research, ICMR Bulletin, ICMR *Patrika* and the Annual Report in English and Hindi. For dissemination of health information, popular lectures were organised by the Council and its Institutes/Centres in addition to open houses /seminar /symposia *etc*. The Council participated in the *Swadeshi Vigyan Mela* in February 2000 and in book fairs in August 1999 and February 2000. A Bioinformatics Centre has been set up in the Council in June 1999 by expanding the activities of the existing Integrated Research Information System (IRIS).

Communicable Diseases

India is undergoing an epidemiologic, demographic and health transition. The expectancy of life has increased, with consequent rise in degenerative diseases of aging and life-styles. Nevertheless, communicable diseases are still dominant and constitute major public health issues.

The research strategy adopted by the Council is a balance between the upstream (fundamental and basic) and downstream (product development/evaluation and operational) research.

Through the network of its disease-specific Institutes/Regional Medical Research Centres and extramural research programme, the Council is supporting and encouraging biomedical research in communicable diseases. New viral and bacterial infections have been identified. Monitoring of anti-microbial resistance to commonly used drugs is being extended to include more organisms. Disease surveillance at the molecular level has been expanded and strengthened. Studies to assess disease burden not only in terms of morbidity and mortality but also economic are high on the Council's agenda. Feasibility of effective strategies under field conditions for control of infectious diseases is being demonstrated. Research support to eradicate target diseases has been intensified. Development and evaluation of diagnostic tools, drugs and vaccines is being undertaken. Programme relevant research to strengthen the national health programmes and human resource development are an integral part of the efforts of the Council towards control of communicable diseases.

BACTERIAL DISEASES

TUBERCULOSIS

Tuberculosis accounts for a loss of approximately 11 million disability adjusted life years (DALYs). The burden of disease may increase further with the emergence of the HIV epidemic. The Revised National TB Control Programme (RNTCP) which covers more than 120 million population has successfully treated approximately 80% of patients in 48 districts of 16 states and Union Territories. Treatment success rates have more than doubled and death rates have decreased by 75 per cent. The ICMR's Tuberculosis Research Centre (TRC) at Chennai is providing research support to the RNTCP through the conduct of basic, applied and operational research to develop better tools and training strategies for tuberculosis control.

Clinical Trials

The TRC initiated a study to examine the feasibility of shortening the duration of treatment for smear positive pulmonary tuberculosis from the present 6-8 to 3-5 months with regimens using ofloxacin in a randomized controlled clinical trial. The regimens were (i) three months of ofloxacin, isoniazid (H), rifampicin (R) and pyrazinamide (Z) daily (Reg.1); (ii) three months of ofloxacin, isoniazid, rifampicin and pyrazinamide daily followed by one month of isoniazid and rifampicin twice a week (Reg 2); (iii) three months of ofloxacin, isoniazid, rifampicin and pyrazinamide daily followed by two months of isoniazid and rifampicin twice a week (Reg 3); and (iv) two months of ofloxacin, isoniazid, rifampicin and pyrazinamide daily followed by two months of isoniazid and rifampicin twice a week (Reg 4). All drugs were given under supervision. Patients who defaulted for treatment were visited at home and motivated to attend. Interim analysis in 352 of the 529 patients admitted to the study showed that at the end of treatment, overall 96 to 99% of the patients had a favourable response. Forty two patients had pre-treatment resistance to isoniazid. Six patients had resistance to rifampicin and isoniazid (MDR tuberculosis), one of whom was also resistant to ofloxacin. Of these six patients, two had an unfavourable response, one relapsed and the other three had favourable response. After amalgamating the results of regimens 1, 2 and 3, all of which had an intensive phase of three months, and comparing it with the fourth regimen, which had an intensive phase of only two months, it was found that the rate of culture conversions was very similar. Culture conversion at two months ranged from 94 to 97%. Analysis in 346 patients in whom results were available showed that the relapse rates were 9, 4, 4 and 13% respectively in the four regimens. Even though the relapse rates in regimens 1 and 4 are higher compared to regimens 2 or 3, the difference was not statistically significant. The follow up of patients would continue upto 5 years.

Studies on Drug Resistance in Tuberculosis

The TRC has completed a study on surveillance of drug resistance in TB in Tamil Nadu to determine the proportion of initial and acquired drug resistance. Out of 400 patients for whom drug susceptibility tests were done, 384 (96%) had no history of previous anti-TB treatment while 16 had had previous treatment. Resistance to isoniazid alone or in combination with other drugs, was observed in 15.4% of the former and 50% of the latter. Any resistance to rifampicin was observed in 4.4% of previously untreated patients as against 25% of patients with previous treatment. These included 3.3% patients with H and R resistance in the untreated group and 25% in the treated group. This study made available, for the first time, authentic basic data on initial and acquired drug resistance from Tamil Nadu.

A study is being conducted at the All India Institute of Medical Sciences (AIIMS), New Delhi to define the magnitude of drug resistant tuberculosis amongst patients with active disease. A total of 215 strains isolated during the year under report were speciated using different biochemical characteristics *viz*. growth rate, pigmentation, niacin production, nitrate reduction, catalase production and growth on MacConkey medium. Susceptibilities to

rifampicin (R), isoniazid (H), streptomycin (S) and ethambutol (E) at their respective critical concentrations were assayed by 1% proportionate method performed on L-J slants. The interim results indicated that among 22 *Mycobacterium tuberculosis* isolates, 9 were sensitive to all drugs, 3 were resistant to isoniazid alone, 4 were MDR (resistant to R+H), 2 were resistant to H+R+S, 1 resistant to R+E and 1 to streptomycin alone. Two isolates were resistant to all drugs. The study is continuing.

Basic Studies

Enzymes involved in the *de novo* purine biosynthesis are important for infectivity, growth and virulence of certain pathogenic bacteria. The *guaA* gene encoding GMP synthetase in *M.tuberculosis* is being studied to help in understanding its role in pathogenicity. The promoter clones isolated during the early phase of this study were sequenced and the transcription start points were determined using primer extension analysis. One of the promoters exhibited very high homology to the putative *guaA* gene encoding GMP synthetase from *M.tuberculosis*. A 1.6 kb coding region along with 400 bp of the upstream region was PCR amplified using specific primers and cloned into pCR2.1 vector. Sequence analysis and restriction mapping confirmed the identity of the cloned fragment to be the *M.tuberculosis guaA* gene (Fig.1). The upstream region of this gene was cloned separately into a promoter-probe vector and studies are underway to determine the transcription start point of this promoter and to study its regulation. The coding region of the gene was cloned into an expression vector and transformed into *Escherichia coli* for overproduction of the gene product. The results show that expression of this gene is lethal to *E.coli*. Hence, attempts are being made to express this gene under the control of heat shock promoter (hsp60) in *M.smegmatis* using a shuttle plasmid vector (Fig.2). The promoter clones isolated in the initial part of this study were further characterised using primer extension analysis. Experiments are in progress to study the ability of these promoters to drive a candidate mycobacterial gene. The immunodominant 38 kDa protein antigen was chosen for this purpose. A 1.1kb coding region of the 38 kDa protein antigen was PCR amplified using specific primers and the product was cloned into pCR2.1 vector. This gene will be used to study the transcriptional strengths of the isolated promoters. The study is continuing.

A study is being supported at the V.P. Chest Institute, Delhi for the purification of plasmid(s) and characterisation of one of the plasmids from *Mycobacterium avium-intracellulare* complex (MAC) isolates obtained from Indian patients having mycobacterial infection. Ninety isolates were analyzed biochemically and were subjected to plasmid screening. Twenty two isolates showed the presence of the plasmid, of which two gave multiple bands which were lost on repeated subculturing. One isolate consistently gave a plasmid band that was purified using the Qualigens column kit. The purified DNA was subjected to transmission electron microscopy that endorsed the circular nature of the plasmid. From restriction digestion using EcoR1, HindIII, Pst1, EcoRV, BamH1 and double digests (BamH1 and Pst1) the exact sizes of individual fragments generated were calculated and the size of the intact plasmid was found to be 24 kb. To localize the origin of replication, a 37-mer oligoprobe designed from the *ori* of pLR7, the *M.avium* plasmid that has been partially sequenced so far, was hybridized using the ECL non-radiolabelled direct labelling and detection system. Signals were obtained with two fragments of 4 kb each of BamH1 and Pst1 double digest plasmid DNA blotted on nylon membrane. Based on these observations, a tentative restriction map could be constructed for the 24 kb wild plasmid that has been isolated from Indian MAC. The methodology standardized for plasmid isolation may be used to screen large number of indigenous MAC isolates for further studies. Probes developed from these plasmids could be of much use in the epidemiology of MAC and it paves the way for the development of a cloning/expression vector and thus opens up a whole new chapter in mycobacterial diagnostics and vaccines.

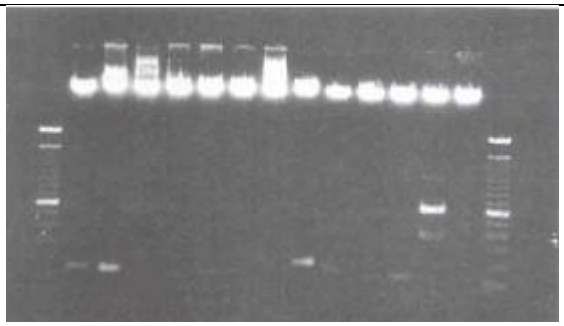


Fig1: Gel photograph showing the restriction analysis of different promoter clones obtained in pJEM13 vector with Apal and Kpn1 enzymes.

Lane 1 & 15-000 bp mol. wt. marker; Lane 14-pJEM13 vector cut with Apa1 & Kpn1; Lanes 2-13-Promoter clones cut with Apa1 & Kpn1.

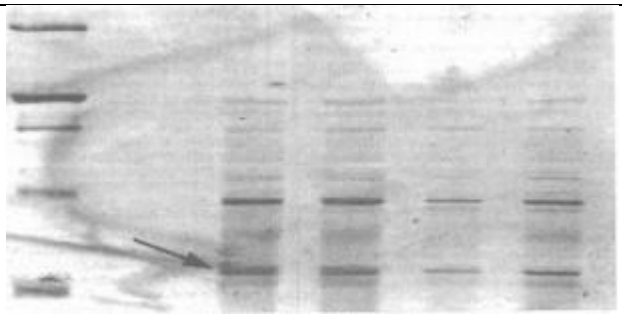


Fig2: SDS-PAGE analysis of pMV/GMP (pMV 261 + gua A gene) recombinant from M. *smegmatis*(mc^2 155) . The arrow indicates the presence of a doublet in induced cultures (lanes 2 & 3) which is absent in the vector control (lane 5).

Lane I-protien mol. wt. marker; Lane 2-induced pMVGMP1 in mc^2 155 for 15 min; Lane 3-induced pMVGMP1 in mc^2 155 for 30 min; Lane 4-induced pMVGMP1 in mc^2 155 for 60 min; Lane 5-pMV 261 in mc^2 155 (vector control).

Studies on Molecular Biology of Mycobacteria

Studies were carried out at Central JALMA Institute for Leprosy (CJIL), Agra to study the relationship of different levels of rifampicin resistance associated with certain mutations earlier observed in the Indian strains of *M.tuberculosis*. Extended studies have provided newer information about type of mutations in case of quinolone resistance and transporter genes. ABC transporters have been amplified by polymerase chain reaction (PCR) from different strains of *M.tuberculosis*. Data show structural as well as functional differences in these transporters in the resistant *vs* sensitive strains thus highlighting the need for investigating other efflux pumps and their functional status. Based on the original data about the type of mutations present in Indian strains of *M.tuberculosis*, new probe systems are being designed.

Studies on developing PCR based ribosomal DNA fingerprinting techniques for pathogenic mycobacteria progressed. Based on the testing of new PCR-RFLP (restriction fragment length polymorphism) system(s) designed

at CJIL, two rDNA-RFLP assays targetting 16 S rRNA gene and spacer region have been found to be potentially useful for rapid identification of clinical isolates of *M.tuberculosis* and other mycobacteria even directly from the lesions specially in tuberculosis.

Application studies on the earlier developed ribosomal DNA fingerprinting techniques as well as random amplification of polymorphic DNA (RAPD), IS 6110 DNA fingerprinting methods on *M.tuberculosis* have made significant progress. These have been used to type large numbers of mycobacterial strains collected in the Mycobacterial Repository Centre at CJIL from different parts of the country and complementary protocol for DNA fingerprinting of Indian strains of *M.tuberculosis*is being formulated. No clustering of any drug resistant type and any particular RFLP type has been observed so far indicating random distribution and selection by drug pressures.

Immunological Studies

The potential role of natural killer (NK) cells in the killing of mycobacteria is being studied at the TRC, Chennai. There was a significant decrease in NK activity in patients as compared to controls, whereas there was no difference between the contact and patient groups. Further, in *M.tuberculosis* infection, it has been proved *in vitro* that reactive oxygen intermediate (ROI) levels were increased. This increased ROI by monocytes or neutrophils may cause suppression of NK activity possibly explaining the decreased activity seen in tuberculosis patients. The mechanism of the defect in tuberculosis patients (cytotoxic effect) was not observed at the recognition/binding stage but probably lies in the subsequent events involved in the lethal hit.

Operational Research

The TRC in collaboration with the Tamil Nadu State TB Programme has established a model centre for directly observed treatment short-course (DOTS) implementation, tuberculosis control, training and research. Five *panchayat* blocks in Tiruvallur district covering a population of 5,00,000 were selected for the model DOTS project. There are 225 villages in these blocks. Since the area has been under observation for a long period of time (as it is the same area where the earlier Chingleput BCG study was conducted), the epidemiological impact of the DOTS programme can effectively be measured here. By the end of the third quarter in 1999, 220 patients had been registered for treatment, of whom 124 were allocated to CAT I, 43 to CAT II and 53 to CAT III. This exercise is continuing.

Further in order to assess the epidemiological impact of DOTS, a base-line and annual risk of infection (ARI) survey was started in December 1998 which is still continuing. The TRC has undertaken a massive training programme as part of the project activity.

Studies conducted earlier at the TRC indicated that 88% of private medical practitioners (PPs) in Chingleput district and Chennai are willing to participate in RNTCP while only 52% are willing for DOTS. During the year, studies were carried out to identify the mode of involvement of PPs in the RNTCP and to assess its feasibility.

In addition the TRC has established an agency called Advocacy for Control of Tuberculosis (ACT) in collaboration with ‘THE HINDU’. The agency has trained and encouraged private practitioners to follow RNTCP guidelines in their private practice.

LEPROSY

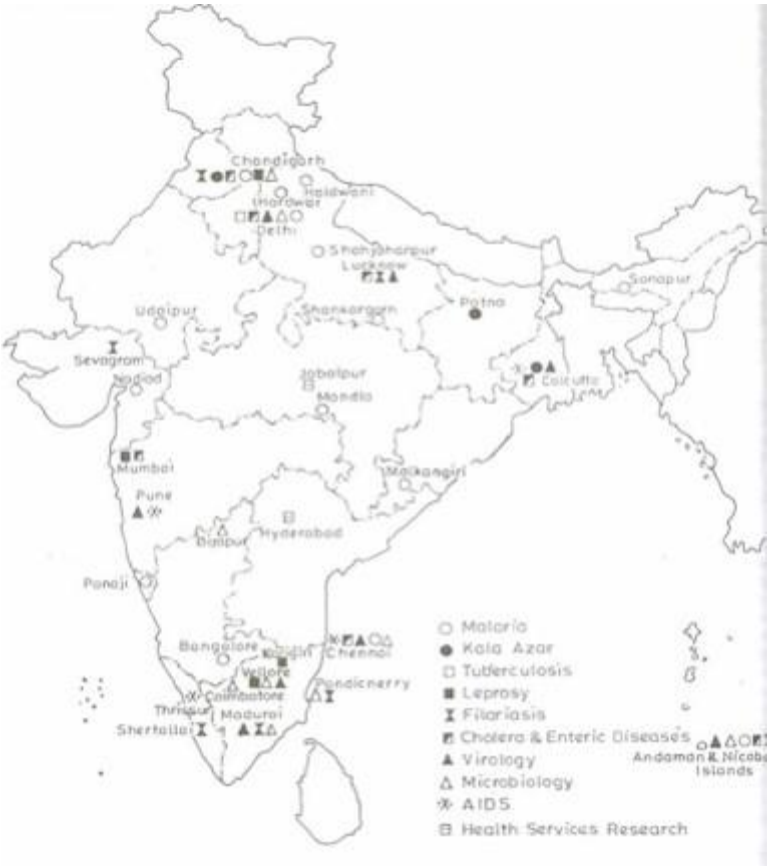
As a result of the introduction of multidrug therapy (MDT) in the national disease control programme, 98 of 122 countries have reached the goal of elimination of leprosy as a public health problem. However, the prevalence of leprosy in India is still around 5/10,000 population. The new case detection rate has also not shown any appreciable decline. Twenty four other endemic countries share a similar situation. For all such countries, the deadline for elimination of leprosy has been extended by the WHO Leprosy Elimination Project to the year 2005. The Council's Central JALMA Institute for Leprosy (CJIL), Agra is focusing its research activities to find solutions to problems related to the persistence of leprosy in India through better understanding of the disease process.

Therapeutic Trials

The follow up of patients treated with a one year MDT regimen for multibacillary leprosy designed at CJIL (comprising rifampicin, ofloxacin, minocycline, clofazimine and dapsone) showed that this regimen was well tolerated and effective in killing the bacilli. Most patients have completed a follow up of more than 3-3.5 years on placebo. Episodes of erythema nodosum lepromatosum (ENL) requiring the use of steroids in highly bacillated group have been observed. The patients have been divided into different groups depending on the initial bacillary index (BI). Some of the patients with initial high BI continued to be bacteriologically positive for a longer period, while others had episodes of ENL. Follow up is continuing.

Studies conducted earlier at CJIL had shown that the duration of MDT therapy, as suggested by the WHO may not be adequate to cure a patient. The efficacy of alternate regimens is being compared with the WHO regimen in terms of persisters, late reactions and relapses. Follow up of patients of paucibacillary (PB) leprosy treated with a six monthly regimen comprising dapsone, clofazimine and rifampicin has confirmed that the patients treated with this regimen have less residual activity, lower reaction rates and no relapses during the first 3.5-4 years of follow up. This regimen appears to be a good alternate regimen for the treatment of PB leprosy.

In a study conducted earlier at National Institute of Epidemiology (NIE), Chennai, single dose of rifampicin, ofloxacin and minocycline (ROM) has been shown to be as effective as six months of MDT for patients with mono lesion leprosy. Subsequently, the study was extended to cover patients with 2 and 3 lesions. The regimen has been found to be equally effective in such patients. A multi-centre double-blind randomized controlled trial is being conducted to evaluate the therapeutic efficacy of single dose ROM for patients with PB leprosy with 2-5 lesions.



Major ICMR Research Projects in Communicable Diseases

In a field study conducted by NIE, Chennai, the WHO design for leprosy elimination monitoring (LEM) activities was tested. The main purpose of this study was to collect information on a limited number of indicators that can describe the performance of the MDT programme for leprosy. The study carried out in 10 randomly selected PHCs of Villupuram district, Tamil Nadu in 1997-98, showed that 97% of 518 patients were treated with M DT. Of the 96 health facilities, 84% provided MDT. All the blister-packs were of good quality. Of the 518 registered patients, 43% had grade 2 disabilities, 22% had multibacillary (MB) leprosy, 22% had single lesions, and 30% were children. There was complete flexibility in delivering MDT. Cure rates were 50 and 64% respectively in patients of MB (115) and PB (403) leprosy. The results suggest that the WHO design is useful to improve the quality of routine reporting and can be incorporated in the National Leprosy Eradication Programme records.

Clinical Studies

Gene probes have been developed for detection of early forms of leprosy in histopathological sections by *in situ* hybridization. Additional data confirm that this method is promising and is able to detect suspicious and indeterminate cases efficiently.

The rationale of classifying leprosy patients on the basis of the number of skin lesions alone was completed during the year. Clinico-bacteriological analysis of a large number of patients has shown that with the increase in the number of skin lesions, the skin smear positivity increases. Further analysis confirms that inadvertently a proportion of patients with MB leprosy could be treated for PB leprosy. These observations have therapeutic implications as

these patients are likely to be undertreated and may relapse later.

Immunology of Leprosy

The CJIL expanded the study on IgG levels to heat shock protein antigens. Additional data further confirmed that there is no difference in the levels of IgG in patients with borderline tuberculoid (BT)/tuberculoid (TT) and lepromatous (LL) leprosy and in those with and without reactions.

An attempt is being made at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh to study the mechanism of T cell anergy or impaired immune response in leprosy patients. Lymphocyte phenotyping of T cells from untreated patients was done by flow cytometry. Eight leprosy patients and 10 healthy controls were studied. Expression of adhesin molecules LFA-1α, Mac-1, LFA-1β and ICAM-1 was also checked on both the lymphocytes and the monocytes of these patients and the expression of the adhesin molecules was compared with the control group. The interim results indicated no significant difference in the per cent values of lymphocyte phenotyping. It was also observed that the adhesin molecules are critical in ensuring the optimum activation of T cells. They have an important role in T cell adhesion and initiation of signal transduction events and may also have a role in immune suppression in leprosy patients. The study is continuing.

In another study at PGIMER, Chandigarh, the mechanism and regulation of apoptosis in the peripheral blood mononuclear cells (PBMCs) of leprosy patients is being studied with the aim of controlling the progression of disease. PBMCs from different categories of leprosy patients were cultured with 2 μg/ml (standardized) of antigen in 5% CO2 for 24 and 48 h. Spontaneous apoptosis at 0 h was also checked. Of the three antigens, *viz*. PGL-1, membrane antigen and cytosolic antigen, membrane antigen has been observed to cause noticeable apoptosis. Phenotypic analysis of apoptotic cells was carried out using anti-CD3, anti-CD4, anti-CD8, anti-CD45 and anti-CD69 each with CD95 antibodies conjugated to FITC and phycoerythrin. It has been observed that the lymphocytes with CD3, CD4 markers labelled with CD95 antibodies show apoptosis. The study is continuing.

Immunoprophylaxis and Immunotherapy

A two-arm double blind, randomized, controlled clinical trial of the ICRC vaccine was recently completed at the Cancer Research Institute, Mumbai. The study was conducted in south-eastern Maharashtra, (Latur, Osmanabad, and Sholapur districts) in which the relative efficacy of the ICRC vaccine (0.5×10^9 bacilli per dose) was compared against one fifth the standard dose of BCG. The immunoprophylaxis trial was launched in August 1986. Nearly 34,000 healthy household contacts of leprosy patients formed the study population. The vaccinees were between 1-65 yr of age, of both sexes, and received either of the two vaccines. Four resurveys were carried out in 1993, 1994, 1997 and 1998 for detection of new cases.

Distribution of vaccinees according to age (child and adult), sex, and BCG scar status was similar in the 2 arms. There were 62 eligible incidence cases (29 belonged to ICRC group and 33 to BCG group) giving an attack rate of 2.1 per 10,000 person years, as against the expected rate of 3.5 per 10,000 person years. The overall protection offered by ICRC vaccine was 18% (95%CI - 35% to 50%, statistically not significant), more than the one fifth dose of BCG vaccine.

The immunotherapeutic efficacy of the ICRC vaccine was analysed in LL patients who were clinically classified as non responders to MDT as they had not shown any fall in BI despite 3-4 years of MDT. Immune functions and clinical parameters were monitored in these patients before and 6-12 months after vaccination. Laboratory

investigations focused on analysis of lymphocyte proliferative responses, cytokine production (IL-2, IFN-γδ) and limiting dilution analysis to determine the frequency of ICRC/*M.leprae* reactive T cells in peripheral blood of LL and TT patients and in ICRC vaccinated LL patients. Lymphocytes from LL patients showed poor responses to *M.leprae* antigens but good response to ICRC antigens. Using the above immunological parameters of T cell function, it was noted that the patients exhibited a marked improvement in T cell responses after vaccination with a concomitant fall in BI and histological upgrading. An increased frequency of *M.leprae*/ICRC reactive T cells was observed in peripheral blood of vaccinated LL patients.

It was also observed that in the vaccinated group there was clonal expansion of lymphocytes expressing T cell receptors Vβ6, Vβ7 and Vβ11 indicating that T cell anergy could be reversed after vaccination.

Studies on Drug Metabolism and Drug Permeability

Studies on clofazimine metabolism were continued at CJIL. In the experimental studies in mice model high levels of clofazimine were observed in the tissues having reti-culoendothelial components. In other tissues the levels were relatively lower. Significant amount of drug was detected in the mouse foot-pad where *M.leprae* is known to multiply. Traces of drug could be detected in pooled nerves. Concomitant administration of isoniazid was found to reduce the distribution profile of clofazimine. It was also noted that with a loading dose of 50 mg of clofazimine daily, the bioavailabilty of the drug in the plasma attained a plateau and did not rise even after further administration of clofazimine.

DIARRHOEAL DISEASES

The National Institute of Cholera and Enteric Diseases (NICED), Calcutta and RMRC, Bhubaneswar continued to pursue their research goals on different facets of diarrhoeal diseases. The NICED, Calcutta has earned an important affiliation with the Japanese International Collaborating Programme. Its active surveillance programme continues to monitor the newly emerging diarrhoeal pathogens and addresses unknown frontiers in clinical diagnosis and disease management.

Entamoeba histolytica

During the course of invasive intestinal amoebiasis, *E.histolytica* actively penetrates the mucosa and submucosa of the host's intestine. Since collagen is a major component of the extracellular matrix and basal lamina of the 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. Attempts were made by NICED, Calcutta to clone and sequence some of the genes that are differentially expressed during activation with human collagen type I and Ca^{2+}. Expression of this gene and further characterization of recombined protein will help in immunodiagnosis of amoebiasis. Preliminary results showed approximately 15 differentially expressed bands in pathogenic amoeba incubated with human collagen type 1 and Ca^{2+}. Incubation showed formation and release of electron dense granules (EDG). Analysis of EDG showed maximum collagenase activity. Purified EDG was used to raise antibodies in rabbit which were used in immunoscreening of the cDNA library constructed from pathogenic *E.histolytica*. Further sub cloning and characterization of cloned fragments is under progress.

Rotavirus

The re-emergence of human group B rotavirus (HuGBR) in India was accompanied by a recognition of the need for

the development of sensitive and rapid diagnostic techniques for the early detection of this potentially highly virulent pathogen. A number of primers were designed from different genes of a previously sequenced adult diarrhoea rotavirus (ADRV) strain for detection of HuGBR strains by reverse transcription polymerase chain reaction (RT-PCR). Altogether 32 primers were selected for detection of gene segments coding for viral structural proteins V4, VP6, VP7 and non structural proteins NSP1, NSP2, NSP3, NSP4 and NSP5. The standardization of the RT-PCR conditions has resulted in amplification of various genes in identical reaction conditions.

An ELISA test developed by the National Institute of Virology (NIV), Pune for detection of rotavirus in stool specimens has been modified and the new rapid test standardized. The test can now be completed in 2-3 hours.

Vibrio cholerae

The genesis of a new cholera causing serogroup *V.cholerae* 0139 formed the impetus to search for *V.cholerae* O139 phages in and around the country.A comparative study of the phage types of the O139 strains isolated in 1992 and 1993 and between 1996 to 1998 showed that during both periods, phage type 1 was the predominant type. The percentage of O139 strains isolated in 1992 and 1993 belonging to phage type 1 (40.46%) was much higher than the percentage of strains recovered from 1996 to 1998 (34.69%). Molecular studies have shown substantial changes in the organization of the CTX phage module of O139 strains isolated from 1996 to 1998 compared to the organization of the CTX phage module of O139 strain isolated in 1992 and 1993.

The most important finding was the almost complete typability of the O139 strains with a set of five phages. This phage typing scheme would be useful in the study of the epidemiology of cholera caused by *V.cholerae* O139.

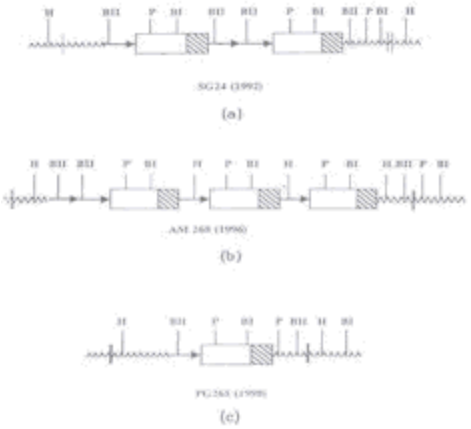


Fig 3 a-c CTX prophage of Vibrio Cholerae 0139 strains

Studies were carried out by NICED , Calcutta on restriction fragment length polymorphism of CTX prophage in view of the drug resistance pattern seen among O139 strains isolated in Calcutta from 1992 to 1998. The results indicated that there is a continuous change in the structure and organization of CTX prophage during the study period along with emergence of a new type of CTX prophage. The 1992-93 strains (Fig.3a) showed two CTX prophages connected by an RS1 element while the 1996 strains (Fig.3b) showed three CTX prophages arranged in tandem. Most of the 1998 strains (Fig.3c) from Calcutta exhibited only one CTX prophage while those isolated from other parts of India are identical to the 1996-97 strains or showed two CTX prophages arranged in tandem. In 1996, O139 strains exhibited two types of CTX prophages with the first of the three prophages being an ElTor-type CTX

prophage and the second and third CTX prophages being a new type of CTX prophage, with the difference primarily lying in the *rstR* gene which codes for the repressor proteins of CTX. In 1998, it was observed that two new clones of O139 have evolved probably from the 1996-97 strains with two epicentres namely Calcutta and Alleppey. Calcutta strains showed only the ElTor-type CTX prophage and not the unique O139 CTX prophage of the 1996 strains while reverse was the case with the Alleppey strains. Therefore, presently, there are two clones of O139 circulating at two locations with different CTX prophages indicating that reassortment in the genome is taking place in the O139 strains. This molecular epidemiological study revealed clonal diversity among the O139 strains and emergence of new epidemic clones, as evidenced by the change in the structure, organization and location of the CTX prophages over a period of seven years.

V.parahaemolyticus

Continued surveillance of *V.parahaemolyticus* mediated diarrhoea implicated the predominant association with disease caused by the O3:K6 serovar during 1998-99. Arbitrarily primed PCR (AP-PCR) of these recently emerged O3:K6 strains with those isolated previously from other countries showed that the new strains exhibited a unique profile different from the old strains. Thus, the Calcutta O3:K6 strains and those isolated from different countries were considered to be clonal. Analysis of the *toxRS* region of the new and old O3:K6 strains was done on the assumption that variation in the *toxR* sequence may be found in phylogenetically distinct clusters of *V. parahaemolyticus*. The difference in the sequence between the new and the old O3:K6 strains ranged from 11 to 14 bp within the 1,364 bp region covering 95.4% of the *toxRS* coding regions, and the sequences differed invariably at 7 base positions (Fig.4). Based on these results a PCR method, referred to as group specific PCR (GS-PCR), was designed to distinguish the new from the old O3:K6 strains. The results indicate that the GS-PCR positive strains belonging to O4:K68 and O1:KUT serovars are genetically very close to the new O3:K6 clone but they also exhibited AP-PCR profiles indistinguishable from that of the new clone. Therefore, GS-PCR positive O4:K68 and O1:KUT strains may have diverged from the existing new O3:K6 clone by alteration of the genes associated with the O:K antigens and followed a spreading pattern similar to the new O3:K6 clone.

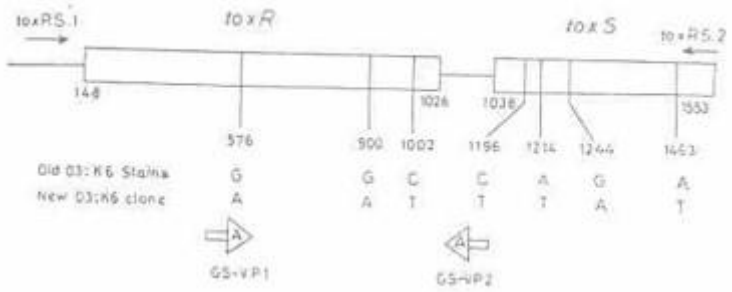


Fig 4: Target positions of the PCR primers used to amplify the *Vibrio parahaemolyticus* tox RS sequences and the essential base difference in the tox RS sequence between the old 03:K6 strain group and the new 03:K6 clone.

Clinical Studies

A double-blind, randomized, controlled clinical trial was conducted by NICED, Calcutta on malnourished children with acute dehydrating diarrhoea to evaluate the efficacy of oral supplementation of zinc as an adjunct therapy to

oral rehydration solution (ORS). Eighty children were randomized to receive zinc sulphate in three divided doses equivalent to 40 mg elemental zinc, in a syrup form and syrup placebo. Clinical parameters and microbiological findings of stool samples were comparable in the two groups at the time of enrolment. All the children (100%) in the zinc supplemented group and 32 (89%) children in the placebo group recovered within 5 days of hospitalization. The zinc supplemented group had a significantly shorter duration of diarrhoea, passed less liquid stool, and consumed less oral rehydration solution and other liquids as compared to the placebo group. These results suggest that zinc supplementation as an adjunct therapy to ORS has beneficial effects on the clinical course of dehydrating acute diarrhoea.

Epidemic Investigations

Following the cyclone in Orissa there was a sudden outbreak of gastroenteritis/diarrhoea in the cyclone affected areas. A total of 107 stool samples were collected from different hospitals/PHCs/CHCs of the cyclone affected areas. Rectal swabs were collected from patients with diarrhoea before any antibiotic was administered. Of the 107 samples, 83 (77.6%) were found to be culture positive and 24 (22.4%) were culture negative. Of the 83 culture positive samples, 66 (79.5%) had *V.cholerae*, 16 (19.3%) *E. coli* and 1(1.2%) had *Shigella flexneri*. Of the 66 *V. cholerae* isolates, 60 were *V. cholerae* 01 Ogawa and 6 *V. cholerae* 0139. Clustering of cases of *V. cholerae* occurred in the worst affected districts of Cuttack and Jagatsinghpur (Erasama, Balikuda, Kujanga, Manijanga) and Astaranga and Kakatpur areas of Puri district.

All isolates were found to be sensitive to tetracycline, ciprofloxacin, furazolidine, strepto-mycin, cotrimoxazole, norfloxacin, gentamicin but resistant to nalidixic acid. The 66 *V.cholerae* isolates were further analysed at the molecular level with the help of NICED, Calcutta. Multiple PCR assay was done using primer specific for *ctx A, tcp A* gene for the detection of cholera toxin and toxin co-regulated pilli gene (Classical and ElTor). It was observed that 59 of 60 *V.cholerae* isolates belong to *V.cholerae* 01 serogroup and ElTor biotype and were positive for *ctx A* gene. Of *the 6 V. cholerae 0139* strains *5* harboured *ctx* A gene.

Besides the antibiogram, the strains were randomly selected from different areas for molecular epidemiological study using random amplification of polymorphic DNA (RAPD) analysis of the isolates. For ribotyping, Bgl 1 digested chromosomal DNA was probed for 16S and 23S rRNA. Almost all the strains exhibited ribotype R3 pattern, as it has been reported from different parts of the country after the emergence of 0139 strains of *V. cholerae*. Primers 1281 and 1283 were used for RAPD to detect clonality, if any. Like the ribotyping results, the *V. cholerae* 01 strains exhibited similarity with Calcutta strains *i.e. V. cholerae* 01 that appeared after the *V. cholerae* 0139 epidemic.

OTHER MICROBIAL DISEASES

A study is being supported at the Vision Research Foundation, Chennai to develop PCR for the detection and genotyping of *Chlamydia trachomatis* in patients with conjunctivitis. This study envisages molecular amplification of *omp-1* gene encoding for major outer membrane protein (MOMP) to help in the epidemiological investigation of *C.trachomatis* infection, identification of individual genotypes to correlate with symptoms, clinical findings and histopathology in conjunctivitis in the hospital-based population. Fifty five consecutive patients of primary conjunctivitis have been clinically examined and conjunctival scrapings were investigated for bacteria, herpes simplex virus (HSV) and adenovirus and *C. trachomatis* infections. Almost half the specimens were smear and culture positive for *C. trachomatis* out of 55 conjunctival scrapings obtained from both eyes. PCR has been standardized to detect *omp-1* gene and common endogenous plasmid gene. DNA extraction from the specimens has

been done. Molecular amplification of *omp-1* gene would now be carried out.

Studies are being conducted at the IOP, New Delhi for development of DNA probe for detection of *C. trachomatis* infection. During the year under report, PCR has been standardized for detection of DNA in clinical samples using plasmid as well as MOMP primers. So far, 135 samples have been tested by PCR using different primers. The presence of an additional lower sized band apart from the usual 540 base pair band was most probably due to some variation in the particular gene sequence that was amplified showing thereby strain polymorphism on the MOMP gene.

In addition to developing a diagnostic method for *C. trachomatis*, fluorescent *in situ* hybridization (FISH) is being used to detect *C.trachomatis* in McCoy cell culture and in clinical specimens. For this, fluorescein labelled probes targeting rRNA sequences are being examined under a fluorescence microscope after *in situ* hybridization.

The incidence of cryptococcosis is expected to rise especially in the wake of HIV/AIDS epidemic. Recently *Cryptococcus neoformans* var. *gattii* has been isolated from patients with HIV/AIDS both from north and south India. This agent has also been isolated from *Eucalyptus camaldulensis* trees from border areas of Punjab. Therefore, a project was initiated at PGIMER, Chandigarh to study the natural habitat of *C. neoformans* var. *gattii* strains in the environment of Punjab and north Karnataka. This would also help in understanding the epidemiology of the disease. In the first phase, various trees like mango, eucalyptus, bamboo, banyan, pipal, neem evaluated in and around Chandigarh and Belgaum have been found to support the growth of *C.neoformans* var. *gattii*. The study is in progress.

To identify the specific immunodominant fractions of various agents of zygomycosis which could be exploited for serological diagnosis of this disease, a study is ongoing at PGIMER, Chandigarh. Hyperimmune sera were raised in outbred healthy New Zealand white rabbits against 12 crude antigens (6 metabolic & 6 homogenate antigens) of 6 medically important agents of zygomycosis. These sera were used in gel diffusion, counter current immunoelectrophoresis (CIEP) and immunoblotting, to find out specific and common immunodominant fractions. Cross reactivity of these antisera was also checked. Several precipitation lines were seen by gel diffusion and CIEP against various antigens. On immunoblotting the cross-reacting and immunodominant antigen was found at 82 kDa fraction. Further characterization of the antigen is being done.

The procedure for the *in vivo* study of zygomycosis was standardised. Immunosuppression of mice was done with cyclophosphamide given intramuscularly. These immunosuppressed mice were injected intravenously with spores. Four categories of inoculum size were taken *i.e.* $2x10^6$, $4x10^6$, $8x10^6$ and $1x10^7$ spores/ml of *Rhizomucor pussilus*. $4x10^6$ spore size was found optimum for development of invasive zygomycosis.

Acinetobacter species are opportunistic pathogens and can lead to invasive diseases in a compromised host. Apart from being important hospital acquired bacterial pathogens, they also commonly colonise the sites of endotracheal tubes, indwelling intravenous cannulae, central venous lines and urinary catheters. The possibility of *Acinetobacter* species becoming multidrug resistant also exists. Studies were initiated at AIIMS, New Delhi to assess the mode of transmission of this bacteria from the hospital environment to the patients especially in the intensive care units (ICU) by typing various isolates obtained from the colonization sites and environmental sites. Strains (147) of *Acinetobacter* species isolated from the neurosurgery ICUs (125 from patients and 22 from the environment) were studied. *Acinetobacter baumm*i was the most common isolate (114/147). Antimicrobial resistance studied by MIC (agar dilution method) showed that 59.2% of the isolates were multidrug resistant (to all the newer antibiotics including third generation cepha-losporins, amikacin, ciprofloxacin *etc*.). However, all the

strains have remained sensitive to Imipenem. Whole cell protein analysis was done by SDS-PAGE. AP-PCR and ribotyping are being standardized and these would be compared with the conventional methods.

A study was recently completed to standardise isolation techniques and to develop immuno-diagnostic methods (IFA and ELISA) for *Mycoplasma pneumoniae* at AIIMS, New Delhi. *M.pneumoniae* was identified as an important cause of community aquired pneumonia (CAP) both in paediatric (29.80%) and adult age groups (36.6%). Using *M.pneumoniae* antigen detection in throat swabs by IFA infection could be demonstrated in 19.87% children and 36.6% adults. Incidence was found to be high in immunocompromised (40%) as compared to immunocompetent subjects (17.5%). If the presence of IgM antibodies alone is considered the number of positive patients would be much higher *i.e.* 29.80% in the paediatric age group. Rapid diagnostic procedures like antigen detection and demonstration of IgM antibodies should be more widely used to detemine the infective etiology early in the course of illness.

Another study was recently completed at PGIMER, Chandigarh on identifying cellular immune resonses in human and experimental cysticercosis. The results revealed that in cysticercosis both humoral and cellular mechanisms may be playing a role in host defence mechanisms. In experimental cysticercosis, studies on kinetics of immune responses showed that the cellular mechanisms were triggered at a late stage compared to humoral responses and may persist longer. In human neurocysticercosis, studies on lymphocyte-proliferative responses indicated that specific antigens might be playing a role in eliciting T cell responses. Immunophenotyping analysis indicated an insignificant increase in B cells and a decrease in total T cells. However, there was a significant decrease in CD8+ cells and no change in CD4+ cells, in contrast to experimental study whereby significant increase in CD8+ T cells was observed. The cytokine profile indicated involvement of TH-I like responses as significantly higher levels of γ-IFN and IL-2 were observed. In chronic helminthic infections, shift from TH-I type immune responses in early infection to TH-2 type response in advanced infection has been reported and might occur as well in long standing human cysticercosis. Since the study was cross-sectional, shift could not be assessed. However, the exact role of cell mediated immune responses in human neurocysticercosis and that of cytokines in patients after medical/or surgical therapy needs to be determined to identify any shift in the TH-I type of response after therapy.

PARASITIC DISEASES

MALARIA

The emergence of chloroquin resistance in *P.falciparum* and vector resistance to commonly used insecticides are the main obstacles in the control of malaria in the country. New technologies are being introduced for malaria control under Enhanced Malaria Control Programme. The roll back malaria programme has been launched simultaneously in all malaria endemic countries. These have thrown new challenges in malaria research. The Council's institutes *viz.* Malaria Research Centre (MRC), Vector Control Research Centre (VCRC) and other institutes are making efforts to address these problems through focused research in vector and parasite biology and ecology, development of malaria control tools, drug development, testing and validation of new technologies.

Integrated Vector Control

Under Integrated Disease Vector Control (IDVC) project, research activities at the field stations were concentrated on the evaluation of new antimalarial drugs, diagnostic kits, insecticides, and repellents; transmission dynamics of malaria in different ecosystems, epidemic investigations, development of an action plan for malaria control; and transfer of technology on bioenvironmental methods for malaria control.

Strategies of bioenvironmental interventions using larvivorous fishes have now been well established by MRC, Delhi and currently preparations are on to extend bioenvironmental interventions to the entire Karnataka state including mosquito control in Bangalore city. The technology has also been transferred to Maharashtra and within two years the bioenvironmental methods have spread to the entire state which is being implemented through the PHC system. In Gujarat 174 fish hatcheries have been established for use in the entire state.

In Panaji, Goa, the MRC has used biopesticides and larvivorous fish in controlling *Anopheles stephensi* breeding and consequently malaria. Bioenvironmental control of malaria has been launched in Panjim (Goa) and Ahmedabad (Gujarat) by the respective city corporations with the technical support of MRC with a marked reduction being seen in mosquito populations and in the transmission of malaria in both the cities. An action plan for the control of malaria for the entire Ahmedabad city has been prepared by MRC. The Goa field station has actively participated during the construction of the Konkan Railway. The technology transfer of the bioenvironmental control project to the State health authorities is being undertaken. Konkan Railway project and Marmugao Port authorities have fully accepted the suggestions made by the Goa field station on malaria control and continue to use their consulting services.

Malaria in Tribal Areas

The VCRC, Pondicherry carried out a study on malaria control in Malkangiri district to assess the feasibility of reducing the morbidity and mortality from malaria in the tribal population by providing early treatment through traditional healers. *Disaris*were willing to treat malaria cases with chloroquine but their record keeping and reporting was poor, as majority of them had no formal education. Therefore, they were trained to provide treatment with the help of a pictorial guide and pre-packed tablets. A total of 110 *disaris* from Malkangiri PHC area were trained. Disaris could follow the recording system and in a period of 9 months (April - December, 1999), they treated 27021 patients in all age groups. Most of them administered the correct dosage and reporting of cases was regular. A total of 29 severe/ complicated cases were referred to the PHC. The impact assessment is being done.

Vector Studies

Susceptibility of Anophelines to P. *vivax*

A study was carried out by MRC, Delhi to assess and compare susceptibility of three recognized malaria vectors *i.e. An. stephensi*, *An. sundaicus* and *An. fluviatilis*species T to *Plasmodium vivax* sporogony. The laboratory colonized mosquitoes of each species were fed through artificial membrane on *P. vivax* infected blood drawn from selected patients. The mean number of oocysts, oocyst rate and sporozoite rates were determined for each of these test species. The results have revealed that *An. stephensi* and *An.sundaicus* are equally susceptible to *P. vivax* sporogony whereas in *An. fluviatilis* species T significantly lower oocyst rate, mean number of oocysts and sporozoite rate were recorded (Fig.5).In field studies, no sprozoite positive specimens were found in *An. fluviatilis* species T and this species was almost totally zoophagic.

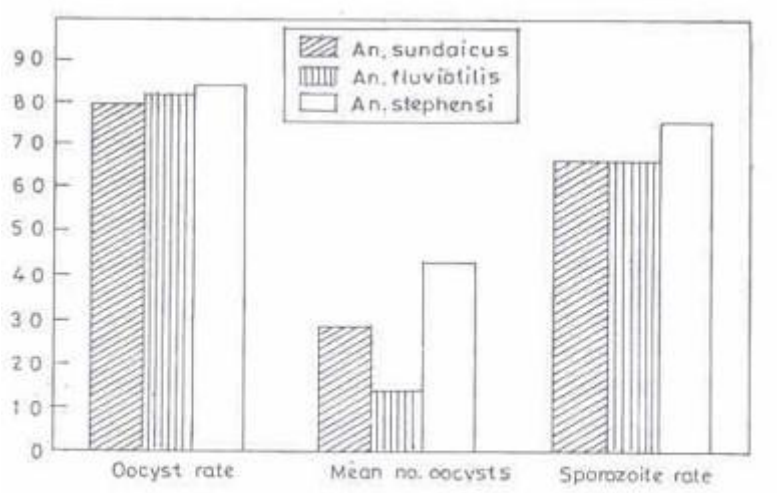


Fig. 5. Comparative susceptibility of *An. sundaicus*, *An. fluviatilis* and *An. stephensi* against *P. vivax*.

Characterization of An. fluviatilis Complex

An. fluviatilis, a major vector of malaria exists as a species complex comprising 3 sibling species. Being morphologically identical, the incrimination of the vector species is difficult. The VCRC, Pondicherry has developed rDNA-ITS2 based primers for two of the sibling species of the *An.fluviatilis* complex. These probes were evaluated for their sensitivity and specificity in the differentiation of *An. fluviatilis* adults collected from different areas of Jeypore and Malkangiri, Orissa.

The VCRC, Pondicherry carried out studies to simplify the PCR technique (both in terms of time and cost). The complete procedure *i.e.*, from DNA extraction to visualizing the product has been brought down from 24 to 5 h. The cost in terms of reagents for DNA extraction has been brought down from Rs. 40 to Rs. 2 per sample. The level of specificity of this PCR assay for the detection of a single *An.fluviatilis* adult in pools of other mosquitoes was studied. It was found that this PCR assay was able to detect a single *An.fluviatilis* adult in a pool containing 40-45 *Culex quinquefasciatus* mosquitoes.

Other Studies

Insecticide treated mosquito nets are known to reduce the man-vector contact, density of the malaria vectors and the incidence of malaria. Therefore, the efficacy of alphacypermethrin, a synthetic pyrethroid, treated mosquito nets was assessed by the VCRC against malaria vectors in Malkangiri district, Orissa. Villages were chosen for evaluation and distribution of alpha-cypermethrin- treated or untreated nets or no-nets before the onset of monsoon season. Indoor resting density of vectors and malaria incidence in the three groups of villages were monitored fortnightly one year before and after the distribution of nets. Re-impregnation of mosquito nets was done in October 1999 to cover the peak transmission season. The reduction in the density of *An.fluviatilis* was 97.1% after the first treatment and 99.5% after re-impregnation compared to the pre-intervention period and the check area. The corresponding values for untreated nets were 66.1 and 62.4% respectively. The reduction in malaria incidence was 79.2 and 85.7% during the corresponding periods. There was no marked effect on the density of *An.culicifacies* after the first treatment and the density was low in all the villages during the next season. The use rate of mosquito nets ranged from 20 to 100%, the lowest was during the colder months, December-January.

The indoor residual application of insecticides reduces the density and longevity of malaria vectors and incidence of malaria. Bendiocarb, a carbamate adulticide has not been studied for indoor residual treatment against malaria vectors under Indian conditions. Therefore, bendiocarb (80% WDP) for indoor residual treatment was evaluated by VCRC, Pondicherry for its efficacy against malaria vectors, *An.fluviatilis* and *An. culicifacies* in Malkangiri district, Orissa.

The spray coverage was about 90% in human dwellings and 100% in cattle sheds. About 50% of the sprayed houses were mud plastered one month after the spray. There was 94.9 and 86.2% reduction in the resting density of *An. fluviatilis* and 16.9 and 26.8% in malaria incidence after the spray of 0.4 g/m^2 and 0.2 g/m^2respectively. The density of *An. culicifacies* was low in all the three groups of villages in the season.

Clinical Trials

Artemisinin, an antimalarial principle isolated from *Artemisia annua* L. is a sesquiterpene lactone with excellent antimalarial activity. Three formulations *viz*. Artesunate, Artemether and Arteether are registered in India. A study has been undertaken to evaluate the comparative safety and efficacy of these formulations administered as follows for the treatment of falciparum malaria (i) α-β Arteether 150 mg i.m. O.D. for 3 days, (ii) Arteether 80 mg i.m. B.D., for 3 days; and (iii) Artesunate 120 mg loading dose i.*v.* and 60 mg i.m. once daily for 5 days.

The results showed fever clearance time of 26.8, 28.09 and 35.65 h and parasite clearance time of 31.2, 31.2 and 28.0 h respectively in groups (i), (ii) and (iii). No significant side effects were seen in any group. Further study to explore the comparative recrudescence rate and gametocytocidal activity is in progress.

Basic Studies

To understand the molecular mechanism of development of chloroquin (CQ) resistance, polymorphism of *pfmdr 1* gene of CQ sensitive (CQS) and CQ resistant (CQR) strains of *P.falciparum* was studied at MRC, Delhi using PCR. Twenty two chloroquine resistant and 18 chloroquine sensitive *P. falciparum* strains were examined for nucleotide changes in *pfmdr 1* gene. Results indicate a strong association but incomplete correlation between CQ resistance and allelic variation of *pfmdr1* gene in *P.falciparum* isolates from India. This suggested that the pfmdr1 gene was not solely responsible for CQ resistance and the study of a combination of mutational changes would be required to determine CQ resistance.

The importance of T cells in malaria immunity has been appreciated for a long time. However, T cell epitopes show variation. Two T helper cell epitopes (Th 2R and Th 3R) have been identifed in circumsporozoite protein (CSP). Genetic variation in Th-epitopes of CSP of 40 *P.falciparum* isolates, collected from Delhi, Jabalpur (M.P.) and Allahabad (U.P.) has been studied. An apparent trend of regionally unbiased restricted polymorphism has been observed among Indian isolates. The nucleotide changes observed have not been reported earlier.

Geographic Information System (GIS)

GIS was used to map the distribution of malaria vector *An.dirus* in India. Topo sheets published by the Survey of India in the scale of 1: 6,000,000 were digitized to prepare thematic maps of soil, altitude, rainfall, temperature and forest area. The digitization and analysis was done using PC based ARC/Info 7.0 and Arc View 3.1. The altitude

map s was taken as the base map, *An. dirus* has been reported up to 4500 m, these areas were extracted from the altitude map. Rainfall >2000 mm and temperature between >20 to <27.5^{o}C and evergreen forest plus tropical moist forest cover areas were taken as favourable zones. Areas having these ranges were extracted and overlaid on altitude map. Using GIS capabilities intersection of these layers was extracted to map areas favourable for *An. dirus* (Fig.6).

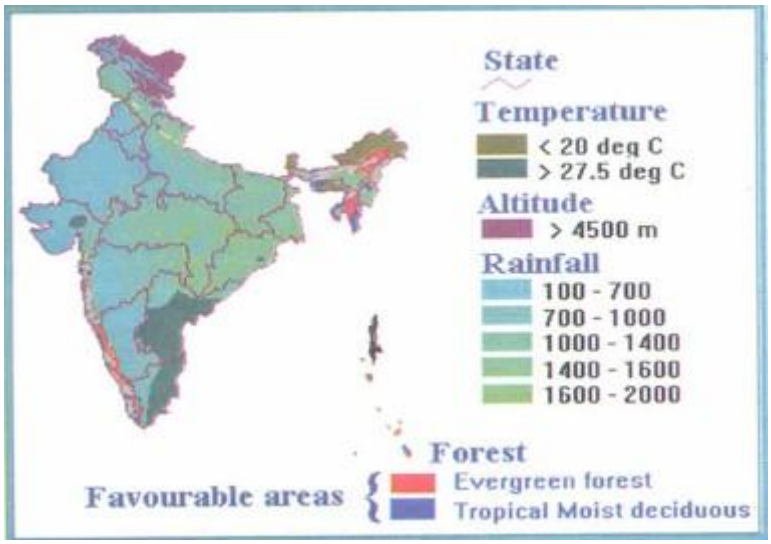


Fig 6 : Distribution of An. dirus in India.

The distribution of *An. dirus* mapped by GIS analysis was compared with the reported distribution. The areas where the species has been reported could be located in the predicted GIS map, with many new areas being found in GIS distribution map. The study is in progress.

Management of Malaria Information System

An efficient management and timely flow of information is crucial for any forecasting system and timely implementation of intervention measures. GIS is a powerful tool for management of information system as it allows integration of both spatial and non-spatial information management. A prototype has been developed for maintaining a Malaria Information System.

With the help of this information system one can reach a street and even the houses, and house-wise information such as number of persons, their names, ages, educational status, malaria history, drug resistance level *etc*. can be attached for instant retrieval. This type of information would allow study of malaria epidemiology in space and time and relate change in the malaria scenario with its determinants for taking timely corrective control measures.

Malaria Parasite Bank

This is a centralized facility at MRC, Delhi to collect human and non-human plasmodial species and strains from different geographical regions. Depending on the species of the parasites, they are cryopreserved in liquid nitrogen or are cultivated *in vitro* and characterized for various studies using standard techniques. The characterized parasites are also cryopreserved for various collaborative studies. The Parasite Bank also supplies biological materials including non-human and human plasmodia to various research organizations mainly for collaborative studies.

FILARIASIS

The Council's Vector Control Research Centre (VCRC) at Pondicherry and RMRC, Bhubaneswar have focused their research in the field of vector biology and control, clinical epidemiology and chemotherapy, applied field research and product development. The Centre has geared its activity towards transferring the technical know-how to the field for optimum and appropriate application for elimination of filariasis so that latest technical knowledge is absorbed into the Programme.

Epidemiological Mapping of Lymphatic Filariasis in India

Rapid mapping methods need to be standardized for prioritisation of areas for intervention. This is an essential step to work towards the elimination of filariasis. The rapid methods for the estimation of prevalence of bancroftian filariasis and its mapping by grid sampling technique are being validated.

An area covering 41,950 km^2 from the eastern coast of India stretching towards the west from Pondicherry, lying between $78^0$9'25'' and $80^0$13'48'' East, and $11^0$0'54'' and $13^0$2'31'' North was selected for the study. For sampling, a 25 x 25 km grid was overlaid over the study area covering 13 districts. Data on filariasis were collected through questionnaire method; physical examination by health workers (PEHW) for scrotal swelling and immunochromatographic card test (ICT) were done.

Spatial analysis were carried out using a GIS software (GS+) to see whether there was any spatial pattern in the occurrence of filarial disease (scrotal swelling) or antigenaemia in the study area.

For this, variogram models were fitted to data on prevalence of scrotal swelling and filarial antigenaemia. Further advanced analyses with S PLUS after removal of trends (detrending) in the data showed that still there were no spatial differences in the prevalence of antigenaemia. Construction of variograms using the residuals obtained showed that still there was no spatial autocorrelation and that there were large-scale trends against longitude and the pattern was apparently random with latitude. Similar analysis is being carried out for disease prevalence also.

No spatial autocorrelation with respect to antigenaemia prevalence was detected. This could have been because the grid used was too big to capture spatial autocorrelation. The use of smaller grids has been planned for future studies. Therefore, a uniform grid sampling procedure may not be applicable globally.

Mathematical Modelling

The VCRC carried out a study to validate the application of epidemiological model LYMFASIM under operational settings for predicting the required duration of interventions for vector control and for mass annual single dose of DEC. The required duration of vector control was determined by simulating the effect of vector control (assuming 80% reduction in monthly vector biting rate, average for 5 yr integrated vector management programme in Pondicherrry) over a period of 5, 10, 11, 12, 13, 14 &15 yr. Simulations were done for about 50 yr since the start of the control programme to predict the trend in prevalence of microfilaria (mf). For chemotherapy programme 4 strategies (5, 10, 15 & 20 annual DEC) were evaluated at 6 different levels of coverage. In simulating these strategies it is assumed that DEC has a microfilaricidal effect of 55% and adulticidal effect of 67% per treatment (based on a VCRC hospital trial). For the treatment programme the required duration of control for each strategy was estimated by calculating the risk of acquiring new infection in children aged less than 5 yr. Each strategy was simulated 50 times. The risk of acquiring new infection is the proportion of simulations that result in a mf

prevalence of 0.033% or more (*i.e.* 1 per 3000 children) over a period of 5 yr after cessation of control. The simulation results suggest that a minimum of 13 yr of vector control with at least 80% reduction in man biting rate of vector mosquitoes is required for elimination of infection and that the minimum coverage required for complete interruption of transmission is 90% and 60% for 5 and 10 annual rounds of DEC in areas with 8.0-10% mf prevalence.

Studies on Mass Chemotherapy

A study is ongoing at the VCRC, Pondicherry to compare the effect of single dose mass drug administration (MDA) with ivermectin and DEC independently and in combination on transmission, microfilaraemia, incidence of acute adeno-lymphangitis (ADL) and prevalence of chronic disease. Four blocks of five villages each were randomly assigned to one of the four arms *viz*., DEC, ivermectin, DEC with ivermectin and placebo. Initial two rounds of MDA were carried out at 6 monthly intervals for DEC, ivermectin and placebo arms in a double blind fashion. The combination arm with DEC and ivermectin was introduced after the completion of two rounds of MDA. Third and subsequent rounds of mass treatment were conducted in an open manner with the placebo village receiving no drug. The mean coverage during the fifth round of chemotherapy in 1999 was 63 and 61% in ivermectin and DEC blocks respectively and 65% for third round of combination drugs. The rate of adverse reactions ranged between 3.5 and 6.2%. Entomological evaluation showed a reduction in vector infection, infectivity and transmission parameters. Parasitological evaluation after the last round of mass treatment showed a reduction of 48 and 60% in mf rate, and 70-95% in mf density in DEC and ivermectin blocks.

Two alternative methods for delivering mass annual single dose DEC treatment are being evaluated for their operational and economic feasibility as well as impact. The methods include delivery through PHC system and community volunteers (CV). Two rounds of treatment have been completed following the pre-designed implementation process.

Post-treatment survey results on the impact of IEC show that posters and public announcements were the most effective community awareness tools. Community compliance estimated through sample surveys in 10 randomly selected villages for each approach showed that about 76% of the respondents in villages under community approach and 68% under PHC approach consumed the drug. Supervised drug administration was relatively higher under PHC approach (35%) than the CV approach (27%). The CVs visited in the evening, while the PHC staff worked during the day. Consequently, the percentage of people available at the time of distribution was higher in areas under CV approach (69%) when compared to that of PHC approach (39%).

There was a significant reduction in mf prevalence in both the areas after two rounds of mass treatment. The reduction was relatively higher in areas under PHC approach, but it was not statistically significant. Microfilaria density showed a reduction of about 70% in both the areas, after two rounds of mass treatment.

The mass DEC fortified salt programme to control filariasis was launched in 1996 to cover the Kanyakumari district of Tamil Nadu. The total target population was about 17 lakhs, distributed in 4 municipalities and 1885 villages. Fortification of salt with DEC (0.2% w/w) was done by the Tamil Nadu Salt Corporation and supplied to the district civil supply department. Distribution of salt to the community was carried out through Fair Price Shops under the Public Distribution System (PDS). A study was initiated by the VCRC to evaluate the impact of this innovative centralized distribution programme designed to achieve good coverage and community compliance. The disease was reported from 28 of 35 units. The prevalence of disease was found to range between 0.002 and 0.132% in different PHCs/Municipalities. Salt distribution (supply) against monthly demands was analyzed and it was found that there

was a steady increase in supply from 3.15% in May 1996 to 34.59% in 1999. Analysis of data on the change in mf prevalence in relation to DEC salt distribution showed that there was a gradual decline in mf rate (Fig.7). Supply against demand was above 30% since July 1998. Microfilaria prevalence reduced to zero after 44 months of DEC salt introduction (August 1999). It is planned to assess antigenaemia prevalence in these seven villages using ICT.

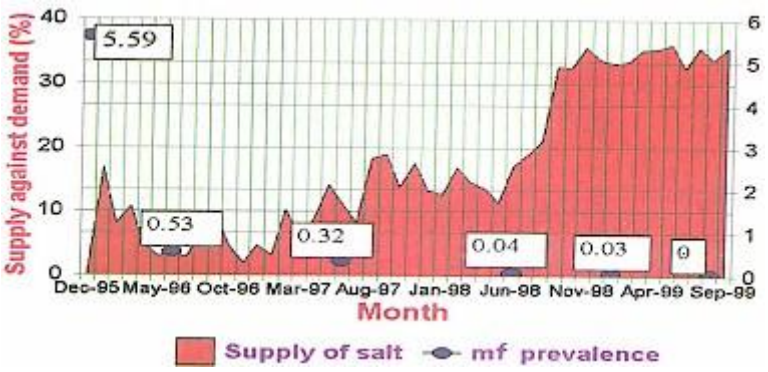


Fig 7: Monthly coverage and mf prevalence in sentinel villages.

Natural History

A study has been carried out by VCRC in 3 selected filariasis endemic urban localities *viz.*Pondicherry, Villupuram and Cuddalore following quantitative research methodology.Simple random sampling procedure was followed to select the respondents from the list of patients. A total of 200 respondents were covered in the three areas and the analysis showed that 55% suffered from adenolymphangitis (ADL), of whom 40.18% had utilized government facilities, 24.30% private health facilities and 35.52% opted for self treatment with drugs from the local drug sellers. However, about 2% of the patients did not take treatment for ADL. About 49% of the patients reported to seek treatment for the chronic disease. Accessibility to health care services, cost of treatment, attitude towards the providers and confidence on the treatment are some of the factors that determine the choice of treatment. Average direct cost for treatment of ADL episodes was estimated to be Rs.2.29, 10.43 and 73.12 when treatment was sought from drug sellers, Government facilities and private practitioners respectively.

Development of Molecular Tools

In order to develop infective stage specific DNA probes, 50 genes expressed in the infective stage larvae (L3) of *Wuchereria bancrofti* were identified by subtractive hybridization and sequenced at the VCRC, Pondicherry. Primers (probes) for six genes were designed and their potential in amplifying the respective genes was tested. Two probes (WbL31 and WbL36) amplified the cDNA of L3 stage larvae but did not amplify cDNA of mf, and L1 and L2 stage larvae. Thus, two infective (L3) stage specific probes developed were evaluated for their usefulness in detecting the infective stage larvae in vectors.

At VCRC, Pondicherry in efforts to develop filarial specific monoclonal antibodies for diagnostic purposes, two clones (B5 and E2) were identified based on their high reactivity with *Wuchereria bancrofti* (mf) antigens. They were moderately reactive with *Brugia malayi* (both mf and adult) antigens and poorly with *Ascaris lumbricoides* and *Setaria* sp. antigens. Clone B5 was tested for its sensitivity and specificity in detecting filarial specific antigens in the sera of individuals who were non-endemic normals, endemic normals, chronic filariasis patients and mf carriers as determined by membrane filtration technique. The antibody was found to be 91.7%

specific and 71.4% sensitive.

In separate studies, in order to develop a simple and rapid method for the extraction of DNA of filarial parasite *Brugia malayi*, suitable for PCR, four different methods (A, B, C & D) were tried. Method D was found to be simple and efficient for the extraction of DNA from a single mf in pools of 25 mosquitoes and the DNA was suitable for PCR amplification yielding a band of 322 bp with primers specific for *B. malayi*. Dot-blot hybridization confirmed the specificity and sequence similarity of the PCR amplified fragment. On blind testing, 50 pools of infected mosquitoes tested positive and 50 uninfected tested negative. The DNA extracted by this method was stable for about one year. The cost of a single PCR reaction using DNA extracted by this method worked out to be Rs. 63.19 which is half that of the standard method and the hands-on time was minimized by five times. The new method besides being specific and sensitive as the standard method is also rapid, safe and cost effective in assessing the *B.malayi* infection in pools of vector mosquitoes.

Development and Testing of New Product

Preliminary characterization of the mosquito pupicidal metabolites of the bacterium, VCRC B426 showed that the active principle is a ~80 kDa protein. The active ingredient was formulated as a flowable concentrate. The LC50 and LC90 of this formulation against pupae of four vector species were determined. Pupae of *Cx.tritaeniorhynchus* were the most susceptible followed by *Cx.quinquefasciatus*, *An. stephensi* and *Aedes aegypti*. The shelf life of the formulation studied indicates that it is quite stable for at least 4 months.

LEISHMANIASIS

Kala-azar is a major public health problem in the states of Bihar, West Bengal and Uttar Pradesh. Cases have also been reported in Delhi. Research on various aspects of kala-azar is being conducted mainly through the Council's Rajendra Memorial Research Institute of Medical Sciences (RMRI) at Patna and various extramural projects. New research areas such as development of DNA/RNA diagnostic probes and their use in mapping of the distribution of the parasite in kala-azar endemic areas and epidemiological modelling have been identified recently. A Leishmania parasite bank has been established. Clinical trials of different combinations of existing drugs for the treatment of kala-azar are being undertaken to optimize the drug dosages and minimize the associated side reactions. Disease epidemiology is being studied to assess the infection dynamics in the population, and prediction of epidemics through application of remote sensing technique.

Epidemiological Studies

A longitudinal study for the estimation of infection dynamics of *Leishmania donovani* in a kala-azar endemic population in Bihar was undertaken at RMRI, Patna. A total of 433 (80%) individuals of all age groups and both sexes from a defined endemic village was examined for their clinical status, and response to direct agglutination test (DAT) and leishmanin skin test (LST). Two rounds of vector surveillance in each household were carried out to assess the morphology, density and infection status of the vectors.

Of the 433 subjects screened, 88 (20%) were found LST positive. No significant difference in leishmanin positivity was observed between males and females. The frequency of leishmanin positives increased with advancement of age reaching a peak in the age group of 35-44 yr. Seropositivity (DAT) was found in 42.75% of the population screened being highest in the age group of 26-34 yr. No significant difference in seropositivity was noticed between males and females. The cohort is being followed up every six months to assess the infection dynamics.

Molecular Biological Studies

Studies were carried out at RMRI, Patna to develop nucleic acid probes and PCR primers for diagnosis and detection of kala-azar, to study strain variation and to develop prototype kit for easy field application. Genomic nuclear DNA from the promastigotes of 17 different isolates was restriction digested using EcoR1, HindIII, Hinf l and HaeIII enzymes. HaeIII pattern was similar at one and different in one restriction site of DNA in KA and post kala-azar dermal leishmaniasis (PKDL) isolates. In a comparative study, the kala-azar isolates reflected that the SAG responsive and unresponsive cases differed at EcoR1 and HaeIII restriction sites. A PCR-RFLP system has been standardized targeting the spacer sequence with rRNA gene. DNA of 17 isolates, 15 visceral leishmaniasis (VL) and 2 PKDL along with one reference strain was amplified by PCR using the same primers. Differences were observed at different sites of 5 VL (4 unresponsive and 1 strain responsive to SAG) and 2 PKDL isolates as evidenced from different banding patterns of nucleotide base pairs. Two SAG responsive and 8 unresponsive strains showed similarity. These strains belong to Patna, Vaishali, Muzaffarpur, Samastipur, Begusarai, Katihar, Madhubani and Buxer districts.

Diagnostic Studies

Field trials were carried out by RMRI, Patna to establish DAT as a diagnostic tool for kala-azar and for mass screening of the population for epidemiological studies. Sensitivity and specificity were found to be 91.6% and 100% at a dilution of 1:800 (cut-off titre). Positive and negative predictive values were 100% and 98% respectively at this dilution.

Validation studies carried out after 6 months in an endemic area, indicated that 18.6% of the subjects were DAT positive during the first survey, of whom 1.9% continued to be DAT positive and developed clinical symptoms of kala-azar during the second survey. None of the subjects DAT negative in the first survey was found positive in the second survey. Periodic evaluation for validity is being monitored at 6th, 9th and 12th months in the same population group.

A study was carried out at RMRI, Patna to assess the efficacy of immunohistochemical (IHC) staining technique in the diagnosis of PKDL in comparison to the conventional methods like tissue smear and culture. The results of the study indicated that IHC technique gave better yield of sensitivity (83%) as compared to biopsy smear (66.6%) and culture (33.3%). More samples are being studied for confirmation and at different stages of treatment.

PCR primers based on kinetoplast DNA were designed at the Institute of Pathology (IOP), New Delhi in order to develop a PCR assay for kala-azar and PKDL. The assay was found to be highly sensitive with culture isolates as well as samples isolated from patients.

Clinical Studies

A study was carried out at RMRI, Patna to assess the frequency of unresponsiveness to SAG (20 mg/kg body wt for 30 days) in 64 previously untreated, confirmed patients of kala-azar and to evaluate whether any factor(s) related to disease are associated with unresponsiveness. Sixty two patients completed the full course of treatment and two developed adverse reactions. The apparently cured subjects (clinical and parasitological cure at the end of treatment) were 30 (48%) and unresponsive at the end of the treatment were 32 (52%). It was observed that unresponsiveness was not associated with age, sex, duration of illness, existence of other associated diseases or Hb levels in the patients. Distribution of patients from different endemic zones was observed to be significantly associated with

frequency of SAG unresponsiveness.

A pilot study to assess the efficacy of SAG in the treatment of PKDL was carried out at RMRI, Patna. Thirteen patients with different clinical forms of PKDL were treated with SAG 10 mg/kg body wt. continuously for 90 days. The patients had macular (7), nodular (5) and papular (1) dermal changes. Only 10 had a past history of kala-azar (2-12 yr prior to the onset of PKDL). Patients(8) who completed the treatment were parasite negative at the end of 3 months and had reduction of dermal lesions, but did not show complete clearance at 2 months post treatment. These patients are being followed up till complete disappearance of lesion or relapse.

Immunological Studies

A study was carried out to find an association, if any, between differentially expressed $CD2^{+}$T cells with immunological profile (IL-2 and MIF) in kala-azar patients during treatment with SAG.

Leishmania antigen failed to induce significant $CD2^{+}$T cells in the peripheral blood (35.07%) and bone marrow (49.85%) of kala-azar patients during active infection presenting with low immunological profile. On the other hand, leishmanial antigen induced significant number of $CD2^{+}$T cells *in vitro* in the sera of cured kala-azar patients (78.26%) and healthy controls (65%). This significant association between $CD2^{+}$T cells in protected subjects was associated with significant MIF (36.85%) and IL-2 release. CD2 induction of T cells in SAG unresponsive cases was 43.64% in the peripheral blood and 46.87% in bone marrow which was associated with low MIF (22.33%) and IL-2 level by the T cells of such patients. The results indicate that $CD2^{+}$T cell proliferation in response to *Leishmania* antigen is indicative of drug response leading to T cell activation and is possibly involved in influencing immunological profile in kala-azar patients.

Basic Studies

A study was undertaken at RMRI, Patna to identify protein antigen fractions recovered from different *Leishmania* isolates from various geographical regions of Bihar by SDS-PAGE, and their diagnostic ability was examined by Western blot. A 8kDa antigen was frequently observed in isolates obtained from untreated and SAG unresponsive patients in kala-azar endemic and non-endemic areas. Sera from all kala-azar patients examined recognised the 8kDa antigen of *L.donovani*. However, sera from cured patients, normal individuals, tuberculosis and leprosy patients did not show any reactvity with 8kDa antigen indicating the specificity of 8kDa antigen to *L.donovani* only. This could be a potential candidate antigen for development of diagnostic tests. Isolation and gene sequencing of 8kDa protein fraction is being carried out.

Studies carried out at the IOP, New Delhi on Western blot analysis of 35 kala-azar positive sera revealed that leishmania antigens of 40, 55, 65, 70 and 82 kDa were recognized most frequently.

Majority (83%) of the sera from kala-azar patients recognized at least four of these five antigens. The 70 kDa antigen, which may include a member of the heat shock protein 70, produced a positive reaction in 94% of patients. Further studies are ongoing.

Studies are being carried out at the Indian Institute of Chemical Biology (IICB), Calcutta to study the role of host protein kinase C (PKC) in the uptake and multiplication of *L.donovani* promastigotes by mouse macrophages. Results showed that staurosporine, an inhibitor of PKC, inhibited phorbol myrsitate acetate (PMA) dependent killing of the parasites, while tyrphostin AG 126, an inhibitor of protein tyrosine kinase showed very little effect. Depletion

of PKC by prolonged incubation with PMA drastically reduced the superoxide anion generation and increased the uptake and multiplication of the parasites. The study has relevance on membrane fluidity and leishmanial infection.

Entomological Studies

Study has been taken up at RMRI, Patna to find out different species of *Phlebotomus argentipes* population in order to incriminate the vector responsible for transmission of kala-azar. Survey has been conducted in different kala-azar endemic districts of Bihar (Patna, Vaishali and Samastipur). Sandflies of different species – *P. argentipes, P. papatasi* and *Sergentomyia* species were collected in different seasons. Besides these, two new species *i.e.P.sergenti* and *P.major* were also identified using the key of Lewis. Morphological variations were observed in specimens of *P.argentipes* in the measurement of genital filament (0.124-0.294 mm), aedeagus (0.017-0.139 mm), coxite (0.077 – 0.124 mm) and style (0.093 – 1.7 mm).

DNA from pooled wild caught sandflies and total DNA probe prepared from reference strain of *L. donovani* were used for dot blot hybridisation assay. The result revealed that out of 92 pools, 59.78% showed the presence of parasite (*Leishmania*) and *P. argentipes* showed 65.8% positivity. High parasite positivity indicates high transmission and is the reason for endemicity.

Establishment of Leishmania Bank

The leishmania parasites isolated from kala-azar/PKDL patients manifesting different clinical pictures/severity of disease, from different geographical regions of Bihar, need characterization on aspects of their growth kinetics pattern, virulence, isoenzyme type and RFLP. So far 45 isolates (KA-36 and PKDL-9) of *Leishmania*promastigotes are being maintained *in vitro,* 33 are under adaptation and a few have been cryopreserved. The isolates are being utilized in various studies and are provided to other institutes on request for research purposes.

Application of Remote Sensing for Prediction of Kala-azar Epidemics

Study has been initiated to evaluate the feasibility of application of remote sensing by use of satellite data for monitoring the macro-ecosystem, specific vegetation cover and human settlements and to relate them with the changing sandflygenic conditions. It has applicability in epidemic prediction in the hyper-endemic Vaishali district and non-endemic Lohardagga district. Five villages were selected randomly in one block of each district. Vector density in both study sites observed in different seasons for the last two years showed consistent pattern. Satellite data of selected foci are being collected to compare with the digitized map of the same foci to generate data on the association of sandflygenic conditions with environmental determinants to assist prediction.

VIRAL DISEASES

Viral diseases are major public health problems. Research in the area of viral diseases is being undertaken at the Council's National Institute of Virology (NIV), Pune, Enterovirus Research Centre (EVRC), Mumbai, National AIDS Research Institute (NARI), Pune, Centre for Research in Medical Entomology (CRME), Madurai and Virus Unit, Calcutta. Studies for developing vaccine against Japanese encephalitis (JE), surveillance of poliomyelitis, molecular epidemiology of wild polioviruses, molecular biological studies in hepatitis and AIDS are some of the important areas of research which have been addressed during the year under report.

Japanese Encephalitis

Vaccine Studies

At NIV, Pune B and T cell epitopes have been identified on the JE virus envelope protein. A chimeric peptide has been synthesized which contains one B and one T cell epitope. The chimeric peptide when used as an immunogen was only partially protective against live virus challenge. Continuing this work further, 14 new T cell epitopes were identified, some on NS1, a nonstructural protein coded by the JE virus. Some of the epitopes were found to have a T helper cell response suggesting their immunogenic potential. These studies will lead to development of a cocktail vaccine representing additional cellular and humoral immune responsive epitopes which would offer complete protection against JE virus infection.

Studies employing monoclonal antibodies suggested that some of the epitopes on the JE virus envelope protein have molecular mimicry with the host's histone proteins. During natural JE infection antibodies generated against such epitopes react with cellular histones as auto-antibodies. Their role in JE virus pathogenesis is under study.

Entomological Studies

The role of *Anopheles subpictus* in JE virus transmission in South Arcot district, Tamil Nadu has now been elucidated. Vector abundance coincided with the time of paddy cultivation but virus isolations were made throughout the year. Generally there were two peaks of both vector abundance and virus isolations – a wet season (August-December) and a dry season (March-June) peak (Fig.8). Being mainly zoophagic, *An.subpictus* appears to play a role in zoonotic cycle of JE transmission.

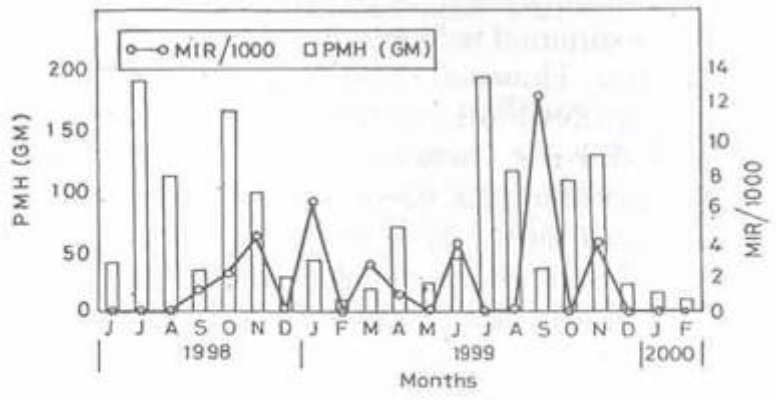


Fig. 8. Comparison of infection and abundance of *An. subpictus*. MIR-minimum infectivity rate; PMH (GM)-per man hour (geometric mean).

Longitudinal study of ecology and JE virus infection of mosquitoes in Kuttanadu (Kerala) seems to have provided a clue to the role of *Mansonia sp.* in JE transmission. The results of the study suggest that *Culex tritaeniorhynchus* and *Mansonia sp*. served as vectors for JE virus transmission in a sequential way – mansonioides maintaining the zoonotic cycle during the period when JE infection in humans is not apparent (April-November) followed by virus amplification in *Cx.tritaeniorhynchus* in the period (December- March) when encephalitis cases are reported (Fig.9). Thus *Cx.tritaeniorhynchus* appears to act as the primary vector and mansonioides as the secondary vector in Kerala.

Poliovirus

Acute Flaccid Paralysis Surveillance

Mumbai

The four metro cities (Delhi, Mumbai, Calcutta and Chennai) have a high incidence of paralytic poliomyelitis. Urban slums are the main breeding ground of the poliovirus. Eradication of poliomyelitis from these cities is considered difficult because of the high population density, large slum population and also because these cities attract patients from all over the country for treatment.

During 1999, 194 patients of acute flaccid paralysis (AFP) were recorded in Mumbai, of these 116 were residents of Mumbai (a decline of 31% over the previous year) and 78 were non-residents. AFP cases were reported from 15 out of 16 municipal wards. Most cases occurred in slums. The four wards (F,G,M and R) historically known to contribute high numbers of poliomyelitis cases had 52.4% of all reported cases of the city. Faecal samples from 109 (94%) cases were studied for enterovirus detection; 69 (63.3%) were found to be virologically negative. Wild poliovirus was isolated only from three cases, vaccine strains from 12 and non-polio enteroviruses were isolated from 25 (22.9%) cases. These results showed that the historical hot spots of wild poliovirus transmission have been completely eliminated by the OPV immunisation.

Four doses of OPV were administered to children in Mumbai during mass immunisation campaigns (October 1999-January 2000) which also included house-to-house mopping up. From January to March 2000, 16 AFP cases were reported. No wild poliovirus has as yet been detected among these cases. Mumbai, therefore, appears to be reaching towards a stage of polio control.

Maharashtra

During 1999, 663 AFP cases from Maharashtra were investigated for poliovirus infection. Wild polioviruses were isolated from 18 cases in ten districts, 12 had poliovirus type 1 and 6 had poliovirus type 3. Wild poliovirus type 2 has not been isolated from Maharashtra since 1996. The results indicate widespread distribution of wild virus in the State. However, there was a significant decline (87%) in the total number of wild virus isolates during 1998. In 1999, vaccine poliovirus strains were isolated from 65 cases.

From January to March 2000, 105 AFP cases have been reported. Only one case of wild poliovirus type 3 infection has so far been detected.

Madhya Pradesh

In 1999, 16 wild poliovirus positive cases of paralytic poliomyelitis were detected in 637 AFP cases studied virologically. These included 8 cases each of wild poliovirus type 1 and 3. Wild poliovirus type 2 was not detected. The 16 wild virus isolates were isolated from cases from 12 districts of MP.

From January to March 2000, of the 139 AFP cases investigated, 1 wild poliovirus has been detected in MP.

Wild Polioviruses

Surveillance

During 1999, the EVRC tested 1849 poliovirus isolates from 1840 cases of AFP from all over India by ELISA and nucleic acid probe hybridization for defining vaccine or wild viruses.

Wild polioviruses were detected in cases from almost all larger states of the country except Kerala, Orissa, Himachal Pradesh, Jammu & Kashmir and north-eastern states. Uttar Pradesh and Bihar together had about 90% of all wild polioviruses isolated in the country. Wild poliovirus type 3 predominated throughout north India. Wild poliovirus type 2 was isolated from Uttar Pradesh (9 cases) and West Bengal (one case) in early 1999.

Wild poliovirus type 1 (8 cases) and poliovirus type 3 (26 cases) have been detected among the poliovirus isolates (113 cases) during the first 3 months of 2000. Majority of these wild virus isolates are poliovirus type 3 indicating the continued transmission of the virus in Uttar Pradesh. However, wild viruses appear to be under control in the southern states of the country.

Molecular Epidemiology

A large number of wild virus isolates from all over the country have now been sequenced to track wild poliovirus transmission routes. The database contains sequences of more than 150 type 1, 70 type 3 and recent type 2 poliovirus isolates. The data show tight clustering of genetically related viruses in parts of UP and Bihar. At least 9 lineages have been identified during 1999 in these two states.

In October 1999, a case of paralytic poliomyelitis due to wild poliovirus type 1 occurred in China after more than a 3 yr gap. The database available with the EVRC helped the Global Polio Eradication Programme in defining genetic relationship of the virus. The virus isolates detected in China during 1999 belonged to the lineage currently (1998-99) circulating in north India. The closest virus was identified from Madhya Pradesh.

Vaccine Derived Poliovirus Isolates

A large number of AFP cases were found to excrete vaccine derived poliovirus strains (observed in all states). Many of these cases may be true vaccine associated paralytic poliomyelitis (VAPP) thus requiring further characterization of the virus isolates. Vaccine-derived poliovirus type 2 isolates were studied by using site-specific PCR and 5′UTR sequencing to detect mutation. Among the 29 isolates so far characterized, 16 revertants at major attenuation site (No. 481), 7 revertants at minor attenuation site (No. 398) and 4 recombinants in 5′UTR region have been found. Further characterization is in progress.

OPV Potency Testing

The most important aspect of the polio eradication programme is administration of potent live oral poliovirus vaccine (OPV) to children. Monitoring the potency of field samples of the vaccine provided information on conditions during storage and transportation. During 1999, 3067 OPV field samples were tested of which 2630 (86%) were found to have satisfactory quality.

Since 1998, OPV vials have a thermo-sensitive label which indicates the cumulative effect of exposure to unfavourable temperatures. In a study to check the correlation between colour change of the vaccine vial monitor (VVM) and thermal exposure, the vaccine vial monitoring system was found to work satisfactorily. However, discrepant results in VVM colour reading and vaccine potency tests have been detected in some field samples. This calls for a large-scale evaluation of VVM.

A study was carried out at AIIMS and Kalawati Saran Hospital, New Delhi to monitor the poliovirus strains for inter- and intratypic variations by RFLP and sequencing. In this study polioviruses were isolated and characterized by RT-PCR for the regions coding for VP1-2A and also the 3D polymerase gene. The positive samples obtained by RT-PCR of 3D region were further characterized by RFLP. Two poliovirus type 1 isolates were obtained from 66 samples.

RT-PCR for 3D region and VP1 region was standardized and both these regions were amplified using separate PCR protocols for all the 40 poliovirus isolates. Fifteen PCR products of 3D region were further characterized by RFLP using Rsa I, HaeIII and Dde I enzymes. The RFLP pattern of 12 of these were similar to poliovirus type 1, three isolates had patterns of poliovirus type 2. Of these 12 RFLP patterns, 7 strains were characterized as wild type poliovirus 1 and five as Sabin type poliovirus 1. All three poliovirus type 2 strains had RFLP pattern of Sabin type poliovirus 2. It was also observed that one strain of poliovirus type 1 had an extra restriction enzyme site with HaeIII.

Hepatitus Viruses

The diagnosis of hepatitis A virus (HAV) is primarily based on detection of virus specific IgM antibodies in blood. An IgM capture ELISA has been standardized for urine samples and blood samples collected on filter paper by finger prick. The sensitivity and specificity of the test is comparable to ELISA performed on conventional blood sample. Since HAV patients are children, collection of urine or finger prick blood would be most ideal in field or clinic settings.

Studies were undertaken at AIIMS, New Delhi to detect and characterize hepatitis B virus (HBV) mutants circulating in acute and chronic hepatitis patients who were serologically negative for all markers of known hepatitis viruses. About 500 sera were screened for the presence of HBV genome using PCR for 'S' and core region. Of these, 23 of the 59 fulminant hepatic failure patients, 24 of the 279 chronic hepatitis patients, 34 of the 137 blood donors positive for IgG anti-HBc and one of the 25 donors positive for antibodies to core and surface antigens were found to carry HBV genome. Approximately 16% of the total cases examined carried HBV genome.

Efforts are also being directed to generate meaningful data on the hepatitis B prevalence among the primitive tribes of the Andaman and Nicobar islands. In order to create awareness about hepatitis B, its modes of transmission and the possibility of eradication through vaccination, a health education campaign involving tribal chiefs, religious leaders and medical and paramedical staff was carried out in Car Nicobar island. Two villages namely Tamaloo and Lapathy having a total population of 3016 were selected randomly from Car Nicobar island for this study. The entire population of these villages was enumerated and information about different risk factors such as family history of jaundice, blood transfusion, major operations, sickness, multiple injections, dental treatment, tattooing, promiscuous behaviour *etc*. was collected. Till date, 900 serum samples have been collected from one of the selected villages. Serological testing of these samples for various markers of hepatitis B infection is in progress. Individuals negative for HBsAg and anti-HBs will be selected for hepatitis B vaccination.

In a study conducted at NIV, Pune, the presence of a new transfusion transmitted virus (TTV) has been detected in voluntary blood donors and individuals at high risk for parenteral transmission. Non parenteral transmission also plays an important role in the transmission of the virus in our setting. The phylogenetic analysis suggests that the majority of them belong to group 1a. Public health importance of TTV infections is being worked out.

Insect Cell Lines

Development of a cell line from lepidopteran insects was reported earlier. During the year under report cell lines were further characterized and it was shown that these could be cryopreserved and revived. The *Spodoptera litura* cell line was used for expression of cloned genes from JE and hepatitis C viruses. These cell lines can be used for large scale growth of baculovirus. This virus has potential application for biological control of pests.

HIV INFECTION / ACQUIRED IMMUNE DEFICIENCY SYNDROME

The human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) is increasing in India. ICMR's research activities have helped to understand the problem of HIV/AIDS and have contributed in formulating strategies for the control and management of the disease. A prospective cohort of HIV seronegative persons attending STD clinics gave the first reliable estimates of incidence of HIV infection in this highrisk population and identified the behavioural and biological risk factors associated with acquiring HIV infection. Presently this cohort is being used for studies on acute pathogenesis and intervention of HIV/AIDS.

Basic research including developmental research has been given special importance. High in the priorities are vaccine related virological and immunological studies, development of diagnostic tests for opportunistic infections, testing of drugs for anti-retroviral and immunopotentiating activity and generation of reagent and virus repositories for use in HIV research. HIV infection is unique due to its social aspects. Studies in the social and behavioural sciences have been continuing specially in areas related to women and education, awareness, reproductive health and treatment seeking behaviour**.**

HIV Prevalence Associated with High Risk Factors

Studies on a cohort of HIV seronegative STD patients established in 1993 have been continued at the National AIDS Research Institute (NARI), Pune. The longitudinal study has enabled detection of HIV seroconverters and persons with p24 antigenaemia who were enrolled for the study of acute pathogenesis of HIV infection. The focus of the study has now gradually shifted from descriptive epidemiology to behavioural studies and intervention trials. Analysis of trends in various categories in the cohort has shown no significant change.

Analysis of results in 5763 referred samples at NARI showed prevalence of HIV in 78.6% sexually promiscuous persons, 48% patients with STD, 70% commercial sex workers and 55% recipients of blood or blood products. As these patients were referred to NARI for confirmation of the HIV diagnosis, the percentages of reactive patients may not reflect the actual prevalence in these risk groups.

There is an association between HIV and tuberculosis infection in terms of predisposition. In studies carried out at the NARI clinic, 27% of the TB patients (1565) were found to be co-infected with HIV. In the Sasson General Hospital, HIV prevalence was 23.0% in TB patients and 3.50% in pregnant women. Sentinel surveillance in the antenatal clinic at Bhosari, and Talera Hospitals, Pune showed 1.25 and 2% HIV seroprevalence respectively. In yet another study carried out by the NIV, Pune at the Sasson General Hospital and TB wards of the Naidu Hospital, a HIV prevalence of 21.35% (112/520) and 34.06% (140/411) respectively, was seen. Some of the samples (7/441) were seroreactive for both HIV-1 and HIV-2 and only 3 samples were reactive with HIV-2.

Studies have been carried out at the All India Institute of Hygiene and Public Health, Calcutta to understand the prevalence of HIV and other STD infections among the commercial sex workers in Calcutta. A total of 584 samples were tested in 1996-97, 79 samples in 1997-98 and 204 samples in 1998-99. HIV seropositivity rate was 12, 7.6 and 17% respectively during these periods. Syphilis had a 45.3, 20.1 and 26.4% prevalence in these groups. Smear

positivity for gonococcal urethritis varied from 33% in the first year to 41.8% in the third year. Sera from patients of gonococcal urethritis tested for IgM antibody for *chlamydiae* showed that 45% were positive indicating the possibility of new infection.

Prevalence of Hepatitis in STD Patients

In a retrospective study to estimate hepatitis B virus (HBV) incidence in STD clinic attendees, 497 subjects who attended the NARI clinics and had returned for follow up, were investigated and the data analysed. Three hundred and eighty six (77.7%) were males and 111 (22.3%) females. Seventy three were HIV infected at entry, whereas 33 seroconverted for HIV during the study period. Interim analysis shows that the incidence of HBV infection as determined by seroconversion to core antibodies may be as high as 13.05%. Further analysis is in progress.

Prevalence of Hepatitis B and C Viruses Amongst HIV Seropositive Intravenous Drug Users

The seroprevalence of HCV among healthy Indians (voluntary blood donors) is estimated to be 0.12-4.0%. HbsAg carrier rate in the Indian population is between 2-7%. Some information on HIV and HBV prevalence among intravenous drug users (IDUs) of Calcutta has been reported. Although IDUs are at much greater risk of HCV infection (70-90%), reports to this effect are hardly available from India. Study was undertaken of the prevalence of HBV and HCV infections among 77 Manipuri couples where the husbands were intravenous drug users and HIV positive. A high prevalence of HCV (92%) and HBV (100%) infection was found in the IUDs from Manipur.

Since HCV and HBV are also transmitted through the sharing of injection equipment amongst IDUs, it is expected that the prevalence of these infections would be high. This study showed that almost all (92%) of the HIV infected IDUs were positive for HCV. Anti-HBc was present in 100% of the IDUs and in 95% of the wives. One wife, however, was positive for HbsAg suggesting recent infection. It is also probable that heterosexual transmission of HCV (11%) took place from male IDUs to their non-injecting wives . Stringent control measures to prevent the transmission of hepatitis viruses (B and C) are urgently required in Manipur.

Immunological Studies

HIV-1 specific cytotoxic T lymphocyte (CTL) response is being studied in HIV seropositives, especially in recent seroconverters and long-term non-progressors. A standard 51Cr release assay using autologous B cell lines infected with HIV expressing vaccinia as target cells measured the CTL response.

Fourteen individuals were assessed for the HIV-1 specific cross-clade CTL activity. Eight of them showed CTL response against env B and/or env C antigens (7 showed cross-clade CTL response against env of subtype B and C while one individual showed CTL response only against subtype C env). This finding has implication on the development of indigenous HIV vaccine in India.

Immunopathogenesis of Acute Primary HIV Infection in Pune

Patients reporting at STD clinics and HIV referral clinics at NARI were screened for anti-HIV antibodies. Those found negative were tested for the presence of p24 antigen to detect acute primary HIV infection before inclusion in the study. Out of the 1547 patients screened, 12 were found to be eligible as p24 antigen positive; 7 of the p24 antigenaemic and 6 seroconverters were enrolled for the study. Five patients with acute HIV-1 infection were studied for proliferative responses against mitogen(PHA), recall antigens (PPD and tetanus toxoid) and HIV antigens

(p24, p55 and gp120). All 5 patients showed good proliferative response against PHA and PPD. None showed response against tetanus toxoid and any of the HIV antigens.

Normal Ranges of Lymphocyte Sub-populations in Indian Population

In view of the large variation observed in human CD lymphocyte counts in different studies conducted in India and the non availability of the range of normal values of CD lymphocytes in the Indian population, a multicentric study was carried out to establish ranges of the important lymphocyte sub-populations in the normal Indian population.

Mean T cell count ($CD3^+$) was slightly lower in Indians (68.55%) as compared to the Western average (73.0%), whereas B cell counts (CD19) were similar (14.5% *vs.* 14.0%). The most remarkable feature appears to be a significantly lower CD4 count in Indians (36.9% as compared to the Western average of 44.0%). CD8 counts were, however, similar which resulted in a lower CD4/CD8 ratio in Indians (1.17 as compared to the Western value of 1.40). Interestingly, CD4/CD8 ratios differed significantly within different states of India. These findings are important for clinical research, drug and vaccine trials and immunological monitoring of patients including HIV/AIDS patients. Further analysis is being done to understand the factors /parameters including the regional differences influencing the CD counts.

Subtype Identification of HIV-1 in Western India

Identification of recombinant strains is very important in HIV control strategies, especially vaccine development. In view of the importance of HIV subtype prevalence and its analysis in the country, NARI has continued subtyping of HIV-1 isolates. During the year under report 134 blood samples were collected from different parts of western India. The commonest subtype prevalent throughout this region is subtype C. In addition a few subtype A samples were also obtained.

Full length amplification and sequencing of 6 HIV-1 strains from seroconverters was carried out. Indian samples collected from Pune by NARI upon heteroduplex mobility assay (HMA) analysis also showed that subtype C is the most predominant subtype. This could be further divided into C2 and C3 genotypes. Additionally, subtypes A and B were also detected suggesting that Pune is experiencing an HIV epidemic where multiple subtypes are involved. Recently 6 HIV-1 subtype C strains isolated by NARI have been completely sequenced. One of the strains was found to be a recombinant between subtype C and subtype A. It is for the first time that a recombinant virus has been detected in India. The majority of the mosaic virus genome was subtype C but the envelope gene and portion of LTR (long terminal repeat) were from subtype A.

Co-receptor Usage

In addition to CD4 molecule, HIV requires chemokine co-receptors (mainly CCR-5 or CXCR-4) for internalization of virus into the cell. For HIV-1 subtype B viruses (which are most common in the developed world) utilization of CXCR-4 correlates with advanced disease condition and poor prognosis. Studies were carried out in samples collected from different parts of the country from individuals presenting with HIV disease ranging from asymptomatic to AIDS defining conditions. HIV (40 strains) was isolated and studied for co-receptor utilization. It was observed that 39 of 40 viruses were CCR-5 dependent suggesting that subtype C viruses, predominant in India, were CCR-5 dependent, irrespective of disease stage. Only one virus, a strain of HIV-2, was found to be dual tropic but predominantly using CXCR-4 co-receptor.

HIV-1 and HIV-2 Repository

A total of 71 HIV-1 and 6 HIV-2 isolates from samples obtained from different parts of India were characterized. Subtyping of 71 HIV-1 isolates by HMA revealed predominance of HIV-1 with subtype C. Further analysis is ongoing. Phenotypic characterization of 35 HIV isolates was carried out using MT2 cell lines and the results indicated that 34 isolates were non-syncytium inducing and syncytium induction was seen in only 1 isolate.

Simian Retovirus

Until now Simian retrovirus (SRV) has not been reported in *Hanuman langur*monkeys in India. At the NIV, Pune a strain of SRV has been isolated from langur PBMCs. This is the first report from India. Nucleotide sequencing of amplified envelope region suggests this to be phylogenetically a unique SRV-6. Further studies are going on.

Knowledge, Attitude and Behavioural Studies

Studies were carried out by NARI to determine the HIV seroprevalence and awareness about AIDS among rural pregnant women. A comprehensive, community based seroepidemiologic study was conducted in the area covered by three PHCs (Chakan, Kadus and Khed Shivapur) in Pune district of Maharashtra .

Out of the 1251 blood samples tested, 15 were seropositive, indicating an overall prevalence of 1.2% among pregnant women in rural areas of Pune district. HIV seroprevalence was significantly higher among villages situated within 1 km of a national or state highway. A majority of the participating women were housewives and 70% of them were aware of the existence of the disease and had heard about AIDS. One third of the respondents were aware of all the main modes of HIV transmission. Among those who were aware of the existence of the disease, almost a third was not aware about the possibility of HIV transmission through blood transfusion or from HIV infected pregnant women to the baby during delivery or through breast milk. Majority also had misconceptions about the mode of transmission of HIV.

Studies were carried out at National Institute of Epidemiology, Chennai to understand AIDS awareness among college students. The results of the study revealed that only about 20% of the Chennai college students had fairly good knowledge (a score of 90% or more) about HIV/AIDS. A small percentage of the students had misconception about the modes of transmission. There is a need to improve the level of awareness among them on various aspects of HIV/AIDS

Reproductive Health

The overall burden of reproductive ill health is very high and many women die every year due to the complications of pregnancy and child birth. Maternal mortality which continues to remain unacceptably high, glaringly reflects the inequity in women's access to basic life saving interventions as well as inadequacy of the health care system. Most maternal deaths occur due to haemorrhage, sepsis, toxaemia, obstructed labour and unsafe abortions while safe and affordable technologies to prevent such deaths do exist. Equally important issues related to this are nutritional anaemia, adolescent pregnancies, and gender discrimination. The high population growth over-shadowing the health gains as reflected by increase in life expectancy and impressive decline in infant mortality, has resulted in increased demand on the already over stretched health care delivery

system. The Council's research relating to reproductive health therefore encompasses interrelated areas of family planning, safe motherhood, prevention and management of complications of abortions, reproductive tract infection (RTIs)/sexually transmitted diseases (STDs), infertility, adolescent health and gender perspective and are directed to address the issues related to reproductive health through basic and clinical research as well as operationalising the existing knowledge and available technologies. Several new initiatives have been launched during the year under report. These researches have been undertaken through the Council's Institute for Research in Reproduction (IRR), Mumbai, the network of Human Reproduction Research Centres (HRRCs) located in different parts of the country and several non-ICMR institutes.

The IRR, Mumbai continued its focus on research in basic reproductive biology. A human sperm antigen, 80kDa, has been identified from human sperm extract and efforts are ongoing to develop this peptide as an immunogen for developing an antifertility vaccine. Efforts are also on to develop integrin as a clinical marker to assess the fertility potential in men. The nucleotide sequence of cDNA clone of bonnet monkey oviductal glycoprotein (OGP) synthesized last year was compared with cDNA nucleotide sequences of human, baboon and rhesus monkey OGP this year. Simultaneously a recombinant protein was also synthesized from cDNA clone of bonnet monkey OGP to raise antibodies against OGP.

Emergency contraception is useful in a situation where the prevalence of use of regular contraceptive is low, in couples using barrier methods or oral pills or in couples having infrequent sex. The wider use of this method can prevent unwanted pregnancies and abortions. Since this method is not widely available or known in the country, a study has been initiated in 31 HRRCs to assess the knowledge and demand of these methods.

Male participation in the Family Welfare Programme is very poor and acceptance of vasectomy particularly is low. Phase III clinical evaluation of indigenously developed male intravasal contraceptive RISUG (styrene maleic anhydride dissolved in dimethyl sulphoxide) has been initiated as a multicentre study.

Evaluation of the feasibility of using pregnancy kits for early detection of pregnancy (within 30 days of the missed period) at the field level, so that women could seek early antenatal or MTP services, revealed that paramedical workers can use the kits effectively in the field, however, there is a need to generate awareness about early detection of pregnancy for better reproductive outcome. A study on the management practices of meconium stained amniotic fluid and meconium aspiration syndrome in the newborn, a major obstetric complication during delivery, has been initiated in 31 HRRCs.

A study on feasibility of using syndromic approach for diagnosis and management of RTI/STDs at the PHC level has been initiated at 10 HRRCs. The training of paramedical workers in identification of symptoms indicative of RTI/STDs is complete and field work is ongoing.

An expert group on neonatal health has been constituted to address neonatal mortality and related issues. Project proposals on innovative approaches for home-based management of sick neonates and other thrust areas identified by the Group have been developed. An Indo–US agreement on bilateral collaboration in maternal and child health research has been finalised and the Council will be acting as a nodal agency to steer this programme.

FERTILITY REGULATION

CONTRACEPTION

Basic Research

Basic research in the area of male and female fertility regulation was carried out mainly at IRR, Mumbai.

Magainin Peptides

Earlier studies at IRR had indicated that Magainin-A (Mag-A) can be used as a safe and effective intravaginal contraceptive in rats and rabbits. In monkeys Mag-A (1 mg) introduced intravaginally on the day of ovulation (mating confirmed by the presence of sperm in the vaginal smears) prevented pregnancy in all five animals. These animals returned to regular cycling, suggesting the suitability of Mag-A for contra-ceptive use.

Role of Disulphide Bonds of the β-subunit in Receptor Binding of hCG and in Heterodimer Formation

The disulphide bond between cysteine (Cys) residues at 93 and 100 of hCG-β is the 'determinant loop' which specifies the activity of the heterodimer to be CG, LH, FSH or TSH. The synthesized disulphide loop peptide (Cys^{93}-S-S-Cys^{100}) 92-101 hCG-β was checked for its ability to inhibit radiolabelled hCG binding to its receptor on the sheep corpora lutea membrane. The results indicated that (i) the disulphide loop structure between Cys residues at 93 and 100 is probably not essential for receptor binding of hCG (ii) the net positive charge of the region between 93 and 100 alone is not sufficient for receptor binding, and (iii) the Cys residues at 93 and 100 along with the net positive charge seem to be the minimum requirement for receptor binding of hCG.

Studies on Mammalian Oviductal Glycoprotein

The earlier studies at IRR had demonstrated the ability of antibodies to glycoprotein secreted from epithelial cells of oviduct (OGP) to interact with ovulated eggs and sperms and inhibit fertilization, implying a critical role for OGP during fertilization and embryo development. The partial cDNA encoding bonnet monkey OGP has been successfully cloned. In the experiments carried out this year, the nucleotide sequence (AF 132 215) showed 96% homology to human, baboon and rhesus monkey estrogen induced OGP. The cDNA clone of bonnet monkey OGP was recloned into pet 20b vector to obtain recombinant protein and to raise antibodies to OGP. The protein could be immunostained with antibodies to human OGP, baboon OGP and antipeptide antibodies to the well conserved region of mammalian OGP. Rabbit antibodies to rOGP were developed and it immunostained enriched human OGP on Western blots and immunostained epithelial cells secreting OGP in murine oviductal section taken during early pregnancy. Ability of these antibodies to interfere in *in vitro* fertilization is being examined.

Evaluation of Antifertility Effect of FSH Binding Inhibitor

Human ovarian follicular fluid is being purified and characterized for follicle stimulating hormone binding inhibitor (FSHBI). The peptide inhibiting FSH binding to ovarian granulosa cells showed a single peak on reversed phase high performance liquid chromatography (RP-HPLC). The effect of this peptide on progesterone (P4) production by granulosa cells was studied *in vitro*. FSH at concentrations of 0.3-30 µg/well gave a dose dependent increase in P4. Partially purified peptide (hGF2 fraction) alone could not affect P4 production but in the presence of 10 ng FSH, it inhibited P4. The highly purified peptide inhibited P4 production at a dose of 1.0

µg. Thus FSHBI acts by regulating P4 production from granulosa cells (Fig.10&11).

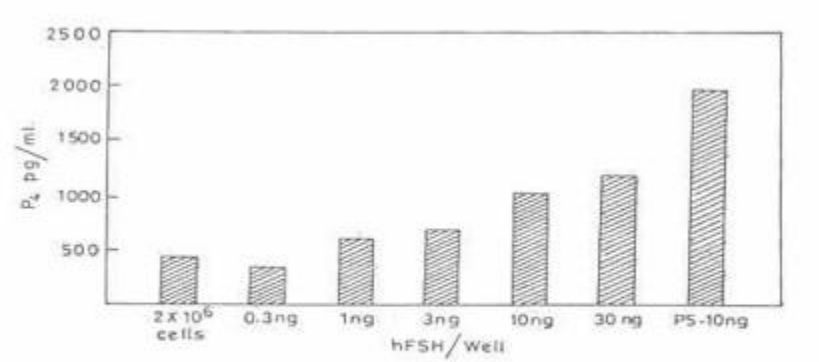


Fig. 10. FSH stimulated P_4 secretion by short term cultures of mouse granulosa cells.

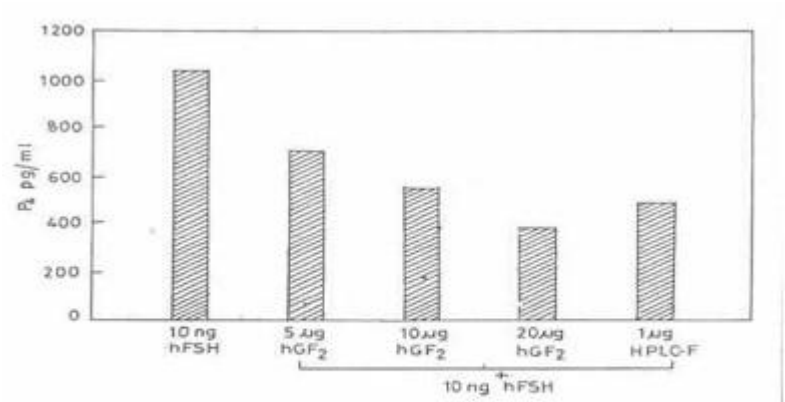


Fig. 11. Effect of FSH binding inhibitor on FSH induced P_4 secretion.

Role of Integrins in Implantation

To date, the role of integrins (ITGs) in mediating embryo-endometrial interactions remains poorly understood. The studies at IRR in the murine model suggest that α_4, α_6, α_1 and β_3 are maximally expressed in the endometrium on day 3 or 4 after fertilization. The expression of α_4, α_6, α_6 β_1, α_5 ITGs on oocytes and blastocysts is stage dependent. Down regulation of α_1 and β_3 ITG expression by interleukin-2 leads to failure of implantation. It is proposed that ITGs may have a role in implantation.

Expression of Endometrial Functional Markers in Fertile and Infertile Bonnet Monkeys

Studies on the expression of selected factors *e.g.* steroid receptors, cytokines and growth factors as well as identification of novel endometrial markers were carried out on the endometrial samples collected from bonnet monkeys during different phases of the menstrual cycle. Studies were also carried out to correlate the expression of these markers during the peri-implantation period with the fertility outcome in the animals treated with different doses of an antiprogestin, onapristone. Results obtained from the studies initiated last year were

substantiated by carrying out similar studies on a larger number of animals. Expressions of progesterone receptor, transforming growth factor (TGFβ) (Fig.12), and its receptor (TGFβR) (Fig.13) were downregulated in the endometria from infertile animals as shown by RT-PCR studies. No significant correlation was seen between expression of these factors and the fertility status of animals.

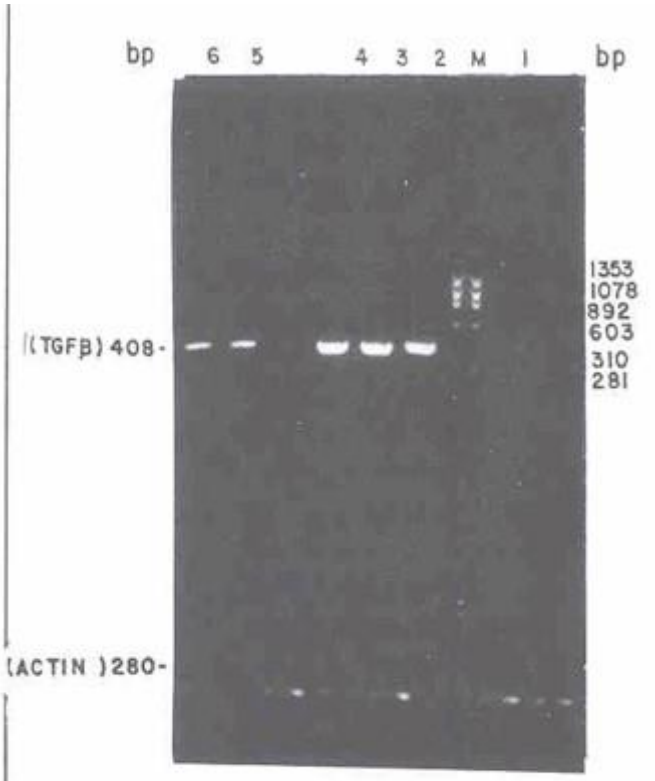


Fig. 12. Expression of transforming growth factor β (TGFβ). Total RNA was extracted from control animals in follicular (lane 1) and luteal (lane 2) phases and from luteal phase of animals treated with 2.5 mg (lanes 3,4), 5 mg. (lane 5) and 10 mg. (lane 6) of onapristone. Total RNA (200 ng) was subjected to RT-PCR analysis using specific primers for TGFβ. A 408 bp RT-PCR product was seen in all endometria.

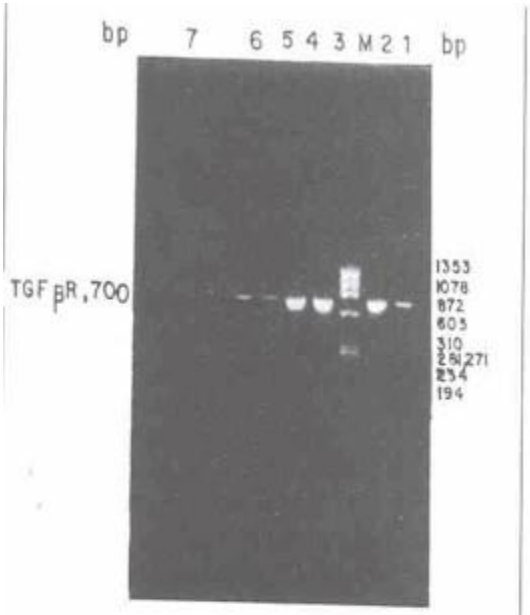


Fig. 13. Expression of transforming growth factor β receptor (TGFβR). Total RNA was extracted from control animals in follicular (lane 1) and luteal (lane 2) phases, and from luteal phase of animals treated with 2.5 mg (lanes 3,4) 5 mg (lane 5) and 10 mg. (lanes 6,7) of onapristone. Total RNA (200 ng) was subjected to RT-PCR analysis using specific primers for TGFβR. A 700 bp RT-PCR product was seen in all endometria.

Several differentially expressed cDNA fragments were identified by DDRT-PCR studies. These fragments either showed upregulation or downregulation in the endometria from treated animals as compared to the control group. One of these cDNA fragments was cloned in pGEMT vector and sequenced using T7 and Sp6 primer. This cDNA fragment of 88 bp showed high expression during the peri-implantation period in the control bonnet monkeys while in the animals rendered infertile with onapristone, expression of this fragment was downregulated. Sequence homology search of this cDNA fragment did not reveal significant homology to any known endometrial factor. Further characterization of this and other differentially expressed fragments and their potential role in implantation may help us to identify the endometrial factors which if expressed aberrantly may lead to infertility. This may also facilitate identification of newer targets of contraception.

Development of an in vitro Screening System for Evaluating the Potencies of Progestins developed for Therapeutic and Contraceptive Applications

An estrogen independent, progesterone receptor (PR) reporter gene system using mammalian cells is being developed at IRR to relate the response of the test progestin to progesterone in a single assay to get the true potency estimates of the test compounds. To achieve this objective a progesterone responsive reporter gene construct pUGCAT was introduced into the mammalian cell line T47D which retained the PR expression in culture. The transfection of T47 cells with pUGCAT has been accomplished. Exposure of the transfected cells to 10^{-5} and 10^{-7}M progesterone expressed the CAT enzyme. Standardization of the progesterone dose related response curve for the transfected UGCAT with six to eight doses of progesterone ranging from 10^{-4} to 10^{-12}M

gave two types of response patterns of CAT expression. To get consistent pattern of CAT expression optimization is being continued.

Purification and Cloning of an Epididymal Sperm Maturation Antigen

An epididymal sperm maturation antigen has been purified from sheep cauda using conventional biochemical techniques. The blue-sepharose bound fraction containing the 26 kDa protein was further subjected to chromatography on HPLC MonoQ column, resulting in a homogeneous preparation of 26 kDa protein as seen by SDS-PAGE electrophoresis. N-terminal sequencing of the purified protein is in progress.

The cDNA clone isolated from a lambda ZAP monkey epididymal cDNA library using monoclonal antibodies to the 26 kDa protein, was sequenced. Sequence analysis of 995 bases at the N-terminal and 1100 bases at the C-terminal have been read and attempts to complete sequencing are underway. No significant homology with sequences in the gene data bank has been obtained so far.

Human Seminal Plasma Inhibin (HSPI) as Sperm Vaccine for Fertility Regulation

The earlier studies at IRR demonstrated that active immunization of adult bonnet monkeys with R-17-BSA conjugate using Freund's complete adjuvant (FCA) resulted in a significant decrease in sperm motility without altering sperm count or serum LH and testosterone levels. An inverse correlation between circulatory antipeptide antibody and sperm motility was observed. These results are promising but as FCA cannot be used as an adjuvant in humans it was decided to use muramyl dipeptide (MDP) as an adjuvant with squalene and arlacel for emulsification. Initial immunization studies with MDP in rabbits resulted in antibodies that were able to recognize native protein and in titres similar to those obtained when FCA was used as an adjuvant. Currently a new group of ten monkeys is being monitored for baseline data on semen parameters and will be immunized with R-17-DT using MDP as an adjuvant and the effects on fertility will be studied.

Studies with Human Sperm Antigen

A 80 kDa human sperm antigen (HSA) is one of the potential candidate antigens for immuno-contraception, as it has been demonstrated to be immunogenic, efficacious, conserved and specific to sperm. It was reported that chemically the antigen is unique as N-terminal amino acid sequence of the native protein and its fragments obtained by enzymatic digestion did not show sequence homology with any of the known proteins in the database. These peptide sequences were synthesized and characterized further. The passive administration of these antipeptide antibodies in male rats caused the agglutination of the epididymal spermatozoa along with almost complete loss of motility while in female rats the passive administration of antipeptide antibodies also rendered the animals infertile. Active immunization with the synthetic peptides evoked a better immune response in female rabbits than in male rabbits. Antifertility studies in female rabbits are in progress.

Clinical Research

Phase III Clinical Trial with Subdermal Implant Norplant^{R}

Norplant^{R} (6 capsules) was offered as one of the contraceptive choices at the Council's 31 HRRCs in a study where all the women seeking family planning methods were given a balanced presentation of the existing (IUD, OC, condom, male and female sterilization) and new (Norplant^{R}, once a week pill centchroman, vaginal pessary

TODAY and diaphragm) methods of contraception during November 1994 to December 1996. The acceptors of Norplant^{R} are being followed up for a period of 5 years of contraceptive use to evaluate the efficacy and continuation rates. A total of 2048 Norplant^{R} acceptors have been observed for 70,744 women months of use, 154 women have completed 5 years of use so far. One method failure has been reported after 3 years of use. The continuation rates were 92.0, 79.4 , 66.4, 52.5 and 41.0 per 100 users at 1,2,3,4 and 5 years of use respectively. The main reason for discontinuation was menstrual irregularities. The cumulative discontinuation rates for this reason were 3.5, 9.0, 14.3, 20.3 and 25.9 per 100 users at 1, 2, 3,4 and 5 years of use respectively. The study is ongoing and women who are willing to continue with the method are being followed upto 5 years of use. Women who have discontinued the use of Norplant^{R} due to some reason and are exposed to the risk of pregnancy are being followed up for two years for return of fertility as judged by pregnancy and outcome of pregnancy.

Emergency Contraception among Women

Emergency contraceptives are the methods to be used within a short time after unprotected intercourse, so as to avoid unplanned pregnancy. A study has been initiated in 31 HRRCs to determine whether awareness regarding emergency contraceptives exists among women of child bearing age and adolescents and to find out such behaviour, attitudes and opinions that would lead to the risk of unplanned pregnancy; to identify the most acceptable route of administration for emergency contraception and; to determine the existing awareness about emergency contraception among providers. A total of 1000 beneficiaries of family welfare services and 300 providers of these services have been interviewed through a detailed questionnaire.

Major ICMR Research Projects in Reproductive Health

Male Intravasal Contraceptive RISUG

The concept of injecting a bioactive compound into the lumen of the vas deferens to obtain a potentially reversible long-term contraceptive effect is a new dimension in the male contraceptive field. The animal studies and phase I and phase II clinical trials with the injectable contraceptive RISUG, a specific copolymer of styrene with maleic anhydride dissolved in 60 mg solvent of dimethyl sulphoxide, have indicated that the new technique is safe and efficacious. A phase III clinical trial with this preparation has been initiated to evaluate the safety and efficacy of the drug in a large number of subjects. All the subjects will be followed up for six months following treatment to study the immediate and long term adverse effects, semenology and pregnancy protection. A total of 16 subjects have been enrolled in the study.

INFERTILITY

Female Infertility

Role of Hyperinsulinaemia in Women with Polycystic Ovaries

A study was undertaken at IRR, Mumbai, to determine whether women presenting with polycystic ovaries (PCO) with or without hirsutism and/or obesity and those having polycystic ovaries only are at risk of developing insulin resistance or have an altered insulin pattern and their responses to insulin sensitizing agents. The study revealed that women who had PCO and obesity irrespective of their androgen status showed significantly enhanced insulin response compared to those who were obese with normal looking ovaries and normal androgen levels as well as those having polycystic ovaries only.

Induction of ovulation by clomiphene citrate in women desiring conception revealed negative response in 14 of the 18 women treated. Treatment with insulin sensitizing agent, metformin resulted in normalisation of menstrual cyclicity and reduction in weight in 8 of the 14 non responders. However, no spontaneous ovulation was observed. Simultaneous administration of clomiphene/ human menstrual gonadotrophin (hMG) with metformin resulted in ovulation in 50% of them with pregnancy in one.

The results suggest that obesity plays an important role in development of PCO leading to hyperinsulinaemia which can be a risk factor for cardiovascular disease and type II diabetes, if left untreated.

Male Infertility

Molecular Identity and Functional Significance of Progesterone Receptor and Expression of Integrin on Human Spermatozoa

A transcript of 536 bp was detected in human spermatozoa RNA using primers specific for uterine progesterone receptor (PR). The transcript was amplified, cloned in pGEMT vector and sequenced using both forward and reverse primers. The partial cDNA clone for the sperm PR showed complete homology to the classical PR in the regions from nucleotide number 2694 to 3230. The cDNA corresponding to this transcript contains the regions corresponding to the DNA binding domain as well as hormone binding domain. This was suggestive of the molecular similarity between the classical PR and sperm PR. The studies at IRR on the expression of progesterone binding sites in fertile and infertile males demonstrated lesser number of PR positive spermatozoa in infertile males. This indicated that the progesterone receptor on spermatozoa may have a predictive value in assessing the functional status of spermatozoa. A preliminary map of antigenic profiles based on SDS-PAGE/ immunoblot analysis has been constructed. The scanning of protein profiles showed the presence of $\cong$ 57 and = 44 kDa proteins unique to fertile samples. The 57 kDa protein was a glycoprotein localized on acrosomal region. Approximately 40% of spermatozoa expressed this protein which was involved in sperm egg interaction. The antigen is being sequenced.

Relevance and Efficacy of Clomiphene Citrate Therapy in Idiopathic Subfertile Males

Of the fifteen idiopathic subfertile men being administered clomiphene citrate 8 were put on an alternate day dose schedule while 7 were put on a daily dose schedule. The former group fared better than the latter in terms of improved sperm density, motility and morphology. There was improvement in two functional parameters related to fertilizing ability *viz.* hypo-osmotic swelling test and sperm mitochondrial activity index in the alternate day group. Two of these individuals with improved seminal and functional parameters could successfully impregnate their

wives. Two pregnancies ensued post- therapy – one each in the alternate-day and daily-dose regimen groups. Men who did not show any improvement in seminal status were associated with aberrant spermatogenesis at the testicular level. The study is ongoing

MATERNAL AND CHILD HEALTH

Management Practices of Meconium Stained Amniotic Fluid and Meconium Aspiration Syndrome

One of the major problems an obstetrician faces while conducting labour is meconium stained amniotic fluid (MSAF) which is present in 10-20% of all deliveries. Meconium aspiration syndrome (MAS) occurs in 2-4% of all deliveries (or 20-25% of MSAF cases) leading to a mortality of 8-48% and 20% of morbidity at various stages of growth. There are no data available in India on the management practices, outcome of pregnancy, morbidity and mortality of MAS babies. The study has been initiated at 31 HRRCs to assess the management practices for pregnant women with MSAF and to study the morbidity and mortality in newborns with MAS. A total of 4066 cases of MSAF have been enrolled so far; 431 (10.6%) babies born to these women developed MAS. The enrolment of MSAF cases and follow up of MAS babies is ongoing.

Feasibility of using Pregnancy Detection Kit in PHC/SC/Villages and Urban Slums

The early detection of pregnancy is essential for safe motherhood and reproductive health of women. At present no pregnancy kit is available in the National Family Welfare Programme. At the request of Ministry of Health and Family Welfare, ICMR initiated a study to assess the demand for early detection of pregnancy and; to evaluate the sensitivity and specificity of pregnancy tests kits when used under programme conditions [(at PHC/ sub-centre (SC) /Urban Health Centre and at field level)] by paramedical staff.

The study was carried out in two urban slum areas (in Delhi and Calcutta) and two rural areas (in Rajasthan and U.P.) covering one lakh population each. The sample size envisaged at each centre was 1500 subjects, 500 at HRRCs and 1000 in PHC/SC/urban slums. Extensive IEC campaign was launched by the participating centres by distribution of pamphlets and organizing group meetings. The medical and the paramedical staff of the HRRCs and the participating health centres were trained in the use of the kits and the method of confirmation of pregnancy. The interim data indicated sensitivity and specificity of these tests as confirmed by clinical findings at follow up visit to be about 90% when used by paramedical staff. The preliminary analysis indicated that while paramedical workers are able to use the pregnancy kit, there is a need to intensify the IEC compaign.

Assessment of Vaccine Wastage during Pulse Polio Immunization Programme

The requirement of oral polio vaccine (OPV) is presently determined by the guidelines laid down by WHO/UNICEF. Accordingly, a wastage multiplication factor (WMF) of 1.33 which corresponds to 25% wastage of OPV is assumed at present. Since no study of this nature has been conducted in India, the Ministry of Health & Family Welfare entrusted this job to the Council. The Council conducted the study through its network of HRRCs and its permanent institutes in 31 districts from 11 states and 3 Union Territories on 17th January 1999 during the Pulse Polio Immunisation (PPI) programme. All the booths were covered in a district amounting to 30,767 booths in 31 districts. The information on wastage was based on number of vials received at a booth, number of vials used and the number of children given vaccine. The study has shown an overall wastage of 14.7 % doses and a WMF of 1.17 of OPV which is well below the present assumption of 25% wastage and a multiplication factor of 1.33. The wastage during the immunisation should be minimised to

make it more cost effective. At the request of Ministry of Health & Family Welfare, it is proposed to initiate a study to determine the amount of wastage during the routine immunization programme for all the six vaccines and suggest methods for reducing it.

Management of Reproductive Tract Infections / Sexually Transmitted Diseases

A study on the feasibility of using syndromic approach for diagnosis and management of RTI/STDs at PHC level where facilities for clinical examination or laboratory facilities are not available has been initiated at 10 HRRCs. A training programme was organized for the Research Officers of HRRCs on interview methodology and syndromic management including wet smear examination. The paramedical staff have been trained in interviewing the men/women in the selected villages and in eliciting information on symptoms indicative of RTI/STDs and high risk sex behaviour. The diagnosis made by paramedical workers will be validated by clinical and wet smear examination of all these men/women irrespective of whether they are symptomatic or asymptomatic. The first part of the study on validity of syndromic diagnosis has been initiated in all the centres. The interview survey is ongoing.

Involvement of Practitioners of Indian Systems of Medicine in the Delivery of RCH Services in Rural Areas

Despite a widespread network of the modern system of medicine and the services available through government and private sources, people in India have utmost faith in the traditional systems of medicine as the services are generally cheaper and available in small towns/ rural areas and the remedies are free from side effects. According to a recent estimate, India has 5.6 lakh formally trained practitioners of Indian Systems of Medicine (ISMPs). These practitioners provide the bulk of primary health care services to the rural population. As such, their services can be utilized for improving the delivery of reproductive and child health (RCH) services. The objective of this study is to involve ISMPs in improving the utilization of RCH services in rural areas within the existing infrastructure available at PHC/district level. The project was implemented in UP, MP and Rajasthan. In each of the selected PHCs, the identification of ISMPs was done and their inclusion in the study was based on their willingness for involvement in the study. The base line surveys of ISMPs and the community have been completed. In the base line community survey 403 ISMPs were identified in the experimental and 357 in the control area. The ISMPs had about 12-16 years in the field; the average area covered was from 8-20 kms. in different centres and the number of villages covered varied from 4-13. On an average every ISM practitioner treated about 292 paediatric cases annually. About 2-5% of ISMPs also provided services for infertility and RTI/STDs. The contraceptive services were provided on an average to around 58 cases annually.

In the experimental area 136 ISMPs were provided orientation training for 3 days on various aspects of RCH care before involving them in the study and were monitored for their involvement in RCH services. These ISMPs have developed close linkages with PHC staff in ensuring the delivery of the services. The data received so far have shown an upward increase in the referral for various RCH services by the ISM practitioners in experimental area by propagating the distribution of contraceptives, antenatal and natal care, MTP, provision of iron and folic acid and vitamin A tablets and ORS packets as well as referral of children for immunisation. In control area no training was provided.

Socio-behavioural Aspects of Menopause

A study was undertaken at IRR, Mumbai to assess the knowledge, attitude and perceptions of women regarding menopause and to study some aspects of sexuality during menopause. A total of 332 women from the low

socio-economic strata with established menopause were interviewed personally. The mean age at menopause was 45.34 yr. Although most women had knowledge about the cause of menopause (*i.e.* menopause is a physiological process), a few (11%) stated that menopause can only occur after the removal of the uterus. Sixty three per cent of women had a positive attitude towards menopause. Majority of them (77%) felt that they were free to take decisions in household matters which were formerly restricted to men. Misconceptions about menopause were reported by 6.3% of women and the most common myth was its association with decrease in eye sight (5%). Overall sex desire was decreased in 40% of women during menopause and total loss of sexual desire was expressed by 18.8% women. The study is ongoing.

Nutrition

Nutritional problems, especially in women and children, continue to be widely prevalent in the country in spite of many nutrition oriented programmes being implemented by the Govern-ment of India. In addition, with increased life expectancy the nutrition problems of the elderly also need attention. To identify the priority areas for research for finding out effective, practical, economically viable and sustainable solutions for the plethora of nutrition related problems affecting people and to prepare project proposals in a multicentre mode, the Council organised a series of national and international workshops and expert group meetings. The areas identified include development of simple biochemical tests for detection of micronutrient deficiencies, the development of a nutritional surveillance system, identification of foods rich in micronutrients, nutritional problems of aged such as osteoporosis, development of intervention strategies to control undernutrition in children up to 2 yr. of age, and prevalence of low birth weight babies and interventions for their growth and development. The Council has also taken steps to revise the recommended dietary allowances (RDA). The research activities related to nutrition were mainly carried out by the National Institute of Nutrition (NIN), Hyderabad and complemented by its three centres *i.e.* Food and Drug Toxicology Research Centre, National Centre for Laboratory Animal Sciences and National Nutrition Monitoring Bureau (NNMB). The Institute continued to focus its research activities to address and find solutions to various unresolved issues in the field of nutrition.

COMMUNITY STUDIES

First Repeat Survey of Tribal Population

The National Nutrition Monitoring Bureau (NNMB) conducted a repeat survey for the diet and nutritional assessment of the tribal populations living in the areas covered by Integrated Tribal Development Agency by visiting the villages that had been surveyed earlier. The results revealed that there was a reduction in the extent of severe undernutrition among preschool children with improvement in their height and weight. There was also a marginal increase in the intake of cereals and millets at individual level.

Nutritional Status of Adolescents

The data on adolescent girls, collected through NNMB surveys during 1996-97, were analysed to assess their current diet and nutritional status. The data were also compared with that obtained in 1975-79 from the same villages. There was an increase in the intake of cereals and millets over the past 20 years among the adolescents. Secular changes in height and weight were observed with an increase of about 2.5 to 3.5 cm and 1 to 1.5 kg

respectively. The extent of undernutrition as measured by weight for age and stunting (low height for age) also showed a decline during the current survey as compared to 1975-79.

Diet and Nutritional Status of the Elderly

The health and nutritional status of the aged has been receiving considerable attention in recent years. In view of this, data collected on the elderly during the 1996-97 NNMB surveys and the district profile surveys conducted in 1994 in non-NNMB states of Punjab, Haryana, Himachal Pradesh and Assam were analyzed and compared with that of the 1975-79 NNMB surveys. The results showed that the consumption of cereals and millets was more than the RDA in all the age and gender groups. Except in the age group of 80 yr and above, the consumption of energy has improved over a period of time. The extent of chronic energy deficiency (CED) appeared to be higher among the aged population than their younger adult counterparts. There was a considerable reduction in the prevalence of CED as compared to 1975-79.

Micronutrient Status and Mental and Physical Performance of School ChildrenSupplemented with a Special Nutritional Beverage

A double blind randomised placebo controlled study is in progress to evaluate the impact of supplementation of a cocktail of micronutrients in the form of a specially fortified beverage on the physical and mental development of school children. Analysis of base line data indicated that the boys achieved higher IQ as compared to girls.

Boys >10 yr receiving the special nutrition beverage achieved significantly higher verbal and performance quotients compared to their counterparts receiving a placebo. In girls receiving the supplement, significant differences were found in all age groups. The study also revealed that nutritional status and height influenced IQ as better nourished (>75% weight for age) boys and girls in the supplemented group scored higher IQ scores than children in the placebo group. Aspects related to bone density were also studied. The base line whole body mineral content and the density at the neck of the femur were not different in the two groups while there was a significant difference between boys and girls. However, all values were much less than those reported in the Western studies. The micronutrient status in several children in this study was found to be inadequate.

Low Cost Nutritious Supplements

Since red palm oil (RPO) is a rich source of β-carotene, NIN in collaboration with AP Foods, has developed a RPO (carotino) fortified ready-to-eat food as a nutritious supplement for children. Preliminary studies showed that the stability and acceptability of the product were satisfactory.

ENERGY METABOLISM

Sports Nutrition/Work Physiology

Energy expenditure in sports persons involved in different athletic events, such as sprinters, and middle and long distance runners, showed changes from transition to competition phase, based on the intensity of training they received. Therefore, contrary to the current practice of giving uniform ration to all the sports persons all through the season, it is essential to formulate diets to meet the nutritional demands of participants in each sport

so as to maintain optimal body composition and achieve optimal performance during competitions.

NUTRITION AND INFECTION

Serum Transferrin Receptor in Children suffering from Infections

To define the iron status in children, normal levels of serum transferrin receptor (STfR) were determined. In addition, the effect of infections on STfR was evaluated. The mean serum STfR was 6.08±.48 mg/l in children who had haemoglobin levels more than 11 g/dl, similar to that reported in literature for healthy children. Using this value as the cut-off level, it was observed that more than 50% of children having Hb more than 11 g/dl also had elevated levels of the receptor, thus identifying the wide prevalence of iron deficiency in children. On the other hand, ferritin, which was also estimated, failed to identify even severe anaemia. Mean receptor levels showed a significant negative correlation with Hb levels while ferritin had no correlation with Hb or STfR. Hence, unlike Hb which diagnoses only anaemia, STfR appears to be a good indicator to assess iron stores in preschool children (Fig.14).

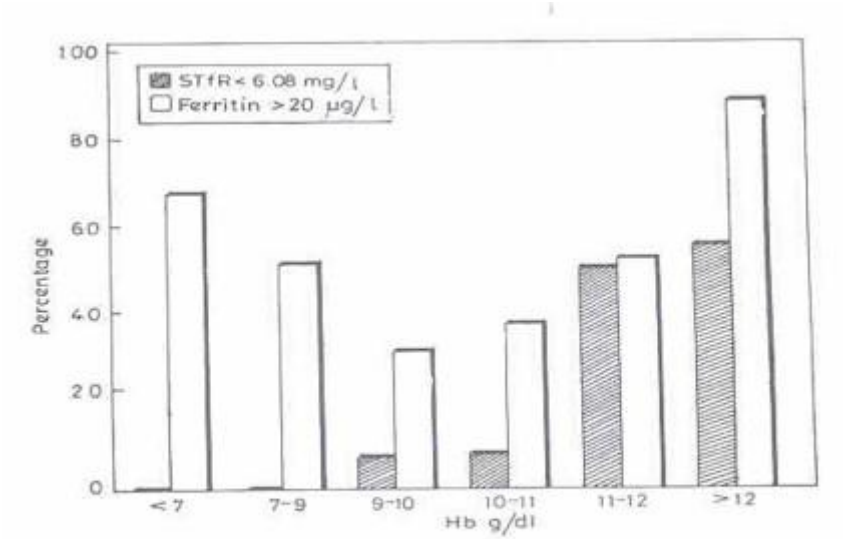
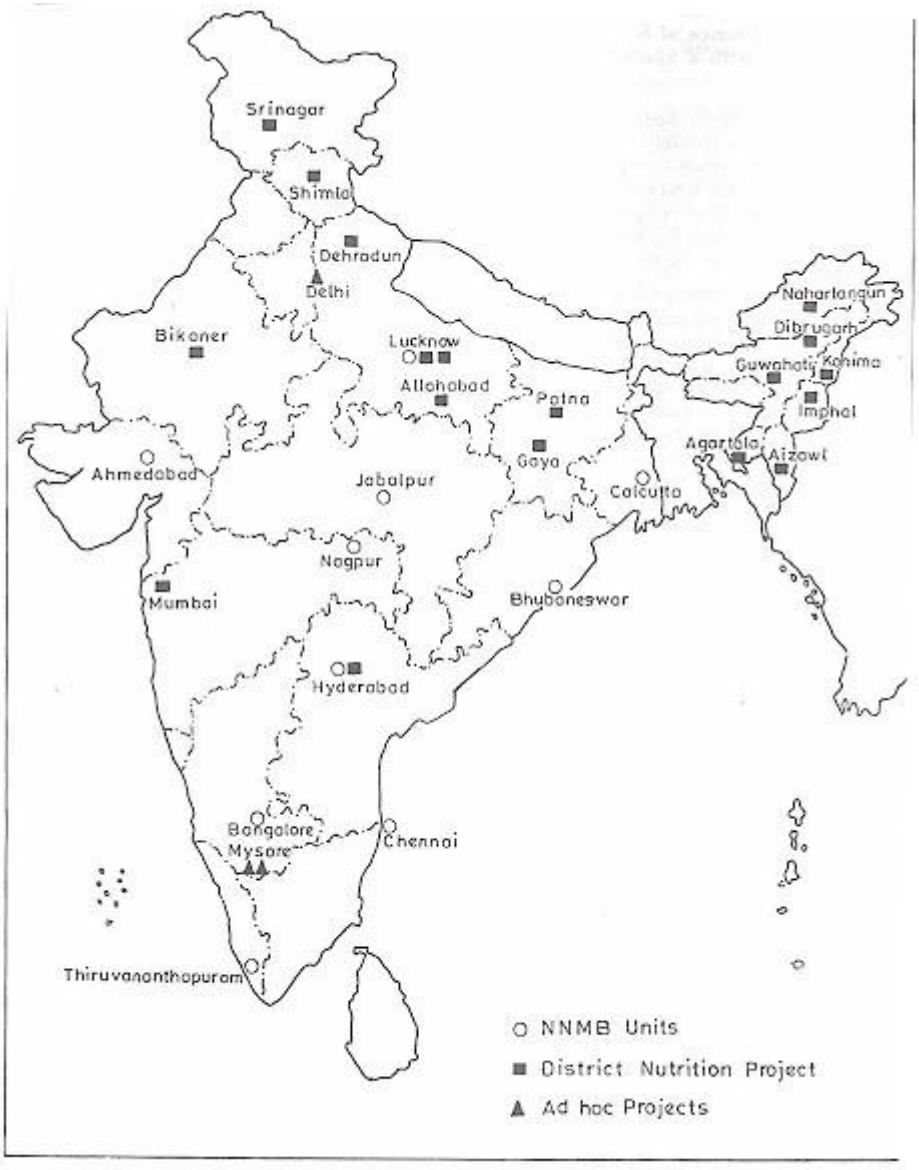


Fig. 14. Serum transferrin receptor (STfR) and ferritin in normal children grouped according to Hb levels.

STfR was determined in preschool children who attended the hospital for various infections. They were followed up at 15-30 days after the infection. No difference in mean receptor levels was found in children with or without infection with similar haemoglobin levels, thereby indicating that in general, STfR is a good indicator of iron status even in the presence of infection, unlike ferritin which shows an acute phase response. The percentage of children having anaemia and elevated STfR levels was similar. However, STfR values returned to basal level by 30 days after infection. These observations suggest that anaemia of infection is due to iron deficiency which could be due to lack of storage iron or non-mobilization of stored iron in the non anaemic children. These results emphasise the importance of controlling infections for improving iron status of children.



Major ICMR Research Projects in Nutrition

Outcome of Acute Bacterial Meningitis in relation to Nutritional Status in Children

The role of nutritional status and secretion of TNF-α in children suffering from acute bacterial meningitis and the outcome of the disease was determined. Bacterial isolation was found to be positive in 76% of CSF samples with *Streptococcus pneumoniae* being the most common organism. *Neisseria meningitidis*, *Haemophilus influenzae*, *Escherichia coli* and Streptococci also contributed to meningitis. TNF-α was detectable in 69% of all cases and children with *S.pneumoniae*, *N.meningitidis* and *H.influenzae* as causative organisms had higher levels of TNF compared to the others. Though TNF levels were similar among children with various nutritional grades, the percentage of children producing the cytokine was higher in severe protein energy malnutrition group. Twenty two per cent of the children died and 40% recovered with sequelae. Severely malnourished children had significantly higher adverse outcome compared to better nourished groups. *S.pneumoniae* contributed to nearly 50% of deaths. Nutritional status and the causative organism appear

to contribute to the outcome of acute pyogenic meningitis in children. However, TNF did not significantly influence the outcome. Similarly, nutritional status had no effect on levels of TNF.

MICRONUTRIENTS AND TRACE ELEMENTS

Trends of Xerophthalmia from 1980-1999

The data collected from the records of the Niloufer Hospital for Women and Children during 1980-99 on the trends of severe vitamin A deficiency manifesting as blindness or potentially blinding corneal lesions revealed that 540 children with corneal lesions attended the hospital. On an average 22 to 28 patients were seen per year between 1980 and 1999. The occurrence of corneal lesions was maximum among children aged 1-3 yr followed by those between 3 and 5 yr. Since vitamin A deficiency is still prevalent in some parts of the country, there is a need to target the under-fives and control the scourge of vitamin A deficiency using innovative methods.

Effects of Food based Vitamin A Supplementation during Pregnancy on Maternal and Child Health

With increase in realization of the importance of vitamin A status in maternal and child health, a cross sectional study was conducted among pregnant women during their third trimester to assess the extent of the problem of clinical and subclinical vitamin A deficiency and relate it to the pregnancy outcome. Night blindness was observed in 5% of the women and about 60% of them had serum retinol levels less than 30 mg/dl. Women with night blindness and those with low retinol levels had a significantly higher occurrence of pregnancy induced hypertension, pre-term deliveries and asphyxiated babies. These results suggest the need to undertake in depth studies to explore the role of vitamin A status on maternal health and pregnancy outcome.

Molecular Mechanisms of Immuno-suppression in Severe Protein Energy Malnutrition

mRNA gene expression for cytokines IL_2 and IL_4 and cytokine profile of lymphocyte culture supernatants for IL_2 were examined in children suffering from anaemia and compared with healthy non anaemic children aged 1-5 yr. Healthy children had mRNA expression for IL_2 and IL_4 whereas anaemic children had it only for IL_4. IL_2 levels were undetectable in their culture supernatants. Since anaemia is widespread among children, these observations are important, particularly in relation to the ongoing immunisation programmes involving newer vaccines.

Mineral and Trace Element Contents of Foods

Apart from reassessing the mineral and trace element composition of commonly consumed plant foods, foods of animal origin were also analysed using atomic absorption spectrophotometer. It was found that country hen eggs had significantly higher amounts of trace minerals like calcium, phosphorus, copper and manganese as compared to eggs of hens bred in poultry farms.

Transferrin Receptor

The indigenous sandwich ELISA developed at the NIN for the quantitation of serum transferrin receptor (STfR) has been validated in adolescent girls receiving 60 mg of iron supplement for 100 consecutive days. The changes in iron status correlated well with STR and not with serum ferritin. The results of the study confirmed

that the indigenous sandwich ELISA technique developed for STfR is a good indicator of iron status.

DIET AND NON-COMMUNICABLE DISEASES

Studies on Fenugreek Seeds

Galactomannan, the soluble dietary fibre present in the fenugreek seeds, was isolated and its effect on the blood glucose and cholesterol levels of obese rats (WNIN/GR-ob) assessed. Incorporation of galactomannan into the control diet at 2.5 and 5.0% levels could significantly decrease plasma glucose and cholesterol levels at the end of 9 weeks both in males and females compared to animals receiving control diet alone.

Biochemical and Metabolic Studies with Sesame Lignans

The high oxidative stability of sesame oil is attributed to the lignans *viz*., sesamol (S1), sesamin (S2) and sesamolin (S3). S2 and S3 are present in seeds and oils. On heating the oils to frying temperature, S1 is formed. The antioxidant properties of S1 (Sigma Co.), S2 and S3 (isolated and crystallized at NIN) in comparison to BHT and tocopherols (a and g) were studied in *in vitro* enzymatic (cumene hydroperoxide induced) and non enzymatic (iron-ascorbate induced) lipid peroxidation systems. The antioxidant activity in cumene hydroperoxide system was in the following order : BHT>αT = γT>S1>S2>S3. The antioxidant properties of lignans in combination with tocopherols showed enhanced inhibitory effects. In the non-enzymatic system, only S1 had inhibitory effects. However, sesame lignans in combination with tocopherols enhanced the inhibitory effects in the non-enzymatic lipid peroxidation system. These findings suggest that sesame lignans can potentiate the antioxidant properties of tocopherols and contribute to their beneficial role as dietary antioxidants.

FOOD CHEMISTRY

Nutrient Composition of Foods

The analysis of total lipid and individual fatty acid contents of selected fresh fruits showed that they contain <1 % total lipids. The α-linolenic acid (ALNA) content is higher in plum, papaya and guava (0.4%) as compared to other fruits (0.2%). On an average about 400 g of fresh fruits provide ~0.1 g ALNA. It was reported earlier that on an average ~60g of green leafy vegetables or ~400g of other vegetables provide 0.1 g of ALNA. Thus, fruits and vegetables can contribute to increasing the n-3 poly unsaturated fatty acid intake in addition to providing several other nutritional benefits.

Fats in Bakery Products

Vanaspati is widely used in the preparation of bakery foods. The data obtained show that biscuits furnish ~12% lipids, ~5% saturated fatty acids (SFA) and 4% trans fatty acids (TFA). Thus, consumption of 7-10 biscuits would furnish about half of the upper safe limit of SFA and TFA together.

FOOD AND DRUG TOXICOLOGY

Food Safety

Application of HACCP to Paneer

The Hazard Analysis Critical Control Point (HACCP) approach which is now well accepted as the best preventive strategy in food safety and quality to prevent food-borne hazards was used for the toxicological evaluation of *Paneer* (cottage cheese). After identifying the critical control points (CCP) in the manufacturing process, it was found that the microbiological contamination of the final product could be considerably reduced by intervention strategies like improving the personal hygiene of the food handlers.

Ochratoxin in Coffee

Studies on the occurrence of ochratoxins in Indian coffee revealed that although ochratoxin A is present in Arabica, cherry and monsoon coffee samples, its level is well below the limit of 5 µg/kg which is considered by the European Union as a safe limit.

Antinutritional Factors in Wild Legume Cassia tora

Studies on the seeds of wild legume *Cassia tora* indicated the possibility of extracting the gum from the seeds in large quantity by a simple process and its use as a thickener in food products. The seed germ meal obtained as a bye product of gum extraction though rich in protein is found to contain antinutritional factors. A detoxification method to remove antinutritional factors has also been evolved. The studies on protein efficiency ratio (PER) and short term toxicity indicated that the detoxified germ could be used as animal feed ingredient.

Analysis of Argemone Oil in Adulterated Oils

A study carried out in collaboration with Director General of Health Services, New Delhi, on validation and harmonization of analytical method for quantitation of argemone oil in adulterated vegetable oils revealed the efficacy of the method in detecting adulteration. However, in the case of non-edible oils like *Karanjia* oil, the analytical method gave false positive results.

Drug Toxicology

Biomarkers of Genotoxicity : Antimutagenicity of Heated Garlic

Earlier studies at NIN have demonstrated the antimutagenic property of garlic in rats exposed to benzo(a)pyrene. In order to verify whether this property is still retained after subjecting the garlic to cooking, a study with cooked, boiled and unboiled garlic was undertaken with *S.typhimurium* TA 98 as tester strain. The results showed that the antimutagenic principles in garlic are not destroyed by heat treatment.

Studies on Medicinal Plants from North Eastern Region of India

In collaboration with Institute of Advanced Study in Science and Technology (IASST), Guwahati, some plants used by tribals in north eastern India were tested for their ability to counter the hepatotoxic effect in a paracetamol-induced liver toxicity model. Aqueous and methanolic extracts of the plants *Costos* and *Leucas lavandulaefolia* were tested. Extracts of both plants have been shown to exert hepatoprotective effect as evidenced by a decrease in SGOT and SGPT enzyme activities and histopathologic examination.

In order to understand the underlying mechanism involved, the antioxidant potential of the extracts of the above plants and those of *Cajanus cajan, Glycosmis* and *Sida rex* were tested using *in vivo* linoleic oxidation assay. Many plant extracts exhibited significant antioxidant potential as demonstrated by a reduction in lipid peroxide levels in the *in vivo* assay. The hepatoprotective properties of the extracts of the plants studied may probably be related to their antioxidant properties.

Drug Metabolism in Obese Rats

Since excess body fat is known to be associated with increased risk of cancer, it was thought that obese rat model developed at the NIN could be a suitable model for fat-cancer studies. Before undertaking such investigations, the levels of drug metabolising enzymes, namely benzo(a) pyrene hydroxylase, microsomal epoxide hydrolase (phase I), uridine diphospho-glucuronyl transferase (UDPGT) and glutathione-s-transferase (GST) (phase II) were estimated in homozygous obese, heterozygous obese and lean rats. The activities of conjugating enzymes GST and UDPGT, which play an important role in detoxifying the xenobiotics, were significantly low in the homo and heterozygous obese rats as compared to lean control, thereby suggesting that the elimination of ingested xenobiotics may be impaired in such animals. These results suggest that obese rat model could be useful in studying xenobiotic metabolism.

OTHER STUDIES

Studies on Obese Mutant Rats

At the National Centre for Laboratory Animal Sciences (NCLAS), Hyderabad research activities realted to obese rats continued. These studies have shown that leptin gene amplification was highest for obese rats as compared to lean and carrier animals. However, nucleotide sequencing of leptin gene isolated from obese animals did not show any change/aberration indicating that the mutation in these animals is not with respect to leptin. The melanocortin receptor (MCR-4) expression in obese rat was found to be low as compared to lean and carrier animals. The random primer OPB_{15} was able to distinguish WNIN/Ob rats from WNIN stock rats as indicated by PCR based DNA fingerprint. The obese mutant stock (including lean, carrier and obese) as a whole was found to be at a greater risk of oxidative damage compared to parental WNIN rat stock, as shown by high levels of protein carbonyls and malic dehydrogenase. Correspondingly, the GSH levels were found to be significantly low in these animals. Amongst the tissues studied, the brain showed consistent ageing pattern with respect to all parameters. The opioid receptor levels (Delta, Kappa, Mu) were significantly reduced in obese animals compared to WNIN control. Binding studies showed lack of leptin receptors in obese animals.

Preliminary studies on spices revealed the hypoglycaemic effect of curry leaves and hypolipidaemic effect of turmeric in WNIN/GR-Ob rats.

Environmental and Occupational Health

During the year under report, studies in the area of environmental and occupational health were carried out by the Council's National Institute of Occupational Health (NIOH), Ahmedabad and its Regional Centres at Bangalore and Calcutta in workers engaged in various industries such as chemicals, automobile, mining *etc.* and

grain and tobacco handlers as well as on air and water pollution.

Assessment of the Health Status of Subjects exposed to Chemicals/Gases evolved due to Accidental Fire in a Godown

An accidental fire broke out in April 1998 in a godown located in one of the industrial estates of Calcutta, used by custom clearing agents for keeping the items pending clearance of custom duties. A huge quantity of chemicals (mainly organic) was stored in the godown. One hundred and thirteen subjects were admitted to hospital, out of which seven died. A study was undertaken to assess the health status of exposed subjects and follow them up to ascertain the effect of the exposure, if any.

A total of 453 exposed subjects (Community 220; Fire Brigade 203; Police 30) were clinically examined. The predominant symptoms were headache (33.48%), vertigo (30.17%), nausea (22.68%), irritation of mucus membrane (28.63%), eye irritation (18.32%), skin irritation, itching and burning (6.60% to 16.74%), tingling (11.26%), joint pain (13.21%), panic attack (5.96%) and anaemia (17.89%). Higher values of SGOT (>40 IU/l) were also found in 50.88% and SGPT (>40 IU/l) in 46.25% of the workers. The pulmonary function test indicated presence of mainly restrictive impairment (Fire Brigade - 11.8%, Police - 13.8%, Community - 10.2%) with obstructive impairment being comparatively less (3.2%). Thus, it seems that nervous system, liver and respiratory systems are mostly affected.

Considering the nature of exposure (chemicals) it was decided to include reproductive outcome as well as genotoxicity in the study. Suitable control subjects for each category will also be examined.

Biological Markers of Manganese Exposure and Effect in Manganese Exposure and Effect in Manganese Miners

Recent revelations of lead toxicity even at very low levels has led to the search for suitable alternate additive to increase the octane number of petrol. One such compound, methylcyclo-pentadienyl manganese tricarbonyl (MMT), has been in use in Canada and some other parts of the world. The toxic effects of manganese at high exposure levels are well known but there are conflicting reports on manganese toxicity at low levels of exposure. To study the effects of manganese at low levels of exposure an environmental and medical study has been initiated by NIOH in Collaboration with US Environmental Protection Agency.

It is planned to measure the environmental exposure in underground manganese mines and study the health effects of manganese at different levels of exposure using magnetic resonance imaging (MRI) and neurobehavioral tests.

During the first phase of the programme, ambient air sampling for manganese was carried out at different work places and in the vicinity of manganese mines at Balaghat, M.P. The samples were collected with stationary samplers and personal samplers for 3-8 h during underground mining and surface mining, and at one ferro manganese plant and its vicinity.

The results show that during surface mining, the respirable dust concentrations ranged from 175.05-295.81 $\mu g/m^3$ at vertical holm shaft and from 99-456 $\mu g/m^3$ at the crusher and manual breaking and dressing units. At drilling points during underground mining the values ranged from 172.8-614.8 $\mu g/m^3$ and at the furnace units in the ferro manganese plant it ranged from 763.1-1282.0 $\mu g/m^3$. The manganese content in the respirable dust

ranged from 1.56-39.16 µg/m^3 during surface mining, from 2.2-83.33 µg/m^3 during underground mining, and from 33.22-75.73 µg/m3 at the ferro manganese plant. In the vicinity (administration building, guest house, and hospital), the respirable dust concentrations were in the range of 4.92-15.7 µg/m^3 with manganese content ranging from 1.3-2.0 µg/m^3.

A total of 476 underground manganese miners with duration of exposure from 5 to 35 yr were evaluated by standard medical questionnaire, computerized spirometry, chest radiography, estimation of manganese in blood and urine and assessment of liver function and thyroid functions. In the second phase of the study, MRI and behavioral tests will be done on subjects selected on the basis of blood manganese levels and clinical parameters.

Effect of Lead in Children and Adolescent Development and Puberty

A long term follow up study was undertaken in school children at Ahmedabad and Calcutta to examine the effects of lead on adolescent development and puberty. The results of the first phase of the study at Ahmedabad showed higher mean age, though statistically non-significant, for various indicators of sexual maturity rating (SMR) in children having blood lead levels higher than 10 mg/dl.

During the current year, the study was extended in 705 children (384 boys and 321 girls) of a school situated near a lead smelter at Calcutta. Analysis of blood lead levels showed that 69.4% of the students had levels <10µg/dl, 25.2% between 10.0 and 14.9 µg/dl, 4.7% between 15.0 and 19.9 µg/dl and 0.7% > 20.0 µg/dl respectively.

SMR for pubic hair in stages-1-3 did not show any significant difference in the mean age of onset in boys with low lead levels (<10µg/dl) and high levels (>10µg/dl). The SMR of external genitalia for boys also showed no difference in the mean age for stages 1-4 in both the high and low lead level groups.

The mean age of onset of menstruation was 13.91 yr and 13.58 yr for low and high blood lead level groups respectively. The SMR of pubic hair for girls with high blood lead levels in stages 2 and 3 was delayed as compared to that in girls with low blood lead levels. The study is continuing.

Air Pollution due to Vehicular Traffic in Major Cities/Towns of Gujarat State

Air pollution caused by motorized vehicles was assessed to examine the air quality in eight cities of Gujarat *viz.*, Ahmedabad, Vadodara, Surat, Rajkot, Bhavnagar, Jamnagar, Vapi and Mithapur. High volume samplers were used to monitor ambient air at four typical traffic junctions in each city during peak hours. Analysis of the samples was made for respirable particulate matter (RPM), NO_2 and CO. The results show that the air quality was found to be very poor in Ahmedabad, Vadodara, Surat and Bhavnagar. The values for RPM, NO_2 and CO were: 163-866 µg/m^3, 11-105 µg/m^3 and 8-33 ppm respectively in Ahmedabad; 99-3193 µg/m^3, 20-113 µg/m^3 and 5-35 ppm in Vadodara; 224-1045 µg/m^3, 20-156 µg/m^3 and 1-9 ppm in Surat; 126-1495 µg/m^3, 6-258 µg/m^3 and 0-9 ppm in Bhavnagar as compared to the air quality standards of 100 µg/m^3, 80 µg/m^3 and 1.75 ppm respectively (National Air Quality Standards). The values for RPM, CO, and NO2 in the four cities were within the recommended air quality standards.

Air Pollution with respect to Levels of Polynuclear Aromatic Hydrocarbons in High Traffic Density

Areas of Bangalore City

The objective of the study was to assess the quality of air in high traffic density areas of Bangalore city with reference to adverse health consequences among the general population. Eight hours continuous air monitoring for total suspended particulate matter (SPM) using high volume sampler was carried out in two high traffic density areas covering eight locations and one residential area (control area) covering three locations. Levels of total SPM were very high ranging 258.93-956.44µg/m^3 in high traffic density area compared to 62.24-205.93µg/m^3 in the residential area. The samples will be analyzed for polynuclear aromatic hydrocarbons with HPLC. The study conducted during summer season will be followed up in the winter season as well.

Development of Toxicity Testing Methods for Industrial Effluents

This multi-institutional project is an ongoing project sponsored by Central Pollution Control Board (CPCB), New Delhi. The aim of the project is to develop an aquatic toxicity parameter for the industrial effluents for regulatory purposes. During the year under report, untreated and treated industrial effluents were collected from six dye and dye-intermediate industries situated at Roha and Mumbai (Maharashtra).

The physico-chemical parameters for the diluent water used in the study were - pH:7.8–8.0, water temperature: 25 ± 1°C, total hardness: 220–240mg/l, alkalinity: 44–60mg/l and conductivity: 0.5–0.7 mS.

The final experiments were conducted using fresh water fish *Brachydanio rerio* in duplicate with the control sets. The fish were exposed to a minimum of five dilutions of the effluents for 48 h. and mortality of the fish was recorded at intervals of two hours for 24 h. The experiments were performed along with the reference toxicant potassium dichromate.

The results show that the value of 48 h. toxicity factor (T_F) for the reference toxicant was 100 mg/l and that of the untreated effluents was in the range of 4-250mg/l, intermediate effluents 2-64mg/l and treated effluents 1-8mg/l.

Reclamation of Vrishabavathi River Water - A Sociological Study

In continuation of our earlier study, the present investigation was aimed to assess the knowledge gained by community regarding water pollution and recycling of contaminated river water. A total of 1800 subjects were covered in the questionnaire survey. Analysis of 200 questionnaires indicates that nearly 82.5% of the population did have the knowledge regarding the existing river water pollution. It was reported that 66.6% of the population knew about recycling of contaminated river water. Acceptance of the recycled river water was reported by 48.5% of the population. Nearly 91% of the population did not use this water for any purpose, while 7.5 % of the population used it for agriculture. The study is being continued.

Occupational Health Hazards among Automobile Transport Workers

In seven public automobile transport garages in Calcutta city, a large workforce of 300-2000 workers is employed. However, very little is known about the health status of this group of workers. Therefore, a study was undertaken to assess the work environment, personal exposure to NO_2, CO, RPM, VOC (volatile organic compound) *etc.* as well as health surveillance covering work stress and postural discomfort from ergonomic

point of view.

Environmental monitoring following standard methods was done using high volume sampler, cascade impactor and personal sampler. The dust concentrations in different areas of the garage varied between 0.131 and 0.307 mg/m^3 for total dust; and 0.039 and 0.133 mg/m^3 for respirable dust. Benzene soluble matter (BSM) in different areas ranged between 0.020 and 0.036mg/m^3. Concentration of trace metals like Fe, Cr, Pb, Cu, Cd was within the prescribed limits. Pulmonary function tests (PFTs) of 181 subjects revealed restrictive (34.3%), obstructive (11.6%) and combined (7.2%) types of impairments. On medical examination of 185 males common symptoms were pain in abdomen (33.5%), cough (30.2%), sputum (34.05%), breathlessness (42.8%), ringing in ears (20.0%), partial hearing loss (10.2%) and itchiness of skin. Chronic bronchitis (23.2%), anaemia (29.2%), and rhonchii (7.0%) were detected on examination. High blood pressure (>140/90 mm of Hg) was noted in 3.2% of the workers (drivers 3.17%; conductors 6.5%). Systolic blood pressure >140 mm of Hg was seen in 10.8% of subjects examined (drivers 7.9%; conductors 19.6%; mechanics 11.3%). Diastolic blood pressure >90 mm of Hg was found in 4.3% of the subjects (drivers 4.6%; conductors 6.96%). The workloads of drivers, conductors and mechanics were 'moderate' to 'difficult' and that of administrative staff 'easy' to 'moderate'. Pain and discomfort felt in different parts of the body were also reported (drivers 67%; conductors 60%). The study is being continued in different garages.

Prevention, Control and Treatment of Silicosis and Silico-tuberculosis in Agate Industry

A new design of agate grinding machine has been developed. An impeller of 12 blades has been incorporated instead of 8 blades made in the earlier design, with the electric consumption remaining more or less the same. The installation of this machine at Khambhat in Gujarat showed that the suction capacity of the exhaust increased to 325 cubic feet/min (cfm) from 200 cfm, with reduction of the respirable dust by 90% and total dust by 95% in the ambient air.

Occupational Health Problems of Tobacco Harvesters and their Prevention

Occupational health problems associated with tobacco cultivation are known as Green Tobacco Sickness (GTS). It is a mild and acute form of nicotine toxicity that affects tobacco workers who have direct dermal contact with tobacco plants during cultivation and harvesting. To detect the chronic health effects of tobacco cultivation, a specially designed questionnaire was used which included tobacco habits, occupational and reproductive history, detailed medical examination, examination of cardiovascular system and the eyes. Another important objective of the study was to find out which types of gloves are acceptable and effective in preventing the dermal absorption of nicotine with reference to the work related symptoms and urinary excretion rate of nicotine and cotinine amongst tobacco harvesters. Further trials are being made with different types of hand gloves such as cotton, rubber, disposable polyethylene, cotton with polyester, nylon (polyamine), polyester, cotton coated on palmer side with PVC polka dots and cotton coated with natural rubber on palmer side.

A total of 685 exposed subjects (457 men and 228 women) were examined. Hypertension was observed in 17.7% of the men and 18.0% of the women. Abnormalities of visual acuity were noted in 26.5% of the men and 26.0% of the women. The work related symptoms such as nausea, vomiting, giddiness, loss of appetite, fatigue, *etc.* were reported by 42.7% of the men and 55.7% of the women. Initial feedback from the workers suggested that cotton gloves were more acceptable and comfortable in wear. Further work is in progress.

Occupational Health Problems among Workers dealing with Newspaper Refuse

During the reporting period, air-borne fungal flora obtained from three newspaper refuse sites using Andersen-6-stage viable sampler were processed for identification. The total number of isolates from sites I, II and III were 1.30×10^3, 1.25×10^3 and 1.41×10^3 respectively.. The number of isolates belonging to genus *Aspergillus* were 19.80, 16.30 and 27.30% respectively. Different species of *Aspergillus* identified morphologically from among these isolates were 4.4, 27 and 25% for *Aspergillus flavus*, 0.5, 10.6% and nil from *A. parasiticus*; and 2.6, 3.6 and 1.2% for *A. glaucus*. Other species included *A. niger, A. nidulans, A. fumigtus, A. versicolor etc.* Special attention was given on the identification of *A. flavus* and *A. parasiticus* since these species are responsible for production of aflatoxin. Identification of toxigenic strains of *A. flavus* and *A. parasiticus* is under progress using qualitative media like Czapex with anisaldehyde, aflatoxin producing ability (APA) agar medium, coconut agar media (CAM) *etc.* Airborne spores of other fungal species like *Cladosporium, Alterneria, Fusarium etc.* were also recovered from these sites. Inhalation of these spores is known to produce bronchial asthma. The study is ongoing.

Assessment of Occupational Health Hazards among Storage Grain Handlers

Foodgrains are stored by different agencies like Food Corporation of India, Central Warehousing Corporation *etc.* The workers are engaged in transporting foodgrains from one place to another inside these godowns for storage and delivery, resulting in exposure to various types of environmental contaminants. These foodgrain handlers are exposed to respiratory hazards from bacteria and fungal spores growing on foodgrains and the proteins of rodents, pesticides, etc. Physical labour results in rapid and deep breathing which makes the workers more susceptible to respiratory hazards. No comprehensive data is available on the health status of these workers.

A study was undertaken to evaluate the health status of the grain handlers along with measurement of fungal spores in the work environment. Measurement of grain dust levels and evaluation of efficiency of the workers was also done.

A total of 140 workers (handling labour 46; quality control 39; ancillary 32; administrative 23) were covered for the present phase of the study. Medical history was recorded using standard proforma with special emphasis on occupational history and history related to allergic symptoms relating to conjunctiva, nose, skin *etc.* The symptoms recorded were redness of eyes (5.79%), eye itching (28.69%) and watering from eyes (10.87%). Running nose, urticaria and pruritis were noted in a relatively small number of subjects. Cough (22.46%), sputum (19.56%), shortness of breath (35.58%), joint pain (30.43%) and low back pain (33.33%) and itching of the skin (5.07%) were the other important complaints. High blood pressure (>140/90 mm of Hg) was seen in 24.63% of the workers. Rhonchii (10.14%) and crepitations (2.89%) were observed in the lungs and the PFTs showed restrictive type of disorder in 7.8%, obstructive disorder in 7.1% and mixed in 1.42% of the workers. The ancillary workers were found to be most affected. Post-shift PFTs showed decrement in 53.8% subjects. Positive broncho dilation test was noted in 4 of 5 subjects tested. Concentration of fungal spores (Aspergillus, *Cladosporium*, Alternaria *etc*.) was very high inside the godown. Some subjects (23.5%) reported pain and discomfort in different parts of the body. The project is ongoing.

Analysis of Industrial Accidents and Structurization of Database

A total of 593 fatal injury cases occurring in Gujarat during 1995-97 were recorded and analysed. About 64% of

the deaths occurred in the chemical, textile, shi p breaking and engineering industries and 60% of the victims were under the age of 30 years. Slips and fall injuries (*e.g.,* fall on ground, fall from height) resulting in death of about 25% of the total cases were recorded during the study period. Machine related accidents (e.g., struck by machine, caught in machine) represent about 19% of the cases. Data suggest that many of the industrial injuries are preventable provided the industrial units follow appropriate method of accident investigation and analysis. For example, about 45% of the victims could have been saved if they were equipped with head gear and harness belt. Detailed analysis of the data is being carried out.

Toxicity and Exposure Assessment through Microbial Screening

The usual practice of evaluation of toxicity screening in case of 'Growth Zone Inhibition test' using sensor organism *Bacillus cereus* is to express either qualitatively or semi-quantitatively results depending upon the production of 'halo'. Considering this, a study has been carried out to establish a quantitative technique as an alternative to 'Growth Zone Inhibition test' using the same sensor organism (*B. cereus)*. The study was initiated with mercury (Hg^{2+}). The toxicity of Hg^{2+} as worked out in 'Growth Zone Inhibition test' was 0.1 ppm. Determination of MIC (minimum inhibitory concentration) and MAC of Hg^{2+} using *B. cereus* as the test organism is under progress.

Identification of Carcinogen-Haemoglobin Adduct in Benzidine exposed Workers

Benzidine is a potent carcinogen. The earlier findings on workers exposed to benzidine and benzidine-based dyes revealed that exposure status and excretion pattern of benzidine metabolites strongly correlated with the level of DNA-benzidine adducts in exfoliated urothelial cells. To examine the haemoglobin-adduct level, the blood samples were collected from 33 exposed (15 exposed to benzidine and 18 to benzidine-based dye *e.g.* Direct Black 38) and 15 control subjects matched for age, sex and socio-economic status. The analysis of samples for acetylated benzidine-Hb adduct level is being done in collaboration with the National Cancer Institute (NCI), USA.

The findings revealed that the Hb adducts of acetylated benzidine were non-detectable in the control subjects. However, it was present at relatively low level in benzidine dye exposed workers and at a very high level among benzidine exposed workers. Comparatively, the Hb adduct content was 18 times higher in benzidine exposed workers than the benzidine dye exposed workers.

NIOH Poison Information Centre - Organophosphate (OP) Pesticide Poisoning

Of the 377 cases of poisoning registered at the Centre, 113 (30%) were found to be of OP-poisoning. The cases of OP- poisoning were highest in the age group of 21-30 yr (46.9%) with 85% males and 15% females. Most frequent cause of poisoning was found to be suicidal (73.5%), the other causes being occupational (15%), accidental (8%), and unknown (3.5%). The exposure through oral route was found to be the most frequent (78.8%) followed by inhalation (15.9%) and combined *i.e.* inhalation and dermal (5.3 %). The OP-poisoning cases (44.2%) were found to be the most severe (severity score-3) requiring 8-38 days of hospitalisation. During the year, the frequency of OP poisoning was found to be higher in August and February. The farmers/farm labourers represented the highest number (42.5%). Sixty nine per cent of cases were either uneducated or had a primary level education. The above data indicate that OP insecticides continue to cause high morbidity. The commonest agents encountered were chlorpyriphos, dimethoate, phrate and monocrotophos.

Non-Communicable Diseases

Non-communicable diseases continue to be important public health problems in India, being responsible for sizeable mortality and morbidity. Demographic changes and changes caused in the environment and the economy are the major reasons for shift against a predominantly communicable diseases scenario. Ageing population allows manifestation of cardiovascular diseases, cancer and mental disorders which also result in high prevalence of chronic disability. The aim of research in non-communicable diseases ongoing at the ICMR is to identify risk factors, their prevention, health services requirements and control strategies.

ONCOLOGY

Research in the field of oncology continued to provide data which would be helpful in the control of cancers and tobacco use. The National Cancer Registry Programme (NCRP) continued to provide information on cancer occurrence and its trends over time. The study on cost of management of tobacco related diseases has provided important insights on the burden imposed by tobacco use. Multidisciplinary study on cervical cancer continues to add useful leads in the etiology and control of this common malignancy among Indian women. Environmental carcinogen testing units aim at identifying important substances/ chemicals of special interest to India and determining their permissible limits in the environment. Dissemination of results of research and their application for control activities was also done.

National Cancer Registry Programme

Generation of authentic data, analysis and interpretation, conduct of epidemiological studies and development of human resources are the major objectives of NCRP, which is functioning since 1981-82. The current network consists of six population based (Mumbai, Bangalore, Chennai, Delhi, Bhopal & rural Barshi) and five hospital based (Thiruvananthapuram, Dibrugarh, Mumbai, Bangalore, & Chennai) cancer registries.

The data from population based cancer registries show that in 1994, the age adjusted incidence rate in urban registry areas varied between 98.7 and 138.3/100,000 among men and between 108.0 and 143.4 /100,000 among women. The age adjusted incidence rate in rural areas of Barshi (Maharashtra) was 41.1 among men and 56.3 among women. The most common site of cancer in men in all the registries (except Chennai where stomach cancer is the commonest) is lung or oesophagus. Other common sites of cancer in men include pharynx and stomach. The common sites of cancer in women include cervix, breast, oral cavity, oesophagus, stomach and ovary. The leading sites for cancer were consistent over the years in all the registries except Barshi. The incidence rate of stomach cancer is high in Chennai and Bangalore. Cancer of the gall bladder is common in Delhi, in both sexes. Over the years, Mumbai and Delhi have shown an increase in the incidence of cancer when all sites were taken into consideration. Cancer of the breast in women has also shown an increase in all urban registry areas. The data from hospital based cancer registries till 1994 showed that the histopathological verification of diagnosis varied from 69.5% (Chennai) to 94.5% (Chandigarh) among men, and from 71.5% (Chennai) to 96.1% (Chandigarh) among women. Proportion of patients with localized disease varied from 5.1% (Chennai) to 24.3% (Dibrugarh) among men, and from 5.6% (Chennai) to 22.8% (Mumbai) among women. The proportion of cases with regional spread varied from 41.6% (Mumbai) to 65.5% (Chandigarh) among men, and from 49.4% (Mumbai) to 78.0% (Chennai) among women. Radiotherapy was the commonest mode of treatment,

followed by surgery or chemotherapy, depending upon the registry. The proportion of patients not receiving/accepting treatment at various centres varied from 16.1% (Dibrugarh) to 45.7% (Chennai) among men and from 15.1% (Dibrugarh) to 39.8% (Chennai) among women. Case control studies on cancers of prostate and gall bladder have been initiated under the NCRP. Two continuing education workshops on cancer registration were held. A three centre study on assessing the coverage of population based cancer registries is being carried out at Bangalore, Chennai and Mumbai.

Cost of Management of Tobacco related Diseases

The project on cost of management of tobacco related diseases [(tobacco-related cancers, coronary heart disease (CHD) and chronic obstructive pulmonary disease - (COPD)] helped in assessing the magnitude of financial burden posed by these diseases. Data on direct as well as indirect expenditure due to the disease were collected from patients and their relatives/ friends. The expenditure incurred by the treating institution for the management of these patients was also collected. The average cost due to a case of tobacco related cancer was Rs.134,449 (discounted at 1990 level). The data from patients of CHD and COPD were collected on a cross-sectional basis, in contrast to a cohort approach followed for tobacco related cancers. The per capita annual direct losses were Rs. 5,130.2 for patients of CHD and Rs. 2,670.7 for patients of COPD. The annual losses indirectly borne by the state/employer were still larger (Rs. 16,863.3 and Rs.11,454.0 per year respectively for patients with CHD and COPD).

Cervical Cancer

The Institute of Cytology and Preventive Oncology (ICPO), New Delhi is conducting a multidisciplinary study on the risk factors of cervical cancer (including HPV) utilizing tools of molecular biology with emphasis on the identification of leads for its control. A multidisciplinary study on breast cancer has also been initiated. Uterine cervical dysplasia II study indicates a significant role of HPV. Other important leads include evidence of specific genetic events in cervical cancer, HPV oncogene expression, and role of some agents in viral oncogene expression. The project on reproductive tract infections (RTI) provided insight into this problem among Indian women, their clinical presentation, association with inflammatory smears and precancerous and cancerous lesions. The pioneering work of the Institute on the clinical downstaging of cervical cancer demonstrated its efficacy for early detection. This was further strengthened by the development of a simple instrument, magna visualiser, which is being patented. A national workshop on clinical downstaging as an alternative strategy for control of cervical cancer is proposed.

Studies on the genetic alteration of cervical cancerous and precancerous lesions involved 16 microsatellite markers belonging to 3p, 4q, 5p, 6q and 10p. Data obtained so far have revealed genetic deletion at 3p and 5p. In a separate analysis, 3p genetic deletions were found to be dependent on HPV whereas 5p genetic deletions at 5S406 were independent of HPV 16/18 infection.

p53 expression was studied in 101 cervical tumours and 36 healthy controls. Overexpression of p53 specific mRNA transcripts did not show any correlation with occurrence of p53 gene mutations. However, overexpression was more common in HPV positive patients. In cervical cancer p53 mutation was found to be infrequent and appears to be not mutually exclusive to HPV infection. In another study of 163 cervical cancer patients, 50 cervical dysplasia patients and 74 healthy controls, p53 gene polymorphism was studied at codon 72 proline/arginine. No strong association of HPV positivity with p53 codon 72 polymorphism was observed.

A DST sponsored workshop on molecular biology in human health and disease was conducted.

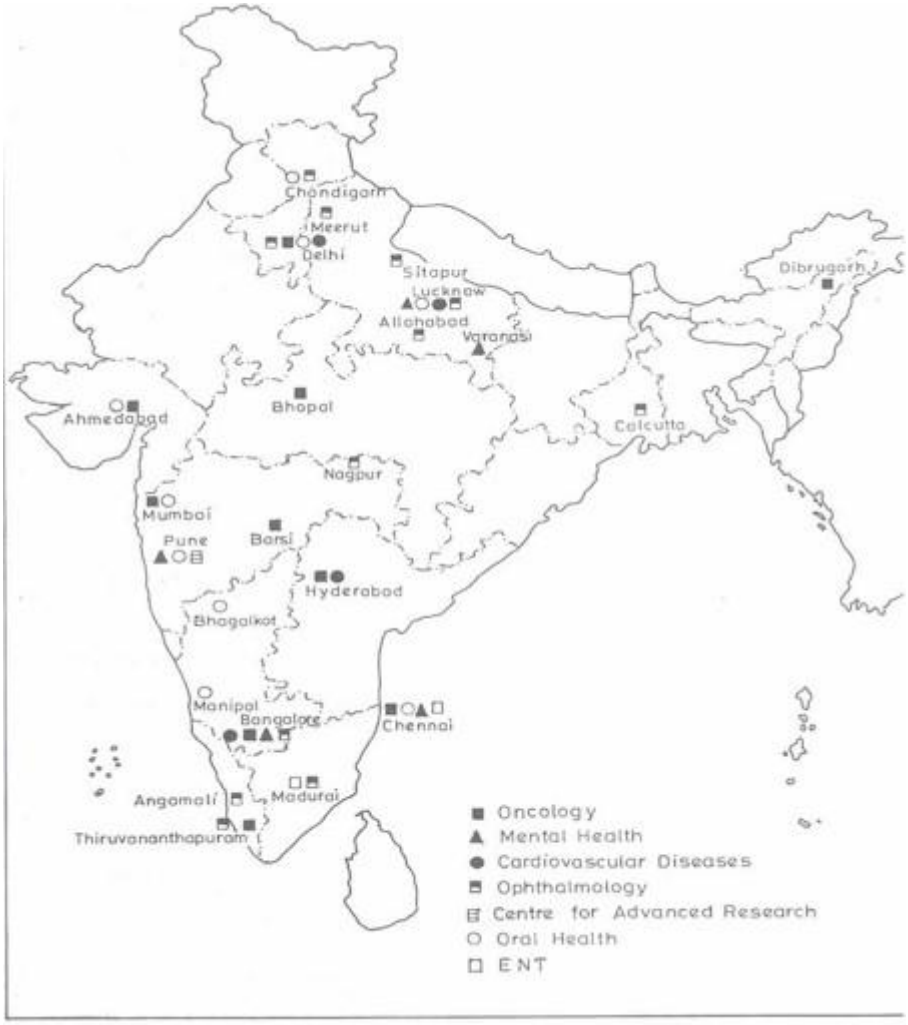
CARDIOVASCULAR DISEASES

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

The conventional risk factors for coronary artery disease (CAD) do not appear to be solely responsible for the higher incidence of ischaemic heart disease in the Indian population. A multicentric case-control study on acute myocardial infarction in Indians was initiated to identify and quantify the association of possible risk factors for CAD. Centres at Delhi, Lucknow, Bangalore and Hyderabad have started collecting data on standardized proformae.

Indo-US Workshop on RF/RHD and Streptococcal Infections

An Indo-US workshop on RF/RHD and Streptococcal infections was held under the US Vaccine Action Programme in April 1999. Fifteen US and 30 Indian scientists were invited for this workshop to explore the development of a joint venture for streptococcal vaccine development. These deliberations helped formulation of a research programme under the *Jai Vigyan* Mission mode.



ICMR Research Projects in Non-communicable Diseases

Jai Vigyan Mission Mode Project on Community Control of RF/RHD in India

Streptococcal infections and rheumatic heart disease have been identified as an area under the *Jai Vigyan* Mission for enhancing research thrust in nationally relevant areas. The ICMR has been actively engaged in research on RF/ RHD and streptococcal infections over the past two decades. The project proposes to study the epidemiology, genetic and immunological host factors, typing of rheumatogenic strains and development of a vaccine against streptococci.

OPHTHALMOLOGY

Blindness is an important national problem because it is an important cause of lost DALYs (Disability Adjusted Life Years).

Glaucoma

Glaucoma is an important cause of preventable blindness. The Council has initiated two studies on glaucoma,

one on epidemiology of glaucoma and other on its management. The project on epidemiology is still continuing while the data collection under the management of glaucoma project has been completed. The data entry and analysis are currently being done at the Council.

MENTAL HEALTH

Epidemiological studies were undertaken in the area of child and adolescent psychiatric disorders at Bangalore and Lucknow. A Centre for Advanced Research was set up at the Maharashtra Institute of Mental Health, Pune to study the health consequences of Marathwada earthquake disaster, with special reference to mental health.

Mental Health Consequences of Earthquake Disaster

The base-line survey of psychiatric and physical disorders in the study area and comparable control area has shown excess psychiatric morbidity especially post-traumatic stress disorders, and other reactions to severe stress in the earthquake affected area. Depressive episodes were also reported more frequently in the disaster affected area. The results of nested case-control study carried out by the Centre showed that significant risk factors of excess psychiatric morbidity in earthquake affected area were disaster injury, disaster deaths, trapping experience and dissatisfaction with social support. One year follow up of cases identified in the base-line survey was carried out. This is the first large community based study in the country that has generated data on course and outcome of post-traumatic stress disorders and other reactions to severe stress. It was found that though nearly two-thirds of psychiatric patients in the disaster affected area recovered (with treatment) within an year of follow up, psychiatric morbidity there was more as compared to the control area. Significant prognostic factors included satisfaction with social support, desirable life events, absence of, or minimal injury during the disaster.

Child and Adolescent Psychiatric Disorders

A task force project was carried out at Bangalore and Lucknow to find the pattern and prevalence of child and adolescent psychiatric disorders in rural and urban areas, and for studying the psychosocial correlates of these disorders. An interim analysis of data shows that following disorders are more prevalent among children in the community : non-organic enuresis, pica of infancy, stuttering, hyperkinetic disorders, conduct disorders, panic disorders, oppositional defiant disorders and specific phobias. Further data analysis is in progress on psychosocial correlates of these disorders.

Tobacco and other Substance Abuse in North-east

In an ongoing survey at the RMRC, Dibrugarh on tobacco and other substance abuse in Arunachal Pradesh, during the year, six selected villages in Khersang PHC area, two substitute villages in Khimiyong PHC area and two villages in Vijainagar PHC area of Changlang district in Arunachal Pradesh were surveyed. A total of 112 persons aged 10 years and above were interviewed during the household surveys. The prevalence of substance use in Khersang PHC area was 46.4% for tobacco (36.4% chewers and 11.1% smokers), 33.7% for alcohol and 1.0% for opium. The prevalence in the surveyed villages under Khimiyong PHC was 35.5% for tobacco (22.9% chewers and 16.7% smokers), 40.4% for alcohol and 15.5% for opium. The least substance abuse was found in Vijainagar PHC area where 5.9% persons were tobacco users (1.9% chewers and 4.6% smokers) and 6.2% alcohol users with no opium user.

Socio-demographic and Behaviour Study of Drug Addicts

Information on drug addicts along the National Highway 37 in Assam and Arunachal Pradesh was collected through Key informants like ex-drug addicts, doctors, NGOs *etc*., by the RMRC, Dibrugarh. Besides the Govt. hospitals, information from public sector hospitals, private nursing homes and leading private practitioners was also collected. So far 31 drug addicts have been contacted and interviewed. Most of the drug addicts were between 20-35 years of age, married and illiterate or educated up to middle standard. Majority of drug addicts were addicted to heroin and frequency of intake was several times per day according to their statements. 'Chasing' was the most preferred route of administration of heroin. However, many preferred the intravenous route of administration. The study is in progress.

Prevalence of Opium Use in Desert Areas of Rajasthan

A study of prevalence of opium use and socio-cultural factors associated with consumption pattern in desert areas was continued at DMRC, Jodhpur and a total of 250 households was covered. The data so far collected indicate that of the individuals examined, nearly 60 were *Doda*/opium consumers, 100 consumed alcohol, while 180 were smokers.

OTORHINOLARYNGOLOGY

Epidemiological, Cultural and Immunological Studies on *Rhinosporidium seeberi*

Rhinosporidiosis is a disease of man and domestic animals. The disease has been reported to be caused by *R. seeberi* or by a unicellular prokaryotic cyanobacterium. In man, it is primarily a disease of the nose, nasopharynx, eye and skin and occasionally affects the viscera and external genitalia.

A study was initiated with the overall objective to identify the specific antigens of *R. seeberi* that cause rhinosporidiosis in humans so as to be able to clone the gene for the above antigen to develop specific diagnostic probes.

During the year under report, work mainly centered around identification of the pathogen. In order to resolve the issue of the pathogenesis, biopsy material from rhinosporidiosis patients and samples of *Microcystis aeruginosa* were independently evaluated by experts from AIIMS, New Delhi; PGIMER, Chandigarh as well as V.P. Chest Institute, Delhi. Work on DNA sequencing of the short fragment of *R. seeberi* genome was also undertaken and compared with the sequence available with the data bank. A genomic library was constructed in ngt11 vector. Immunological studies of the pathogen were also attempted . The pathogen was isolated from pond water and attempts were made to grow the organism in axenic culture.

HAEMATOLOGY

The Institute of Immunohaematology (IIH), Mumbai continued basic, clinical and epidemiological research in haematological disorders which included haemoglobinopathies, bleeding and thrombotic disorders, generation of monoclonal antibodies, transfusion medicine *etc*.

Haemoglobinopathies

Prenatal Diagnosis of Thalassaemia Syndromes

Oligo probes were designed for inclusion of one more mutation in the reverse dot blot hybridization ship making it possible to screen for 6- β-thalassaemia mutations (IVS 1-5(G-C), IVS 1-1(G-T), Codon 8/9 +G, Codon 41/42 -CTTT, Codon 15G-A and Codon 30G-C along with HbS and HbE in a single step (Fig.15). Evaluation was done to check the stability of a PCR premix prepared containing the primers, dNTPs, buffer *etc* as well as the oligoprobe blotted ships. Both these were stable for up to 6 months and could be provided in a kit for detection of common Indian mutations for β-thalassaemia and abnormal haemoglobins.

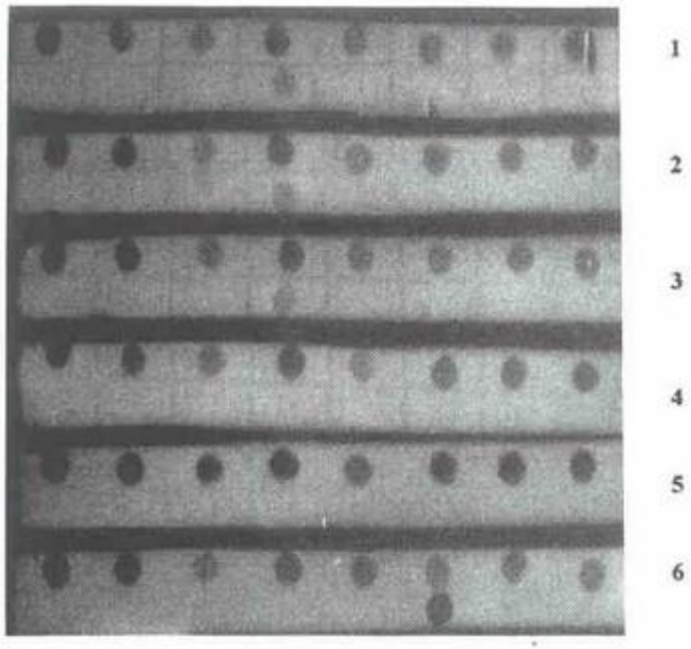


Fig. 15. Reverse dot blot hybridization for 6 β-thalassaemia mutations along with HbS and HbE.
Samples 1-3–IVS-1-5 (G->C) heterozygotes (spot in lower row at 4th position).
Samples 4-5–Normal (spot seen only with normal probes in the 1st row).
Sample 6–codon 30 (G->C) heterozygote (spot in lower row in 6th position).

Antenatal Screening for Thalassaemia

Antenatal screening for thalassaemia was done in 12098 pregnant women. Among these 196 had β–thalassaemia trait and 37 had other abnormal haemoglobins. A total of 126 women were counselled and their husbands checked subsequently and 9 couples at risk were identified prospectively, 8 of whom underwent antenatal diagnosis. One woman was already in the 7th month of gestation and was advised to check the baby's cord blood.

Isolation of Foetal Cells from Maternal Blood

Further work on isolation of foetal cells from 7 ml sample of maternal blood for non invasive prenatal diagnosis was done. By percol density gradient centrifugation carried out in 30 pregnant women at 10 to 23 weeks of gestation, nucleated erythroblast (NRBCs) counts at the interface were found to be 0.6 to 5. Immunogenetic sorting using CD71 resulted in isolation of 5 to 16 cells, while flow cytometry using a monoclonal anti-HbF as a foetal marker gave about 200 cells (Fig.16).

Generation of Monoclonal Antibody by Hybridoma Technology

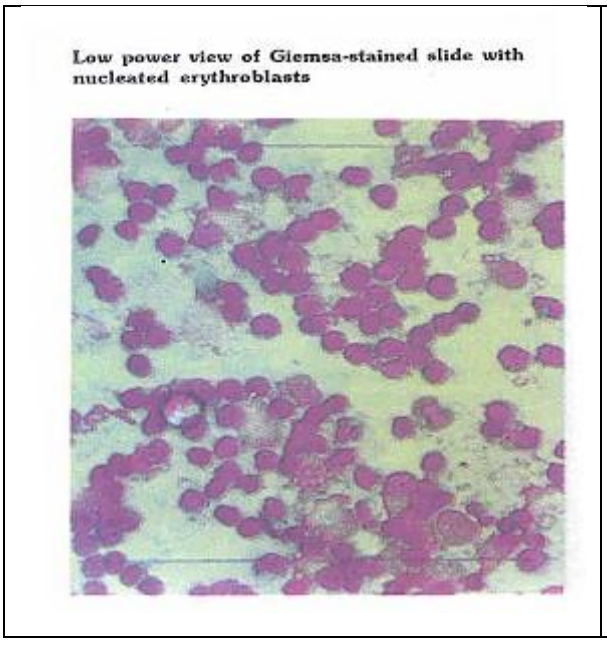
A monoclonal anti HbF was generated and its specificity was tested by flow cytometry to obtain accurate estimation of haemoglobin F in various conditions.

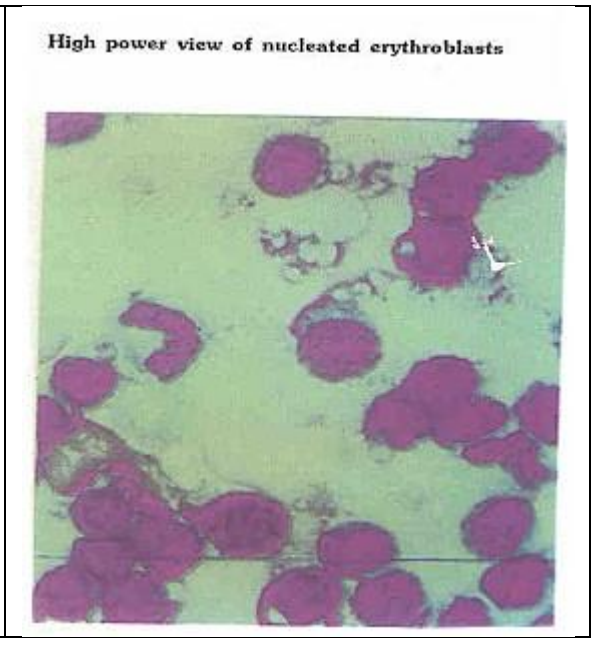
Molecular Studies in G6PD Deficiency

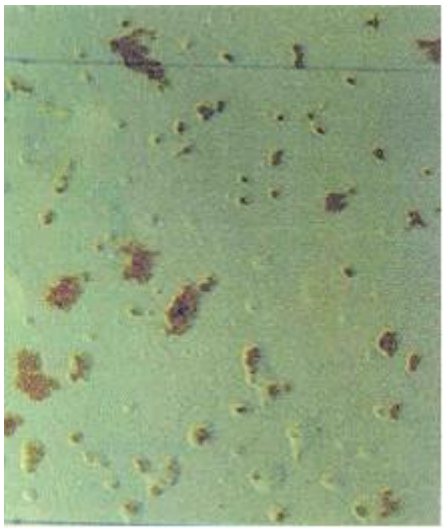
Seventy five subjects screened for mutations underlying G6PD deficiency showed G6PD Kerala Kalyan in 20, G6PD Mediterranean in 18 and G6PD Orissa in 6. Twenty five uncharacterised samples were negative for G6PD Seattle. SSCP of all exons was standardised and uncharacterised samples screened but no altered mobility was found. The 1311 polymorphism was also studied in all samples and both the C and T polymorphisms were seen. Correlating the degree of haemolysis and type of mutation it was observed that all the cases with severe haemolysis did not have Mediterranean type of mutation only as reported earlier.

Haemostasis

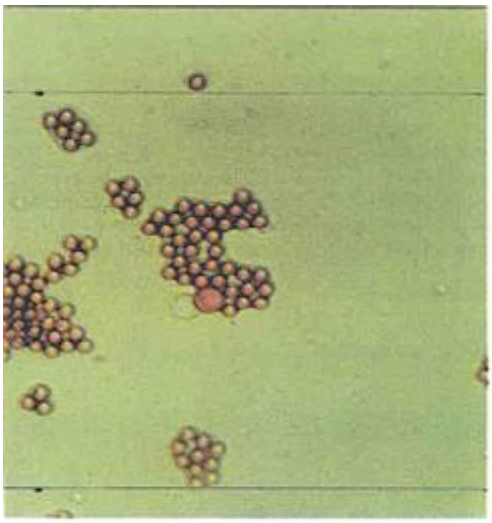
Carrier detection and antenatal diagnosis in families of haemophilia was continued. In the year under report, 28 families of haemophilia A and 8 families of haemophilia B were referred for carrier diagnosis. Out of 43 females examined, 20 were diagnosed as carriers, 22 as non carriers and status of one could not be ascertained. Antenatal diagnosis in haemophilia by chorionic villus sampling was performed in 15 haemophilia A families and 3 haemophilia B families. One family was referred at 18 weeks and the results were given following cordocentesis.


Low power view of Giemsa-stained slide with nucleated erythroblasts


High power view of nucleated erythroblasts



Low power view of Dynal™ beads complexed with CD 71 +ve cells



High power view of Dynal™ beads complexed with CD 71+ve cells

Fig 16 : Immunomagnetic sorting and Giemsa staining of nucleated RBCs using DYNL beads conjugated to CD71.

The etiology of thrombophilia was studied in 248 patients (aged below 40 years) with deep vein thrombosis (DVT). Factor V Leiden mutation which is a major risk factor for thrombophilia in Western countries (*i.e.* 20 – 30%), was found to have minimal role in its etiology in these patients *i.e.* 3% prevalence in DVT patients against a control prevalence of 2.7%. However, patients with Budd- Chiari syndrome still showed a very high prevalence of factor V Leiden mutation *i.e.* 20%. The prothrombin gene polymorphism G 20210 A was found to be rare in the studied population. The MTHFR gene polymorphism showed similar prevalence in control population as well as in the DVT patients.

Carrier detection in von Willebrand (VW) disease which is an autosomal disorder of factor VIII deficiency is another major achievement during the year. Earlier an extensive study of the allele frequency and heterozygosity frequency of the two polymorphic markers of the intron 40 of VW factor gene in 250 unrelated subjects was carried out (Fig.17). The carrier detection was performed in 3 severe von Willebrand families and they were counselled.

Fig. 17. Detection of carriers in a von Willebrand disease family by intron 40 VW1 and VW2 polymorphic markers of the VWF gene. Sister is a carrier (lane 5 & 10). Lane 1–Samples from marker V (Roche Mol. Biochemicals); Lane 2–Father; Lane 3–Mother; Lane 4–Affected sibling (index case); Lane 5–Sister (carrier); Lane 6–Marker pBR 322/MspI digest (GENE I); Lane 7–Father; Lane 8–Mother; Lane 9–Affected sibling (index case); Lane 10–Sister (carrier); Lane 11–Marker V (Roche Mol. Biochemicals).

Platelet Alloantigen in Indian Population and Detection of Neonatal Alloimmune Thrombocytopenic Purpura (NAITP) by Allele Specific Amplification

As information on the distribution of platelet specific alloantigen in the Indian population is not available, this study was undertaken. The population screening so far included 300 subjects who were selected randomly from among voluntary blood donors and attendees of antenatal clinics at Mumbai. The results revealed PLA1 homozygosity of 84% and PLA2 homozygosity of 1% and the rest 15% were found to be heterozygous. One per cent of this female population having PLA2 are at risk of having neonatal alloimmunisation and alloimmune thrombocytopaenia in the newborn.

Transfusion Medicine

Population Screening for Detection and Molecular Characterisation of Partial 'D' Antigen and Rh Variant

Recent studies have suggested that Rh antigen has more than 30 well defined epitopes. A panel of epitope specific monoclonal anti- D culture supernatant was obtained from USA and UK and 983 blood samples of various caste groups and communities were screened. Interestingly, 20 to 49% samples showed reactivity with all monoclonal antibodies indicating the presence of majority of D antigenic epitopes. However, 4.5% of the population showed absence of more than 5 epitopes. The same panel of monoclonal antibodies when used to investigate 16 known cases of weak D antigen showed absence of 25 to 70% epitopes. Rh genotyping was performed in all the 16 cases and the results matched with the overall incidence of these genotypes.

Bone Marrow Transplantation

The Council's Centre for Advanced Research for Bone Marrow Transplantation at Christian Medical College,

Vellore completed five years of sanctioned duration. The Centre aims to develop bone marrow transplantation technology for thalassaemia in India with appropriate modification of specific transplant techniques to suit Indian conditions. Attempts were made to reduce the incidence of graft rejection by increasing the dose of busulphan and estimating the blood levels of busulphan achieved in individual patients and to evaluate the place of additional immunosuppression with antilymphocyte globulin (ALG). A total of 51 patients with thalassaemia major have been given bone marrow transplantation, 26 in Group I receiving Regimen A comprising busulphan 600mg/m2+cyclophosphamide 200mg/kg and 25 in Group II receiving Regimen B (busulphan 16mg/kg+cyclophosphamide 200mg/kg+ALG). The overall survival was 72.5% with both groups having similar results. However, the overall survival was found to be 93.3% amongst 15 cases in class II and 65.7% in class III patients which is comparable to best results in the world. Only 40 cases were evaluable for rejection of which 4 from class III had rejection, (10%) with no rejection in class II. Overall mortality was 27.5% with 13 in class III and one in class II, of these 11 were not related to rejection. The hospital stay varied from 28-84 days depending on post-transplant complications. The study has shown that 600mg/m2 busulphan dose is not more toxic than the standard dose of 16mg/kg. Further addition of ALG to the conditioning regimen had no additional benefit thereby suggesting that omitting ALG can reduce the cost without compromising with the outcome.

Major achievements of the Centre include development of a HPLC based method for assaying busulphan levels in plasma. The assays can be done in a hospital setting and results made available quickly for clinical decisions in individual patients. Documentation of busulphan levels in thalassaemia patients undergoing bone marrow transplantation using 16mg/kg and 600 mg/m2 showed 2-12 fold variation in levels between individuals irrespective of the dosing strategy. The results have shown for the first time that plasma busulphan levels correlate with hepatic glutathione S transferase levels. An increased incidence of gastrointestinal bleeding in patients whose busulphan mean residual value(MRV) is>500ng/ml and area under concentration curve(AUC) >5000ng/ml has been documented.

An increased risk of rejection was observed in patients whose systemic exposure to busulphan is sub-optimal. No patient in whom the MRV was greater than 300 ng/ml rejected while all patients whose MRV was below 150ng/ml rejected the transplant. There was also a correlation with the first dose minimum concentration (C min) and the mean of the first, second and thirteenth dose C min with the probability of rejection being increased if levels were below 200 ng/ml. The data suggest that individualized busulphan dosing based on first dose pharmacokinetics would be the best way to reduce toxicity and rejection.

The Centre has facilities of antenatal diagnosis of thalassaemia for clinical documentation of the molecular defects. DNA fingerprinting for documenting mixed chimerism post -bone marrow transplantation and for maternal contamination in chorionic villus sampling has been standardized. The Centre is now comprehensive and is able to offer all services from antenatal diagnosis to bone marrow transplantation for patients with thalassaemia major.

Intervention Programme for Nutritional Anaemia and Haemoglobinopathies amongst Primitive Tribal Population of India

In view of the prevalence of blood disorders in various primitive tribal populations this multicentric study was initiated in October 1999 at 5 centres in four states namely Maharashtra, Gujarat, Orissa and Tamil Nadu to assess nutritional and sickle cell anaemia in the study population, introduce appropriate intervention and follow up for a period of 3 years. Initial training of the staff appointed at various centres was conducted to obtain uniformity of procedures to be adopted by all the centres. The pilot testing is in progress.

Community Control of Thalassaemia Syndromes - Awareness, Screening, Genetic Counselling and Prevention

The project has been chosen as one of the mission mode projects under the *Jai Vigyan* Science and Technology Mission. The project aims at educating, screening, counselling and identifying couples at risk of having thalassaemic children and developing regional and national referral centres for control of thalassaemia major in the country. The study on college students and pregnant women has been launched in 6 states *viz*. Maharashtra, Gujarat, Assam, West Bengal, Punjab and Karnataka.

Basic Medical Sciences

Research in basic medical sciences is supported by the Council in all its permanent institutes/centres as well as through extramural funding to various research institutions, medical colleges, universities *etc*. The results of studies carried out in the area of pathology (at the Council's Institute of Pathology, New Delhi), pharmacology, biochemistry, molecular biology and toxicology are given below.

PATHOLOGY

Tumour Biology

To study the regulation of tumour suppressor protein p53 by estrogen and antiestrogens in breast cancer cells, estrogen receptor positive breast cancer cells were cultured in media containing 5% foetal calf serum and the cell proliferation and level of p53 expression were studied. Exogenous addition of 17β-estradiol (E2) in the medium had no significant effect on either cell proliferation or p53 expression. However, a significant decrease in cell number and p53 expression was found on addition of tamoxifen in the media. On culture of these cells in growth media devoid of serum but containing hydrocortisone, cholera toxin, sodium, insulin and ascorbic acid, cell number and p53 levels declined but the addition of 17β-estradiol to the medium increased cell proliferation and p53 expression.

In the project on genetics of breast cancer in the Indian population, preliminary work done on mutation analysis of BRCA1 and BRCA2 breast cancer susceptibility genes showed presence of mutations in both the genes in approximately 20% Indian breast cancer patients. Characterization of the mutation spectrum is being further pursued.

Study of oncogenes, tumour suppressor gene and growth factor status in premalignant and malignant prostate enlargement was carried out at the IOP, New Delhi. Forty patients with prostate enlargement due to adenocarcinoma (20), prostatic intraepithelial neoplasia (PIN) (10) and benign hyperplasia (10), studied for expression of tumour suppressor protein p53 and ras onco-protein p21 showed that the lower grades of prostate cancer were associated with higher p53 nuclear reactivity as compared to p21 positive patients who showed inverse correlation. Out of the 10 patients of PIN, p53 positivity was found in 40% while none of these patients showed positive p21 reaction.

Indian Childhood Cirrhosis

In continuing studies on the experimental model of Indian childhood cirrhosis (ICC) three of the four mice kept on herbal diet with garlic and borax showed evidence of mild to moderate fibrosis in liver tissue. Mice kept on garlic and *hing (Ferula asafoetida)* showed moderate degree of definite hepatic fibrosis.

Immunohistochemical localisation of metallothionein by ABC (avidin biotin complex) method on liver biopsy sections from patients of clinical ICC and from animals in ongoing studies on an experimental model of ICC showed positive results in all the cases tested so far. Further studies are in progress.

Vitiligo

A guinea pig model for vitiligo to evaluate the therapeutic potential of new treatment modalities has been developed at IOP, New Delhi. A vitiligo like depigmented patch was produced on the dorsal aspect of black/brown ear lobe of coloured guinea pig by the application of a cream of 4-hydroxy anisole once a day for about two and half months. The ear lobes were divided into matched pairs of equal extent of depigmentation.

The repigmentation completion status at the end of 11 weeks of photochemotherapy revealed that 68.75% (11/16) of psoralen ultra violet A (PUVA) treated ear lobes were completely repigmented as against 25% (4/16) in control group (Fig.18).

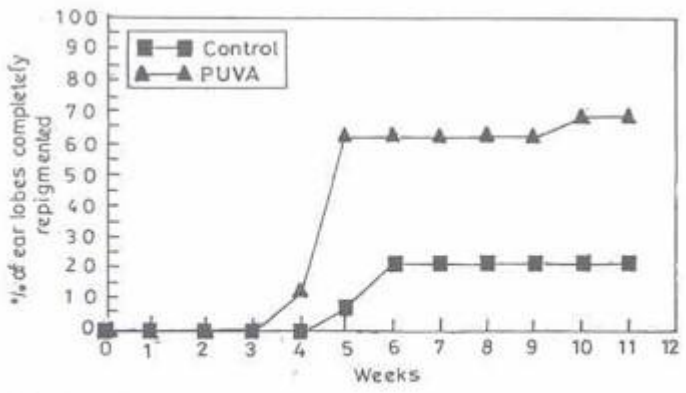


Fig. 18. Repigmentation completion status of PUVA treated guinea pig ear lobes.

The depigmentation produced experimentally in this study not only resembled human vitiligo both histologically and clinically but also responded to a comparatively successful and more popular photo-chemotherapeutic modality, PUVA suggesting that the guinea pig model could be a very useful tool for screening the efficacy of unknown/unscreened medications for vitiligo.

PHARMACOLOGY/TOXICOLOGY

A study was supported at the Industrial Toxicology Research Centre, Lucknow on the toxicological and immunotoxicological potential of commonly used plastics and the identification of leachates. Fifty eight brands of plastic biomedical (40 samples) and food packaging (18 samples) products collected from different major

cities of UP were evaluated. Of these six brands of intravenous sets showing temperature dependent global migration above the permissible limit, were evaluated for detailed *in vitro* and *in vivo* studies. The main parameters studied were neurobehavioural alterations, changes in clinical biochemistry, immunoglobulin profile and histopathology. Migration of Zn from all the six brands of i.v. sets was observed above the permissible limits in simulatory solvents *viz.*sodium carbonate (5%), acetic acid (3%) and ethyl alcohol (8%). The migration of Mn and Cd was above the permissible limits only in simulating solvent sodium chloride (0.9%) and sodium carbonate (5%). Subchronic oral toxicity studies with two brands of i.v. sets containing Mn beyond the permissible levels, revealed significant effect on some of the parameters of the immune system, especially with higher doses (0.8ml/kg b.wt./day). Out of 58 samples, six samples of i.v. sets (*i.e.* 10% of the sample) did not meet the requirement of physico-chemical parameters. Of the six samples subjected to detailed toxicological investigations, only two did not meet the safety requirements. Hence, there is a need of proper checking to ensure that the prescribed standards are being met by the manufacturers.

A study was undertaken at the Central Drug Research Institute (CDRI), Lucknow to design and synthesize novel oligopeptides as antiasthmatic/antiallergic agents. Synthesis of all the peptides and various amino acid derivatives was done using standard procedures. The peptides were tested for anti-PCA (passive cutaneous anaphylaxis) mast cell stabilising and bronchodilator activity in male rats. A convenient route for the solid phase synthesis of IgE related hexapeptide having a troublesome sequence Asp-Ser and Asp-Gly was standardised and an Indian patent filed. Thirty three new congeners of IgE-Fc hexapeptide were synthesized; 96/199 was identified as the most potent compound exhibiting high order of antiallergic activity and was found to be more potent than at least the clinically used drug disodium chromoglycate in experimental animals. A suitable formulation of 96/199 for administration by the nasal route has been prepared and evaluated.

At the Jamia Hamdard, New Delhi, a study was undertaken to investigate the neuropsychopharmacological properties of metallic preparations used in the Indian systems of medicine and study the rationale of their therapeutic action so as to establish their LD_{50}/minimum therapeutic dose and therapeutic index. Calcined preparations of gold and silver used in Ayurveda (*swarna bhasma*, *raupya bhasma*) and Unani Tibb (*Kushta Tila Kalan*, *Kusha Nugra*), thin silver leaves used in India on sweets and betel and on tonic pills *(chandi warf)*, and oral gold preparation (Auranofin) used in modern medicine were subjected to a battery of >30 screening tests for general neuropsychopharmacological effects, cognitive functions, anti-depressant, anxiolytic, neuroleptic and serenic activities as also for the effects on endurance and fatigue. Both gold and silver preparations showed moderate to marked analgesic effects which appear to be mediated through opioidergic mechanisms. Other interesting effects included reduction of haloperidol-induced catalepsy in rats (in both gold and silver preparations), nootropic effects in rats and mice against both active and passive avoidance models, anxiolytic effects observed by Vogel's conflict test and elevated plus maze studies (in gold preparations) and antiaggressive action (in silver preparations). Some pro-convulsant effects were observed with silver preparations, which need further evaluation.

BIOCHEMISTRY AND CELL & MOLECULAR BIOLOGY

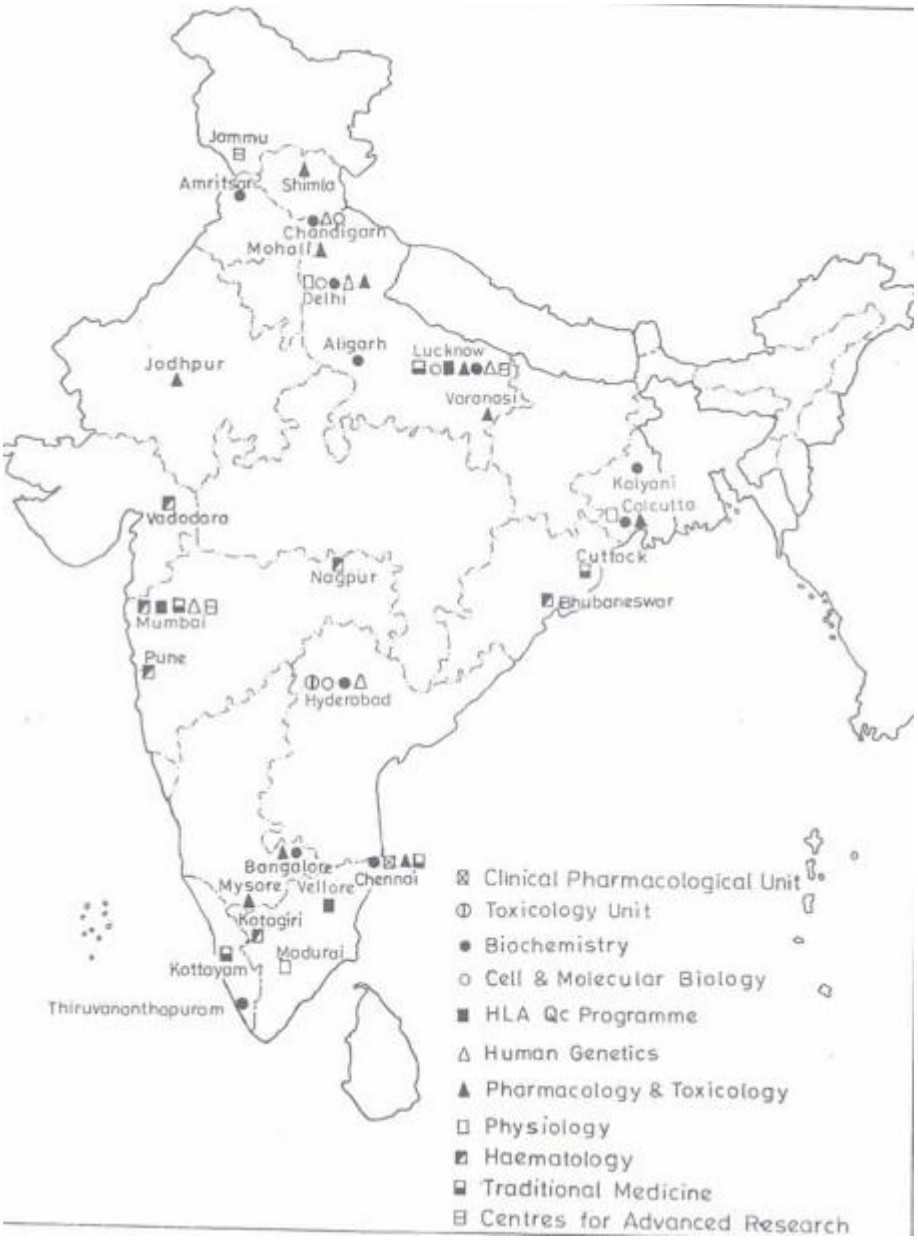
A project aiming at elucidating the biochemical mechanisms involved in Ca^{2+} release from mitochondria of the bovine pulmonary vascular smooth muscle tissue under oxidant stimulation has been completed at the University of Kalyani, Kalyani. The results indicated that H_2O_2 mediated stimulation of lipid peroxidation in mitochondria of bovine pulmonary vascular smooth muscle occurs predominantly *via* hydroxyl ion (OH). Iron release caused by H_2O_2 from the mitochondria plays an important role in this process. The reactive OH is generated, at least partly, extra-mitochondrially and the anion channels appear to play an important role in mediating the response

produced by H_2O_2 on lipid peroxidation in the mitochondria. H_2O_2 induced Ca^{2+} efflux from bovine pulmonary artery smooth muscle mitochondria does not occur primarily *via* non-specific permeability alteration of the mitochondrial inner membrane, instead it appears to occur *via* a Ca^{2+} selective, oxidant dependent release pathway(s). OH plays an important role in H_2O_2 induced stimulation of Ca^{2+} release. Treatment of bovine pulmonary artery smooth muscle mitochondria with H_2O_2 stimulated oxidation of GSH and NAD(P)H alongwith an increase in Ca^{2+} release. Addition of oxaloacetate to mitochondrial suspension stimulated Ca^{2+} release and oxidation of NAD(P)H while GSH level remained unchanged. Subsequently, addition of β-hydroxybutyrate which reduced mitochondrial pyridine nucleotides caused reuptake of the released Ca^{2+} without causing appreciable alteration of GSH level. These results indicate that the redox state of pyridine nucleotides, but not glutathione, regulates Ca^{2+} release from the pulmonary smooth muscle mitochondria under oxidant stimulation.

Elevated levels of lipoprotein (a) [Lp(a)] have been regarded as an independent risk factor for coronary, peripheral and cerebral atherosclerosis. The enormous inter-individual variation in the plasma concentration of Lp(a) is almost entirely controlled by the apolipoprotein (a) [apo(a)] gene locus on the chromosome 6q26-27. In a study conducted at the All India Institute of Medical Sciences(AIIMS), New Delhi 127 angiographically assessed male coronary artery disease (CAD) patients (aged 30-70 yr) and 133 age and sex matched controls were analysed. The apo (a) molecule exists in multiple, genetically determined isoforms, which differ from each other in the number of K-4 type-2 repeats. These variations may be responsible for different promoter activity and thereby variation in Lp(a) concentration. For analysis of the penta nucleotide repeat (PNR) polymorphism, PCR amplified products were loaded on 12% polyacrylamide gel for electrophoresis. Apo(a) K-4 size polymorphism was studied by SDS-agarose gel electrophoresis and immunoblotting. The important observations of the study are: PNR alleles 8 & 9, in general associated with high Lp(a) levels, were the wild ones whereas alleles 10 & 11 associated with low Lp(a) levels, were rare. 12 PNR allele was also detected and confirmed by DNA sequence analysis. A trend for high Lp(a) levels was observed in subjects with PNR sum<20 and low in those having PNR sum>20. The number of K-4 type 2 repeats varied between 12-50 in the subjects. The most frequent allele among the patients was 23K-4 repeats whereas in controls it was 32. An inverse correlation was found to exist between the size of K-4 repeats and serum Lp(a) levels. Subjects with small (<21 K-4 repeats) and intermediate allele (21-28 K-4 repeats) showed high levels of Lp(a) (>40mg/dl) when compared with the subjects with large allele (>28K-4 repeats). K-4 type 2 polymorphism has a profound effect on Lp(a) levels as compared to PNR polymorphism. Although an inverse correlation has been observed between the number of K-4 type 2 repeats and plasma levels of Lp(a), there were also exceptions to this finding.

TRADITIONAL MEDICINE

The Council continued the centrally co-ordinated multicentric clinical trial on *Vijaysar(Pterocarpus marsupium)* for diabetes mellitus at the Madras Medical College, Chennai, Cuttack Medical College, Cuttack and Kottayam Medical College, Kottayam through the task force approach. *Vijaysar* has repeatedly shown promising results in newly diagnosed diabetic patients as evident from the data of the recently concluded 36 and 72 weeks study, a trend similar to that seen in the earlier 12 weeks study. In order to validate the findings in known uncontrolled diabetics, further multicentric trial has been initiated at the same centres. On account of the expected increase in demand for this plant drug, steps were taken for a dialogue between related Government agencies to conserve *Vijaysar* trees, prevent their misuse as timber and start their cultivation by using appropriate agro-technology.



For providing support to the Traditional Medicine (TRM) Programme, two Centres for Advanced Research were initiated, one for clinical pharmacology in traditional medicine at the Seth G.S. Medical College and KEM Hospital, Mumbai and the other for drug development from natural/plant sources at CDRI, Lucknow. For pre-clinical toxicological studies of new plant based drugs or chemical entities, studies are proposed to be undertaken at NIN, Hyderabad. The Central Biostatistical Monitoring Unit (CBMU) of the National Institute of Epidemiology (NIE) at Chennai earlier known as the Institute for Research in Medical Statistics (IRMS) continued to lend its support in designing the protocols and monitoring the multicentric trial.

As part of the expanded activities in traditional medicine, a closer interaction with the Department of Indian Systems of Medicine and Homeopathy (ISM & H) and the respective Councils was maintained. The National Institute of Pharmaceutical Education and Research (NIPER), Chandigarh has been identified for establishing a

second Unit for Standardisation and Quality Control of Selected Herbal Remedies/Natural Products. For cultivation of selected medicinal plants and for agro-technology of endangered species of medicinal plants like *Picrorrhiza kurroa*, Institute of Himalayan Bioresource Technology, Palampur has been identified.

At University College of Medical Sciences, Delhi, four compounds with anti-diabetic activity have been isolated from *Eugenia jambolana* and for these Indian and international patents have been filed.

Standardisation, Quality Control and Formulations for Selected Natural Products/Herbal Drugs

The activities carried out in this area at the Advanced Centre at the Regional Research Laboratory (RRL), Jammu involved studies on microbial and heavy metal load of natural products or herbal drugs, characterisation of the active principles and isolation of biomarkers to facilitate preparation of monographs. Out of 13 markers isolated from *Vijaysar*, 6 have been reported. Two new markers VS-12 and VS-13 were isolated and the structure of VS-08 was revised. VS-08 and VS-12 possessed a very rare isoaurone skeleton. HPLC fingerprinting of the extract with quantitative estimation of the markers and their concentration ranges were established. In addition to six months' accelerated stability studies, the shelf life of *Vijaysar* capsules for 2 years at room temperature was also studied. VS-04 and VS-09 showed hypoglycaemic activity at 10mg/kg orally. General pharmacology showed no anti-inflammatory and antipyretic activities. The Centre continues to do further studies on the pharmacology of *Vijaysar* and preparation of formulations for the clinical trial.

Drug Development from Natural/Plant Products

Studies were carried out at the Advanced Centre at CDRI, Lucknow on Picroliv and plant products from *Terminalia chebula* and *Centella asiatica*. Picroliv is undergoing clinical trial as a hepatoprotective agent. Phase II multicentric trials have been completed and phase III trials are to be initiated. LC-MS fingerprinting of 7 compounds has been carried out besides identifying the two markers, picroside I and II. The HPLC method for estimating the active marker compound of *T.chebula*, a hepatoprotective plant and marker compounds asiaticoside (active) and madicassoside of *C.asiatica*, a wound healing plant drug was also standardised. Further work on the pharmacology of these products is being continued.

Clinical Pharmacology in Traditional Medicine

At the Advanced Centre at the Seth GS Medical College and KEM Hospital, Mumbai, controlled clinical trials are proposed to be undertaken on *Azadirachta indica* for wound healing and on medicated oral rehydration solution (containing in addition to the WHO recommended ORS, *Zingiber officinalis*, *Cyperus rotundus* and *Cumminum cyminum*) for diarrhoea. On the basis of fingerprinting, in-house standardisation of *A.indica* formulation for use in the study has been taken up. The Centre also proposes to study the mechanism of action of *Vijaysar* which has shown effective antidiabetic properties in various clinical trials undertaken.

Supporting Facilities

The National Institute of Epidemiology (NIE) was established in July, 1999 by merging the CJIL Field Unit, Avadi

with the Institute for Research in Medical Statistics (IRMS), Chennai with the main objective of strengthening the epidemiological base in the country. Epidemiological studies were also conducted at the Institute for Research in Medical Statistics (IRMS), New Delhi.

NATIONAL INSTITUTE OF EPIDEMIOLOGY, CHENNAI

In collaboration with the Diabetes Department of the Voluntary Health Services, Chennai, the NIE conducted a cluster sample survey in Chennai City to find the prevalence of known diabetics. Thirty Corporation Divisions were chosen by PPS linear systematic sampling procedure. A cluster of 1200 households was surveyed in each selected Division. Analysis of the data indicated that the age-standardized prevalence of known diabetics was 2.55% (95% CI 2.5% - 2.8%). The prevalence of type II diabetes was 4.2% (95% CI 4.0%-4.3%).

A survey was conducted in a district in Tamil Nadu to identify the disabilities and handicaps in the elderly population. Thirty villages were selected by PPS techniques and 105 households were covered in each village. A total of 974 individuals were studied. The interim findings of this study reveal that 68% of the elderly had at least one functional limitation and visual disability (50%) was found to be most important preventable disability influencing the daily activities of the geriatric population.

INSTITUTE FOR RESEARCH IN MEDICAL STATISTICS, NEW DELHI

The IRMS, New Delhi has undertaken several studies of current national health importance. Coverage evaluation surveys have been undertaken in 90 districts of the country giving due representation to all States and Union Territories. The evaluation covered all vaccines *viz.* BCG, DPT, OPV, measles for children and TT for pregnant women. For this the WHO 30 cluster survey methodology was used. Information was collected for about 19,000 children and an equal number of pregnant women. The survey revealed that the immunisation programme covered about 90 per cent of target children and over 85 per cent of pregnant women. About 63 per cent of children received all the vaccines and 78 per cent of pregnant women received both the doses of TT booster. Further, 53 per cent of pregnant women received full package of antenatal care (ANC) *i.e.* minimum three ANC visits, 2 doses of TT booster and iron-folic acid tablets. In the states of Bihar, Rajasthan, UP, MP and NE states (combined) coverage levels were relatively lower. Further, the coverage levels were also lower for children of illiterate mothers and in small, inaccessible and tribal villages. Efforts are needed for information, education and communication (IEC) activities targeted to educate the mothers specially in rural areas.

INDO-FOREIGN COLLABORATION

The Indo-Foreign Cell (IFC) of the Council coordinates collaboration in biomedical research between India and other countries/international agencies. During 1999-2000, the IFC facilitated (with financial support) the organisation of two Indo-German Workshops _ one on `Molecular Aspects of the Regulation of Ovarian Function' at AIIMS, New Delhi, in October, 1999 and another on `Biological Aspects for the Individualisation of Radiotherapy' at Thiruvananthapuram in February, 2000. An Indo-US Meeting on HIV/AIDS was organised at TRC, Chennai in January, 2000. The IFC also supported the visit of Government of India delegates for various international meetings.

The WHO Country Budget for 1998-99 facilitated the organisation of Workshops on Leprosy, Tribal Health,

Leishmaniasis and Research Management in ICMR institutes during the year 1999-2000.

INTELLECTUAL PROPERTY RIGHTS

The activities relating to intellectual property rights continued during the year under review. The ICMR institutes as well as the Technical Divisions of the Hqrs. are being provided necessary technical inputs in terms of advice and assistance on all intellectual property rights related issues. Some patents were filed during the year.

TRAINING PROGRAMMES

The IRMS continued to provide necessary consultancy services and support to biomedical scientists. Need-based training and orientation programmes were organised for students and trainees from International Institute for Population Sciences, Mumbai; Central Statistical Organisation, Delhi and M.Sc. students of Kurukshetra University.

The Institute continued its collaborative arrangement with various Universities for Ph.D. in Statistics. Other ICMR institutes such as IRR, Mumbai; NIN, Hyderabad; IOP, Delhi; NIOH, Ahmedabad *etc. c*onducted training programmes in their respective areas.

The facilities of the TRC have been utilized by the WHO and the Central Tuberculosis Division to organize a training programme for newly recruited WHO TB consultants. The TRC has also been chosen by International Clinical Epidemiology Network (INCLEN) to impart training to laboratory technicians attached to various medical colleges in the country. The Centre is also assisting the National Tuberculosis Institute, Bangalore to carry out a national sample survey to determine the prevalence of infection in the country.

Publication,Information and Communication

During 1999-2000, the Council continued to publish its periodicals - the Indian Journal of Medical Research, the ICMR Bulletin, the ICMR *Patrika* as well as English and Hindi versions of the Annual Report of the ICMR. For dissemination of health information, the Council organized popular lectures in Hindi and English, participated in the *Swadeshi Vigyan Mela* and the World Book Fair, 2000.

PUBLICATIONS

Periodicals

During the period under report, the Indian Journal of Medical Research (IJMR) continued to be indexed and abstracted by all major global current awareness and alerting services. An Expert Group for the IJMR was constituted during the year to have suggestions for the overall improvement of the Journal. The first meeting of the Group was held in November, 1999. The recommendations/suggestions made by the Group are being implemented. A number of articles published in the IJMR were also featured in the media including newspapers.

The ICMR Bulletin published articles on various topics of general interest *viz.* Increased male responsibility and participation : A key to improving the reproductive health; Silicosis _ An uncommonly diagnosed common

occupational disease; Multi-drug resistant tuberculosis *etc*. The December 1999 issue of the Bulletin featured an article on "Children and young people in the context of HIV/AIDS : Listen, learn, live! World AIDS campaign with children and young people" to commemorate the World AIDS Day. Articles published in the Bulletin such as `*Alliums* as food for healthy life' and `Risk of aluminium toxicity in the Indian context' were featured in news stories.

Other Publications

ICMR *Patrika*, a monthly Hindi publication of the Council was brought out simultaneously with its English version *i.e.* ICMR Bulletin.

The Annual Report of the Director-General continued to be brought out this year too both in English and Hindi but with increased (A4) size, better lay out and incorporating details on the publications of ICMR institutes, ICMR aided seminars, symposia *etc.*, research schemes and fellowships funded during the year, and training courses held.

The Council's National Institute of Nutrition brought out a manual titled `Dietary Guidelines for Indians' and another publication `Dietary Guidelines for Vulnerable Groups' (in Telugu) in collaboration with CARE.

Monograph on Medicinal Plants of India

It has been planned to update, revise and enlarge the first volume of Monograph on Medicinal Plants of India so as to cover scientific information on medicinal plants upto 1998. The activities during the year focussed on collection of additional data on about 300 medicinal plants which included not only plants covered in Vol.I but also those not covered earlier. In addition computerization of data collected earlier is also being done.

INFORMATICS AND COMMUNICATION

Biomedical Information

The ICMR-NIC Centre for Biomedical Information continued to provide biomedical information services from the MEDLARS databases of the National Library of Medicine (NLM). Access to Medline database available at NIC Hqrs. was provided to 8 medical colleges during this period. User centres have been provided access to data from 1990 onwards; data prior to 1990 is provided from MEDLINE database on CDROM. A total 1791 search requests were received at the Centre both over NICMAIL/e-mail and from users visiting the Centre. Information was provided from the MEDLARS as well as resources available over Internet plus CDROM databases. The Centre also continued to provide full text of journal articles from ADONIS database and articles not available in ADONIS were procured from NLM's DOCLINE.

New CDROM databases - Cochrane, Patient Education Library, Drug Information Full text, IPA, Pascal Biomed and Allied & Complementary Medicine were procured. Out of these, IPA, Patient Education Library and Cochrane databases are full text while the rest are bibliographic.

Disease Updates were prepared on Japanese encephalitis (for Andhra Pradesh) by compiling information from the resources available on Internet. This information was distributed to health professionals tackling the

epidemic. A video conference of specialists from New Delhi, Pune and Hyderabad was organised to discuss the prevention and management of Japanese encephalitis.

The IndMED database developed through this Centre at present has 75 journals from 1986 onwards and is accessible from the website *http://indmed.delhi.nic.in.* The Union Catalogue of Biomedical Periodicals (currently till December 1998) is being updated. Holding data of all the libraries are being collected for 1999.

A number of training programmes were conducted on the online searching of bibliographical databases in different cities across the country. A Workshop on Biomedical Research and the Internet was also organised in March 2000. The participants were medical/library professionals from ICMR institutes as well as from medical institutions in Delhi.

Scientometrics

A new edition of the Directory of Journals Publishing Papers from ICMR Institutes (earlier called Publishing Journal Directory of ICMR) has been brought out with additional value-added inputs, updating analysis of the publications of ICMR institutes up to 1998 and initiating analysis of global AIDS research.

The present edition of the directory contains information on 634 publishing journals from the Council's permanent institutes for the period 1980-94. The coverage profile of these journals (brought out from 37 countries) in various secondary services indicates that the maximum number of journals are covered in BIOSIS (467) followed by Current Contents (384), Index Medicus (368), Excerpta Medica (363), Science Citation Index (Source Journals) (349), Indian Science Abstracts (133) and Tropical Diseases Bulletin (78). When the country of publication of these journals was studied, India tops the tally with 169 journals followed by USA (153), UK(127), The Netherlands (31), Switzerland and Germany with 26 journals each and Japan (15) and Denmark (10).

The analysis of HIV/AIDS research was taken up with publications downloaded from the MEDLARS database for the period 1990-94. Analysis showed that there was a gradual decline in the published literature on AIDS during the study period _ 1990 (3765); 1991 (3237); 1992 (3204); 1993 (2970) and 1994 (2079). The major countries publishing papers on HIV/AIDS were USA (6841); France (759); UK (753), Italy (633) and Germany (529). India ranked 17th in the hierarchy with just 74 papers. A total of 1982 journals were used to communicate this research; core journals being AIDS, Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology, AIDS Research and Human Retroviruses, AIDS Education and Prevention, Journal of Virology, Journal of Infectious Diseases and AIDS Care. The authorship profile showed that in common with other areas, multi-authorship trend was clearly visible.

Analysis of SCI/JCR-based research output of ICMR institutes in terms of average impact factor/paper has been initiated.

Bioinformatics Centre

The Bioinformatics Centre has been set up in the Council in June 1999 by expanding the activities of the existing Integrated Research Information System (IRIS). These activities include the following: to publish information available with and generated by ICMR on the web; to work as a platform to publish information

available with other key institutes on the web; to provide good internet access to ICMR institutes and other key institutes; to establish communication links with other ICMR institutes, Bioinformatics Centres of DBT, other key institutes and funding agencies; and to provide internet related services for health research planning to ICMR scientists and program managers.

Work on networking of seven ICMR institutes was initiated during the year. These institutes are being provided with Local Area Network (LAN), Internet connectivity of 64 kbps or higher, network server, scanner, CD writer *etc.* Good internet connectivity using RF and VSAT from the NIC is available to the Council. Users on the network are provided access to the internet through proxy server and to the e-mail through Microsoft exchange server. The ICMR web site *(http://www.icmr.nic.in)* has been developed in-house and hosted from a server in the NIC. The site gives highlights of ICMR activities and achievements, history of ICMR, e-mail directory of ICMR scientists, information on ICMR awards, news and announcement of events, ICMR Bulletin, list of ICMR publications, informative write ups on ICMR institutes/centres, searchable list of scientists and their publications, details of various extramural research grants including application forms for downloading, searchable information on funded projects since 1982 *etc*. Research results of ICMR institutes and of epidemiological surveys *etc.* will also be published on the site.

Biomedical Exhibitions/National Science Day Celebrations/Book Fairs

The Council and its Institutes/Centres organized various activities during the year for dissemination of biomedical information and information on ICMR's activities to different target groups.

As part of the Hindi Day celebrations of the Council, a popular lecture (in Hindi) on "Health, Environment and Law" *(Swasthya, Paryavaran aur Kanoon)* by Dr.M.C.Gupta, Professor and Head, Department of Education and Training, National Institute of Health and Family Welfare, New Delhi was organized at the Council's Headquarters.

The various Institutes/Centres of the Council celebrated the National Science Day (NSD) in February/March 2000 with focus on the theme "Recreating interest in basic sciences". Various events like lectures/ discussions, open houses / seminars /symposia, display/ demonstrations/ exhibitions *etc.* were organized for general public and school children in addition to debate/ essay/ drawing /quiz competitions for school children. CJIL, Agra; RMRC, Jabalpur; DMRC, Jodhpur and RMRI, Patna organised programmes in Hindi including debate competition, quiz programmes for school children, popular lectures, exhibitions, demonstrations *etc*. for laymen. The ICMR Headquarters organized a lecture on "New Challenges in Molecular Medicine" by Dr.Indira Nath, INSA S.N.Bose Research Professor, Department of Biotechnology, All India Institute of Medical Sciences, New Delhi.

The ICMR Headquarters, NIN, Hyderabad; NIOH, Ahmedabad and MRC, Delhi participated in a science and technology exhibition organized as part of the *Swadeshi Vigyan Mela* at New Delhi during February 2000.

The Council participated in the 5th Delhi Book Fair (August, 1999) and 14th New Delhi World Book Fair (February, 2000) organized at New Delhi.

Human Resource Development

As part of the image-building exercise of the Council, a new initiative was taken up to strengthen the capability of ICMR Institutes towards communicating with the mass media as also the lay public. Such a capability strengthening is most essential at the peripheral level as several institutes are not adequately equipped to face the new challenges and demands of the media and the public. A Workshop on IEC in Biomedical Research was held at the National Institute of Nutrition, Hyderabad during December, 1999 to address this issue. The participants for this in-house training programme included middle level scientists and other staff from various ICMR Institutes. The basic objective of the Workshop was to prepare the ICMR Institutes to have a nucleus and infrastructure relating to communicating with the media. This would also serve as an interface between the institutes' scientists and the media to improve the overall image of the ICMR in a positive way. The participants were exposed to various facets of how the print and electronic media operates as also the various constraints faced by the media personnel in getting information from science agencies. The participants and the media people interacted on issues relating to the better coverage of health science in the media and how to mutually cooperate to promote better media coverage. In addition, the participants were also trained to access latest information from the internet and electronic databases. They were also trained to present scientific information to lay people essentially to relay messages of public health interest.

A pre-tested questionnaire was used to evaluate the Workshop. The feed-back received showed that the participants felt that the Workshop was very useful. As this was the first Workshop of this kind some suggestions received for partial reconstructing would be incorporated in the future training programmes.

Appendix IV

List of Publications of ICMR Institutes

Adak, T., Kaur, S., Singh, O.P. Comparative susceptibility of different members of the*Anopheles culicifacies* complex to *Plasmodium vivax. Trans R Soc Trop Med Hyg* 93 (1999) 573.

Adak, T., Wattal, S., Kaur, S., Sharma, V.P. Genetics of creamish white, an eye color mutant in *Anopheles stephensi. J Hered* 90 (1999) 573.

Adhikari, P., Pereira, P., Padbidri, V.S., Chowta, N., Thakare, J.P. Lesser known clinical features of dengue fever. *J Assoc Physicians India* 47 (1999) 1158.

Ahamed, J., Gangopadhyay, J.,Kundu, M., Sinha, A.K. Mechanisms of quinolone resistance in clinical isolates of *Shigella dysenteriae. Antimicrob Agents Chemother* 43 (1999) 2333.

Anitha Kumari, S., Sree Ramkumar, N., Singotamu, L. Scanning electron microscope studies on the gills of fishes collected from a polluted fresh water lake. *Scanning* 21 (1999) 157.

Ansari, M.A., Vasudevan, P., Tandon, M., Razdan, R.K. Larvicidal and mosquito repellent action of Peppermint *(Mentha piperata)* oil. *Biores Technol* 71 (1999) 267.

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lack of intrafamilial spread. *Indian J Gastroenterol* 19 (2000) 24.

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Babu, B.V., Naidu, J.M. Genetic variability of blood and saliva antigens and serum proteins among sub tribes of Mali from Andhra Pradesh, India. *Anthropol Anz (Germany)* 57 (1999) 105.

Babu, B.V., Naidu, J.M. Sickle cell disease: a neglected public health problem among scheduled tribes. In: *Current Status of Scheduled Tribes in India* (Ed. H.C. Upadhyay) Anmol Publications, New Delhi (1999).

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Appendix V

Training Programmes Conducted by ICMR Institutes during 1999-2000

Tuberculosis

At the Tuberculosis Research Centre, Chennai:

• Workshop on Involving Private Practitioners in RNTCP (November 12-13, 1999).

Leprosy

At the Central JALMA Institute for Leprosy, Agra:

• Training Course for Medical Officers working under the National Leprosy

Eradication Programme (April and September, 1999).

At the National Institute of Epidemiology, Chennai:

• Workshop on Simulation Model for Leprosy Transmission and Control (April 5, 1999; WHO sponsored).

• Workshop on Strategies of Impact Assessment in Leprosy Elimination (April 6-8, 1999; WHO sponsored).

Diarrhoeal Diseases

At the National Institute of Cholera & Enteric Diseases, Calcutta:

• Training Course on Management of Acute Diarrhoea with Special Emphasis on Cholera at Dibrugarh and Guwahati (Assam) and Malda (W. Bengal) (November 9-11 and 27-29,1999; December 10-16, 1999 and March 22-24, 2000; UNICEF sponsored).

Leptospirosis

At the Regional Medical Research Centre, Port Blair:

• A Three Week Workshop on Laboratory Diagnosis of Leptospirosis (from April 19, 1999).

Malaria

At the Malaria Research Centre Field Station, Nadiad (Distt Kheda):

• Training Course on Malaria Microscopy for Laboratory Technicians (January 3-7and 17-21, 2000; and February 7-11, 2000).

Filariasis

At the Vector Control Research Centre, Pondicherry

• Workshop on Community Directed Treatment of Lymphatic Filariasis (November 1-5, 1999; WHO sponsored).

Leishmaniasis

At the Rajendra Memorial Research Institute of Medical Sciences, Patna:

• Workshop on Integrated Control of Leishmaniasis (April 7-9, 1999; WHO

sponsored).

Vector-borne Diseases/Entomology

At the Vector Control Research Centre, Pondicherry:

• International Training Course on Comprehensive Vector Control (August 30 - September 11, 1999; WHOsponsored).

• Postgraduate Diploma in Medical Entomology (from July 1999).

At the Malaria Research Centre, Delhi:

• Training Course on Vector-borne Diseases for Entomologists/Biologists (January 10 - February 18, 2000).

Virology

At the National Institute of Virology, Pune:

• Intercountry Workshop on Immunology, Vaccinology and Biotechnology Applied to Infectious Diseases (November 24 - December 10, 1999; WHO/IUIS sponsored).

At the Enterovirus Research Centre, Mumbai:

• Laboratory Workshop on Intratypic Differentiation of Poliovirus Isolates (February 14-23, 2000).

• Laboratory Workshop on Isolation and Identification of Polioviruses (March, 2000).

Reproductive Biology

At the Institute for Research in Reproduction, Mumbai:

• Training Course on Molecular Techniques in Ovarian Function (September 27 - October 2, 1999).

• Indo-US Contraceptive and Reproductive Health Research Initiatives Clinical Trial Methodology Training Course (October 30 - November 5, 1999).

• Training Course on Cytological Detection of Reproductive Tract Infections (December 13-17, 1999).

Endocrinology

At the National Institute of Nutrition,, Hyderabad:

• Annual Certificate Course on Endocrinological Techniques and their Application (August 1 - September 15, 1999).

Nutrition

At the National Institute of Nutrition, Hyderabad:

• M.Sc. in Applied Nutrition (June 1, 1999 - February 28, 2000).

• Postgraduate Certificate Course in Nutrition (December 1, 1999 - February 28, 2000).

Occupational/Environmental Health

At the National Institute of Occupational Health, Ahmedabad:

• Seminar on Occupational Health and Diseases (April 18, 1999; WHO sponsored).

• Workshop on Occupational Health Related Problems of Agate Workers and its Prevention (April 24, 1999; WHO sponsored).

• Training Programme on Occupational Health and Dust Diseases in Miners (May 29 - June 3, 1999; WHOsponsored).

• Training Programme on Occupational Health for ESIS/ESIC Medical Officers (June 21-25, 1999; WHOsponsored).

• Training Courses on Industrial Hygiene (July 5-10; October 25-30, 1999; WHO sponsored).

• Training Programme on Environmental Epidemiology (November 15-19, 1999; WHO sponsored).

• Workshop on Preventing Illness and Injury related to Industrial Accidents (December 15-17, 1999; sponsored by CDC, Atlanta, USA).

• Training Programme for Research Engineers of Indian Council of Agricultural Research (February 14-18, 2000).

• Workshop on Chemicals and Women's Health (March 2-4, 2000; WHO

sponsored).

• Training Programme on Dust related Diseases - Silicosis (March 7-8, 2000).

Oncology/Molecular Biology

At the Institute of Cytology and Preventive Oncology, New Delhi:

• Contact Programme for Medical and Biomedical Postgraduates on Basic Molecular Biology in Human Health and Disease (February 16-25, 2000; DST sponsored).

Haematology

At the Institute of Immunohaematology, Mumbai:

• Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 31 - October 29, 1999).

• Training Course in Blood Group Serology and Blood Bank Methodology for Blood Bank Technicians (August31 - September 30, 1999).

• Training Course in Advanced Haematology and Immunohaematology (October 15-29, 1999).

Laboratory Animal Technology

At the National Centre for Laboratory Animal Sciences, Hyderabad:

• Training Course for Laboratory Animal Technicians (June 14 - July 30, 1999).

• Training Course for Laboratory Animal Supervisors (September 1 - November 30, 1999).

Biomedical Statistics/Epidemiology

At the National Institute of Epidemiology, Chennai:

• Basic Course in Statistics for Medical Officers (August 16-21, 1999).

• Basic Course in Statistics for Postgraduate Medical Students (October 25-28, 1999).

At the Vector Control Research Centre, Pondicherry:

• Training Course in Epidemiology and Control of Infectious Diseases (March 2000).

At the Tuberculosis Research Centre, Chennai:

• National Workshop on Health Research Management (September 14-16, 1999; WHO sponsored).

Appendix VI

ICMR Aided Symposia/Seminars/Workshops/Conferences

The following ICMR aided Symposia/Seminars/Workshops/Conferences were held during the year 1999-2000:

1. Workshop on HIV/AIDS/STDs and Healthy Life Style organised by Department of Social and Preventive Medicine, MKCG Medical College, Berhampur (April 10-11, 1999).

2. International Symposium on Transcription Assembly and Nucleic Acid-Protein Interaction organised by Department of Microbiology and Cell Biology, Indian Institute of Science, Bangalore (June 5-7, 1999).

3. Symposium on Bone Health organised by National Institute of Nutrition, Hyderabad (June 7, 1999).

4. Workshop on Research Methodology and Writing a Scientific Paper for Publication organised by Department of Pharmacology, Perundurai Medical College, Perundurai (June 18, 1999)

5. Workshop on Medical Communication: Writing in the Margins organised by

L.V. Prasad Eye Institute, Hyderabad (July 24-25, 1999).

6. Workshop on Stereology, Image Processing and Quantitative Image Analysis in Biomedical Research organised by Department of Anatomy, All India Institute of Medical Sciences, New Delhi (July 26-28, 1999).

7. International Symposium on Atraumatic Restorative Treatment organised by SHIRAZ-47, 3rd East Street, Kamraj Nagar, Chennai (August 12-14, 1999).

8. Biennial National Conference of the Association of Gerontology on Challenges of ageing in the 21st Century organised by Heritage Medical Centre, Hyderabad (August 20-21, 1999).

9. X Annual Meeting of the Indian Society for the Study of Reproduction and Fertility and National Symposium on Signal Transduction in Reproduction, Hormones, Receptors and Growth Factors organised by Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram (September 9-11, 1999).

10. Symposium on Cardiology for the Next Millennium organised by Sri Ramachandra Medical College and Research Institute, Cardiac Care Centre, Chennai (September 10-12, 1999).

11. Symposium on Research in Molecular Biology and Biotechnology in India: Challenges in the Next Millennium organised by Indian Institute of Chemical Biology, Calcutta (September 13-14, 1999).

12. International Seminar on Disability Caused by Mental Disorders organised by Schizophrenia Research Foundation, Chennai (September 15-17, 1999)

13. XXI Biennial Conference of Indian Association of Leprologists organised by Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Chandigarh (September 17-19, 1999).

14. I Conference of the Council of Behavioural Scientists organised by Central JALMA Institute for Leprosy, Agra (October 2-3, 1999).

15. National Symposium and Update on Problem Areas in Diagnostic Oncopathology organised by Department of Pathology, Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha (October 8-10, 1999).

16. IV Postgraduate Course on Endocrine Surgery and International Workshop on Endocrine Telesurgery organised by Department of Endocrine Surgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow (October 25-29, 1999).

17. India Consensus Development Workshop on Standards of Care in HIV

Disease organised by YRG Centre for AIDS Research and Education, Chennai (October 28-30, 1999).

18. International Workshop on Challenges to Scientists to Preserve the Mother Earth in the Next Millennium organised by National Environmental Science Academy, New Delhi at Pondicherry (October 28-30, 1999).

19. X All India Congress of Cytology and Genetics organised by Department of Zoology, University of Kalyani, Kalyani (October 29-31, 1999).

20. III National Conference of the Indian Association of Cardiovascular and Thoracic Anaesthesiologists organised by Department of Cardiac Anaesthesia, Cardiothoracic Centre, All India Institute of Medical Sciences, New Delhi (November 12-14, 1999).

21. XIX Annual Convention of Neonatology Forum organised by Agadi Hospital, Bangalore (November 18-19, 1999).

22. Symposium on Microbial Infections of the Central Nervous System organised by Department of Parasitology, Postgraduate Institute of Medical Education and Research, Chandigarh (November 20, 1999).

23. XXXII Annual Meeting of Nutrition Society of India organised by Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore (November 25-26, 1999).

24. National Conference on Challenges in HIV/AIDS in the Next Millennium organised by Department of Medicine, All India Institute of Medical Sciences, New Delhi (November 25-27, 1999).

25. National Symposium on Advances and Applications of Animal Sciences for Human Welfare and Zoological Congress of Eastern India organised by Department of Zoology, University of North Bengal, Siliguri at Darjeeling (November 25-28, 1999).

26. International Conference on Man, Environment and Nature organised by Centre for Study of Man and Environment, Parivesh Kendra, Calcutta (November 26-28, 1999).

27. XXIII All India Cell Biology Conference organised by Centre for Cellular and Molecular Biology, Hyderabad (November 27-29, 1999).

28. XXIV National Conference and International CME of Indian Society of Blood Transfusion and Immuno-haematology organised by Department of Transfusion Medicine, Sanjay Gandhi Postgraduate Institute of Medical

Sciences, Lucknow (November 27-30, 1999).

29. International Symposium on Chemotherapy: Problems and Perspectives in 21st Century organised by Department of Pharmacology, K.G. Medical College, Lucknow (November 28-29, 1999).

30. XI Annual Conference of the Physiological Society of India organised by Department of Physiology, Vallabhbhai Patel Chest Institute, Delhi (November 28-30, 1999).

31. International Congress on Frontiers in Pharmacology and Therapeutics in 21st Century organised by Department of Pharmacology, All India Institute of Medical Sciences, New Delhi (December 1-4, 1999).

32. XVII Annual Conference of Indian Society for Medical Statistics organised by Department of Biostatistics, National Institute of Mental Health and Neurosciences, Bangalore (December 2-4, 1999).

33. Workshop on the Role of Nitric Oxide Gas in the Treatment of High Altitude Pulmonary Edema and Adult Respiration Distress Syndrome organised by Defence Institute of Physiology and Allied Sciences, Delhi at Pune (December 4, 1999).

34. XVII Annual Conference of Indian Academy of Neurosciences organised by School of Studies in Zoology, Jiwaji University, Gwalior (December 6-8, 1999).

35. Indo-European Seminar-cum-Workshop on Advances in Human Cytogenetics organised by Department of Medical Genetics, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow (December 6-9, 1999).

36. XXXI Annual Conference of the Society of Nuclear Medicine organised by Department of Imaging Science, Meenakshi Mission Hospital and Research Centre, Madurai (December 8-11, 1999).

37. National Seminar on Newer Vistas in Bioactive Agents organised by Gandhigram Rural Institute, Gandhigram (December 9-10, 1999).

38. International Symposium on Cancer Control in Developing Countries organised by Chittaranjan National Cancer Institute, Calcutta (December 10, 1999).

39. XV Asia Pacific Cancer Conference organised by Cancer Institute (WIA), Chennai (December 12-15, 1999).

40. II International Conference on Contaminants in the Soil Environment in Australasia - Pacific Region organised by Council of Scientific and Industrial

Research, New Delhi (December 12-17, 1999).

41. International Conference on Medical Diagnostic Techniques and Procedures organised by Department of Applied Mechanics, Indian Institute of Technology, Chennai (December 15-17, 1999).

42. III International Symposium on Cognition, Education and Mental Health organised by Department of Psychology, Banaras Hindu University, Varanasi (December 16-19, 1999).

43. LXVIII Annual Meeting of Society of Biological Chemists (India) and Symposium on Current Trends in Biology organised by Indian Institute of Science, Bangalore (December 27-29, 1999).

44. XVIII National Symposium on Reproductive Biology and Comparative Endocrinology organised by Department of Zoology, Madras Christian College, Chennai (December 27-29, 1999).

45. XLIII All India Congress of Obstetrics and Gynaecology organised by Department of Obstetrics and Gynaecology, K.G. Medical College, Lucknow (December 27-30, 1999).

46. LXXXVII Session of the Indian Science Congress organised by University of Pune, Pune (January 3-7, 2000).

47. XXV Annual Conference of Indian Society of Human Genetics and II Conference of South Asia-Pacific Society of Human Genetics organised by Anthropological Society of India, Nagpur (January 9-10, 2000).

48. Seminar on Foods and Nutrition Update_Challenges Ahead organised by Department of Food and Nutrition, Lady Irwin College, New Delhi (January 14-15, 2000).

49. XIX Annual Convention of Indian Association for Cancer Research organised by Amla Cancer Research Centre, Thrissur (January 21-23, 2000).

50. Workshop on Gene Amplification Techniques in Disease Diagnosis and National Conference of Laboratory Medicine organised by Department of Laboratory Medicine, All India Institute of Medical Sciences, New Delhi (January 21-25, 2000).

51. Symposium on Biomedical Engineering and Nuclear Medicine and Workshop on Medical Imaging organised by Electronics Division, Modular Laboratories, Bhabha Atomic Research Centre, Mumbai (January 24-29, 2000).

52. International Symposium on Cataract: Molecular and Epidemiological

Aspects organised by Department of Genetics, Dr. A.L. Mudaliar PG Institute of Basic Medical Sciences, University of Madras, Chennai (January 31- February 1, 2000).

53. National Seminar of the New Millennium on Medicinal Plants Cultivation _ Problems, Packages, Practices and Marketing organised by St. Xavier's College, Palayamkottai (February 3-5, 2000).

54. I International Symposium on Mycoses in the New Millennium: Challenges and Strategies organised by Sri Ramachandra Medical College and Research Institute, Chennai (February 9-11, 2000).

55. Annual Conference of UP Chapter of Cardiological Society of India organised by M.L.B. Medical College, Jhansi (February 11-12, 2000).

56. V International Symposium on Vectors and Vector-borne Diseases organised by Department of Zoology, Punjabi University, Patiala (February 16-18, 2000).

57. International Conference on Radiation Biology organised by Regional Cancer Centre, Thiruvananthapuram (February 17-19, 2000).

58. National Conference on Naturopathy and Yoga organised by *Nisargopchar Gramsudhar*Trust, Pune (February 17-20, 2000).

59. International Workshop on Neonatal Surgery organised by Department of Paediatric Surgery, All India Institute of Medical Sciences, New Delhi (February 18-20, 2000).

60. International Symposium on Good Laboratory Practice organised by Centre of Cellular and Molecular Biology, Hyderabad (February 27-28, 2000).

61. VIII Annual Meeting of the Molecular Immunology Forum organised by Department of Biochemistry, Indian Institute of Science, Bangalore (March 3-5, 2000).

62. V World Conference on Injury Prevention and Control organised by Indian Institute of Technology, New Delhi (March 5-8, 2000).

63. National Workshop on Hospital Waste Management organised by International Development Centre, New Delhi (March 7-8, 2000).

64. Symposium on Public Health Challenges in the New Millennium organised by Department of Community Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh (March 25-26, 2000).

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43. LXVIII Annual Meeting of Society of Biological Chemists (India) and Symposium on Current Trends in Biology organised by Indian Institute of Science, Bangalore (December 27-29, 1999).

44. XVIII National Symposium on Reproductive Biology and Comparative Endocrinology organised by Department of Zoology, Madras Christian College, Chennai (December 27-29, 1999).

45. XLIII All India Congress of Obstetrics and Gynaecology organised by Department of Obstetrics and Gynaecology, K.G. Medical College, Lucknow (December 27-30, 1999).

46. LXXXVII Session of the Indian Science Congress organised by University of Pune, Pune (January 3-7, 2000).

47. XXV Annual Conference of Indian Society of Human Genetics and II Conference of South Asia-Pacific Society of Human Genetics organised by

Anthropological Society of India, Nagpur (January 9-10, 2000).

48. Seminar on Foods and Nutrition Update_Challenges Ahead organised by Department of Food and Nutrition, Lady Irwin College, New Delhi (January 14-15, 2000).

49. XIX Annual Convention of Indian Association for Cancer Research organised by Amla Cancer Research Centre, Thrissur (January 21-23, 2000).

50. Workshop on Gene Amplification Techniques in Disease Diagnosis and National Conference of Laboratory Medicine organised by Department of Laboratory Medicine, All India Institute of Medical Sciences, New Delhi (January 21-25, 2000).

51. Symposium on Biomedical Engineering and Nuclear Medicine and Workshop on Medical Imaging organised by Electronics Division, Modular Laboratories, Bhabha Atomic Research Centre, Mumbai (January 24-29, 2000).

52. International Symposium on Cataract: Molecular and Epidemiological Aspects organised by Department of Genetics, Dr. A.L. Mudaliar PG Institute of Basic Medical Sciences, University of Madras, Chennai (January 31- February 1, 2000).

53. National Seminar of the New Millennium on Medicinal Plants Cultivation _ Problems, Packages, Practices and Marketing organised by St. Xavier's College, Palayamkottai (February 3-5, 2000).

54. I International Symposium on Mycoses in the New Millennium: Challenges and Strategies organised by Sri Ramachandra Medical College and Research Institute, Chennai (February 9-11, 2000).

55. Annual Conference of UP Chapter of Cardiological Society of India organised by M.L.B. Medical College, Jhansi (February 11-12, 2000).

56. V International Symposium on Vectors and Vector-borne Diseases organised by Department of Zoology, Punjabi University, Patiala (February 16-18, 2000).

57. International Conference on Radiation Biology organised by Regional Cancer Centre, Thiruvananthapuram (February 17-19, 2000).

58. National Conference on Naturopathy and Yoga organised by *Nisargopchar Gramsudhar*Trust, Pune (February 17-20, 2000).

59. International Workshop on Neonatal Surgery organised by Department of Paediatric Surgery, All India Institute of Medical Sciences, New Delhi (February

18-20, 2000).

60. International Symposium on Good Laboratory Practice organised by Centre of Cellular and Molecular Biology, Hyderabad (February 27-28, 2000).

61. VIII Annual Meeting of the Molecular Immunology Forum organised by Department of Biochemistry, Indian Institute of Science, Bangalore (March 3-5, 2000).

62. V World Conference on Injury Prevention and Control organised by Indian Institute of Technology, New Delhi (March 5-8, 2000).

63. National Workshop on Hospital Waste Management organised by International Development Centre, New Delhi (March 7-8, 2000).

64. Symposium on Public Health Challenges in the New Millennium organised by Department of Community Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh (March 25-26, 2000).

List of Research Schemes Funded During 1999-2000

Epidemiology and Communicable Diseases

Sl. No.	*Title of the Project*	*Investigator/Institution*	*Grant released during the yr (Rs. in lakhs)*
1	Assessment of health and nutritional profile among the elderly population of Orissa primitive tribes	Dr. Gandham Bulliyya Regional Medical Research Centre Bhubaneswar	0.59
2	A comprehensive study on delivery of health care research for capacity building amongst the primitive tribes of orissa	Dr. G.P. Chhotray Regional Medical Research Centre Bhubaneswar	3.38
3	Study of prevalence of nosocomial infection in a medical college hospital	Dr. Piaray Lal Kariholu B.L.D.E Association's Shri B.M. Patil Medical College Bijapur	0.43

4	Comparative evaluation of vectors of Japanese encephalitis and bio-environment factors in JE prone and apparently JE free zones of West Bengal	Dr. Neelam Tandon Calcutta School of Tropical Medicine Calcutta	1.32
5	NADPH-oxidase associated components and their fate in macrophage associated disorders	Dr. M.K. Basu Indian Institute of Chemical Biology Calcutta	1.67
6	Identification and characterization of multiple genes in *Entamoeba histolytica* during human collagen type I and CA2+ interaction : use of mRNA differential display	Dr. Pradeep Das National Institute of Cholera and Enteric Diseases Calcutta	3.84
7	Potential of polysaccharide-cholera toxin B subunit conjugate for respiratory mucosal immunity	Dr. Sanjay Chibber Panjab University Chandigarh	0.82
8	Serodiagnosis of invasive zygomycosis	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	3.17
9	Natural habitat of *Cryptococcus neoformans* var. *gattii* strains in the environment of north india and north Karnataka	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	1.70

10	Molecular characterization of group A *Streptococcus*	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	2.31
11	Molecular cloning, sequencing and expression of adhesin gene of enteroaggregative *E.coli* (EAggEC) towards development of a specific probe	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	4.22
12	Monoclonal antibody based ELISA system to detect malaria antigen in cerebrospinal fluid for diagnosis of cerebral malaria	Dr. M.L. Dubey Postgraduate Institute of Medical Education and Research Chandigarh	1.19
13	Study on the mechanism of action of a biologically active excretory secretory product of *G.lamblia* in mice enterocytes	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.61
14	Study on the cellular responses by a mannose sensitive adhesin of *Salmonella typhimurium*	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.39
15	Cellular immune response in human and experimental cysticercosis	Dr. Nancy Malla Postgraduate Institute of Medical Education and Research Chandigarh	1.67

16	Human filariasis : Immunological (immuno- globulin and cytokine) responses in *W.bancrofti* and *B.malayi* infections in endemic areas in India	Dr. Nancy Malla Postgraduate Institute of Medical Education and Research Chandigarh	1.79
17	Study of typhoid carriers through culture of bile specimen obtained during routine endoscopy and surgical procedures	Dr. Chetana Vaishnavi Postgraduate Institute of Medical Education and Research Chandigarh	0.96
18	A study of possible mechanism(s) for T cell anergy in lepromatous leprosy	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	2.50
19	Interactions of galactose- binding lectin of *Entamoeba histolytica* with immune-competent cells	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	0.94
20	Studies on regulation of apoptosis in leprosy patients	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	3.22
21	Mechanism of target cell death induced by GAL/GALNAC lectin of *E.histolytica*	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	2.38

22	Studies on the prevalance, serotype and electropherotyping pattern of human rotavirus associated gastroenteritis among children 0-2 years of age	Dr. S. Ananthan Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences Chenna	1.72
23	Use of small fragment restriction endonuclease analysis in the typing of group *A Streptococci*	Dr. Thangam Menon Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences Chennai	1.10
24	Polymerase chain reaction for detection and genotyping of *Chlamydia trachomatis* in conjunctivitis	Dr. H.N. Madhavan Vision Research Foundation Chennai	3.50
25	Hybridization studies on aminoglycoside modifying enzyme and b-lactamase gene sequences as diagnostic marker in *P.aeruginosa* infections	Dr. N. Abitha Devi P. S.G. College of Arts and Science Coimbatore	0.33
26	Integrated vector control of malaria, filaria and other vector-borne diseases	Dr. Sarala K. Subbarao Malaria Research Centre Delhi	57.50
27	Application of remote sensing and geographical information systems for decision support in malaria control	Dr. Aruna Srivastava Malaria Research Centre Delhi	19.79

28	Delineation of breeding habitats and landscape features suitable for *Anopheles culicifacies* abundance using satellite remote sensing	Dr. R.C. Dhiman Malaria Research Centre Delhi	6.05
29	The role of proinflammatory cytokines in the induction of nitric oxide from human mononuclear phagocytes of patients suffering from pulmonary tuberculosis	Dr. Mridula Bose Vallabhbhai Patel Chest Institute Delhi	2.76
30	Development of computer based health management information system in Rajasthan	Dr. R.C. Sharma Desert Medicine Research Centre Jodhpur	4.84
31	Lactoferrin and antibodies to lactoferrin in tears of leprosy patients	Dr. Ebenezer Daniel Schieffelin Leprosy Research and Training Centre Karigiri	1.12
32	Viability of *Mycobacterium leprae* in leptomatous patients after completion of 12 month and 24 months multidrug therapy	Dr. Gigi J. Ebenezer Schieffelin Leprosy Research and Training Centre Karigiri	1.61
33	Factors affecting susceptibility / resistance of the host to hepatic amoebiasis	Dr. Sheela Ghoshal Central Drug Research Institute Lucknow	0.81
34	Herpes simplex encephalitis in children	Dr. Rashmi Kumar K.G's Medical College Lucknow	1.17

35	Purification and characterization of dengue virus-induced human cytotoxic factor	Dr. Asha Mathur K.G's Medical College Lucknow	0.88
36	Isolation, characterization and pattern of drug- resistance of indigenous strains of *Giardia lamblia*	Dr. Prem Kumari Misra K.G's Medical College Lucknow	1.47
37	Establishment of a field station in South Arcot district, Tamil Nadu, for control trials of Japanese encephalitis	Dr. A. Gajanana Centre for Research in Medical Entomology Madurai	14.73
38	Cultivation and identification of human pathogenic *Leptospira* and comparison of dark field microscopy with agglutination tests	Dr. Sivasubramanian Chandrasekaran Madurai Medical College and Government Rajaji Hospital Madurai	0.14
39	*Clostridium difficile* associated diarrhoea	Dr. Alka Gogate Lokmanya Tilak Municipal and L.T. M.G. Hospital and Medical College Mumbai	0.86
40	Immunotherapeutic clinical trial with ICRC vaccine as an adjunct to chemotherapy to be conducted along with immunoprophylactic clinical trial with ICRC vaccine	Dr. Shubhade V. Chiplunkar Tata Memorial Hospital Mumbai	2.07

41	A prospective evaluation of clinical profile and natural course of water-borne viral hepatitis in adults and seroepidemiology of HAV in children in India	Dr. S.K. Acharya All India Institute of Medical Sciences New Delhi	1.64
42	Efficacy of zinc supplementation in acute diarrhoea with malnutrition	Dr. Arvind Bagga All India Institute of Medical Sciences New Delhi	1.61
43	Monitoring of poliovirus stains for inter and intratypic variability by restriction pattern analysis and sequencing	Dr. Shobha Broor All India Institute of Medical Sciences New Delhi	0.49
44	Molecular typing of *Acinetobacter* Sp. isolated in AIIMS hospital	Dr. Arti Kapil All India Institute of Medical Sciences New Delhi	3.86
45	Hepatitis B virus mutants in acute non A to E hepatitis patients	Dr. S.K. Panda All India Institute of Medical Sciences New Delhi	6.17
46	Molecular characterization of VP^3 gene of human rotavirus strains associated with severe diarrhoea and without diarrhoea in children	Dr. Pratima Ray All India Institute of Medical Sciences New Delhi	1.32
47	Construction of a genomic library of *C.trachomatis* serovar 12, identification & characterisation of the immunoreactive recombinant clones	Dr. Gita Satpathy All India Institute of Medical Sciences New Delhi	3.62

48	Surveillance of anti-tuberculosis drug resistance	Dr. Pradeep Seth All India Institute of Medical Sciences New Delhi	5.42
49	Generation and *in vitro* characterisation of recombinant phage display antibodies to hepatitis B surface antigen	Dr. Subrata Sinha All India Institute of Medical Sciences New Delhi	1.19
50	To study the role of host genetic factors in hepatitis B viral infection in family contacts of HBV related liver disease patients	Dr. S.K. Sarin G.B. Pant Hospital New Delhi	4.07
51	Serotypic characterization of human rotavirus strains from children with diarrhoea	Dr. Anita Chakravarti Maulana Azad Medical College and associated hospitals New Delhi	1.93
52	Prospective study of hepatitis C virus infection in voluntary blood donors from Delhi city hospitals	Dr. Premashis Kar Maulana Azad Medical College and Associated Hospitals New Delhi	2.52
53	Surveillance of hepatitis E virus in sewage and drinking water : Prevention strategies against infection in a resettlement colony of Delhi	Dr. Premashis Kar Maulana Azad Medical College and Associated Hospitals New Delhi	3.44

54	Application for remote sensing in identifying and mapping sandfly distribution in endemic and non-endemic kala-azar	Dr. S.K. Kar Rajendra Memorial Research Institute of Medical Sciences Patna	3.54
55	Antibiotic susceptibility pattern of *Streptococcus pneumoniae* in childhood carriers in Pondicherry	Dr. Reba Kanungo Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	2.67
56	Malaria control through strengthening the traditional health care personnel (traditional healers) in the tribal community	Dr. P.K. Das Vector Control Research Centre Pondicherry	0.22
57	Application of remote sensing (RS) and geographical information systems (GIS) for epidemiology and control of lymphatic filariasis	Dr. P.K. Das Vector Control Research Centre Pondicherry	0.22
58	Prevalence of haemoglobinopathies and G6PD deficiency among the primitive tribal population of Andaman and Nicobars	Dr. K.sM. Murhekar Regional Medical Research Centre Port Blair	2.75
59	Prevalence of viral hepatitis among the tribes of Andaman and Nicobar islands	Dr. M.V. Murhekar Regional Medical Research Centre Port Blair	2.50

60	Studies on transmission dynamics of diurnally subperiodic *W.bancrofti* infection in Nancowry group of islands	Dr. S.C. Sehgal Regional Medical Research Centre Port Blair	2.13
61	Estimate of disease burden due to shigellosis in rural community in the Andamans	Dr. S.C. Sehgal Regional Medical Research Centre Port Blair	1.50
62	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	18.00
63	AIDS research and reviews National AIDS Research Institute	Dr. R.R. Gangakhedkar Pune	6.21
64	Testing of the traditional medicines for their toxicity, anti-HIV activity and immuno-potentiating activity	Dr. R.S. Paranjape National Aids Research Institute Pune	5.42
65	Studies on mosquitoes of southern Rajasthan	Dr. P.N. Sharma M.L.Sukhadia University Udaipur	0.47
66	Serological diagnosis of melioidosis - an evaluation of ELISA, indirect haemagglutination (IHA) and indirect fluorescent antibody test (IFAT)	Dr. Mary V. Jesudason Christian Medical College and Hospital Vellore	4.41
67	A molecular approach to the detection of enteroviruses in acute and chronic neurological illnesses	Dr. Gopalan Sridharan Christian Medical College and Hospital Vellore	4.41

Reproductive Health and Nutrition

68	Quality assurance in immunoassay-isotopic and non-isotopic : role of external quality assurance	Dr. D.K. Hazra S.N. Medical College and Hospital Agra	0.72
69	District nutrition project for prevention and control of micronutrients deficiency disorders-phase II	Dr. K. Ropari Directorate of Health Services Aizwal	4.56
70	Human Reproduction Research Centre	Dr. Krishna Mukherjee Moti Lal Nehru Medical College Allahabad	12.28
71	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Krishna Mukherjee Moti Lal Nehru Medical College Allahabad	0.39
72	District nutrition project for prevention and control of micronutrients deficiency disorders-phase II	Dr. Krishna Mukherjee Moti Lal Nehru Medical College Allahabad	1.92
73	Promotion of vasectomy by training the providers and community education	Dr. Vijay Srinivasan The Gandhigram Institute of Rural Health & Family Welfare Trust Ambathurai	1.56
74	National Nutrition Monitoring Bureau	Dr. J. Sundaram Directorate of Health and Family Welfare Services Bangalore	8.83

75	Relative role of FSH and LH in regulation of differentiation of progenitor mesenchymal cells in the rat testis and monkey	DR. A. Jagannadha Rao Indian Institute of Science Bangalore	2.35
76	Human Reproduction Research Centre	Dr. B.S. Kodkany Jawaharlal Nehru Medical College Belgaum	7.50
77	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. B.S. Kodkany Jawaharlal Nehru Medical College Belgaum	0.39
78	National Nutrition Monitoring Bureau	Dr. K. Satyanarayana Regional Medical Research Centre Bhubaneswar	8.83
79	Human Reproduction Research Centre	Dr. Durga Gehlot S.P. Medical College and Associated Group of Hospitals Bikaner	10.98
80	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Durga Gehlot S.P. Medical College and Associated Group of Hospitals Bikaner	0.39
81	District nutrition project for prevention and control of micronutrients deficiency disorders-phase I	Dr. S.S. Swami S.P. Medical College and Associated Group of Hospitals Bikaner	0.33

82	Studies on structural and functional characterization of aberrant prolactin secretion in asymptomatic hyperprolactinaemic women	Dr. S.N. Kabir Indian Institute of Chemical Biology Calcutta	0.66
83	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. Abha Sarkar Institute of Postgraduate Medical Education and Research Calcutta	14.52
84	Human Reproduction Research Centre	Dr. Kartick Chandra De Medical College and Eden Hospital Calcutta	11.88
85	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Kartick Chandra De Medical College and Eden Hospital Calcutta	1.26
86	Human Reproduction Research Centre	Dr. A.K. Mondal R.G. Kar Medical College and Hospital Calcutta	12.60
87	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. A.K. Mondal R.G.Kar Medical College and Hospital Calcutta	0.39
88	National Nutrition Monitoring Bureau	Dr. A. Roy Chowdhury Regional Occupational Health Centre(Eastern) Calcutta	8.83

89	Use of natural products in reproductive biology	Dr. Asima Chatterjee University College of Science and Technology Calcutta	2.58
90	Human Reproduction Research Centre	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	9.72
91	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	0.39
92	Maternal immunoprophylaxis against hepatitis B virus and assessment of maternal immune response and antibody transfer to their infants	Dr. Indu Gupta Postgraduate Institute of Medical Education and Research Chandigarh	1.38
93	Quantitative changes in body water contents, occurrence of SIADH and their significance in children with acute bacterial meningitis	Dr. Sunit C.Singhi Postgraduate Institute of Medical Education and Research Chandigarh	1.36
94	Biodegradable polymeric implants for the delivery of contraceptive steroid	Dr. K..P. Rao Central Leather Research Institute Chennai	1.85

95	National Nutrition Monitoring Bureau	Dr. K.C. Viswanathan Directorate of Public Health and Preventive Medicine Chennai	8.83
96	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. V.S. Devaki Government Kasturba Gandhi Hospital for Women and Children Chennai	0.39
97	Human Reproduction Research Centre	Dr. S. Janaki Government Kasturba Gandhi Hospital for Women and Children Chennai	11.98
98	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Dharani Srinivas Government Kilpauk Medical College and Hospital Chennai	0.39
99	Human Reproduction Research Centre	Dr. A. Sundaravalli Government Kilpauk Medical College and Hospital Chennai	11.95
100	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. R. Lakshmi Government R.S.R.M. Hospital Chennai	0.39
101	Human Reproduction Research Centre	Dr. Dharani Srinivas Government R.S.R.M. Hospital Chennai	11.65

102	Human Reproduction Research Centre – Regional Centre for Clinical Research	Dr. Gajalakshmi Subramanyam Institute of Obstetrics and Gynaecology and Government Hospital for Women and Children Chennai	13.22
103	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Gajalakshmi Subramanyam Institute of Obstetrics and Gynaecology and Government Hospital for Women and Children Chennai	1.32
104	Human Reproduction Research Centre	Dr. S.N. Das S.C.B. Medical College Cuttack	8.52
105	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Pratima Patnaik S.C.B. Medical College Cuttack	0.39
106	District nutrition project for prevention and control of micronutrients deficiency disorders- phase II	Dr. V.B. Prakash V.C. Prakash Cancer Research Foundation Dehradun	3.25
107	Human Reproduction Research Centre	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	10.57

108	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	0.39
109	District nutrition project for prevention and control of micronutrients deficiency disorders-phase I	Dr. F. U. Ahmed Assam Medical College Dibrugarh	2.67
110	National Nutrition Monitoring Bureau	Dr. Nargis Naseem Directorate of Health, Medical Services and Medical Education Gandhinagar	8.83
111	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. P. K. Sharma Gauhati Medical Guwahati	13.22
112	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. P. K. Sharma Gauhati Medical College Guwahati	0.39
113	Central Reference Laboratory of the National Nutrition Monitoring Bureau	Dr. K. Vijayaraghavan National Institute of Nutrition Hyderabad	8.83
114	National Nutrition Monitoring Bureau	Dr. K. Vijayaraghavan National Institute of Nutrition Hyderabad	8.83

115	Purification and characterization of LTC 4 synthase from sheep uterus	Dr. P. Reddanna University of Hyderabad Hyderabad	1.90
116	District nutrition project for prevention and control of micronutrients deficiency disorders-phase II	Dr. E. Yaima Singh Regional Institute of Medical Sciences Imphal	5.21
117	National Nutrition Monitoring Bureau	Dr. Tapas Chakma Regional Medical Research Centre for Tribals Jabalpur	8.83
118	Human Reproduction Research Centre	Dr. Anju Taly S.M.S. Medical College and Hospital Jaipur	11.04
119	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Anju Taly S.M.S. Medical College and Hospital Jaipur	0.39
120	Feasibility of using pregnancy detection kits at PHC/ subcentre/village/urban slum level	Dr. Anju Taly S.M.S. Medical College and Hospital Jaipur	1.00
121	Human Reproduction Research Centre	Dr. Sadhna Sharma Government Medical College and S.M.G.S. Hospital Jammu	9.99

122	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Sadhna Sharma Government Medical College and S.M.G.S. Hospital Jammu	0.39
123	Human Reproduction Research Centre	Dr. V.K. Singh G.S.V.M. Medical College Kanpur	11.99
124	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. V.K. Singh G.S.V.M.Medical College Kanpur	0.39
125	District nutrition project for prevention and control of micronutrients deficiency disorders-phase II	Dr. Viu Meru Directorate of Health Services Kohima	2.24
126	Human Reproduction Research Centre	Dr. Chandrawati K.G's Medical College Lucknow	13.60
127	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Chandrawati K.G's Medical College Lucknow	0.39
128	District nutrition project for prevention and control of micronutrients deficiency disorders-phase I	Dr. Uday Mohan K.G's Medical College Lucknow	0.90
129	Human Reproduction Research Centre	Dr. P. Meenambal Madurai Medical College and Government Rajaji Hospital Madurai	14.90

130	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. P. Meenambal Madurai Medical College and Government Rajaji Hospital Madurai	0.39
131	Human Reproduction Research Centre	Dr. Usha Sharma L.L.R.M. Medical College Meerut	8.00
132	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Usha Sharma L.L.R.M. Medical College Meerut	0.39
133	Role of leaf extract of*Stephania hernandifolia (aknadi)* on fertility regulation in male : an evaluation for male pill of plant origin for 21st century	Dr. Debidas Ghosh Vidyasagar University Midnapore	0.61
134	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. K.E. Bharucha Grant Medical College and Sir J.J. Group of Hospitals Mumbai	0.39
135	Human Reproduction Research Centre	Dr. Rekha G.Dever Grant Medical College and Sir J.J. Group of Hospitals Mumbai	9.19

136	Human Reproduction Research Centre- Regional Centre for Clinical Research	Dr. Mina Bhattacharya Seth G.S. Medical College and K.E.M.Municipal Hospital Mumbai	9.68
137	Studies on cholesterol and oxidized lipids from dairy and egg products on lipid metabolism related to cardiovascular diseases	Dr. Belur R. Lokesh Central Food Technological Research Institute Mysore	0.63
138	Studies on antioxidant properties and hypocholesterolemic effect of sesame oil	Dr. K.. Sambaiah Central Food Technological Research Institute Mysore	1.16
139	National Nutrition Monitoring Bureau	Dr. N.R. Khan Public Health Institute Building Nagpur	8.83
140	Role of cytokines in premature ovarian failure	Dr. Anand Kumar All India Institute of Medical Sciences New Delhi	2.41
141	Regulation of collagenase - IV and plasminogen activator activity in human placenta : mechanism of control of trophoblast invasion	Dr. Chandana Das All India Institute of Medical Sciences New Delhi	2.18

142	Role of phospholipase C, cAMP and cGMP signal transduction mechanisms in the regulation of testosterone production in purified mouse Leydig cells	Dr. M.L. Khurana All India Institute of Medical Sciences New Delhi	0.90
143	Human Reproduction Research Centre	Dr. Deep Takkar All India Institute of Medical Sciences New Delhi	9.25
144	Mechanism of antiprogestin interaction with experimental animal and human target tissues	Dr. Urmila Vij All India Institute of Medical Sciences New Delhi	3.02
145	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. Gulshanjit Singh Deen Dayal Upadhyay Hospital New Delhi	3.51
146	Feasibility studies on the use of indigenous ELISA kits of cortisol and testosterone	Dr. G. Lakshmi Kumari Hormone Research Foundation New Delhi	2.78
147	Development of simple, sensitive and rapid low cost pregnancy test for early detection of pregnancy	Dr. G. Lakshmi Kumari Hormone Research Foundation New Delhi	3.20
148	Central Co-ordinating Unit for Contraception Research	Sh. N.C. Saxena Indian Council of Medical Research New Delhi	9.51

149	Feasibility of using pregnancy detection kits at PHC/ subcentre/village/urban slum level	Dr. Padam Singh Indian Council of Medical Research New Delhi	13.80
150	Development of indigenous thread to be used for the production of copper T 200B	Dr. B.L. Deopura Indian Institute of Technology New Delhi	3.86
151	National Nutrition Monitoring Bureau Institute for Research in Medical Statistics	Dr. Padam Singh 8.83 New Delhi	
152	Morphological changes of placenta in tobacco users and non tobacco users	Dr. Gayatri Rath Lady Hardinge Medical College and Associated Hospitals New Delhi	4.72
153	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. H.C. Das Lok Nayak Jaiprakash Narayan Hospital New Delhi	3.51
154	Nutritional status of affluent school going children in Delhi	Dr. C. Gopalan Nutrition Foundation of India New Delhi	4.85
155	Effect of seasonality on the birth weight of infants and on the haemoglobin of women in reproductive age group	Dr. C. Gopalan Nutrition Foundation of India New Delhi	4.28

156	Phase III clinical trial of an injectable intravasal contaceptive for the male	Dr. S.K. Basu Rural Hospital New Delhi	3.51
157	Human Reproduction Research Centre	Dr. Sudha Salhan Safdarjang Hospital New Delhi	9.54
158	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Sudha Salhan Safdarjang Hospital New Delhi	0.39
159	Human Reproduction Research Centre	Dr. M.N. Pal Goa Medical College Panaji	8.00
160	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. M.N. Pal Goa Medical College Panaji	0.39
161	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Raj Kumari Narone Patna Medical College and Hospital Patna	0.39
162	Human Reproduction Research Centre	Dr. Shakuntala Sharan Patna Medical College and Hospital Patna	10.56

163	Human Reproduction Research Centre	Dr. Asha Oumachigui Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	10.48
164	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Asha Oumachigui Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	0.39
165	A study on the maternal and child health care among the four primitive tribals of Nilgiri Hills in Tamil Nadu	Dr. T. Subramanyan Naidu University of Pondicherry Pondicherry	4.15
166	Human Reproduction Research Centre	Dr. Aparna Shrotri B.J. Medical College and Sasoon General Hospital Pune	10.15
167	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. Aparna Shrotri B.J. Medical College and Sasoon General Hospital Pune	0.39
168	Human Reproduction Research Centre	Dr. K. Coyaji King Edward Memorial Hospital Research Centre Pune	7.34

169	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. K. Coyaji King Edward Memorial Hospital Research Centre Pune	1.24
170	District nutrition project for prevention and control of micronutrients deficiency disorders-phase II	Dr. Abdul Rauf Government Medical College and Chest Diseases Hospital Srinagar	1.17
171	Reproductive health problems of women among the fishing communities in Kerala	Dr. V. Gopalakrishnan Central Institute of Development Research Thiruvananthapuram	2.18
172	Improving the quality of family planning services in the national family welfare programme at the PHC level through the ICMR HRRCs	Dr. C.G. Chandrika Devi Medical College and Sat Hospital for Women and Children Thiruvananthapuram	0.39
173	Human Reproduction Research Centre	Dr. P.K. Syamala Devi Medical College and Sat Hospital for Women and Children Thiruvananthapuram	11.60
174	National Nutrition Monitoring Bureau	Dr. K.A. George State Nutrition Bureau Nutrition Research Centre Thiruvananthapuram	8.83

175	Influence of endogenous and exogenous ovarian steroid hormones on functions of submandibular salivary gland of laboratory mammals	Dr. Ami P. Raval M.S. University of Baroda Vadodara	0.41
176	Promotion of vasectomy by training the providers and community education	Dr. R.K.Baxi Medical College and S.S.G. Hospital Vadodara	0.06
177	Human Reproduction Research Centre	Dr. M.R. Desai Medical College and S.S.G. Hospital Vadodara	11.80
178	Improving the quality of family planning services in the National Family Welfare Programme at the PHC level through the ICMR HRRCs	Dr. M.R. Desai Medical College and S.S.G. Hospital Vadodara	0.39
179	Study of altered cell biology and signal transduction in platelets in pregnancy toxemia	Dr. Debabrata Dash Institute of Medical Sciences Banaras Hindu University Varanasi	0.50

Non-communicable Diseases

180	Rural Cancer Registry	Dr. D.V. Bala The Gujarat Cancer and Research Institute Ahmedabad	2.52

181	Sensitive detection of occult metastases in breast cancer : demonstration of CD44 variants and K-19 in peripheral blood by reverse transcriptase-polymerase chain reaction	Dr. Jyotsna M.Bhatavdekar The Gujarat Cancer and Research Institute Ahmedabad	2.50
182	Prognostic significance of DNA ploidy, S-phase fraction and cell proliferative marker KI-67 in large cell non-Hodgkin's lymphomas	Dr. Nilkamal H. Karelia The Gujarat Cancer and Research Institute Ahmedabad	1.03
183	Possible correlation between heteromorphism of constitutive heterochromatin and susceptibility mutagens in patients with oral cavity cancer	Dr. Amit H. Trivedi The Gujarat Cancer and Research Institute Ahmedabad	0.91
184	Epidemiology of glaucoma	Dr. S.T. Fernandez Little Flower Hospital and Research Centre Angamally	10.84
185	Management of glaucoma under Indian conditions	Dr. S. Chandrasekhar Shetty Bangalore Medical College and Victoria Hospital Bangalore	0.67
186	National Cancer Registry Co-ordinating Unit (Technical Wing)	Dr. A. Nandakumar Kidwai Memorial Institute of Oncology Bangalore	5.54

187	Vasectomy and cancer of prostate : a multicentric case control study - Coordinating Unit	Dr. A. Nandakumar Kidwai Memorial Institute of Oncology Bangalore	0.58
188	National Cancer Registry - Hospital Based	Dr. P.S. Prabhakaran Kidwai Memorial Institute of Oncology Bangalore	1.29
189	National Cancer Registry - Population based	Dr. P.S. Prabhakaran Kidwai Memorial Institute of Oncology Bangalores	3.68
190	Antioxidant defenses in arteries of cigarette-smoke exposed rats and the effect of supplementation with vitamin E	Sh. C.V. Anand M.S. Ramaiah Medical College Bangalore	1.01
191	Urban hospital-based case- control study toidentify risk factors for acute myocardial infarction - Control Data Unit	Dr. Prem Pais St.John's Medical College Bangalore	1.45
192	Urban hospital-based case-control study to identify risk factors for acute myocardial infarction (Paticipating Centre)	Dr. Prem Pais St.John's Medical College Bangalore	0.74
193	Bhopal Cancer Registry	Dr. Shiela Kanhere Gandhi Medical College and Associated Hospitals Bhopal	14.78
194	Studies of glutaminase enzyme from malignant cells and mammal organs as an antineoplastic agent	Dr. Putul Maity Chittaranjan National Cancer Institute Calcutta	2.01

195	Evaluation of dopamine as a potential protective agent against cytotoxic drug-induced myelosuppression	Dr. M.R. Ray Chittaranjan National CancerInstitute Calcutta	1.09
196	Comparative evaluation of 99m TC - MAG3 in normal and chronic renal failure patients	Dr. Mridula Misra Indian Institute of Chemical Biology Calcutta	2.03
197	Inhibition of experimental hepatocarcinogenesis by *Mikania cordata* : a cellular and biochemical Study	Dr. Malay Chatterjee Jadavpur University Calcutta	1.34
198	A study of factors affecting bacterial adherence to various IOLS materials (polymethyl methacrylate and foldable intraocular lenses)	Dr. Jagat Ram Postgraduate Institute of Medical Education and Research Chandigarh	2.41
199	A community-based study to estimate the excess expenditure on health care attributable to smoking	Dr. S.K. Jindal Postgraduate Institute of Medical Education and Research Chandigarh	2.41
200	Role of CD44 and NM 23 in benign and malignant lesions of the human breast	Dr. Kusum Joshi Postgraduate Institute of Medical Education and Research Chandigarh	2.32

201	Community-based follow up and treatment of children identified to have psychiatric disorders	Dr. Savita Malhotra Postgraduate Institute of Medical Education and Research Chandigarh	1.67
202	T cell signals to M peptide 5 streptococcal antigen in a model of immunologically mediated carditis in rhesus monkeys	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	2.12
203	*Jai Vigyan* mission mode project on community control of RF/RHD in India	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	10.72
204	National Cancer Registry - Hospital based	Dr. V. Shanta Cancer Institute (W.I.A.) Chennai	1.72
205	National Cancer Registry - Population based	Dr. V. Shanta Cancer Institute (W.I.A.) Chennai	4.65
206	Virological and immunological studies on herpes simplex keratitis	Dr. S.P. Thyagarajan Dr. A.L.Mudaliar P.G.Institute of Basic Medical Sciences Chennai	1.95
207	Clinical trial on a stainless steel band material	Dr. N.R. Krishnaswamy Ragas Dental College and Hospital Chennai	0.04
208	Development and evaluation of bioactive ceramic coating	Dr. S. Rajeswari University of Madras Chennai	3.18

209	Assessment of immunobiological effects induced by organophosphorus pesticides in human subjects due to accidental poisoning and occupational hazards	Dr. B.D. Banerjee University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	0.80
210	Comparison of conventional and objective auditory tests for early diagnosis of hearing impairment of high risk neonates, infants and young children in some rehabilitation colonies for timely intervention	Dr. S.K. Vishwakarma University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	13.63
211	National Cancer Registry - Hospital based	Dr. F.U. Ahmed Assam Medical College Dibrugarh	2.38
212	Etiology of endemic goitre in North-Eastern India : role of environmental goitrogens	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	1.67
213	Cancer chemopreventive potential of certain vegetables, fruits and medicinal plants of the north- eastern region of India	Dr. Rupjyoti Bharali Gauhati University Guwahati	1.67

214	Clinical trial on chlorella E - 25	Dr. Kamala Krishnaswamy National Institute of Nutrition Hyderabad	1.00
215	Etiology of endemic goitre in North-Eastern India : role of environmental goitrogens	Dr. Kamala Krishnaswamy National Institute of Nutrition Hyderabad	9.29
216	Urban hospital based case control study to identify risk factors for acute myocardial infarction (Participating Centre)	Dr. Sudhir R. Naik Osmania Medical College and Associated Hospitals Hyderabad	0.74
217	Mode of action of calcium glutarate in skin tumorigenesis	Dr. K.P. Gupta Industrial Toxicology Research Centre Lucknow	1.68
218	Role of reactive oxygen radicals and herbal preparations in anterior uveitis	Dr. Basant Lal K.G's Medical College Lucknow	1.36
219	Clinical trial on a stainless steel band material	Dr. D.N. Kapoor K.G's Medical College Lucknow	0.04
220	Urban hospital-based case-control study to identify risk factors for acute myocardial infarction	Dr. V.K. Puri K.G's Medical College Lucknow	0.74
221	Recidivism : a study to identify risk factors to formulate preventive and rehabilitative strategies	Dr. S.C. Tiwari K.G's Medical College Lucknow	2.41

222	Study with human retinal S-antigen : epitope mapping in uveitis patients	Dr. V.K. Singh Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	6.90
223	Evaluation of PCR and other parameters for detection of intraocular tuberculosis in South Indian patients	Dr. P. Namperumalsamy Aravind Eye Hospital and Postgraduate Institute of Ophthalmology Madurai	2.40
224	Value of culture and serology in ophthalmic complications of leptospirosis	Dr. P. Namperumalsamy Aravind Eye Hospital and Postgraduate Institute of Ophthalmology Madurai	7.52
225	Studies on epidemiology, culture, immunology and molecular biology of *Rhinosporidium seeberi*	Dr. C. Rajamanickam Madurai Kamaraj University Madurai	3.97
226	The role of HPV, p53 alterations, Ras mutations and Bcl-2 expression in cervical cancers in India	Dr. D. Saranath Cancer Research Institute Mumbai	4.68
227	National Cancer Registry - Population based	Dr. M.R. Kamat Indian Cancer Society Mumbai	4.77
228	Cancer Registries' Rural Cancer Registry	Dr. K.A. Dinshaw Tata Memorial Hospital Mumbai	1.07

229	Alternating triple therapy regimen in aggressive lymphomas (B - cell type) : correlation with distinct biologic entities	Dr. R. Gopal Tata Memorial Hospital Mumbai	7.81
230	Mechanisms of protein phosphorylation and signalling pathways during tumour promotion by two new liver tumour promotors in primary cultures of normal and preneoplastic rat hepatocytes	Dr. K.V.K. Rao Tata Memorial Hospital Mumbai	2.54
231	Management of extra-hepatic portal hypertension in childhood : efficacy and efficiency of endoscopic sclerotherapy and porto-systemic shunt surgery	Dr. N.K. Arora All India Institute of Medical Sciences New Delhi	2.62
232	A study on MAG3 (mercapto acetyl triglycine) as a single modality investigation for the evaluation of dynamic and absolute renal function and indirect dynamic cystography (using effective filtration fraction analysis)	Dr. Minu Bajpai All India Institute of Medical Sciences New Delhi	1.93

233	Assessment of human cardiac allograft rejection using light microscopy, electron microscopy and immunohistochemistry	Dr. Prem Chopra All India Institute of Medical Sciences New Delhi	1.13
234	Changing spectrum of lower respiratory tract infection : a study of community acquired spneumonia in adults with special reference to geriatric population	Dr. A.B. Dey All India Institute of Medical Sciences New Delhi	2.71
235	Urinary screening of school children of Delhi : a preliminary study	Dr. A.K. Dinda All India Institute of Medical Sciences New Delhi	2.71
236	The development of neuropsychological battery for use on hindi knowing children	Sh. Surya Gupta All India Institute of Medical Sciences New Delhi	1.48
237	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	3.82
238	Feasibility of transporting blood dried on filter paper for the measurement of lipids, lipoproteins and markers of glycaemic index, glucose, glycosylated haemoglobin and insulin for cardiovascular diseases	Dr. B.L. Jailkhani All India Institute of Medical Sciences New Delhi	3.64

239	Role of nutritional factors in laryngeal cancers in India	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	0.62
240	Validation and reproducibility of the food frequency method in the Indian context	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	0.19
241	Stress in children	Dr. Manju Mehta All India Institute of Medical Sciences New Delhi	0.65
242	Relationship of tobacco consumption to health care expenditure of families : an organised sector study	Dr. D. Prabhakaran All India Institute of Medical Sciences New Delhi	3.76
243	Urban hospital based case control study to identify risk factors for acute myocardial infarction (Participating Centre)	Dr. K. Srinath Reddy All India Institute of Medical Sciences New Delhi	0.74
244	Molecular genetic basis of platelet derived growth factor induction and tyrosine phosphorylation in astrocytic tumours of the brain	Dr. Chitra Sarkar All India Institute of Medical Sciences New Delhi	0.02
245	Study of oral health status and treatment needs of the elderly population in the community	Dr. Naseem Shah All India Institute of Medical Sciences New Delhi	0.76

246	The effect of aspirin on biliary mucin	Dr. R.K. Tandon All India Institute of Medical Sciences New Delhi	0.53
247	National Cancer Registry-Population based	Dr. Kusum Verma All India Institute of Medical Sciences New Delhi	5.72
248	Vasectomy and cancer of prostate : a multicentric case control study	Dr. Kusum Verma All India Institute of Medical Sciences New Delhi	1.84
249	Risk factors for gall bladder carcinoma in Delhi - a population-based case-control study	Dr. Kusum Verma All India Institute of Medical Sciences New Delhi	1.09
250	The purine metabolic enzyme adenosine deaminase and 5' nucleotidase (NT) activity in peripheral blood T cells in multiple sclerosis patients	Sh. S. Vivekanandhan All India Institute of Medical Sciences New Delhi	2.05
251	Antioxidant status in Parkinson's disease	Sh. S. Vivekanandhan All India Institute of Medical Sciences New Delhi	2.54
252	National Cancer Registry-Coordinating Unit (Operational Wing)	Dr. Bela Shah Indian Council of Medical Research New Delhi	6.73
253	Urban hospital-based case-control study to identify risk factors for acute myocardial infarction (Co-ordinating Unit)	Dr. Bela Shah Indian Council of Medical Research New Delhi	1.07

254	Biorheological and biochemical study of pathological synovial fluid	Dr. R.K. Saxena Indian Institute of Technology New Delhi	2.42
255	Nutritional deficiencies and supplementation therapy in patients with alcoholic and non- alcoholic liver disease	Dr. S.K. Sarin Maulana Azad Medical College and Associated Hospitals New Delhi	7.12
256	Role of serum and hepatic iron content in chronic liver disease and hepatocellular carcinoma in India	Dr. S.K. Sarin Maulana Azad Medical College and Associated Hospitals New Delhi	4.46
257	Centre for Advanced Research for Health Consequences of Earthquake Disaster with special reference to Mental Health	Dr. Neha R.Pande B.J. Medical College and Sasoon General Hospital Pune	7.27
258	Role of transforming growth factor alpha and epidermal growth factor as potential indicators of aggressiveness in gestational trophoblastic disease	Smt. Molykutty John Regional Cancer Centre Thiruvananthapuram	1.02
259	National Cancer Registry - Hospital based	Dr. M. Krishnan Nair Regional Cancer Centre Thiruvananthapuram	3.02

260	Tumour response to radiation therapy in carcinoma of the uterine cervix : The role of Ras gene mutation	Dr. M. Krishnan Nair Regional Cancer Centre Thiruvananthapuram	1.91
261	Cellular immortality and apoptosis during tumour progression in the uterine cervix	Dr. M. Radhakrishna Pillai Regional Cancer Centre Thiruvananthapuram	1.87
262	Programmed tumour cell death and proliferative Dr. V.M. Pradeep fraction ratio in the staging of thyroid cancer	Regional Cancer Centre Thiruvananthapuram	0.88
263	Genotyping of the CYP1a1 and GSTM 1 genes in tobacco associated oral cancer	Dr. K. Ramadas Regional Cancer Centre Thiruvananthapuram	2.11
264	Effect of selenium and copper on lipid profile and histopathological changes in experimental chicks	Dr. G. Subramanyam S.V. Institute of Medical Sciences Tirupati	1.52

Basic Medical Sciences

265	A systematic study on the photoconjugation between amino acids and nucleic acids and their possible role in the pathogenesis of SLE	Dr. Asif Ali Jawaharlal Nehru Medical College Aligarh	3.40
266	Role of DNA fragmentation and prolonged immediate early gene expression in the neuropathogenesis of diabetes and hypoglycemia in rat	Dr. Gurcharan Kaur Guru Nanak Dev University Amritsar	1.00

267	Studies on regulation of synthesis and secretion of GnRH in the placenta	Dr. A. Jagannadha Rao Indian Institute of Science Bangalore	2.95
268	A study of the long-term effects of antiepileptic drugs on learning and memory	Dr. N. Pradhan National Institute of Mental Health and Neurosciences Bangalore	2.97
269	Alpha adrenergic receptor linked second messenger response to antidepressants in rat brain	Dr. M.N. Subhash National Institute of Mental Health and Neurosciences Bangalore	1.04
270	A study of serum nitrate levels in pregnant woman	Dr. Rani Gupta St.John's Medical College Bangalore	0.15
271	*Jai Vigyan* mission project on community control of thalassaemia syndromes – Awareness, screening, genetic counselling and prevention	Dr. Cecil R. Ross St.John's Medical College Bangalore	7.92
272	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. G.P. Chhotray Regional Medical Research Centre Bhubaneswar	4.41
273	Effects of early postnatal undernutrition on the development of synaptosomal membrane protein kinase C and GAP-43 protein in rat pups	Dr. Sasanka Chakrabarti Dr. B.C.Roy Postgraduate Institute of Basic Medical Sciences Calcutta	0.99

274	Studies on haemorrhagins of Russell's viper (*Vipera russelli*) venom	Dr. Debashish Bhattacharyya Indian Institute of Chemical Biology Calcutta	0.56
275	Pharmacological aspects of gastrointestinal motility with special reference to development of prokinetic drugs	Dr. Lalima Chaudhury Indian Institute of Chemical Biology Calcutta	1.52
276	Antibody - mediated drug delivery in visceral leishmaniasis	Dr. P.K. Das Indian Institute of Chemical Biology Calcutta	0.80
277	Pharmacological and biochemical investigation on the poisonous sea-anemones occurring in the eastern coastal line of India	Dr. A.K. Nag Chaudhuri Jadavpur University Calcutta	1.18
278	*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 Calcutta	8.22
279	Neuropharmacological studies in rats having D- galactosamine - induced hepatitis	Dr. Dipankar Bhattacharyya University College of Medicine Calcutta	2.09
280	Further studies on the snake venom neutralizing factor from *Hemidesmus indicus* and *Pluchea indica*	Dr. Antony Gomes University College of Science and Technology Calcutta	0.75
281	Nicotine and hypertension : role of kidney	Dr. Juthika Koley University College of Science and Technology Calcutta	1.63

282	Impact of nutrition supplements and psychological counselling on performance of young sports persons : a community-based controlled study	Dr. M.S. Ghosh West Bengal State Council of Sports Calcutta	1.72
283	Molecular mechanisms responsible for the defective allele of human hepatic cytochrome p4502c19	Dr. K.K. Kohli Postgraduate Institute of Medical Education and Research Chandigarh	0.50
284	Role of thyrotrophin releasing hormone in the modulation of SP-A receptor and its ligand binding affinity in different cell types in lungs of prenatal and postnatal rabbits	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.72
285	Vitamin E and atherosclerosis : studies on LDL receptor expression in hypercholesterolemic rhesus monkeys following alpha-tocopherol treatment	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	2.44
286	Clinical trial on traditional remedies for diabetes mellitus	Dr. R.S. Hariharan Chennai Medical College and Government General Hospital Chennai	1.90
287	Flexible dose open trial on*Vijayasar* for known diabetes	Dr. R.S. Hariharan Chennai Medical College and Government General Hospital Chennai	2.80
288	Central Biostatistical Monitoring Unit for Traditional Medicine Research	Dr. M.D. Gupte National Institute of Epidemiology Chennai	12.42

289	Flexible dose open trial on *Vijayasar* for known diabetes	Dr. M.D. Gupte National Institute of Epidemiology Chennai	2.00
290	Clinical trials on traditional remedies for diabetes mellitus	Dr. P.K. Mishra S.C.B. Medical College Cuttack	1.74
291	Flexible dose open trial on *Vijayasar* for known diabetes	Dr.P.K. Mishra S.C.B. Medical College Cuttack	2.75
292	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 Delhi	2.79
293	Role of lipoprotein(a) and its phenotypes as a risk factor for premature coronary artery disease in Indian subjects	Dr. Jasvinder K.Gambhir University College of Medical Sciences and Guru Hospital Teg Bahadur Delhi	1.87
294	Investigations on the hypoglycaemic activity of *Eugenia jambolana* in rabbits	Dr. Suman Bala Sharma University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	3.74
295	Biochemical investigations on the mechanism of action of hypoglycaemic compound from the water extract of the bark of *Ficus bengalensis*	Dr. Rimi Shukla University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	1.13
296	Behaviour of pulmonary vagal sensory receptors on opening of an arteriovenous shunt in dogs	Dr. K. Ravi Vallabhbhai Patel Chest Institute Delhi	2.68

297	*Jai Vigyan* mission project on community control of thalassaemia syndromes - awareness, screening, genetic counselling and prevention	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	7.92
298	Investigation into the tumouricidal action of essential fatty acids and their metabolites	Dr. U.N. Das L.V. Prasad Eye Institute Hyderabad	1.94
299	Human serum mannose-binding lectin (MBL) – development of a quantitative enzyme-linked immunosorbent assay and biochemical characterization of MBL receptors on immune cells	Dr. M. Ramanadham University of Hyderabad Hyderabad	0.50
300	DNA polymerases in developing and aging rat brain : levels and mechanism of modulation of enzyme activities	Dr. K. Subba Rao University of Hyderabad Hyderabad	1.14
301	Centre for Advanced Research on Standardisation and Quality Control and Formulation of Selected Traditional Remedies/ Natural Products	Dr. K.L. Bedi Regional Research Laboratory Jammu Tawi	3.59
302	Rapid diagnostic test for C-reactive protein (CRP) based on whole blood agglutination by a conjugated protein of monovalent lectin and FAB fragment of anti human C-reactive Immunoglobulin	Dr. T.K. Maiti Indian Institute of Technology Kharagpur	0.50
303	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. K.S. Suresh Kumar Nilgiris Adivasi Welfare Association Kotagiri	5.13

304	Flexible dose open trial on*Vijayasar* for known diabetes	Dr. R.V. Jayakumar Medical College and Hospital Kottayam	2.80
305	Centre for Advanced Research for Drug Development from Natural/Plant Products	Dr. C.M. Gupta Central Drug Research Institute Lucknow	41.00
306	Design and synthesis of novel oligopeptides as an antiasthmatic /antiallergic agent	Dr. Bijoy Kundu Central Drug Research Institute Lucknow	1.45
307	Enzyme based design and synthesis of new class of malaricides and drug transport inhibitors for chloroquine reversal	Dr. Vishnu Ji Ram Central Drug Research Institute Lucknow	1.43
308	Rational approach to new remedies for mycotic infections	Dr. Vishnu Ji Ram Central Drug Research Institute Lucknow	1.06
309	Effect of hexachlorocyclo-hexane – a chlorinated group of pesticides on the development processes and cardiotoxic potential in iron deficient rats	Dr. Mohini Anand 0.85 Industrial Toxicology Research Centre Lucknow	
310	Mechanism of tumour suppression by nicotinamide	Dr. K.P. Gupta Industrial Toxicology Research Centre Lucknow	1.75
311	Ameliorative potential of *Picrorhiza kurroa* in cadmium induced hepato- and renal toxicity in rat model	Dr. Shashi Khandelwal Industrial Toxicology Research Centre Lucknow	0.74

312	Reactive metabolites of benzene with the ability to induce oxidative stress as component of the mechanism of benzene toxicity	Dr. G.S. Rao Industrial Toxicology Research Centre Lucknow	0.37
313	Studies on toxicological and immunotoxicological potential of commonly used plastics and identification of leachates	Dr. P.K. Seth Industrial Toxicology Research Centre Lucknow	3.00
314	Studies on the mechanism of neurotoxic action of methanol – biochemical,behavioural, morphological and clinical aspects	Dr. P.K. Seth Industrial Toxicology Research Centre Lucknow	5.72
315	Delineation of molecular mechanisms of developmental neurotoxicity of selected environmental chemicals : role of early response genes	Dr. P.K. Seth Industrial Toxicology Research Centre Lucknow	1.39
316	Immunoblot analysis of *Cysticercus fasiolaris* antigen and its role in the diagnosis of neurocysticercosis	Dr. Nuzhat Husain K.G's Medical College Lucknow	0.31
317	Prevalence and molecular characterization of alpha- thalassaemia in Uttar Pradesh	Dr. Sarita Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	0.79

318	Production of HLA-cell tray from pregnant mother's sera with a view to produce complete HLA typing sera in India	Dr. Suraksha Devi Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.31
319	*Jai Vigyan* mission project on community control of thalassaemia syndromes – awareness, screening, genetic counselling and prevention	Dr. R.P. Britt Christian Medical College and Brown Memorial Hospital Ludhiana	7.92
320	Development and evaluation of few drug delivery systems for peptides and proteins	Dr. N. Udupa Kasturba Medical College and Hospital Manipal	1.76
321	Animal model for transdermal drug delivery systems	Dr. Ramesh Panchagnula National Institute of Pharmaceutical Education and Mohali	1.82 Research
322	Role of cytokines and cytotoxic cells in inflammation and tissue damage in juvenile rheumatoid arthritis in comparison with adult rheumatoid arthritis	Dr. Sudha S. Deo Bai Jerbai Wadia Hospital for Children and Institute of Child Health Mumbai	1.14
323	Development of potent uterine relaxants for better management of premature labour	Dr. C.L. Viswanathan Bombay College of Pharmacy Mumbai	2.37

324	Production of HLA-cell tray from pregnant mother's sera with a view to produce complete HLA typing sera in India	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	0.46
325	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	55.70
326	*Jai Vigyan* mission project on community control of thalassaemia syndromes - awareness, screening, genetic counselling and prevention	Dr. Dipika Mohanty Institute of Immunohaematology Mumbai	99.89
327	Centre for Advanced Research for Clinical Pharmacology in Traditional Medicine	Dr. Sharadini A. Dahanukar Seth G.S. Medical College and K.E.M. Municipal Hospital Mumbai	27.13
328	Circumvention of drug resistance by phenoxazine MDR modulators in antibacterial chemotherapy	Dr. K.N. Thimmaiah University of Mysore Mysore	1.80
329	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	0.62

330	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. D.L. Jain Government Medical College and Hospital Nagpur	5.64
331	To study the chronomodulatory role of melatonin Dr. R.L. Bijlani in control of experimental tumours in rats	All India Institute of Medical Sciences New Delhi	1.93
332	Endocrinological effects of 50 Hz electromagnetic Dr. P. Jha fields of moderately high intensity in rats	All India Institute of Medical Sciences New Delhi	2.37
333	Role of angiotensin converting enzyme (ACE) inhibitors in myocardial stunning	Dr. S.K. Maulick All India Institute of Medical Sciences New Delhi	1.78
334	Quinolone binding to DNA : spectroscopic and computer modelling studies	Dr. M.R. Rajeswari All India Institute of Medical Sciences New Delhi	1.36
335	Monitoring of adverse drug reactions in India- Coordinating Unit	Dr. Vasantha Muthuswamy Indian Council of Medical Research New Delhi	1.45

336	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Vasantha Muthuswamy Indian Council of Medical Research New Delhi	4.79
337	*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	4.79
338	To investigate the molecular mechanism of REM sleep deprivation induced norepinephrine mediated increase in Na-K ATPase activity in rat brain	Dr. B.N. Mallick Jawaharlal Nehru University New Delhi	1.65
339	Intervention programme for nutritional anaemia Dr. Mridula A. Phadke and haemoglobinopathies amongst some primitive tribal populations of india	B.J. Medical College and Sasoon General Hospital Pune	4.17
340	Biological status of tribal groups of Bihar	Dr. B.N. Pandey Purnia College Purnia	2.04
341	Indigenous plant lectins and their use as reagents in immunology and pathology	Dr. P. Remani Regional Cancer Centre Thiruvananthapuram	0.37

342	Effects of antioxidants isolated from lemons and *Allium* species as compared to alphatocopherol on the damages induced by nicotine in rats	Dr. P.L. Vijayammal University of Kerala Thiruvananthapuram	2.18
343	Investigations on the anticancer activity of reagents compounds isolated from garlic	Dr. Girija Kuttan Amala Cancer Hospital and Research Centre Thrissur	1.08
344	*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	8.16
345	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Y.M. Italia Valsad Raktadan Kendra Valsad	5.64
346	Experimental evaluation of some ayurvedic rasayanas on peptic ulcer and gastric muscosal offensive and defensive factors	Dr. R.K. Goel Institute of Medical Sciences Banaras Hindu University Varanasi	0.71
347	Behavioural teratology of some centrally acting drugs	Dr. Mandavi Singh Institute of Medical Sciences Banaras Hindu University Varanasi	2.22

Publication and Information

348	Scientometric studies on ICMR-sponsored research	Dr. K. Satyanarayana Indian Council of Medical Research New Delhi	1.57
349	ICMR-NIC Centre for Biomedical Information National Informatics Centre	Smt. S. Naina Pandita New Delhi	7.93

List of Fellowships Funded During 1999-2000

Epidemiology and Commmunicable Diseases		
1	HPLC methods for the determination of antifilarial drugs and their metabolites in different body fluids and their applications in pharmacokinetic studies	Dr. Reema Sarin Institute of Life Sciences Bhubaneswar
2	Studies on the vector of lymphatic filariasis in the coastal areas of Digha, West Bengal	Sh. S.N. Chatterjee The University of Burdwan Burdwan
3	Studies on the proteolytic pathways involved in the degradation of erythrocyte membrane proteins during anaemia in visceral leishmaniasis	Dr. Gargi Sen Indian Institute of Chemical Biology Calcutta
4	Characterization of fumerate reductase mediated succinate formation from L*eishmania donovani* promastigote for potential target of chemotherapy	Sh. Gautam Datta Jadavpur University Calcutta
5	Life cycle study of *Artyfechinostomum oraoni*	Dr. Indrani Paul University College of Science Calcutta
6	A systematic epidemiological survey of sporotrichosis in Parwanoo (Himachal Pradesh) Medical Education and Research	Sh. A.K. Ghosh Postgraduate Institute of Chandigarh
7	Antibody mediated selective targeting of isonicotinic acid hydrazide (INH) entrapped in PLG microparticles specifically to *Mycobacterium tuberculosis* infected macrophages	Smt. Indu Mehta Postgraduate Institute of Medical Education and Research Chandigarh

8	Role of anaerobic stress proteins in pathophysiology of *Salmonella typhimurium* infection	Sh. Raman Deep Singh Postgraduate Institute of Medical Education and Research Chandigarh
9	A study on calcium homeostasis of promastigote and axenic amastigote of *Leishmania donovani*	Sh. B.Anil Prasad Postgraduate Institute of Medical Education and Research Chandigarh
10	Protective efficacy and immunogenicity of iron regulated outer membrane proteins (IROMPs) of *Salmonella typhi*	Km. Shaloo Sood Postgraduate Institute of Medical Education and Research Chandigarh
11	To study the oxidative stress in rotavirus infected liver and small intestine of malnourished infant mice	Sh. Ranjan Katyal Postgraduate Institute of Medical Education and Research Chandigarh
12	To study the protective efficacy of antioxidants and Indian herbal antidiarroheals in rotavirus diarrohea	Sh. Ranjan Katyal Postgraduate Institute of Medical Education and Research Chandigarh
13	To study the immune response against lipopolysaccharide and outer membrane proteins and role of free radicals during experimental *H.influenzae* infection in mice	Km. Jaya Sahni Postgraduate Institute of Medical Education and Research Chandigarh
14	Immunoscreening of cDNA library of L_4 larval stages of B*rugia malayi* to identify potential vaccine candidate antigens for human lymphatic filariasis	Sh. D.Eswaran A.C.College of Technology Chennai
15	Rapid diagnosis of tuberculosis using purified antigens	Km. K.R.Uma Devi Tuberculosis Research Centre Chennai

16	Immunomodulatory effect of immune complexes in experimental tuberculous infections	Dr. H.Shakila Tuberculosis Research Centre Chennai
17	Studies on the influence of human leucocyte antigens (HLA-DR and- DQ) on immune responses in pulmonary tuberculosis	Sh. H. Uma Hariharan Tuberculosis Research Centre Chennai
18	HLA - DR2 and granulysin producing potential of $CD8^+$ and $CD4^+$ cells in pulmonary tuberculosis	Dr. Anila Anna Mathan Tuberculosis Research Centre Chennai
19	Epidemiology, socio-cultural and biomedical aspects of malaria	Dr. Kumud Sarin University of Delhi Delhi
20	Natural habitats of *Cryptococcus neoformans* var. *gattii* and var. *neoformans* and their serotypes	Sh. S.R.Nawange Rani Durgawati Vishwavidyalaya Jabalpur
21	Studies on cerebral microvessels and effect of antimalarial treatment during experimental malaria	Dr. Anju Agarwal K.G's Medical College Lucknow
22	Evaluation of newer laboratory techniques for early diagnosis of extra-pulmonary tuberculosis	Smt. Vandana Tiwari K.G's Medical College Lucknow
23	Is leptospiral infection a significant public health problem in north India	Smt. M.Martha Prem Latha All India Institute of Medical Sciences New Delhi
24	Prevalence and molecular typing of enterotoxigenic *Bacteroides fragilis* (ETBF) in diarrhoeal diseases	Dr. Nidhi Sharma All India Institute of Medical Sciences New Delhi
25	Molecular fingerprinting of clinical isolates of *Mycobacterium tuberculosis* by IS 6110-based restriction fragment length polymorphism (RFLP)	Smt. N.Vijaya Bhanu All India Institute of Medical Sciences New Delhi
26	Phenotypic and genotypic characterisation of methicillin resistant *Staphylococcus aureus* and its role in epidemiological typing	Sh. N.P. Mohapatra Lady Hardinge Medical College and Associated Hospitals New Delhi

Reproductive Health and Nutrition		
27	Sperm surface protein phosphorylation mechanism - a possible regulator of sperm maturation and its function	Smt. Debjani Nath Indian Institute of Chemical Biology Calcutta
28	Role of nitric oxide as an effector molecule in the process of implantation	Km. Shampa Biswas Indian Institute of Chemical Biology Calcutta
29	Fertility failure in intrauterine insemination : its causes with special reference to oxidative damage	Dr. Anuradha Chakrabarty Indian Institute of Chemical Biology Calcutta
30	A study of health and nutritional status in relation to some biosocial factors among the *kora* and *mahali* tribes of West Bengal	Dr. Bechuram Mondal Indian Statistical Institute Calcutta
31	Studies on further development of progesterone releasing intrauterine device (IUD) to enhance its duration of release	Dr. A.K.Ghosh Jadavpur University Calcutta
32	Studies on protein-fat interaction and its influence on serum and tissue lipid profile	Smt. Malabika Sen University College of Science and Technology Calcutta
33	Studies on the influences of different selenium levels on spermatogenesis and the possible role of selenium binding proteins in mice testis	Sh. Leelank Panjab University Chandigarh
34	Biodegradable polymeric implants for the controlled release of contraceptive agents	Sh. D.Selvaraj Central Leather Research Institute Chennai
35	Dietary efficacy of edible mushrooms along with vitamin E in modulating the risk of coronary heart disease in experimental rats	Km. G.K .Poongkodi Dr. A.L. Mudaliar P. G.Institute of Basic Medical Sciences Chennai
36	Studies on the placental proteins involved in differentiation of trophoblasts during first trimester of pregnancy in human	Km. Meena Jaggi University of Delhi Delhi
37	Characterization of cadherin and catenin expressed during implantation and establishment of its role in embryonic attachment	Km. Deeksha Saxena Devi Ahilya Vishwavidyalaya Indore

38	Studies on the contraceptive effects of leaf of the common mint *(Mentha arvensis* L.) in the male albino rat : Isolation and evaluation of the active antifertility principles	Dr. Nidhi Sharma University of Rajasthan Jaipur
39	Luteal protein secretion during early pregnancy in rat	Dr. Rajeev Chandra Central Drug Research Institute Lucknow
40	A study on free radical scavengers in infertile male spermatozoa	Sh. Kalbe Jawad K.G's Medical College Lucknow
41	The effect of administration of low, non-lethal doses of methyl parathion, phorate and monocrotophos on reproduction of male rats	Dr. Vijay Verma Punjab Agricultural University Ludhiana
42	Biochemical and histological investigations on antifertility effects of plants *Andrographis peniculata, Tylophora indicaand Vinca rosea* on gonads of male albino rats	Km. Surbhi Mittal D.N. College Meerut
43	A case-control study to identify the risk factors for lower limb amputation in diabetics	Dr. Shailendra Bajpai All India Institute of Medical Sciences New Delhi
44	Study of seminal plasma alpha-glucosidase activity and its possible role in male infertility	Dr. Komal K. Gaur All India Institute of Medical Sciences New Delhi
45	Modulation of integrin and cytokine expression in mouse blastocysts by steroid hormones :mechanisms of embryo implantation	Km. Sayantani Basak All India Institute of Medical Sciences New Delhi
46	Effect of food flavour cinnamaldehyde on kidney- a molecular approach	Dr. J.T.Sivakumar All India Institute of Medical Sciences New Delhi
47	Study of prevalence of anaemia, vitamin-A deficiency and goitre, dietary intake pattern and nutritional status of pregnant mothers belonging to schedule caste communities	Km. Priyali Pathak All India Institute of Medical Sciences New Delhi
48	Study of profile of diabetic complications in presence of different types of urinary protein excretion	Dr. Marumudi Eunice All India Institute of Medical Sciences New Delhi
49	Sonohysterography	Dr. Chetna Tiwari Army Hospital (Research & Referral) New Delhi

50	Study of laproscopic scoring of endometriosis and management with danazol in 50 patients of diagnosed endometriosis	Dr. Sarabjit Kaur Army Hospital (Research & Referral) New Delhi
51	Nutrition knowledge of medical practitioners in hospitals : an assessment, intervention and impact	Km. Charu Institute of Home Economics New Delhi
52	To study the influence of maternal haemoglobin and ferritin on placental volume in less than 20 weeks gestation	Dr. Poonam Sachdeva Maulana Azad Medical College and Associated Hospitals New Delhi
53	Evaluation of the effects of estrogenic environmental contaminants in male reproduction of adult rats	Sh. C.Latchoumycandane University of Pondicherry Pondicherry
54	Gender discrimination and child mortality : a sociological study in Salem district of Tamil Nadu	Sh. P. Murugan Bharathidasan University Tiruchirapalli
55	A study on physical and psychosocial development of pre-school children of urban slums of Varanasi	Dr. Prithviraj Sen Institute of Medical Sciences Banaras Hindu University Varanasi
	Non-communicable Diseases	
56	Biochemical, histopathological and cytogenetical studies of cadmium toxicity in different tissues of mice	Sh. Ranajit Karmakar Jadavpur University Calcutta
57	Antitumour potential of 1 alpha , 25 - dihydroxyvitamin D3 in n-nitrosodiethanolamine induced rat liver carcinogenesis : a mechanistic approach	Sh. Ranjan Basak Jadavpur University Calcutta
58	Carcinoma - associated mucin antigens (Tn, S-Tn and T) : efficacy in detecting and monitoring patients with squamous cell carcinoma of the head and neck, oral, oesophagus, lung and cervix	Sh. K.Sankaranarayanan University of Madras Chennai
59	Improving mental health of high school students with psychotherapeutic interventions in relation to examination anxiety	Dr. Anita Gupta University of Delhi Delhi

60	Carrier detection strategies for Duchenne muscular dystrophy	Sh. Tajamul Hussain Institute of Genetics and Hospital for Genetic Diseases Hyderabad
61	Study of crystals in osteoarthritis knee and the evaluation of colchicine as a disease modifying drug for osteoarthritis	Dr. Ragini Srivastava K.G's Medical College Lucknow
62	Argyrophilic nucleolar organizer regions and KI-67 proliferation markers in fine needle aspirates of thyroid lesions	Dr. Anju Mehrotra K.G's Medical College Lucknow
63	Rehabilitation surgery for lower limb deformities due to poliomyelitis	Dr. Rahul Khare K.G's Medical College Lucknow
64	A study on oxidative stress and anti-oxidant status in gynaecological malignancies	Dr. A.A.Mahdi K.G's Medical College Lucknow
65	Effect of certain antiviral agents on the modulation of radiosensitivity of HeLa cells *in vitro*	Smt. K.Aruna Kumari Kasturba Medical College and Hospital Manipal
66	Evaluation of the role of TPS determination in management of cancers in a north Indian population	Smt. Padmamalika Khanna L.L.R.M.Medical College Meerut
67	Studies on BRCA 1 and BRCA 2 gene mutations in breast cancer patients	Dr. T.M. Valarmathi All India Institute of Medical Sciences New Delhi
68	The role of retinoblastoma antioncoprotein in the progression and prognosis of primary brain tumours	Km. Annapurna Rathore All India Institute of Medical Sciences New Delhi
69	Comparative evaluation of low energy lasers, ultrasonic energy and microwave diathermy in the treatment of oral submucous fibrosis	Dr. Padma Prasanna Kumar All India Institute of Medical Sciences New Delhi
70	A study of genetic alterations overriding the cell arrest effect of normal p53 overexpression in an *in vitro* glial tumour model	Sh. S.Ilanchezhian All India Institute of Medical Sciences New Delhi

71	Colonic mucosal changes in patients with portal hypertension - a clinicohistopathological study	Dr. Sumeet Sethi Army Hospital Research & Referral) New Delhi
72	A study of prevalence of hepatitis C virus infection among armed forces personnel	Dr. Rajni Parmar Army Hospital (Research & Referral) New Delhi
73	To evaluate the efficacy of non - invasive ventilation in acute respiratory failures due to chronic obstructive pulmonary disease (COPD)	Dr. Anjali Chawla Army Hospital (Research & Referral) New Delhi
74	Ultrasonographic evaluation of posterior segment in ocular injuries with opaque media - a clinical study	Dr. Simaljit Kaur Army Hospital (Research & Referral) New Delhi
75	To study the prevalence and clinical course of ophthalmopathy associated with autoimmune thyroid disorders in defence forces hospital dependent population	Dr. Hema Rawal Army Hospital (Research & Referral) New Delhi
76	Rehabilitation of patients of severe arthritis of hip joint by hybrid total hip arthroplasty	Dr. Naval Bhatia Safdarjang Hospital New Delhi
77	A survey on coronary risk factor profile in relation to prevalence of CHD in Tirupati urban population	Sh. S.A.Abdul Latheef S.V. Institute of Medical Sciences Tirupati
Basic Medical Sciences		
78	Antihyperglycaemic effect of *Phaseolus vulgaris* L. (kidney bean) and *Coccinia indica* W.and A. (little gourd) in experimental diabetes:effects compared with troglitazone, a new oral antidiabetic agent	Sh. S.Venkateswaran Annamalai University Annamalai Nagar
79	Effect of seizures and antiepileptic drug on the sleepwake- fulness cycle in kainic acid model of epilepsy in rats	Sh. Y.H. Raol National Institute of Mental Health and Neurosciences Bangalore
80	Biochemical and pharmacological studies on serotonin-1 and serotonin-2 receptors in human post-mortem brain of neuropsychiatric disorders	Sh. V.K .Yaragudri National Institute of Mental Health and Neurosciences Bangalore
81	Anti-thyroid action of phenylhydrazine: studies on the	Dr. Mitali Pramanik

	hypothalamopituitary - thyroid axis in juvenile and adult male rats	Bose Institute (New Campus) Calcutta
82	Studies on growth and melanization of epidermal cells by selected ceramides and cerebresides to compare the action of ceramides present in a human placental extract meant for vitiligo therapy	Km.. Shampa Mallick Indian Institute of Chemical Biology Calcutta
83	Study of cell cycle and induction of apoptosis by centchroman and its enantiomers – a contraceptive and a candidate drug for breast cancer in V79,CHO,MCF-7 and MDA-MB-231 cell lines	Sh. Amitabha Mukhopadhyay Indian Institute of Chemical Biology Calcutta
84	9-O-acetyl sialoglycoconjugate (9-O-AC-SG), a novel biomarker on the surface of leukemic blasts-specific target molecule for drug targetting in childhood acute lymphoblastic leukemia (ALL) using an unique lectin and specific antibodies	Sh. Satyabrata Biswas Indian Institute of Chemical Biology Calcutta
85	Involvement of calcium in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine - induced neurotoxicity	Dr. Supriti Samanta Ray Indian Institute of Chemical Biology Calcutta
86	Ischaemic myocardial damage and red blood cells : role of antiarrhythmic drugs	Smt.Aindrila Chattopadhyay Jadavpur University Calcutta
87	Cigarette smoke-induced oxidative damage and its prevention	Sh. Koustubh Panda University College of Science Calcutta
88	Estimates of genetic and environmental variances for body measurements from twin and family data	Sh. Somnath Basu University College of Science Calcutta
89	A gastric antiulcer activity of vestibulo-cerebellum and role of mast cells	Smt. Neeta Sarkar University College of Science and Technology Calcutta
90	Identification and role of intestinal lactase gene in hypolactasia in adult rats	Km. Jaspreet Kaur Panjab University Chandigarh

91	Purification, biochemical characterization and nuclear localization of calmodulin in *Microsporum gypseum*	Sh. D.D. Deo Postgraduate Institute of Medical Education and Research Chandigarh
92	Human genetic polymorphism of omeprazole hydroxylation (CYP2C19) in Indian subjects	Km. Jatinder Kaur Postgraduate Institute of Medical Education and Research Chandigarh
93	Effect of co-administration of isoniazid, rifampicin and pyrazinamide on hepatic oxidative stress, DNA damage and repair in mice	Sh. Vishal Lamba Postgraduate Institute of Medical Education and Research Chandigarh
94	Purification and characterization of zinc binding protein from renal cortex of rat	Sh. Rajendra Kumar Postgraduate Institute of Medical Education and Research Chandigarh
95	Evaluation of neuroprotective role of dl-alpha-lipoic acid in ageing rats	Sh. P. Arivazhagan Dr. A.L. Mudaliar P. G. Institute of Basic Medical Sciences Chennai
96	Studies on the insulin like effects of sodium tungstate on streptozotocin induced diabetes in rats	Sh. P. Ravichandran University of Madras Chennai
97	Effect of diclofenac and piroxicam with and without vitamin E supplement on the ovarian function in adult albino rats	Km. Vinolia Azariah Bharathiar University Coimbatore
98	Ischaemia induced alterations in c-fos, HSP70 and excitatory amino acid neurotransmitters in gerbil brain under differential thyroid status	Dr. Meenakshi Bawari Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow

99	Development of antibodies against human sodium/iodide symperter (HNIS) and development of assay procedures for NIS	Dr. Amita Mehrotra Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
100	Fluorescence response in chlortetracycline loaded cells : characteristics of the response with various methods of calcium release from intracellular stores in different cell types	Km. P.R. Vijayalakshmi Varma Kasturba Medical College and Hospital Manipal
101	The prognostic significance of the expression of resistance gene (mdrl and mrp) and glutathione S transferase in acute leukaemias	Dr. S.K.Gurbuxani All India Institute of Medical Sciences New Delhi
102	Modulatory role of ascorbic acid on oxidative modification of human low density lipoprotein and on atheroma formation in rabbits	Smt. Sabari Das All India Institute of Medical Sciences New Delhi
103	Molecular genetic studies in glaucoma	Km. R. Vijaya All India Institute of Medical Sciences New Delhi
104	The septal noradrenergic mechanism for elaboration of male sexual behaviour in rats	Dr. Kamlesh Kumari Gulia All India Institute of Medical Sciences New Delhi
105	VMN modulation of tonic pain in chronically sucrose fed rats	Smt. Kaushiki Chatterjee All India Institute of Medical Sciences New Delhi
106	Role of the medical preoptic neurons in the regulation of sleep and brain temperature under different environmental temperatures	Dr. A.P. K.. Mahapatra All India Institute of Medical Sciences New Delhi
107	The design of peptide inhibitors using alpha, beta dehydro residues	Dr. Sneh Arora All India Institute of Medical Sciences New Delhi

108	Immunohistochemical studies of effect of prenatal sound overstimulation on synaptogenesis in chick brainstem auditory nuclei	Smt. Phalguni Anand Alladi All India Institute of Medical Sciences New Delhi
109	Heparin from the seaweed *Grateloupia filicina*	Sh. A. Muruganantham Centre of Advanced Study in Marine Biology Parangipettai
110	Studies on goat uterine nuclear estrogen receptors: (a) association of nuclear estrogen receptors with small nuclear ribonucleoproteins (SnRNPs) as an indirect measure of the receptor influence in splicing process. (b) ubiquitination of nuclear estrogen receptors	Sh. Thomas Sebastian Rajiv Gandhi Centre for Biotechnology Thiruvananthapuram
111	Antineoplastic evaluation of alkaloidal principles of *Amoora rohituka* based on flow cytometry	Dr. T. Rabi Regional Cancer Centre Thiruvananthapuram
112	Studies on the metabolism of extracellular matrix components by hepatic non-parenchymal cells	Km. P. Pranitha University of Kerala Thiruvananthapuram
113	Biochemical investigations on the flavonoids from *Emblicaofficinalis* and *Mangifera indica*	Km. L. Anila University of Kerala Thiruvananthapuram
114	Effect of algal toxins *(Ptychodiscus brevis)* on the spinal monosynaptic transmission *in vitro*	Sh. J.N. Singh Institute of Medical Sciences Banaras Hindu University Varanasi
115	Search for *Brahmi* - a comparative study of *Bacopa monnieri*and *Centella* species	Dr. Deepa Arora Institute of Medical Sciences Banaras Hindu University Varanasi
116	Neuropsychopharmacological studies on Indian *HypericumPerforatum* L.	Sh. Vikas Kumar Institute of Technology Varanasi