

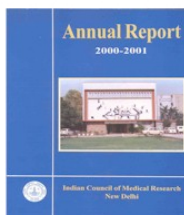
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Overview

The Indian Council of Medical Research is an autonomous organization under the Ministry of Health and Family Welfare, Government of India and is the main funding agency for medical research in the Country. During the year 2000-2001, modernization of laboratories of ICMR institutes/centres initiated during 1998-99 was continued.

To increase awareness about ethical issues and intellectual property rights in medical research among the scientific community, workshops were organized during the year. Indo-foreign collaborative projects were also supported by the Council.

Highlights of research activities of the Council are presented below:

Communicable Diseases

The Council continued research on the basic, clinical and epidemiological aspects of a number of prevalent bacterial, parasitic and viral diseases including acquired immunodeficiency syndrome (AIDS). The Chennai based Tuberculosis Research Centre (TRC) of the Council is conducting various studies on tuberculosis to strengthen the revised national tuberculosis control programme. Attempts are being made to develop more effective drug regimens and monitoring of drug resistance. Operational studies for better implementation of DOTS (directly observed treatment short-course), and immunological and biochemical studies have also been carried out.

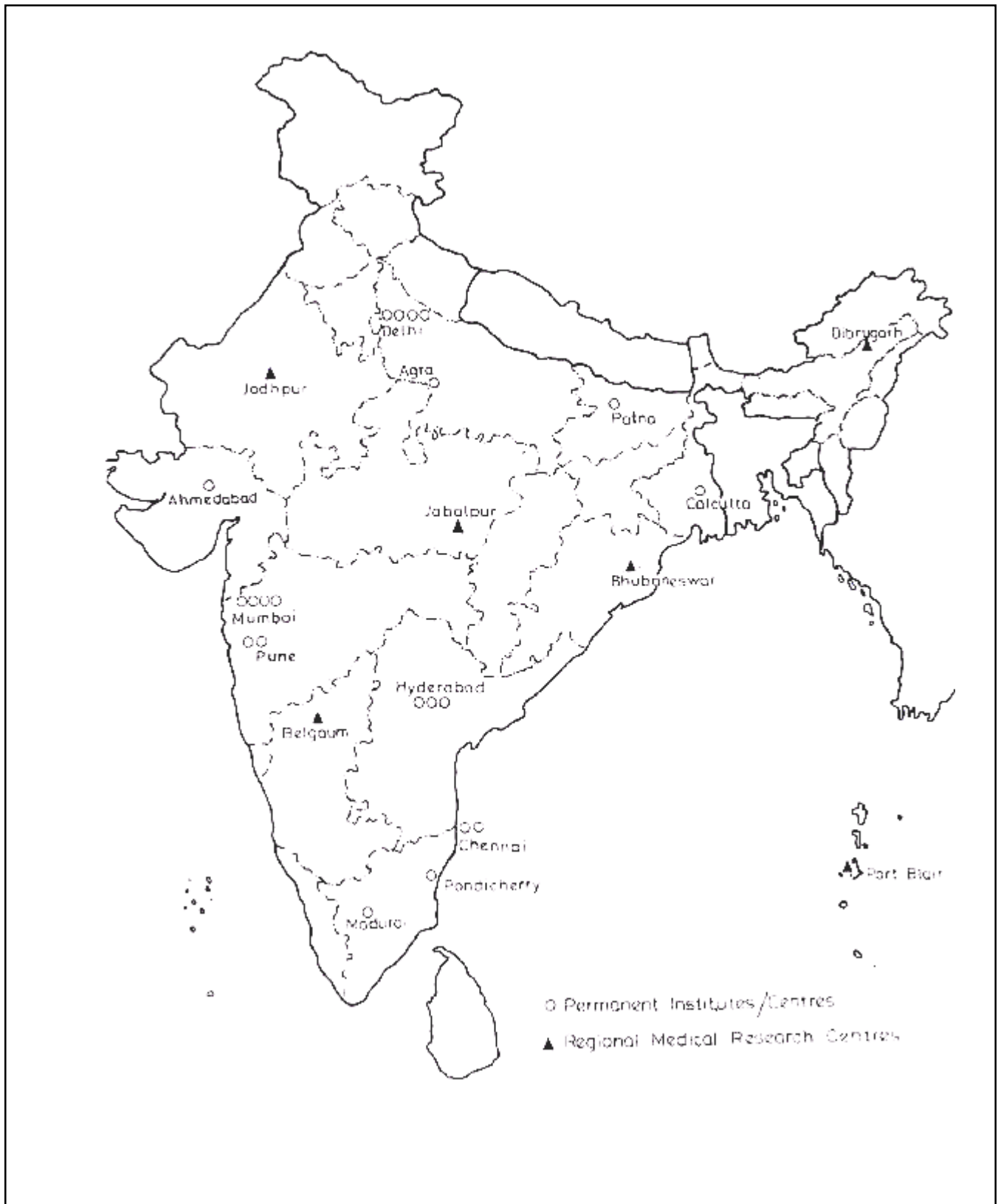
In the field of leprosy, the Council's Central JALMA Institute for Leprosy (CJIL) at Agra is assisting the National Leprosy Eradication Programme (NLEP) which has shown considerable improvement in terms of reduction in prevalence rates. Therapeutic trials have been conducted for testing the efficacy of a number of multidrug regimens. Immunological studies to

understand local immunity in leprosy and immunotherapeutic studies on the efficacy of *Mw* vaccine were also conducted during the year.

The National Institute of Cholera and Enteric Diseases, Kolkata is conducting studies on a number of diarrhoea causing pathogens such as *Vibrio cholerae*, *Shigella* spp., *V.parahaemolyticus*, *Salmonella typhimurium*, rotavirus and *Entamoeba histolytica*. During the year, outbreaks of leptospirosis reported from various parts of the country were investigated by the Council's Regional Medical Research Centre, Port Blair besides clinical, serological and epidemiological studies on leptospirosis.

The Council has taken up studies on vector and parasite biology, chemotherapy, molecular epidemiology, entomology and diagnostic studies on malaria, filariasis and leishmaniasis. Under the integrated vector control programme, a study has been initiated in Sundergarh district of Orissa to develop a field site for vaccine trials besides the roll back malaria initiative in pilot districts (Jodhpur, Aizwal, Tumkur, Keonjhar) and entire Goa state. Distribution of malaria and filariasis has been studied using geographical information system maps.

During the year under review, studies were continued for development of vaccine against Japanese encephalitis, surveillance of poliomyelitis, molecular epidemiology of wild polioviruses, molecular biology of hepatitis and epidemiology of dengue. Acquired immunodeficiency syndrome (AIDS)/human immunodeficiency virus (HIV) infection continue to remain a priority area of research by the Council. Socio-behavioural and epidemiological studies, development of AIDS vaccine and studies on molecular pathogenesis and immunological aspects of HIV infection were continued during the year. The National AIDS Research Institute (NARI) at Pune is participating in a feasibility study of azidothymidine treatment for reducing mother to child transmission of HIV infection.



ICMR Institutional Network

Reproductive Health

Research in the field of reproductive health was focussed on male and female contraceptives, emergency contraception, male and female infertility and expression of functional markers in primate endometrium. An operational study was conducted to assess the contraceptive knowledge and practices of women seeking abortion. Four kits have been developed for quantitation of reproductive hormones and a separate study was conducted to assess the feasibility of using pregnancy detection kit in PHCs/villages and urban slums. Management practices of pregnant women with meconium stained amniotic fluid and meconium aspiration syndrome were studied by 21 Human Reproduction Research Centres of the Council.

Nutrition

The Council's National Institute of Nutrition (NIN) at Hyderabad and the National Nutrition Monitoring Bureau conducted a series of community surveys in different parts of the country for assessment of diet and nutritional status of the population. Drought surveys were undertaken in Andhra Pradesh, Gujarat and Rajasthan. Safety and feasibility of administering vitamin A alongwith oral polio vaccine was assessed in five randomly selected districts of Orissa. Other areas of research included bioavailability of micronutrients and trace elements, food and drug toxicology and role of diet in cancer. Basic and applied studies on obese mutant rats were continued.

Environmental and Occupational Health

The National Institute of Occupational Health (NIOH) at Ahmedabad and its regional centres at Bangalore and Calcutta continued studies on health problems of industrial workers engaged in manganese mining, tobacco harvesting, quartz and agate grinding and pesticide formulation. A study was undertaken in child labour employed in match industry at Sivakasi (Tamil Nadu) and in cycle rickshaw pullers in Kolkata. Psychological evaluation of children exposed to lead (through lead smelting units) revealed that their performance IQ was depressed significantly.

Non-communicable Diseases

During 2000-2001, priority areas of research in non-communicable diseases comprised cancer (breast, cervical and prostate), cardiovascular diseases, glaucoma, psychiatric disorders in children, suicide behaviour, disability and rehabilitation. *Jai Vigyan* Mission mode project on community control of rheumatic fever/rheumatic heart disease was continued to study the epidemiology and vaccine development for streptococcal infections. A study of mental health service needs of the earthquake affected population in Gujarat was initiated during the year. For community control of thalassaemia syndrome, screening of population has been started and education, awareness and counselling material has been prepared under the *Jai Vigyan* mission mode project. The Council is continuing studies on other haematological disorders also such as G-6-PD deficiency, myelodysplastic syndrome, bleeding disorders and haemoglobinopathies in tribal populations of India.

Basic Medical Sciences

Multidisciplinary studies in traditional medicine were continued by the Advanced Centres at Lucknow and Mumbai and at other institutes in the country. During the year the Clinical Pharmacology Unit established at TRC, Chennai studied the herbal immunomodulators and hepatoprotective drugs as adjunct to anti-tuberculosis drugs. Multicentric studies were conducted on *Pterocarpus marsupium* (Vijaysar) and *Picrorrhiza kurroa*, *Terminalia chebula* and *Centella asiatica*. An in-house *neem* oil preparation has been standardized at the Advanced Centre in Clinical Pharmacology at Seth G.S. Medical College and KEM Hospital, Mumbai.

A programme has been initiated to develop standards for 160 therapeutically important medicinal plants.

Studies were continued on the pathogenesis of systemic lupus erythematosus, antioxidant effects of garlic/onion oil, development of novel uterine relaxants, pharmacokinetics of rifampicin and ofloxacin and role of angiotensin converting enzyme inhibitors in myocardial stunning.

Publication, Information and Communication

The ICMR continued to bring out the Indian Journal of Medical Research, ICMR Bulletin, ICMR *Patrika* and Annual Report in English and Hindi. This year the ICMR *Patrika* was awarded the *Utkrishta Patrika Samman*, in Millenium World Hindi Conference. The ICMR-NIC Centre for Biomedical Information has developed a webpage (<http://indmed.nic.in>) giving

details of the services being provided. ICMR web page (<http://www.icmr.nic.in>) gives information on ICMR institutes, research projects and publications *etc.* of the Council. The ICMR Hqrs. And its institutes organized National Science Day (NSD), lectures, discussion, open houses, exhibitions *etc.* for dissemination of health information to general public including school children. The theme of the NSD for the year 2001 was Information Technology for Education.



Communicable Diseases

Infectious diseases remain a cause of major public health concern. Currently, known communicable diseases dominate the disease pattern. Malaria and kala-azar have re-appeared. An added cause of concern is the emergence of drug resistant tuberculosis, malaria and gonococcal infections. Equally alarming have been the reported outbreaks of leptospirosis in some parts of the country. New diseases like HIV infection have spread to all parts of the country. Diarrhoeal diseases continue to be one of the leading causes of childhood deaths. In addition, Japanese encephalitis, dengue and dengue haemorrhagic fever have made significant in-roads in the country while hepatitis B, C and E are perceived as major public health threats.

The ICMR through its network of disease specific Institutes/Regional Medical Research Centres (RMRCs) and extramural research programmes has initiated activities to meet the challenges, both old and new, for prevention and control of emerging, re-emerging and other communicable diseases. 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 kills one person per minute in India. It has emerged as a major public health problem especially in association with HIV. In fight against tuberculosis, the Tuberculosis Research Centre (TRC), Chennai, is conducting studies to strengthen the Revised National TB Control Programme (RNTCP) through development of more effective drug regimens, monitoring of drug resistance, improving microscopy techniques, conduct of basic immunological and genetic studies and

operational research for better implementation of directly observed treatment short-course (DOTS).

Clinical Trials

The TRC is currently undertaking a randomised clinical trial to assess the efficacy of 3, 4 and 5 month regimens in the treatment of sputum positive pulmonary tuberculosis *viz.* (i) three months of ofloxacin(O) isoniazid (H), rifampicin (R) and pyrazinamide (Z) daily (Reg.1); (ii) three months of OHRZ daily followed by one month of H and R twice a week (Reg 2); (iii) three months of OHRZ daily followed by two months of H and R twice a week (Reg 3); and (iv) two month of OHRZ daily followed by two months of H and R twice a week (Reg 4). All drugs were given under supervision. Patients who defaulted were visited at home and motivated to attend. Interim analysis demonstrated that 360 of the 529 patients had bacilli sensitive to all drugs while in 56, bacilli were resistant to one or more drugs. The results of sputum culture conversion are shown in Fig.1. Results of the bacteriological status at end of treatment are shown in Fig.2. Forty seven patients had pre-treatment resistance to H, all but two of whom had a favourable response. Eight patients had resistance to R and H, one of whom was also resistant to O. Of these, five patients had an unfavourable response, one relapsed and the other two had favourable response. Patients have now been followed up for 20 to 48 months after the start of treatment. The relapse rates are shown in Fig.3. The difference in the relapse rates between regimens 2 and 3 (each had an intensive phase of three months) compared to regimen 4 (which had an intensive phase of only two months) was statistically significant. Follow up is continuing.

In another study, evaluation of an oral 8-month regimen in the treatment of sputum positive pulmonary tuberculosis was carried out to study the efficacy of a regimen with the same initial intensive phase (2ERHZ thrice weekly), but with a continuation phase of 6 months

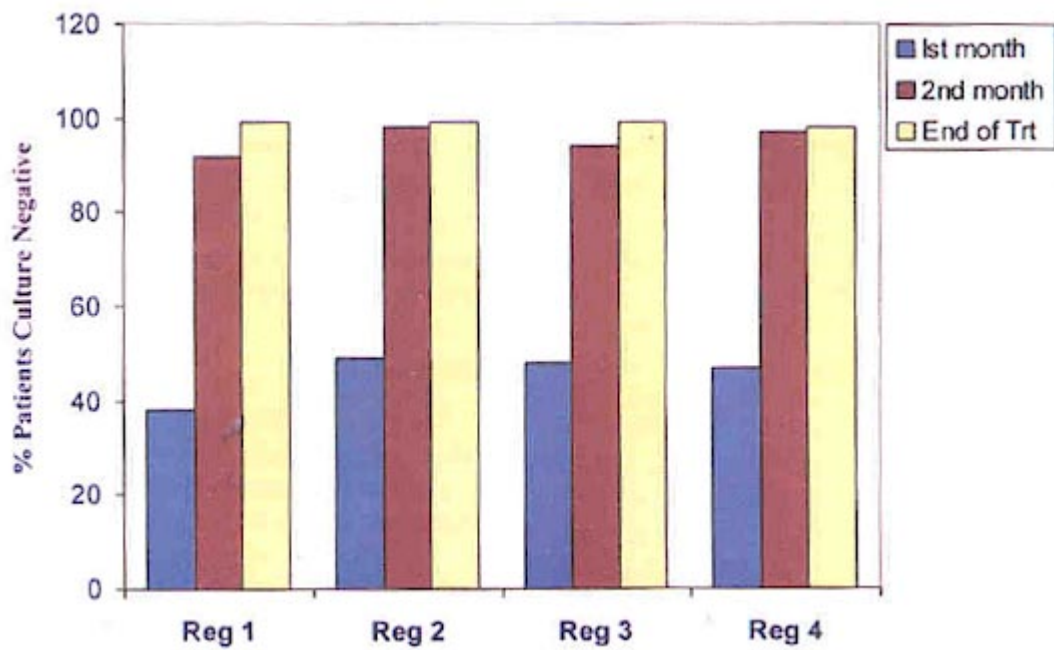


Fig.1. Sputum culture conversion.

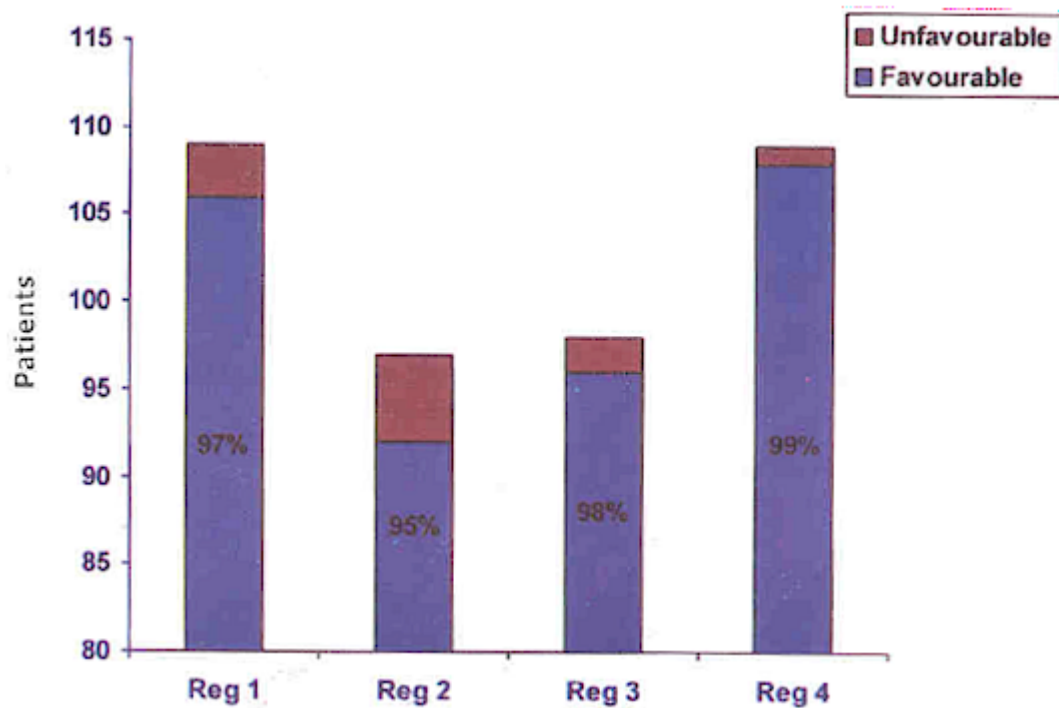


Fig.2 Bacteriological status at end of treatment.

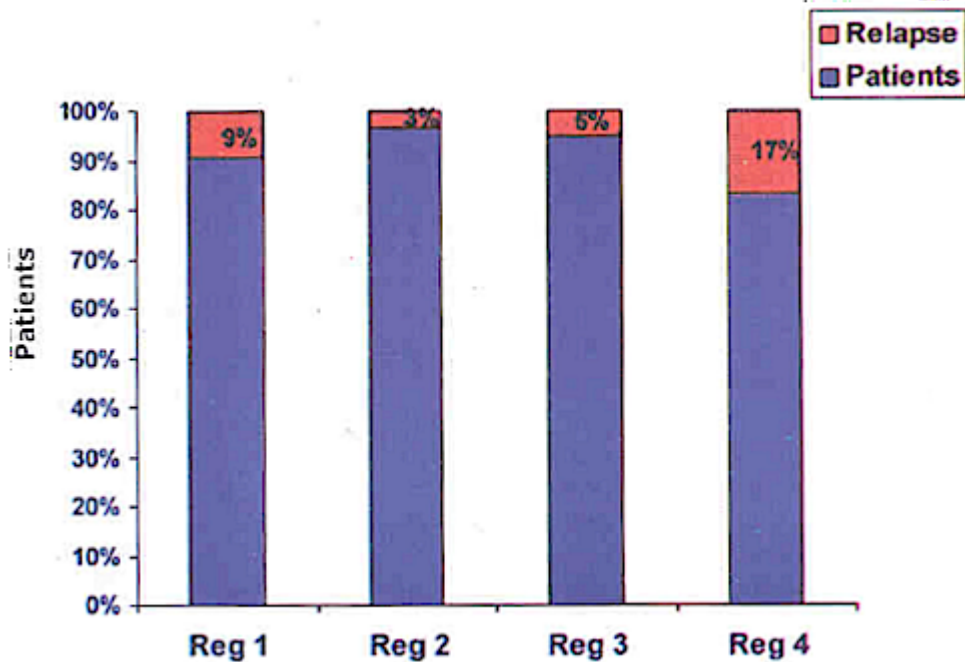


Fig.3 Relapse after treatment.

of daily ethambutol (E) and isoniazid given as once weekly supply. Of the 200 patients admitted to the study, 20 were excluded from analysis for various reasons. 1.90% had bacilli susceptible to all anti-tuberculosis drugs, while 9% were resistant to H and 1% to H and R. The lone patient with MDR-TB had a doubtful response at the end of chemotherapy. All patients will be followed up for a period of 2 years. The study is in progress.

A study is ongoing at TRC to assess the efficacy of the category 1 regimen (2EHRZ₃/4RH₃) in relation to both cure and relapse rates in non insulin dependent diabetes mellitus (NIDDM) patients suspected with pulmonary tuberculosis. Among the 52 patients enrolled till date 15.4% are still on treatment while 7.7% were lost to follow up. The proportion of patients who became smear negative at each month was 37%, 66%, 79%, 87%, 92% and 89% respectively. The patients who had unfavourable response became smear and culture negative by 2nd month but became smear positive by 3rd month and culture positive by 5th month and remained positive subsequently. Follow up is continuing.

Studies on Drug Resistance

In order to examine the issue of emergence of resistance among patients treated with the currently used drugs in the programme, a retrospective analysis of studies using the regimens *viz* (i) 2 HRZE₇/6 HE₇ (ii) 2 HRZE₂/4HRE₂ (iii) 2 HRZE₃/4HR₂ (iv) 3 HRZE₃/3HR₂ was carried out. Of the 1817 patients studied, 79% had organisms susceptible to all drugs of which 2% had unfavourable response, 7% bacteriological relapse and 1% developed resistance to H or R or both. Pre-treatment H resistance of 21% was noted and the emergence of resistance to R occurred among 2% of the patients treated with standard short-course treatment. The results indicated that sputum positive pulmonary tuberculosis patients can be successfully treated with standard short-course chemotherapy regimens.

Operational Research

The TRC has undertaken a project in collaboration with the Government of Tamil Nadu with the main objectives to (i) establish a model centre for DOTS implementation in a population of approximately 5 lakhs

in Thiruvallur district (ii) establish a centre for DOTS demonstration and training, (iii) strengthen the infrastructure at state level, particularly in the districts surrounding the project area, (iv) assess epidemiological impact of DOTS using annual risk of infection (ARI) (tuberculin surveys), disease survey, RFLP and drug resistance surveys and (v) to conduct operational research on key aspects of the DOTS strategy. Five *Panchayat* unions in Thiruvallur district covering a population of 5,87,000 in 218 villages were selected for this project. So far a number of medical and paramedical personnel have been given field training. A baseline survey to estimate the prevalence of disease and infection is in progress in the project area. ARI is being estimated in 45,000 children below 15 yr. The survey methodology involves enumeration of the study population, identification of children aged 2 months to 14 yr, BCG scar reading, tuberculin testing with 1TURT23 and reading and reaction size 72 to 96 h after testing. Of the 17,788 children examined, 38% had a BCG scar. In order to study the drug susceptibility pattern and the profile over a period of time, two additional sputum samples were collected from 1060 patients in the model DOTS area, preferably within a week after starting treatment. A total of 500 clinically proven cases of tuberculosis were identified for molecular epidemiological studies from model DOTS area. Data is being examined to identify gender differences with respect to infection and disease in the community. Data on cases identified in the model DOTS project area will help to understand the self-reporting and diagnosis of the disease in service programme.

Epidemiological Studies

At TRC, a study was conducted in a random sample of villages in Kadambatur and Thiruvalangadu blocks of Thiruvallur district to evaluate the risk of tuberculosis among tobacco smokers. An association between tobacco smoking and pulmonary tuberculosis was found. The cumulative effect of duration of smoking also showed a highly significant trend.

Bacteriological Studies

In a study carried out at TRC, comparative efficacy of two sedimentation agents *viz.* sodium hydroxide-ammonium sulphate (SAS) and phenol-ammonium sulphate (PAS) in detecting AFB in sputum of TB patients

was evaluated. By this method the smears can be prepared with ease and less time is required to grade them. The results of the study revealed that PAS is more sensitive in picking up the positives than the SAS.

Rifampicin (R) resistance serves as a surrogate marker for the detection of MDR-TB as 90% of R resistant (R) isolates are also H-resistant (H). A total of 66 clinical isolates of *M.tuberculosis*, 3 quality control strains and a reference strain, namely, *M.tuberculosis* H₃₇Rv were tested for their susceptibility to 1 and 2 mg of H and R/ml respectively, using luciferase reporter phage (LRP) assay. Modifications to the original protocol of growing the isolates in 7H9 broth for 7 days and exposing the same to the action of the drugs for 48 h were found necessary to overcome sample contamination. Among the four LRP procedures used, results of direct LRP sensitivity assay using phAE85 showed a better correlation with those of the conventional susceptibility test. With a growth inhibition index breakpoint of 50%, the agreement of the direct LRP results with the conventional method was 95%, both for H and R. While all the drug susceptible isolates were correctly identified by this test, the sensitivity of the assay to detect drug resistance was 90% and 85% for H and R respectively. The level of sensitivity increased to greater than 92% with both the drugs, if an inhibition index breakpoint of 90% was used. These results suggest that direct LRP assay with phAE85 can be used as an alternate method for the conventional sensitivity test for *M.tuberculosis*.

Immunological Studies

Numerous studies have emphasized the importance of host genetic factors in resistance/susceptibility to tuberculosis. The host genetic factors may be divided into major histocompatibility complex (MHC) genes, human leucocyte antigens (HLA) and non-MHC/non-HLA genes. A study has been carried out at TRC to identify a gene or multicandidate genes associated with susceptibility to TB which may serve as genetic marker(s) to predetermine the development of the disease. Earlier studies conducted at the Centre had shown that the HLA-DR2 is associated with susceptibility to pulmonary tuberculosis. An increased frequency of HLA-DR2 was seen in the pulmonary tuberculosis patients when compared to control subjects. DNA typing of HLA-DR2 sub-types using sequence specific oligonucleotide probes (SSOP) revealed that DRBI 1501 was significantly

associated with susceptibility to tuberculosis and a trend towards decreased frequency of DRBI 1502 and 1503 was seen in patients. The results suggest that DRBI 1501 is the main allele of the HLA-DR2 subtypes *i.e.* associated with susceptibility to pulmonary tuberculosis.

In addition, a study was also carried out to understand the role of HLA-DR2 and non-DR2 (DR2 negative) genes/gene products on the innate immune mechanism associated with susceptibility to tuberculosis. The effect of binding of lysozyme on live *M.tuberculosis* H₃₇Rv on its viability and plasma lysozyme levels was studied. The plasma samples of active TB patients and normal healthy subjects treated with live *M.tuberculosis* H₃₇Rv showed decreased lysozyme levels. The results suggest that lysozyme plays a role alongwith other lysosomal enzymes in the innate immune mechanism against *M.tuberculosis* infection. Initial infection in HLA-DR2 positive normal subjects may be associated with a high responder status, in turn making them tolerant for the pathogens.

It has been earlier demonstrated that nitric oxide, the product of the arginine dependent pathway of human mononuclear phagocytes effectively kills *M.tuberculosis in vitro*. The release of reactive nitrogen intermediates was triggered by incubation with various proinflammatory cytokines namely IFN- γ , TNF- α and IL-1 β . By using colony forming assay, it was demonstrated that human mononuclear phagocytes can effectively kill *M.tuberculosis* by using a NO dependent pathway.

A project is ongoing at V.P.Chest Institute, University of Delhi, to study the role of proinflammatory cytokines in the induction of nitric oxide from human mononuclear phagocytes of pulmonary tuberculosis patients.

To ensure that the inducible nitric oxide synthase (iNOS) pathway of nitric oxide is actually occurring, mRNA isolation (for iNOS gene) from activated monocytes and macrophages of active tuberculosis patients will be performed by reverse transcriptase polymerase chain reaction (RT-PCR). The study is continuing.

In studies done at Institute of Pathology (IOP), New Delhi immunohistochemical (IHC) staining showed mycobacterial antigen in 74% cases compared to 44% stained with Z-N stain in tuberculous lymphadenitis. IHC staining highlighted the antigen either as solid or beaded rods within epithelioid cell cytoplasm, caseous

areas and giant cells or as antigenic dust within caseous areas.

Biochemical Studies

Ofloxacin (O) has proved to be a valuable addition to the available anti-TB drugs. Since limited information is currently available on the pharmacokinetic interactions of O with other anti-TB drugs, *viz.*, R, H and Z, a study was undertaken to investigate the bioavailability of O when given alone and in combination with the above mentioned drugs in healthy subjects. Twelve male healthy volunteers were randomly allocated to different groups, namely, O alone, O+R, O+H, O+Z and O+R+H+Z. Blood and saliva samples were collected at 1,2,3,6 and 8 h after drug administration and total urine excreted during 0-4 and 4-8 h was collected. Plasma concentrations of all the four drugs, salivary concentrations of O and urinary excretion of O, total R, H and its metabolites (acetyl H and isonicotinic acid), Z and pyrazinoic acid were determined after coding the samples. The pharmacokinetic variables such as peak concentration (C-max), time taken to attain the peak concentration (t-max), the area under the time-concentration curve (AUC) and half-life (t_{1/2}) were calculated from the plasma and salivary concentrations. Further, the proportion of doses excreted as unchanged drugs and their primary metabolites in urine collected during 0-4 and 0-8 h were also calculated. The results of this study indicate that the pharmacokinetic properties of O are not modified when administered with other anti-TB drugs *viz.*, R, H and Z and also the bioavailability of these drugs do not get altered when given alongwith O.

A simple and rapid high performance liquid chromatography (HPLC) method for determination of O in plasma and urine has also been standardised. The method is simple, sensitive and precise with an accuracy of greater than 90%. The assay is less laborious and time consuming than the bioassay and permits processing of more samples and, therefore, it is more suitable for kinetic studies. An HPLC method for determination of R concentration in plasma has also been standardised. The method is specific and none of the other anti-tuberculosis drugs interfered in the estimation.

LEPROSY

As India moves closer to the goal of elimination of leprosy, The Council's Central JALMA Institute for Leprosy

(CJIL) at Agra is assisting the National Leprosy Eradication Programme by focusing its research activities on early detection of cases and putting them on appropriate treatment schedule for an adequate duration to prevent relapses and late reactions. Markers are being identified to monitor treatment and for detecting genetic susceptibility. Basic research is being pursued for developing these tools. In addition, behavioural, sociological as well as operational research is also being conducted.

Therapeutic Trials

The relapse rates among multibacillary (MB) patients who were given 2 yr. fixed duration therapy till the point of smear negativity (conventional therapy) are being followed up. In a follow up of 3-7 yr., relapses have been observed to be significantly higher in patients treated with 24 months fixed duration MDT as compared to those treated till smear negativity. Further, among both the groups relapse rate was significantly higher among those with high bacterial load (>4+).

The 4 yr follow up of patients treated with a one year MDT regimen (comprising rifampicin, ofloxacin, minocycline, clofazimine and dapsone) for MB cases progressed satisfactorily. The regimen was observed to be well tolerated and effective in killing the bacilli. 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. Relapse was observed in three patients who had initial pre-treatment BI of more than 2+. No relapses have been observed in patients with initial pre-treatment BI of 1+ and less.

A multicentric double-blind randomized controlled trial to evaluate the therapeutic efficacy of single dose of rifampicin, ofloxacin and minocycline (ROM) in 1600 paucibacillary (PB) leprosy cases with 2-5 lesions and 1200 monolesion cases is being carried out at 6 centres, (Chittor, Cuddappah, Chingleput, Chennai City, Champa and Naini Leprosy Mission). Follow up of patients is in progress.

A simulation model for leprosy (SIMLEP) was prepared at National Institute of Epidemiology (NIE), Chennai to study the effect of various interventions such as early case detection, various chemotherapy

regimens, vaccination *etc.* Attempts are being made to develop a simple, practical, user-friendly model in collaboration with CSIR Centre for Mathematical Modelling and Computer Simulation (CMMACS), Bangalore for use by programme managers.

Histopathological Studies

During the year studies on development and application of *in situ* hybridization (ISH) technique based on gene probes for detecting early forms of leprosy were continued. ISH was found to be much more sensitive than immunocytochemical method. Further, some of probes proved better for *in situ* detection of *M.leprae* specific sequences which was related to size as well as G+C content of the probes. Probes could also detect sequences in 6-9 yr old paraffin sections.

Immunological Studies

A study has been continuing at CJIL to understand the local immunity in leprosy. Earlier it was reported that by employing organotypic skin culture kinetics of production, antibodies were produced in borderline tuberculoid (BT) lesions. Using the same methods, skin in borderline lepromatous (BL)/lepromatous (LL) lesions has been observed to produce large quantities of IL-4, IL-6 and very minimal quantities of TNF- and IFN-. On the other hand BT lesions produced large quantities of TNF- and IFN- as well as IL-4 indicating both TH1 and TH2 expression in the same lesion. Further, the immunohistological study showed that many of the BT lesions are populated with B and plasma cells. These observations indicate down-regulating role of Th2 interleukins in Th1 functions in BT lesions.

The additional data further confirmed that in a proportion of long treated LL cases the lymphocytes were capable of producing IL-2, IFN- and IL-12 in response to *M.leprae* antigen stimulation thus indicating the tendency for upregulation of CMI responsiveness in these patients. The immunosuppressive cytokines are also being produced by these patients.

The study on IgG levels to recombinant heat shock protein antigens has been further expanded during the year. No difference in the antibody levels in BT/TT and LL patients was observed. Further, no difference in the levels of proliferative response was noted in leprosy patients with and without ENL reactions. Significantly higher levels of antibodies to recombinant proteins of

M.leprae were found in patients with reversal reactions compared to TT/BT, BL/LL and patients with erythema nodosum lepromatosum (ENL) reactions. Studies on IgG subclasses against lipoarabinomannan (LAM) in leprosy patients with ENL and reversal reactions continued during this period. Significantly low levels of IgG₃ have been found to correlate with severity of reactions.

Studies were continued at CJIL to compare the sensitivity and specificity of antigen and antibody detection with PCR. Further data confirm that the PCR detection is sensitive and specific whereas there were some problems of false positivity with antibody detection procedure. In order to focus on antigen detection, a modified serum antibody competition test (SACT) by coating the plates with monoclonal antibody was attempted. While the test was found to be specific, a reduced sensitivity was observed. The study is continuing to assess and improve these approaches.

A project is ongoing at Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh to study the mechanism of T cell anergy seen in leprosy patients. The phenotype profile of lymphocytes and expression of adhesion molecules has been studied in control and MB patients. The total percentage of CD3+, CD4+, CD8+, CD19, HLA DR+ and NK cells did not vary in BL/BT, tuberculoid (TT) forms of leprosy except LL form, as compared to the controls. The percentage of CD8+, CD19+ and NK cells was significantly reduced in LL cases as compared to BL, BT and TT cases. The expression of adhesion molecules CD₁₁a,b,c and CD54 was significantly affected. ICAM-1 (CD 54) was maximally affected in LL cases. Reduced expression of CD 11 was seen in lymphocytes and monocytes of all cases. CD11b expression was maximally reduced in LL forms and was unaffected in BL cases. CD11c expression was also significantly reduced in LL forms but the level of expression on TT, BL and BT forms was same. The T cell clones have been established from lymphocytes of all forms of leprosy and these were stimulated with *M.leprae* sonicated antigen (1mg/ml) to study the proliferation. 40-60% reduced transformation was observed in T cell clones of LL cases whereas it was reduced by 15-20% in BL cases as compared to control (stimulated by conA), BT and TT forms. HLA DR3 and DQ1 expression was not affected in any of the leprosy patients. The study is continuing.

Another project is being funded at PGIMER, Chandigarh to study the mechanism of apoptosis in

the peripheral blood mononuclear cells (PBMCs) of leprosy patients and the role of *M.leprae* cytosolic and membrane antigens in apoptosis. Apoptosis in BT/TT patients with PGL-1 antigen and cytosolic antigen ranged from 30-40% which was only 4-6% in case of BL patients with both the antigens. Only PGL-1 caused apoptosis in LL patients (7-15%). The DNA fragmentation analysis on agarose gel confirmed death of cells by apoptosis. The EM pictures of PBMC's after interaction with antigens (4 h) confirmed apoptotic changes induced by PGL-1 and cytosolic antigens as compared to normals. The mRNA levels for Fas/Fas L were not upregulated in cells undergoing apoptosis. The expression of CD28 and B7 was reduced on T cells and monocytes and this was more significant in BL/LL patients than BT/TT patients. The study is progressing.

Immunoprophylaxis and Immunotherapy

A double blind immunoprophylactic and immunotherapeutic trial to study the efficacy of *Mw* vaccine was carried out at CJIL jointly with Institute for Research in Medical Statistics (IRMS), New Delhi. MB index cases received 8 doses of vaccine every 3 months alongwith MDT, while household contacts (HHCs) received 2 doses of the vaccine at an interval of 6 months. The study population comprised about 28,000 HHCs of MB and PB cases spread in 272 villages of the above area with a pre-survey prevalence of 18 per 1000 in 1989. Decoding was done in January 2001 and detailed analysis is in progress.

A survey to determine the incidence and prevalence of leprosy has been undertaken in Agra district. Of a total of 63370 subjects surveyed in 6 *tehsils* during July 1999 to February 2001, 275 leprosy cases have been detected. Prevalence ranged from 25.3 to 74/10,000 with an average of 43.4/10,000. New case detection rate varied from 21.7 to 59.5/10,000 with an average of 36.1/10,000. Out of all cases detected, 83.3% were new cases.

Programme Evaluation

An appraisal of the National Leprosy Eradication Programme (NLEP) including validation of Modified leprosy Elimination Campaign (MLEC) II was undertaken in March-April, 2000, jointly by the NIE, WHO, World Bank, DANLEP and GOI. The objective of this evaluation was to assess the progress of NLEP in terms of coverage



Major ICMR Research Projects in Communicable Diseases

and achievements and yield of MLEC and to assess the quality of care and accessibility of services. The progress of the NLEP at the national level has shown considerable improvement in terms of reduction in prevalence rate. However, the progress has been uneven in some of the States (Orissa, Maharashtra and Tamil Nadu), which require special inputs to accelerate the goal of elimination. There is, however, no appreciable change in new case detection rate. MDT services are available in all the districts. All the states have completed training of health personnel for integration of leprosy with general health services.

DIARRHOEAL DISEASES

Diarrhoeal diseases are the major cause of illness among children. The institutes involved in research on diarrhoeal diseases are National Institute of Cholera and Enteric Diseases (NICED), Kolkata, National Institute of Virology (NIV), Pune and Regional Medical Research Centre (RMRC) at Bhubaneswar.

Epidemiological Studies

A community based intervention study was conducted by NICED, Kolkata to see the impact of zinc supplementation in reducing diarrhoeal morbidity in a cohort of rural children aged 6 to 41 months. The preliminary results revealed that both weekly as well as daily supplementation of zinc protects significantly against diarrhoea.

With an aim to understand the epidemiological features of diarrhoea caused by *Escherichia coli*, the NICED, Kolkata carried out a community based longitudinal study among rural children. Preliminary results showed more than 51.2% isolation rate of this pathogen which was further classified by DNA colony hybridization assay as enteropathogenic *E.coli* (23.8%), enterotoxigenic *E.coli* (17.9%) and enteroaggregative *E.coli* (9.5%).

Clinical Studies

A double blind, randomised, clinical trial was carried out at NICED, Kolkata to compare the efficacy of standard and hypo-osmolar oral rehydration solution (ORS) in 64 marasmic children (6-48 months old) suffering from dehydrating acute diarrhoea. Clinical parameters and

microbiological findings of stool samples were comparable in both groups at the time of admission. Stool output, duration of diarrhoea, intake of ORS and fluid intake were significantly less in hypo-osmolar group as compared to standard group. Ninety one per cent children in standard group and all children in hypo-osmolar group recovered within 5 days of initiation of therapy. The study showed that hypo-osmolar ORS has beneficial effects on clinical course of dehydrating acute watery diarrhoea in severely malnourished (marasmic) children. Furthermore, children did not become hyponatremic after receiving hypo-osmolar ORS.

Entamoeba histolytica

The NICED, Kolkata continued studies on identification and characterization of multiple genes in *E.histolytica* using mRNA which are differentially expressed in pathogenic *E.histolytica* during incubation with human collagen type 1 and Ca²⁺ and their comparison with non-activated pathogenic *E.histolytica*. Two hour interaction of *E.histolytica* with human collagen type 1 and Ca²⁺ resulted in maximum mRNA synthesis and 15 differentially expressed new or overexpressed bands were seen. The sequencing of some of these bands will help in understanding the genes involved in collagenase secretion and the role of collagenase in pathogenesis of amoebiasis.

E.histolytica colonizes the bowel lumen and invades the intestinal epithelium to cause colitis, liver abscess or cysts that are excreted out. Parasite recognition of glycoconjugates plays an important role in the pathogenesis of amoebiasis. A study was initiated at PGIMER, Chandigarh to understand the interaction of galactose-binding lectin of *E.histolytica* with immune competent cells *in vitro*. The preliminary results of the study showed that the lectin induced immunomodulation was evident in intestinal and amoebic liver abscess cases. The immunomodulation was checked by co-culturing the stimulated antigen presenting cells (APC) of the patients with lymphocytes *in vitro*. The lectin stimulated APCs induced death of naive T cells but lymphocytes from patients showed blast formation. The proliferating lymphocytes were of CD⁸⁺ subset and produced IFN- γ , IL-2 and IL-10 in abundance as compared to other cytokines. The APCs showed reduced co-stimulator molecules and reduced phagocytic/bactericidal activity.

Salmonella typhimurium

A study was initiated at PGIMER, Chandigarh to investigate the mechanism by which a mannose sensitive adhesin of *S.typhimurium* induces cellular response. The study indicated the involvement of adenylate cyclase dependent cAMP and protein kinase A in the adhesin triggered activation of host cell signalling events. Further, the level of inflammatory cytokines like IL-6 and TNF- α in culture supernatant of Henle 407 cells was found to have increased 2-fold in the presence of adhesin. The study is in progress.

Rotavirus

Three strains of group A rotavirus were isolated by NIV, Pune in tissue culture from fecal specimens (two specimens showed reactivity to G2/4 MAbs and one was non-typable) collected from hospitalized children. These isolates were detected at passage level P5-P7. Further passages were made to increase the infectivity titre. All these isolates were lyophilized and stored. Two strains had sub-group I and one subgroup II specificities. None of these isolates reacted with MAbs against G1-G4, G8 (human strains), G3 (simian strain) and G6 and G10 (bovine strains) rotavirus serotypes. Further characterization is underway.

To study the relation between maternal immunity and susceptibility of infants to rotavirus, a study was carried out by NIV, Pune in convalescent children (<2 yrs) hospitalized for rotavirus diarrhoea, and their respective mothers. They were tested for the presence of neutralizing antibodies (NAbs) to human rotavirus serotype G9 (F45 strain). The fecal specimens of these patients were serotyped earlier by MAbs against serotypes G1 to G4, G6, G8 and G10. Out of 64 sera tested, 54% mothers' sera and 60% child patients' sera were positive for NAbs to G9 serotype at 1:100 dilution. The serum samples from child patients were divided into two groups. In group-1 (specimens contained non-typable rotaviruses), out of 26 sera 38.5% were positive to G9 serotype whereas in group-2 (fecal specimens were typable with available MAbs), of the 38 sera 18.4% were positive. The respective mothers' sera were negative for G9 serotype, indicating that NAbs may have been acquired as a result of infection due to G9 serotypes among the child patients.

Vibrio cholerae

Seven rough strains of *Vibrio cholerae* isolated as the sole infecting agent from patients with cholera-like diarrhoea were examined at NICED, Kolkata for the presence of the regulatory element *toxR* and certain virulence-associated genes of the CTX genetic element and *V.cholerae* pathogenicity island (VPI). Multiplex PCR analysis using *wb* specific genes of either 01 or 0139 strain showed that 6 of the 7 isolates produced an 01 *wb* specific amplicon while one isolate produced an 0139 specific amplicon. While analysis of lipopolysaccharide profiles of smooth variants of *V.cholerae* revealed the presence of long repeated units of 'O' polysaccharide side chains, all the rough variants appeared to be devoid of the same and possessed only core oligosaccharide. PCR experiments with primers specific to the *ctxA*, *ctxB*, *tcpA*, *tagA*, *int*, *aldA*, *toxT*, *LJ*, *RJ* and *toxR* genes revealed that 6 of the 7 rough strains were positive for these genes. One strain was found to be negative for *tagA* and *RJ* indicating the presence of an altered VPI. Each of these strains showed media-dependent expression of cholera toxin and produced higher amount of toxin as compared to the reference *V.cholerae* 01 EITor (strain VC20) or 0139 (strain ISG24) under comparable conditions. Studies on the clonality of these strains by the analysis of rRNA genes indicated their relatedness to strains of *V.cholerae* 01 EITor or 0139 isolated during the same time period.

The toxigenic Inaba serotype of *V.cholerae* 01 biotype EITor reappeared in India in 1998 and 1999, almost 10 years after its last dominance in Calcutta in 1989. Extensive molecular characterization was done at NICED, Kolkata by ribotyping RFLP and pulsed-field gel electrophoresis (PFGE). It was observed that recent Inaba strains are remarkably different from the earlier Inaba strains but are similar to the prevailing *V.cholerae* 01 Ogawa EITor biotype strains. The antibiograms of the Inaba strains were also similar to those of the recent *V.cholerae* Ogawa strains. These *V.cholerae* 01 Inaba strains appear to have evolved from currently prevailing Ogawa strains and are likely to dominate in the coming years.

The virulence of a pathogen is dependent on a discrete set of genetic determinants and their well-regulated expression. The *ctxAB* and *tcpA* genes are known to play a cardinal role in maintaining virulence

in *V.cholerae* and are believed to be exclusively associated with clinical strains of 01 and 0139 serogroups. Studies at NICED, Kolkata examined the presence of 5 virulence genes, including *ctxAB* and *tcpA*, as well as *toxR* and *toxT*, involved in the regulation of virulence in environmental strains of *V.cholerae* cultured from three different freshwater lakes and ponds in the eastern part of Calcutta. PCR analysis revealed the presence of these virulence genes or their homologues among diverse serotypes and ribotypes of environmental *V.cholerae* strains. Sequencing of a part of the *tcpA* gene carried by an environmental strain showed 97.7% homology to the *tcpA* gene of the classical biotype of *V.cholerae* 01. The study provided new insights into the ecology of *V.cholerae*.

Ciprofloxacin and norfloxacin are second generation fluoroquinolone broad-spectrum antimicrobial agents and possess excellent activity against *V.cholerae* 01 and 0139 serogroups. From 1995, progressive increase in ciprofloxacin and norfloxacin resistance among *V.cholerae* 01 strains has been recorded with highest occurrence of 38.8% in 1999 and 25% in 2000. The minimal inhibitory concentration (MIC) for ciprofloxacin resistant *V.cholerae* strains ranged from 9 to >32 mg/ml and that for norfloxacin from 192 to >256 mg/ml when tested with the E-test strips on Mueller Hinton agar. The incidence of nalidixic acid resistance among *V.cholerae* 01 was low before 1993 (<10%) and peaked during subsequent years (100% in 1999).

V. parahaemolyticus

V. parahaemolyticus is a halophilic bacterium, capable of causing gastroenteritis in humans following the ingestion of contaminated seafood. *V. parahaemolyticus* of serovars 03:K6, 04:K68 and 01:KUT are reported to be pandemic clones, since these serovars share many genotypic features. Active surveillance carried out by NICED, Kolkata has shown emergence of a new serovar 01:K25, which shared clonality with other pandemic serovars. In the year 2000, 1633 stool samples were screened, out of which 49 were positive for *V. parahaemolyticus*. Analysis of isolation profile of *V. parahaemolyticus* showed the emergence of 01:K25 and drop in 03:K6 serovar which was dominant earlier.

Shigella Species

As the sensitivity of the conventional technique for identifying *Shigella* is low, a PCR assay was evaluated by NICED, Kolkata. Analytical sensitivity of the PCR technique was obtained by artificially spiking the negative stool samples with a standard strain of *Sh.flexneri* type 2 and then determining the detection limit. Specificity of the method was determined by testing a number of known *Shigella* and enteroinvasive *E.coli* (EIEC) strains and organisms other than *Shigella* species. A total of 300 stool samples, collected from acute childhood diarrhoea cases were plated onto two selective agar media after enrichment in Luria broth. *Shigella* species was isolated from 7.7% children and EIEC from 1% patients. All enriched stool samples were subjected to PCR to amplify the target sequence of invasive plasmid antigen H locus, a multicopy element found on the chromosomes and invasion plasmid. It was observed that only 38% of acute diarrhoea cases actually had *Shigella* or EIEC infection, as confirmed by laboratory methods. Moreover, this PCR assay could identify a number of untypable *Shigella* strains which could have remained undiagnosed otherwise. Therefore, the PCR may be considered as sensitive, easy to perform and rapid.

Studies carried out at NICED, Kolkata showed that *Sh.flexneri* is the predominant serotype followed by *Sh.boydii* and *Sh.sonnei* isolated from diarrhoea cases. No *Sh.dysenteriae* was detected thus indicating the endemicity of *Shigella* in and around Kolkata. *Shigella* strains were found to be resistant to co-trimoxazole, tetracycline, ampicillin and furazolidone and sensitive to gentamicin, cefuroxime, nalidixic acid and fluoroquinolones. About 73% of the isolated strains of *Shigella* spp are multidrug resistant. To analyze clonal relationship among isolates of multidrug resistant *Sh.flexneri* strains, molecular typing to determine changes at the genetic level and to understand their implications in the epidemiology of the disease was undertaken by NICED, Kolkata. Of the 22 different plasmids ranging in size from 3.0 to 105 kb, 86.4% were of 105 kb size. Digestion of chromosomal DNA with the restriction endonuclease XbaI produced clearly resolvable pattern after PFGE. Different patterns were identified amongst the isolated strains consisting of 12-14 DNA fragments showing the origin of *Sh.flexneri* strains from different clones.

EMERGING AND OTHER MICROBIAL INFECTIONS

Leptospirosis

To obtain data on disease burden due to leptospirosis, a multicentric study has been initiated. Fifteen research and teaching institutions across the country have been identified to act as collaborating centres and RMRC, Port Blair is the coordinating centre. Each Centre would enroll 600-700 patients and paired sera samples would be collected and subjected to lepto dipstick test and microscopic agglutination test (MAT). A total of 1768 patients have been enrolled so far.

A clinical, bacteriological, serological and epidemiological study on leptospirosis was undertaken in a rural community at RMRC, Port Blair. Majority of the cases were from agricultural families. During the study period 2177 fever cases were reported to the PHC. Out of these, 11.4% were suspected and 3.3% confirmed as leptospirosis. Follow up serum samples collected every two months from patients from whom leptospire were isolated revealed that IgM antibodies disappeared earlier than microscopic agglutinating antibodies. The serogroup specific antibodies disappeared earlier than homologues/serovar specific antibodies. Findings of the study also showed that the infecting serovar cannot always be assessed based on MAT results as some of the patients showed low titres against serogroup specific antigens.

Lepto lateral flow, a newly developed test by Royal Tropical Institute, Amsterdam for rapid diagnosis of leptospirosis at peripheral level was evaluated at RMRC, Port Blair. All the indices of efficacy of lepto-lateral flow were comparable to that of IgM ELISA. The test can be performed at peripheral levels where electric supply is erratic or absent by persons with low technical skill and the results obtained within 10 minutes thus making it a useful tool for rapid diagnosis of leptospirosis. The Centre is also in the process of developing IgM based ELISA test for rapid diagnosis of leptospirosis.

Outbreaks of febrile illness were reported in Mumbai and Thane districts of Maharashtra in July 2000 after heavy rainfall. Sera samples were collected from suspected cases, healthy controls residing in this area and domestic animals and were tested with MAT and two IgM based tests (IgM ELISA and lepto-dipstick). 47.2% of the suspected cases were diagnosed as leptospirosis on the

basis of serological tests. 15.2% healthy controls and 25% domestic animals tested had anti-leptospiral antibodies. In outbreaks of the disease in several districts of Kerala during September 2000, 48.5% cases were reported as leptospirosis. The common serovars in MAT positive sera belonged to sero-groups *autumnalis* (66.6%), *grippotyphosa* (8.3%), *hebdomadies* (8.3%) and *javanica* (8.3%) and mixed equal reaction was found in 8.3%. Sero-prevalence among healthy individuals was very low, ranging between 7 and 9%.

The RMRC, Port Blair is also involved in characterisation of leptospira isolates by using monoclonal antibodies. Of a total of 27 isolates (23 human, 2 from dogs and 2 from rats) identified, none could grow at 13° C and in the presence of azaguanine, revealing the pathogenic nature of leptospira. The MAT with group sera and monoclonal antibodies showed that out of 23 isolates from human source, 18 belonged to serogroup *grippotyphosa*, 2 to *icterohaemorrhagiae*, 2 to *canicola* and remaining one to *sejroe*. Two isolates from rats belonged to serogroup *grippotyphosa* whereas two from dogs to *canicola*.

B. pseudomallei

A study has been funded at CMC Hospital, Vellore to know the prevalence of antibodies to *B. pseudomallei* in patients presenting as pyrexia of unknown origin (PUO) whose sera is negative for typhoid fever, brucellosis, toxoplasmosis, malaria and filariasis and in serum samples from ten laboratory personnel who had been handling *B. pseudomallei*. IHA, ELISA and indirect fluorescent antibody (IFAT) tests have been standardised for detection of antibodies to *B. pseudomallei*, using pooled antigen from 3 strains isolated from blood culture in the laboratory. Out of 200 samples from patients, 24 have been confirmed for melioidosis by culture. The study is progressing.

Streptococcus pyogenes

A study is ongoing at PGIMER, Chandigarh to detect polymorphism within the *Streptococcus pyogenes* strains. Three reference strains (M1, M5 and M12) of *S. pyogenes* belonging to different M serotype and 14 contemporary isolates (8 cultured from patients suffering from pharyngitis and 6 from RF/RHD patients) of *S. pyogenes* were analyzed. RFLP of *vir* regulon provided 11 different restriction fragment patterns for the 14 clinical isolates

showing great amount of variation within the strains. Two strains from pharyngitis patients showing an identical *vir* restriction pattern as well as two strains from RF/RHD patients showing same *vir* pattern when amplified for *emm* gene, showed PCR product at similar position *i.e.* 1.1 and 1.3 kb respectively. However, the RFLP pattern of *emm* gene showed distinct fragment patterns in all the four isolates. Further analysis of the samples is in progress.

Escherichia coli (EaggEC)

E.coli associated diarrhoea is an important cause of infant morbidity and mortality in developing countries. The ability of *E.coli* to adhere to epithelial surfaces is an essential first step in the pathogenesis of this organism in animals and humans. It is the expression of specialised adhesin that enables *E. coli* to stick to and colonize various intestinal mucosal sites. A study has been initiated at PGIMER, Chandigarh to clone and sequence for entero-aggregative *E.coli* (EaggEC) which will be used further as a probe to identify clinical samples. One of the strains was used for preparation of genomic library. After screening the library with adhesin specific antisera adhesin clone has been identified. The recombinant plasmid DNA was prepared and run on 0.7% agarose gel for size analysis of cloned fragments. Southern hybridisation of the DNA with oligonucleotide probe gave strong positive signal with few cloned DNA fragments containing approximately 1Kb insert. The selected recombinant plasmid was further subjected to determine the DNA sequence. So far almost 900 bp of nucleotide has been sequenced. The study is ongoing.

E.coli (STEC)

A study has been initiated at Eastern Regional Station of Indian Veterinary Research Institute at Kolkata, to assess the prevalence of shiga-toxin producing *E coli* (STEC) in stool samples of animals and humans and to look into virulence loci and phenotypic traits. The possibility of their occurrence in food chain and zoonotic transmission by way of molecular fingerprinting would also be evaluated. A total of 452 stool samples from 265 cattle, 177 human and 10 poultry samples was screened. STEC were isolated from 12.83% cattle and 4.51% human stool diarrhoea samples, while none of the poultry samples had STEC. Additionally PCR based studies revealed that *hlyA* was the only plasmid encoded

marker present in 47.05% animal strains as all the STEC strains did not reveal the desired amplicon for *KatP* and *etpD*. Enterohaemolysin production was demonstrated in 55.88% cattle and 25% human strains. The study is continuing.

PARASITIC DISEASES

MALARIA

Malaria incidence in the country remained around two million cases; of these, the *Plasmodium falciparum* constituted little over 50 per cent. In many areas malaria outbreaks and deaths have been reported. The Council has taken up many initiatives through research at Malaria Research Centre, (MRC) Delhi, Vector Control Research Centre (VCRC), Pondicherry and RMRCs to strengthen the National Anti-Malaria Programme.

Integrated Vector Control

The Integrated Disease Vector Control of malaria is being carried out through MRC's field stations in different geo-ecological sites in the country. The activities at these field stations were carried out keeping in view the needs of the programme. Collaboration with health authorities like Ahmedabad Municipal Corporation by Nadiad field station, Mormugao Port Trust by Goa field station, Municipal Corporation in Bangalore and state malaria control programme in district Hasan by the Bangalore field station, and National Thermal Power Corporation (NTPC) by Hardwar field station for preparing malaria/mosquito control action plans, providing technical know-how and facilitating transfer of technology for malaria control were fruitful. Bioenvironmental control strategy was found suitable in reducing the vector population and disease prevalence. In addition to applied and operational activities related directly to the control programmes at many field stations, basic research to isolate new molecules/agents for mosquito or parasite control were carried out. Many field stations participated in the trials to evaluate new drugs, insecticides and diagnostic kits.

All the field stations planned activities involving communities to enhance the awareness of malaria and the control strategy being implemented in the national programme. For the first time, a study has been initiated in Sundergarh district of Orissa to develop a field site for vaccine trials. Sonapur, Goa, Bangalore and Rourkela

field stations participated in situational analysis at five pilot districts namely, Jodhpur (Rajasthan), Aizwal (Mizoram), Tumkur (Karnataka), Keonjhar (Orissa) and the entire state of Goa under Roll Back Malaria (RBM) initiative.

Urban malaria problem in Ahmedabad city was studied in depth and feasibility of bioenvironmental control was demonstrated. The epidemic investigations for malaria were carried out in Hoshangabad and Beitul districts of Madhya Pradesh. The villages under Hoshangabad district were highly malarious and 3 PHCs of Beitul district were worse affected. *An.culicifacies* was the dominant species followed by *An.subpictus* and *An.fluviatilis* in both these places.

No mosquito breeding was observed in rainwater harvesting resources (percolation pits, well-cum-canal-cum-percolating pits, borewells etc.) in urban conglomerations.

A collaborative study was carried out with Ispat General Hospital, Rourkela and International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi to understand malaria transmission dynamics and to characterize parasite populations and immune responses in tribal population. The study showed that the tribal area is under the influence of very efficient vector species and the parasite load in the community is high to maintain persistent malaria transmission.

A technology transfer project on bioenvironmental control of mosquitoes in Mormugao Port Trust area in Vasco-de-Gama made significant progress in reducing mosquitogenic conditions. The project on bioenvironmental control of malaria in PHC Kamasamudram in district Kolar has concluded successfully. Geographical reconnaissance for mapping of mosquito breeding sites was carried out in urban areas of Shahjahanpur (U.P.). Results of one year survey revealed high mosquitogenic conditions in the area.

Vector Biology

Earlier studies done by MRC, Delhi on *An.culicifacies* populations from Rameswaram Island, Tamil Nadu indicated the existence of both species B & E acrocentric and sub-metacentric karyotypes. The sub-metacentric karyotype with vectorial potential detected by sporozoite positivity was recognized as a new species and provisionally designated as species E. In Rameswaram

Island species E and B are sympatric. Molecular studies were carried out on these species to find variations that could distinguish these two species. Universal primers were used to amplify different regions in the given gene by PCR and further analysis was made. A total of six sets of primers was used for PCR amplification of mitochondrial and nuclear regions of the mosquito genome. Of these, primers for D3-28S rDNA region could distinguish species A and D from species B, C and E on heteroduplex analysis (HDA) of the derived amplicon.

The RMRC, Bhubaneswar carried out a survey in Orissa to study *An. fluviatilis* sibling species composition and its bionomics in three highly malarious districts - Keonjhar, Bolangir and Kalahandi. In these districts species B and C were sympatric and primarily zoophagic. In contrast, *An.fluviatilis* species S in the above mentioned districts was found highly anthropophagic and resting predominantly in human dwellings. Man hour density ranged from 10 to 45. These observations strongly indicate that species S of *An.fluviatilis* complex is the principal vector in the districts surveyed in Orissa state. Ninety seven per cent of samples tested were found to feed on human blood.

Presently the differentiation of sibling species is done based on polytene chromosomes, which is time-consuming and cumbersome and requires the samples to be in a particular stage of development. Hence, PCR assay was developed by VCRC, Pondicherry based on the rDNA ITS2 region for differentiating sibling species of malaria vector *An.fluviatilis* complex. Field evaluation of the PCR assays showed that the assay for species 'X' has 94% sensitivity and that for species 'T' or Y 84%, compared to cyto-taxonomic technique. Majority of the indoor resting mosquitoes (69%) and man landing collections (79%) were species X, while 85% of the light trap collections from cattle sheds and 55% from pit shelters were species Y. Seventy five per cent and 3.4% of the Malkangiri population and 29.8% and 56.2% of the Jeypore population was found to be species X and Y respectively.

Studies have been carried out at MRC, Delhi to map malaria vector in NE states. *An.minimus* is the species of hill and foothill areas (up to the altitude of 1600 m) but is also found in valleys at low altitudes. It breeds in upstreams, ditches and channels preferably in unpolluted, slow moving waters with grassy, partially

shaded edges and forest fringe areas. In this study, thematic maps of altitude, forest, soil, temperature and rainfall were used. The plates on various themes were reconstructed on NT-platform. The conditions favourable for the species were extracted from literature. Overlaying and integration of thematic maps was done using Arc/info NT and analysis by Arc/info view 3.3 GIS ESRI software. Integration of the themes resulted in mapping of areas favourable for *An. minimus*. The distribution of *An. minimus* mapped by Geographical Information System (GIS) analysis was compared with reported distribution. There was indication of potential sites for the presence of *An. minimus* in many areas, but no survey records are available from these areas.

Studies on Insecticide Resistance

Various strains of insecticide resistant and susceptible *An. culicifacies* comprising field collected deltamethrin resistant and laboratory colonized strains of species A, B and C with different susceptibility to DDT, malathion and deltamethrin were biochemically assayed to explore the basis of resistance. The analysis of data revealed that the mean glutathione-S-transferase (GST) activity was significantly higher in DDT resistant strains (species B and *An. culicifacies s.l.* Rameswaram strain) than in susceptible strain (species A), which suggests GST based DDT resistance in *An. culicifacies*.

Earlier it was established by MRC, Delhi through synergistic study that malathion carboxylesterase is responsible for malathion resistance in *An. culicifacies*. Preliminary results indicate that malathion is metabolised to mono and dicarboxylic acid in malathion resistant strains indicating the involvement of malathion-carboxylesterase. This is an important finding as it indicates that malathion resistant mosquitoes will not show cross resistance to carbamate and other organophosphates.

Clinical Studies

Azithromycin, an azalide antibiotic similar to erythromycin, has been shown to possess good antimalarial activity in human malaria challenge studies. It can be given to pregnant women and infants. Considering the potential of the drug and the limitations of existing drugs to treat malaria, a study was undertaken by MRC, Delhi to explore antimalarial activity of azithromycin (1g/day for 3 days) in *P. vivax* malaria in

comparison to standard chloroquine treatment. Results showed that although the clinical and parasitological recovery on day 3 *i.e.* 74% and 44% in azithromycin group was low, it increased to 88% and 84% respectively on day 7. In chloroquine group recovery was 95-100% on these days. Both the drugs were well tolerated and there was no recrudescence in either group upto 28 days.

Parasite Biology

Parasite bank is fully established as a national resource centre for cryopreserved human and non-human parasites. Other biological materials produced in the bank are being used for supply to various organizations and for collaborative studies.

Parasite bank now has 555 *P. falciparum* isolates. Periodically few cryopreserved isolates were revived and tested for sensitivity to chloroquine. Isolates were also maintained in running culture for educational purpose and for supply. In addition to the human plasmodia, parasite bank is also maintaining rodent, avian and simian plasmodia for research studies.

Geographical Information System (GIS)

During the year, a 3-dimensional TIN model was generated which depicts the depression areas in Mewat (Haryana). There is a general slope of the area from west to east. Most of the area is prone to flooding. Streams originating from small hills converge to Kotla lake. Drains in Nuh fill the Ujjina lake. Run off water causes floods and depression areas hold water and become potential breeding sites for mosquitoes (Fig. 4a). A remote sensing image of August, 1998 was procured and classified in various land use classes. Bare land was further classified in three classes 1, 2 and 3. Barren 1 class category was found to have good correlation with annual parasite incidence (API). Further ground verification revealed that these are man made depression areas which become potential breeding sites during rainy season.

Villages in the depression areas constitute potential malaria receptive belt (API 13 – 24 during epidemic and post epidemic period) (Fig. 4 b,c). This belt acts as the foci of malaria in the region. The foci expand in high rainfall (flood) years and shrink during drought. In post epidemic period, (1997), villages surrounding

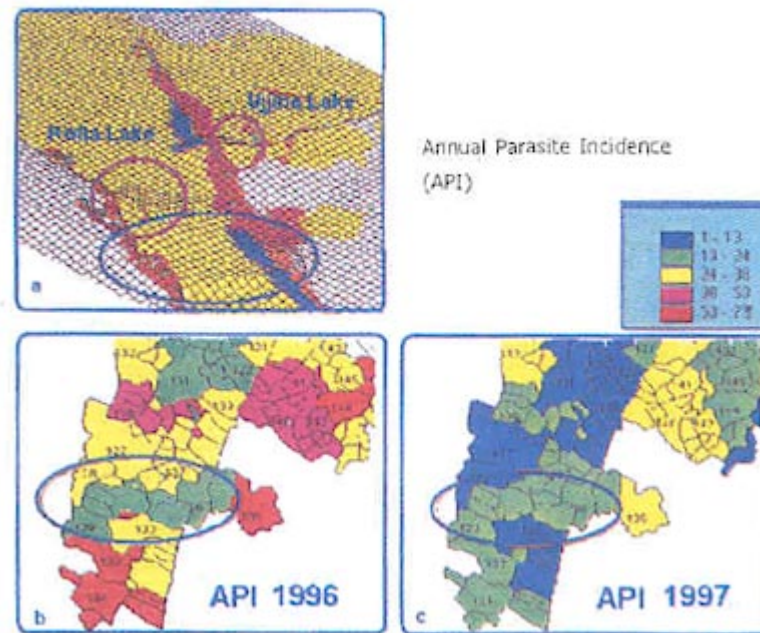


Fig.4 3-D model of south Mewat (Haryana) showing depression areas in Nuh block as foci of malaria.

the belt had low API as compared to epidemic year (1996). GIS helped in identifying the depression areas and therefore the villages falling in sink area have high probability of malaria.

A task force project was initiated in Tumkur district of Karnataka by MRC, Delhi to find out the feasibility of detecting breeding habitats of *An.culicifacies* and the landscape features which make areas suitable or unsuitable for endemicity of malaria, based on satellite remote sensing technique. Ten villages from each PHC were selected for the survey of breeding habitats, adult malaria vector density and mapping of biotope for landscape features. Of the 13 villages in high incidence areas, *An. culicifacies* was collected from 11 and the man hour density (MHD) ranged from 1 to 27. In PHCs with moderate incidence, of the 11 localities, vector species was collected from seven and the MHD ranged from 1 to 18. Satellite data in respect of some sites have been analysed while entomological and ecological data are being collected.

Basic Studies

With the aim of developing a monoclonal antibody based ELISA system for detection of malaria antigen

in CSF, a project was initiated at PGIMER, Chandigarh. The *in vitro* culture of *P.falciparum* was prepared. The hyperimmune antiserum to crude *P. falciparum* antigens has been raised to identify different fractions of parasite antigen by sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE). The monoclonal antibodies to various *P. falciparum* antigens will be produced and clones capable of identifying malaria antigens in CSF of cerebral malaria patients will be recognised. The study is in progress.

A project has been initiated at AIIMS, New Delhi with the aim to develop rapid and sensitive immunodiagnostic method to detect malaria antigen HRP-2 of *P.falciparum* in the blood. Two commercial kits detect HRP-2 antigen by chromatographic immunoassay. The peptides of HRP-2 antigen have been synthesized and characterized. The mono-specific antibody against HRP-2 peptides has been generated using ELISA.

In Orissa 30-40% of the population is found infected with asexual stages of *P.falciparum* but is free of clinical manifestations. The complicated malaria (multi-organ failure including CNS involvement) is associated with a very high percentage of mortality in spite of appropriate

chemotherapy. The investigations conducted by RMRC, Bhubaneswar have indicated that TNF- α (tumor necrosis factor) induced inflammatory response is the primary cause of pathology in complicated cases since pentoxifylline adjunct, a TNF- inhibitor could decrease significantly the duration of coma post-therapy without significant decrease in mortality. It appears that nitric oxide produced as a result of increased TNF- levels directly causes the pathology associated with complicated malaria.

Malaria in Tribal Areas

A drug delivery strategy involving traditional healers was developed by VCRC, Pondicherry to increase the accessibility of anti-malaria treatment to the tribals in remote areas. The traditional healers, though illiterate, were able to treat the suspected malaria cases administering correct dosages with the help of a pictorial guide. 85000 incidences of fever, recorded in 40000 population, were treated. Of these 68 severe cases were referred to PHCs in 2 years. There was a marked reduction in the average number of fever days (days suffering from fever) in the experimental area, compared to the check area. The outpatient attendance of fever cases in the PHCs has come down.

Malariogenic stratification was considered to be an essential component for developing the appropriate malaria control measures in Mandla, a tribal forested district. The mathematical equation used for stratification in this study was developed by MRC, Delhi taking into consideration factors such as topography, average annual rainfall of last five years, vectors prevalent in the area, average API for the last 10 years, epidemic potential (the highest value of API during last 10 years) and vulnerability. The results indicate that all nine PHCs had high risk of malaria. Further, stratification revealed that among 223 sections, only one section fell under medium risk, while 222 sections were under high risk. Similarly, stratification at the village level revealed that out of 1256 villages, 83.7% were under high risk and 16.2% under medium risk. It was observed from this analysis that in majority of sections villages had the highest value of each factor.

FILARIASIS

Filariasis in man is caused by lymphatic dwelling nematode parasites, *Wuchereria bancrofti*, *Brugia malayi*

and *B. timori*. The disease is an important public health problem in many parts of the world and is the second most important cause of permanent disability. India is signatory to the World Health Assembly (WHA) resolution to eliminate lymphatic filariasis. To make elimination a reality, the Council's Vector Control Research Centre (VCRC) at Pondicherry and RMRC, Bhubaneswar have focussed their research on various aspects of filariasis.

Molecular Epidemiology

A study was undertaken by VCRC, Pondicherry to analyse the genome of the parasite using genetic markers to elucidate genetic variability studies on *Wuchereria bancrofti* using random amplified polymorphic DNA (RAPD) markers among the populations of the parasite sampled from different localities. The study revealed that the parasite populations of rural areas are homogenous while those from urban areas are heterogenous (Fig.5). At least three genetically distant populations of *W. bancrofti* occur in Pondicherry. Ribosomal RNA (5.8 S) gene of Pondicherry isolate of *W. bancrofti* was amplified and sequenced. Nucleotide sequence comparison showed that the gene is highly conserved.



Fig.5 Genetic variability studies on *Wuchereria bancrofti* using random amplified polymorphic DNA (RAPD) markers.

A simple, sensitive, rapid, safe and less expensive PCR amplification method for the extraction of DNA has been developed by VCRC, Pondicherry for detection of *W. bancrofti* infection in vectors. Pool sizes of 10-30 gave 100% positivity for infection.

Geographical Information System

Filariasis distribution maps have been created for southern states *viz.* Tamil Nadu, Kerala, Karnataka and Pondicherry, based on the historical data (*i.e.* published records available as of 1995). Such data was available only for 40 districts out of a total of 58 districts (pre-bifurcation) in these states.

Studies have been initiated by VCRC, Pondicherry using GIS. These districts have now been re-stratified (based on quantiles approach) into the following categories *viz.*, very low endemic, low endemic, moderately endemic and highly endemic.

Space-borne remote sensing data (IRS-WiFs data) on various time points (January, May, October and November, 2000) acquired for Karnataka region has been processed jointly by the VCRC and the Indian Space Research Organization (ISRO), Bangalore. A scheme for image interpretation has been worked out and thematic maps of land use pattern, slope and relief and normalized difference vegetation index (NDVI) have been created for Karnataka region (Fig.6). Important confounding factors/dummy indicators of risk for the occurrence of the disease have been enlisted. Preliminary analysis of composite NDVI values revealed that there

is a negative correlation with the filarial endemicity. However, a large database in a wider area and a combination of factors need to be analyzed further for fitting a model in the decision making process. Study is in progress.

Studies on Mass Chemotherapy

Tolerability and efficacy of single dose of albendazole (400 mg) and DEC (6mg/kg b.wt.) alone or combined in asymptomatic *W.bancrofti* microfilaria carriers was determined in a double blind hospital study by VCRC, Pondicherry. Single dose DEC alone was found useful for the control of filariasis, however, albendazole alone can be recommended in areas endemic both for filariasis and helminthiasis, provided the cost is met.

Role of co-administration of daflon-500 (90% diosmin and 10% hesperidin) with diethylcarbamazine (50 mg daily) in comparison with DEC alone in the management of filarial lymphoedema (grade II cases) was evaluated by VCRC, Pondicherry in a double blind design. Daily co-administration of two drugs for 90-day period resulted in significant reduction in oedema volume while no change in oedema volume was seen in cases receiving DEC alone.

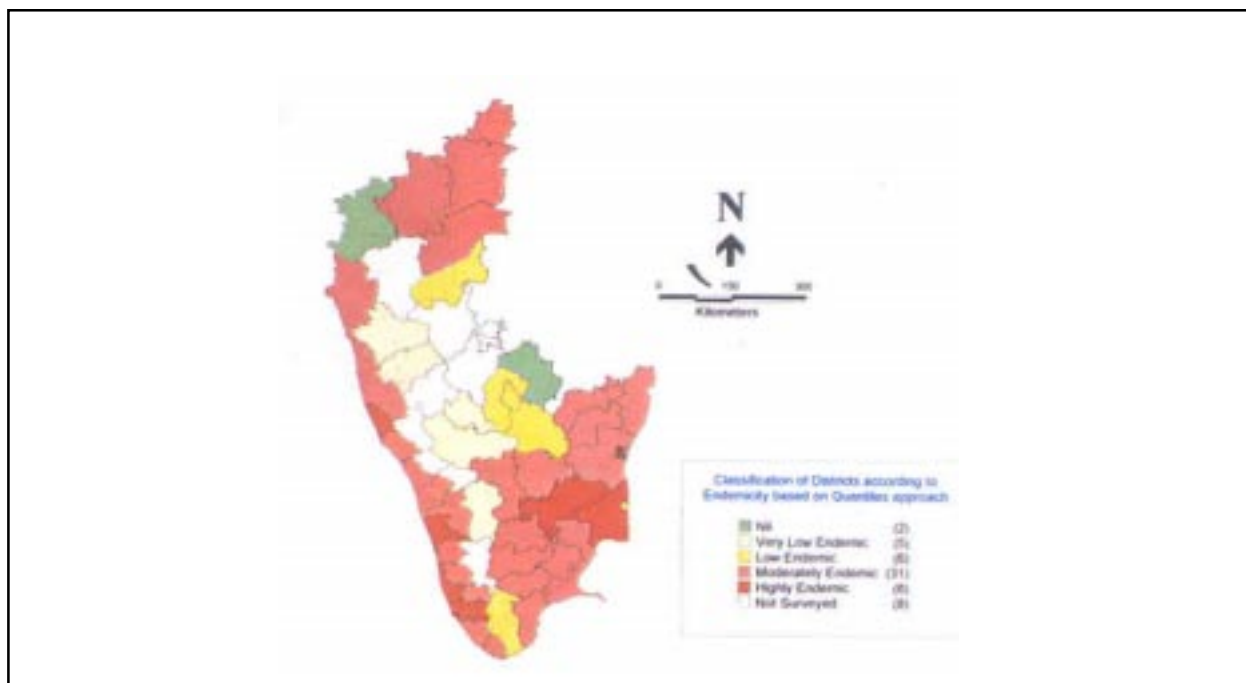


Fig.6 Filariasis distribution in Karnataka, Kerala, Tamil Nadu and Pondicherry.

Evaluation of the impact of mass drug administration with DEC or ivermectin or both on transmission of bancroftian filariasis is being carried out in 20 villages (covering a population of about 34000). Five rounds of mass treatment reduced the prevalence of microfilaria (mf) in the communities receiving DEC or ivermectin by 70% and 62% respectively. The geometric mean mf count declined by 89% and 81% respectively in these groups. Three rounds of mass co-administration of DEC+ivermectin resulted in reduction in mf prevalence by 63% and mf density by 72%. After six rounds of mass drug administration, the infection rate of resting mosquitoes declined by 83% in DEC and 86% in ivermectin treated communities. The infectivity rate in these communities declined by 80% and 82% respectively. In the communities receiving DEC+ivermectin, reduction in vector infection and infectivity rates was 59% and 64% respectively after four rounds of mass drug administration. The results show that DEC is as effective as ivermectin in drastically reducing the transmission levels after five successive rounds of mass drug administration. Comparable level of transmission reduction was also observed after only four rounds of DEC+ivermectin, indicating the superiority of the drug combination over single drug mass administration. However, complete interruption of transmission was not achieved in any of these arms, suggesting that more number of rounds of mass drug administration is required for achieving elimination.

Basic Studies

Immuno-epidemiological investigations carried out by RMRC, Bhubaneswar have revealed that acquisition of filarial infection in human communities is inversely related to production of antibodies to mf sheath. Antibodies to mf sheath are acquired very early in life. Filarial infection as revealed by circulating filarial antigens (CFA) is acquired with increasing age. A dynamic balance is maintained between the two parameters. Presence of antibodies in about 80% paediatric population who are yet to acquire patent filarial infection indicates that antibodies to mf are induced by filarial larvae and not by mf. Study is in progress.

In human filariasis, parasite carriers are often asymptomatic and patients with chronic disease are generally free of active infection. In a study carried out by RMRC, Bhubaneswar, endemic normals, who are

asymptomatic and free of infection (as shown by absence of circulating filarial antigens) were found to contain significantly higher levels of filarial specific IgA in comparison to other categories of subjects in filariasis endemic areas. The filarial IgA was found to be significantly more in females than in males, an observation compatible with decreased susceptibility of females to filariasis. Significantly, there was a direct association between increased filarial IgA and total eosinophils in circulation. Recognition of filarial antigens which selectively induce IgA response is expected to offer further insights into selection of appropriate filarial antigens for vaccine development.

The RMRC, Bhubaneswar has also very successfully used animal models to address issues on the nature of protective immunity in filariasis. Normal immunocompetent mice are resistant to human filarial parasites. X-linked immunodeficient mice show enhanced susceptibility to infection, (both in terms of development of larvae as well as persistence of circulating mf). XID-mice, known to be deficient in production of antibodies to T-independent antigens were shown by VCRC, Pondicherry to be prone to Th1 polarized T-cell immune responses and their macrophages were significantly deficient in production of nitric oxide.

Development and Testing of New Products for Vector Control

B426, a pupicidal formulation of bacterium metabolites developed at VCRC, Pondicherry was field tested against *Cx. quinquefasciatus*. The formulation was effective at 904 µg protein/l applied for a period of 9-12 days.

Under WHO's pesticide evaluation scheme, the institute tested pyriproxifen granules, an insect growth regulator against the immatures of *Cx. quinquefasciatus* in different habitats. The treatment at 0.1 kg/ha caused >90% emergence inhibition in cess pits (for 6 weeks) and at 0.5 kg/ha (for 4 weeks) in drains.

LEISHMANIASIS

Kala-azar is a major public health problem in the states of Bihar, West Bengal and Uttar Pradesh. Major initiatives were launched by Council's Rajendra Memorial Research Institute of Medical Sciences (RMRI) at Patna. During the year the Institute continued its research

activities and conducted training programmes on various aspects of kala-azar. Evaluation of nucleic acid probes, direct agglutination test (DAT) for detection of kala-azar, assessing the unresponsiveness to sodium antimony gluconate (SAG) and epidemiological studies are some of the areas where efforts were made. Studies on HIV and visceral leishmaniasis coinfection studies have also been taken up at the Institute.

Epidemiological Studies

A study has been carried out with the objectives to estimate the background infectivity, immuno-reactivity and incidence of clinical disease with DAT and leishmanin skin test (LST) in a defined kala-azar endemic population and to obtain conversion rate of above status in relation to disease occurrence by follow up study of the cohort clinically and with DAT and LST.

LST results showed increase in population reactivity rate from 200 per 1000 at initial survey to 524 per 1000 at the end of follow up. Both in active visceral leishmaniasis (VL) and post kala-azar visceral leishmaniasis (PKDL), leishmanin skin test was found negative. DAT results showed decrease in infectivity rate from 435 per 1000 at initial survey to 300 per 1000 at the end of follow up. The prevalence of kala-azar in the study area was found to be 34 per 1000.

Diagnostic Studies

In routine diagnosis, DAT was found to have 91.66% sensitivity and 91.15% specificity in assessing kala-azar cases in field conditions. The study was further extended for validation of DAT in a group of kala-azar patients and in persons without VL symptoms living in the same risk area. A high DAT reactivity to leishmanial parasite was observed in contacts living with current cases of kala-azar (57%) as compared to non-kala-azar families (22%). The antigenic analysis of *L. donovani* isolates from different endemic areas showed presence of new polypeptides, a band at 8.6 kDa detected in all the *L. donovani* isolates but not in PKDL cases. This finding may be useful for differential diagnosis of kala-azar.

A nucleic acid based method, suitable for diagnosis of kala-azar and for detection and characterization of leishmania parasites is being developed at present. A PCR – RFLP system has been standardized targeting the spacer sequence within rRNA gene. DNA of 34 isolates

(29 VL and 5 PKDL) in addition to the reference strains (*L. donovani* and *L. tropica*) was amplified by PCR using same primer. Preliminary results indicated the potential of this technique for documenting variation within *L. donovani*.

Under the project ongoing at Institute of Pathology (IOP), New Delhi on immunohistological studies on skin lesions in post-kala-azar dermal leishmaniasis, of the 50 cases, LD bodies could be detected in 43 cases while they were detectable in 23 cases by H&E only. Parasites were seen as dark brown spherules of 3-5 μ m both within and outside the macrophages. The technique is useful especially in cases with a low parasite load.

In another study aiming at identifying novel genes that exhibit stage specific expression in leishmania parasites isolated from Indian kala-azar patients using AP-PCR (arbitrary-primed PCR), a gene fragment of *L. donovani* showing significantly higher expression in the promastigote form was identified. The gene coded for centrosome protein called centrin which was functionally localized in the anterior part of the parasites.

A PCR assay capable of amplifying kDNA of *L. donovani* in a species specific manner has been developed which is sensitive enough to detect kDNA in an amount equivalent to a single parasite or less.

Entomological Studies

A cross-sectional study was carried out in an epidemic affected village in Nalanda district to assess the magnitude of the disease. The survey revealed the presence of vector (*P. argentipes*) in the household. The house index of *P. argentipes* was 18.4 and MHD was 4.5. Using remote sensing data on sandfly distribution, seasonal and spatial changes in land use of both endemic and non-endemic foci have been collected. This will facilitate overlaying of remote sensing data for accurate observation and evaluation of index eco-epidemiological factors. Preliminary results from the study have indicated association and discrimination of distinct bio-ecological parameters and vegetation index with distribution/abundance of *P. argentipes*. It will be correlated with disease distribution.

Vector identification as well as incrimination in visceral leishmaniasis through conventional methods like mass dissection of sandflies and demonstration of parasite in them has not been achieved largely. Morphological

differences among *P. argentipes* have been studied using hybridization with the rDNA probe and detection of zymodeme pattern of leishmania parasite.

Immunological Studies

In order to investigate the cause of T-cell unresponsiveness to *L. donovani* antigen, role of CD 2 antigen on T-cells in immunity to this parasite was assessed. Initially data on distribution of CD 2 + T cells in peripheral blood of kala-azar patients during course of treatment with SAG were obtained enabling comparison of results between responsive and unresponsive cases.

As compared to fresh cases, there was two-fold increase in the expression of CD2 antigen and migration inhibition factor (MIF) levels while there was almost six-fold increase in the levels of IL-2 in responsive cases and no change in unresponsive cases. Upon stimulation, an increase in CD 2 + T cells was observed in patients with active infection (45.33%), which was comparable to clinically cured cases (52.55%). This suggests that anti CD 2 can potentially be used to stimulate leishmania sensitised T-cells. CD-2 antigen is important in initiating phosphorylation in proteins of CD4 molecules.

Clinical Studies

A study was undertaken to assess the rate of unresponsiveness to SAG treatment in fresh VL cases and to see association of various factor (s) with drug unresponsiveness. For the study, 104 fresh VL cases were administered SAG at a dose of 20 mg/kg body weight i.m. daily for 30 days. Investigations were carried out 0, 15 and 30 days after initiating treatment. The proportion of unresponsive cases in high endemic areas (58%) was more as compared to low-endemic areas (36%) of kala-azar. The level of MIF in host prior to treatment was observed to be significantly associated with rate of unresponsiveness. The unresponsiveness was observed more in the patients having MIF level less than 30% before the start of therapy. Out of 52 initially cured cases, 7 relapsed in course of follow up after 1-2 months, thus the ultimate cure rate of SAG observed became 44%.

A control randomized clinical trial of amphotericin B as compared to pentamidine carried out to study its efficacy and toxicity in 230 clinically and parasitologically confirmed unresponsive kala-azar cases revealed that

the cure rate was 100% in amphotericin group while in pentamidine group it was 85%. The study is being continued.

HIV and VL Co-infection Studies

Keeping in view an urgent need for proper evaluation of the extent of the problem of VL-human immunodeficiency virus (HIV) co-infection in Bihar, studies have been initiated in collaboration with National AIDS Control Organization (NACO), New Delhi.

368 sera samples of kala-azar (130 parasitologically confirmed and 238 serologically positive) cases have been tested for HIV antibodies by various HIV test kits. So far, three have been found positive for HIV-antibodies. Rest of the sera samples were found non-reactive for HIV antibodies during screening.

VIRAL DISEASES

Research in 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), studies on dengue viruses, surveillance of poliomyelitis, molecular epidemiology of wild polioviruses, molecular biological studies in hepatitis and AIDS are some of the important areas of research addressed during the year under report.

Japanese encephalitis (JE)

Epidemiological Studies

Karnataka, Andhra Pradesh and Tamil Nadu

During the year, of a total of 216 specimens from suspected encephalitis cases received from 15 districts of Karnataka, four of Andhra Pradesh, and one of Tamil Nadu, 76 were diagnosed as JE. All specimens were tested for IgM antibodies for JE virus (JEV) by M antibody capture enzyme linked immunosorbent assay (MAC-ELISA) and haemagglutination inhibition (HI) test against JE, WN and DEN-2 antigens. Maximum JE cases occurred in November (39) followed by October (24).

Kushinagar district, U.P.

During the year, Kushinagar district experienced a small outbreak of JE. A total of 234 cases with 42 deaths

were reported from all 14 PHCs. Cases started appearing in July and continued till October. Children aged 6-10 yr. were worst affected. The cases are being investigated.

Entomological Studies

A total of 59608 adult mosquitoes comprising 40 species were collected from three JE affected villages viz., Gulehla, Gopalpur and Ghoghra in Kushinagar district of Gorakhpur region, *Cx. tritaeniorhynchus*, incriminated vector of JE showed relatively high density and accounted for 20.2% of the total collection followed by *Mansonia uniformis* (16.9%), *Cx. pseudovishnui* (15.6%), *An. peditaeniatus* (13.9%), and *An. vagus* (13.2%) during the epidemic season i.e., July to October. About 12463 mosquito larvae belonging to 34 species were sampled from a variety of breeding habitats. Larvae of *Cx. tritaeniorhynchus* were collected in highest numbers and accounted for 57% of the total collection during August. This indicates that there is a build up of the *Cx. tritaeniorhynchus* population during August preceding the peak of human cases, which was reported in September.

A three-year longitudinal study on primary and secondary vectors of JEV infection was completed in Kuttanadu, which had experienced an insular JE outbreak in 1996. *Mansonioides* were identified to play secondary role and probably helped in the maintenance of JEV in the environment before paddy season in this unique ecological setting.

Attempts were made to assess the utility of goats as sentinel animals to reflect the JEV infection load in the mosquitoes and the risk of infection to human population. The magnitude and timing of JE infection in the principal JE vector, *Cx. tritaeniorhynchus*, as measured by MIR per 1000 and a new index linking percentage of JE positive mosquito pools with abundance of JE vectors (named as infected vector abundance), were reflected by the seroconversion in goats. This is easier and practicable at regional level and may be useful for the prediction of JE infection risk of human population.

The technology to impregnate cheap polypropylene material (urea bags) with pyrethroid (deltamethrin) for covering open spaces as curtains (to reduce JE vector-man contact) was transferred to 69 villages of two PHCs by the Govt. of Tamil Nadu. Evaluation revealed 90%

reduction of *Cx. vishnui* and *Cx. quinquefasciatus* mosquitoes in experimental villages compared to control villages. Complete fixation of curtain material was observed by 51% of those who received them. Remaining households had partial coverage with curtains. Almost all (95%) were willing to pay for re-spraying of curtains to increase their active life span and about 2/3 (61.7%) were willing to pay for replacement of damaged curtains.

A pyrethroid product "Kingfog" (1% ultra low volume formulation of deltamethrin) was evaluated for its efficacy in reducing the JE vector population and JE vector-man contact in one village. Adult mosquito population was reduced drastically and parity rate was lowered for 2 days. Peridomestic fogging of pyrethroid appears to be a potent weapon during epidemic period to reduce the JE vector-man contact for a limited period thereby reducing the JE virus transmission potential.

Conventional diagnosis using 3 available systems indicated high prevalence of JEV infection (59%) in acute encephalitis syndrome (AES) in children. The results of conventional tests were confirmed with RT-PCR technique carried out at National Institute of Immunology (NII), New Delhi. Majority of the positive samples (5 out of 7) were confirmed as JEV infection with RT-PCR technique also.

A newly designed medium was made by substituting the conventional Luria broth medium for the production of *Bacillus thuringiensis* serovar *israelensis* toxins and larvicidal activity of the toxins could be demonstrated in the laboratory. Further work is in progress.

Attempts were made to develop a simplified immunospot assay (ELISPOT) for detecting JEV infection at low levels without using sophisticated equipments. The ELISPOT results can be preserved and cross-checked at a later date.

Immunopathogenesis of JEV

Nude Mouse as a Model for Studying JE Pathogenesis

Earlier a mouse model employing adult BL6 nude (athymic) mice inoculated *via* subcutaneous route for studying JE pathogenesis have been evaluated. Since antibodies were detected in the sera of both the apparently healthy and sick euthymic (BL6 +/nu) and Swiss mice, experiments employing passive transfer of monoclonal antibodies (MAbs) revealed a protective

role of antibodies especially when given one day before the virus challenge in mice. Studies were continued employing a combination of two MABs especially those which showed lowering of average survival time in mice challenged with the virus.

JEV Replication and Expression in Cells

Studies on JEV replication in cells indicated an important role of nucleus during early phase of replication. An essential role of glycosylation in native epitope conformation and expression/presentation on the virus 'E' glycoproteins has been established. Assaying the virus from culture supernate and cell lysates yielded low virus content along with drastic reduction of haemagglutinating activity in tissue culture fluid indicating the down regulation of virus maturation inside the cells and loss of biological activity.

Vaccine Related Studies

Development of Chimeric Peptide Vaccine against JEV

Conformation of B cell epitope is an important factor in deciding the appropriate immunogenicity of chimeric Th-B cell peptides. In order to confirm this, studies on reactivity of chimeric peptide with MABs were carried out. Chimeric peptides containing B cell epitope 40-TLDVRMINIEASQ-52 and T helper epitope 439-SIGGVFNSIGKAVHQ-455 were synthesized in two different orientations, T-B and B-T. Results showed that reactivity with JEV specific MABs Hs-1 and Hs-2 remains intact with the chimeric peptides. In the case of chimeric peptide containing 40-TLDVRMINIEASQ-52, it was observed that the earlier nonspecific reactivity with flavivirus cross-reactive MAB Hx-2 actually decreases. These studies will help to decide the appropriate combination of chimeric peptides as JE vaccine. Similarly, both T-B and B-T chimeric peptides induced similar immune response against JEV in mice. In addition, induction of anti-JEV antibodies was observed using aluminum hydroxide gel as an adjuvant.

Study on prediction of T helper epitopes was continued. Using various prediction methods, T helper peptide epitopes on structural and nonstructural proteins of JEV were predicted. Six peptides from envelope glycoprotein (Egp), membrane (Mem) and nonstructural (NS) protein 1 of JEV have shown promise as T helper peptides in stimulation assays.

In order to ascertain potentiation of immune response by T helper peptides, mice were primed with T helper peptides in aluminium hydroxide followed by two booster doses, two weeks apart, of propiolactone inactivated JE virus mouse brain antigen. Sera were collected two weeks after each booster and virus neutralization assay was carried out. The results indicated that priming by T helper peptides from both structural and non-structural proteins can enhance virus neutralizing antibody response (Fig.7). The augmentation was seen both in Balb/c and Swiss mice. Incorporation of T helper peptides in booster doses further augmented the neutralizing antibody responses.

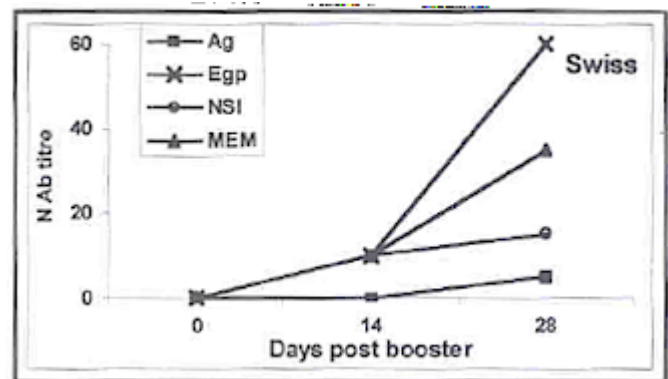


Fig.7 Priming of neutralizing antibody response by T helper peptides.

Once the immunopotential effect of NS-1 and Mem T helper peptides was known, chimeric peptides containing T helper peptides and B cell epitopes capable of inducing neutralizing antibodies were synthesized. Balb/c, C3H, Swiss mice were immunized with chimeric peptides. The results indicated that mice could produce JEV reactive antibodies after immunization with chimeric peptides containing NS-1 and Mem T helper epitopes. Challenge studies showed that most of the chimeric peptides could protect mice from lethal challenge of JEV. The best results were obtained with peptide containing B cell epitope along with NS-1 T helper epitopes.

Nucleic Acid Vaccine for JEV

Studies on development of DNA vaccine for JEV are being conducted. To increase the efficiency of the DNA vaccine, a truncated form of prM-E and the complete prM-E of JEV were cloned into the mammalian expression

vector, pCDNA 3.1C. To target the CMI response, the NS1 gene of the same strain has also been cloned into the TA vector and will be further subcloned into pCDNA 3.1C. The core of JEV has been cloned into the baculovirus and its expression confirmed by ELISA and immunoblot.

Attenuated JE Vaccine

To develop an attenuated vaccine for JEV, four mutants were selected from the persistently infected cell line. The mutants replicated in PS cells to reasonably high titres, were avirulent, induced neutralizing antibodies in mice and protected against virus challenge. Neutralization (NT)-resistant escape mutants of two strains of JEV, Vellore and Bankura, were isolated against a panel of neutralizing monoclonal antibodies. The Mabs recognized specific and conserved sites on the E protein. The mutants are being passaged further to identify NT epitopes conserved between different Indian strains.

Dengue (DEN)

Epidemiological Studies

Karnataka, Andhra Pradesh and Tamil Nadu

From April 2000 to March 2001, specimens were received from a total of 740 suspected dengue fever cases from 15 districts of Karnataka, four districts of Andhra Pradesh and one district of Tamil Nadu. Of these, 131 cases had paired sera and 609 had single serum sample. All the specimens were tested for IgM antibodies against dengue-2 antigen by MAC-ELISA and HI test against JE, West Nile and DEN-2 antigen. Virus isolation in mice was done from 258 sera samples of acute viral fever cases and of these, 85 groups were cross challenged intracerebrally with live dengue-2 virus for indirect demonstration of dengue viraemia.

Out of 740 cases, 212 were diagnosed as dengue and 528 were negative based on dengue IgM or cross challenge test. Dengue positive dengue haemorrhagic fever (DHF)/dengue shock syndrome (DSS) cases were seen from May to October 2000. 46 cases had clinical symptoms of DHF/DSS of which 37 were DHF-II, six DSS-II and three DSS-IV grade. About 65% of these were children below 10 yr. and 20.7% were adults aged 16-65 yr. Of the 740 cases, 289 were recorded from 22 villages covering five districts; 51.6% of these were diagnosed as dengue. Altogether 11 virus isolations were made in suckling mice. The outbreaks occurred

between April and October 2000 in different districts involving all age groups and both sexes.

Generation of Monoclonal Antibodies (MAbs) against DEN Virus

Murine Mabs were generated against DEN-1 (Hawaii) and DEN-2 (P23085) viruses. Four Mabs (II G7A6, III E5G5, VE6A11 and 1VE3B6) were characterized for their reactivity in HI, ELISA, IF and NT. Two of these Mabs (VE6A11 and III E5G5) showed DEN group reactivity in ELISA as well as in IF while one Mab (II G7A6) showed flavivirus cross reactivity. Two group reactive Mabs, III E5G5 and VE6A11, were different from one another in their reactivity. Only VE6A11 showed neutralization against DEN-I virus in *in vivo* N test.

Monoclonal antibody based antigen detection ELISA was developed to study prevalence of CHIK virus in field collected *Ae. aegypti* mosquitoes.

Insect Genetics

Enhanced Esterase Activity in Dengue Infected Mosquitoes

Salivary glands and midgut play an important role in virus transmission. It was observed that esterase enzyme level increases in these organs of dengue-infected mosquitoes which is suggestive of defense response of mosquitoes to virus infection.

Dengue Virus Binding Proteins in the Midgut of Ae. aegypti

Western blot studies showed that 38kDa protein from the brush border membrane fraction of midgut epithelium of *Ae. aegypti* binds specifically to E-protein of dengue virus thus suggesting that this protein plays an important role in viral entry into the gut epithelial cells.

Haemagglutinins in the Midgut of Mosquitoes and their Role in Dengue Virus Susceptibility

Midgut extracts of mosquitoes showed haemagglutinin activity. Among many carbohydrates tested, five showed inhibition of this activity in the gut extracts. Incorporation of these into the dengue virus infected mosquito bloodmeal showed reduction in susceptibility of mosquitoes to virus suggesting that these sugars compete with virus receptors in the midgut.

This may be one of the factors affecting the susceptibility of mosquito to dengue viruses.

Hepatitis

Hepatitis A Virus (HAV)

ELISA based technology developed by NIV, Pune for the detection of hepatitis A IgM and total antibodies has been transferred to industry. A project has been initiated in collaboration with the industry for preparation of hepatitis A vaccine.

Hepatitis B Virus (HBV)

Basal Core Promoter HBV Mutants

Basal core promoter (BCP) region of HBV genome was sequenced among symptomless HBsAg carriers, patients suffering from chronic, acute and fulminant hepatitis B. No correlation between BCP HBV mutants and disease severity or presence of pre-core HBV mutants was noted.

Genotyping of HBV

Based on the sequencing of S gene of HBV, phylogenetic analysis of three samples each from Pune and Andaman and Nicobar islands was carried out. All the samples belonged to genotype D.

Hepatitis C Virus (HCV)

HCV Genotypes in Different Parts of India

During the current year, 120 serum samples from chronic hepatitis C patients representing western (45) eastern (14) southern (30) and northern (31) parts of India were genotyped based on the sequencing of 5'-noncoding region of the genome. The results showed that genotype 3 was most prevalent in northern and eastern India; genotypes 1 and 3 were equally prevalent in western India whereas multiple genotypes were almost equally distributed in southern India.

Hepatitis E Virus (HEV)

Hepatitis E in Animal Species

The prevalence of IgG antibodies to HEV (IgG-anti-HEV) was determined among different animal species. Seropositivity varied from 4.4 to 6.9% in cattle, 54.6 to 74.4% in pigs and 2.1 to 21.5% in rodents. Of the

44 dogs screened, 10 were positive. None of the 250 goat sera tested was found to be anti-HEV positive. Of the 22 serum samples from *Bandicota bengalensis* collected in 1985, 12 were found to be positive for anti-HEV antibodies. Among the 400 rodent sera tested in year 2000, none of the 125 house mice (*Mus musculus*) and 75 shrews (*Suncus murinus*) was positive. Fifty nine of the 200 house rats (*Rattus rattus rufescense*) were positive for IgG anti-HEV antibodies. No evidence of HEV infection was obtained following experimental inoculation of an Indian strain of HEV into anti-HEV negative pigs, rats and goats. Retrospective analysis of sequential serum samples collected in 1985-86 from 45 pigs from Karnataka state documented sero-conversion to IgG anti-HEV antibodies in 42 pigs. Mean age at sero-conversion was 4.8± 2.8 months.

Swine HEV

Of the 284 pig serum samples from western India screened for the presence of HEV RNA employing nested PCR, four were found positive. Phylogenetic analysis based on partial sequencing of ORF-2 placed all swine HEV isolates in genotype 4 which include the human HEV isolates from Taiwan and China and swine HEV isolates from Taiwan (Fig.8). In contrast to the US and Taiwan wherein both human and swine HEV isolates grouped together in genotype 3 and 4 respectively, human HEV isolates from India belong to genotype 1 whereas genotype 4 circulates in swine. Experimental transmission of swine HEV to Indian pigs was documented.

Molecular Epidemiology

During the year, 38 outbreaks of viral hepatitis in different parts of Maharashtra were serologically confirmed to be due to hepatitis E. Phylogenetic analysis placed all the 17 HEV isolates examined so far in the most prevalent genotype 1a representing Asia-Africa.

Multiple Viruses

Monitoring of Sewage Treatment Plant for the Presence of Hepatitis Viruses

Affluent and effluent samples from a local sewage treatment plant were collected twice a week for one year and screened by PCR for the presence of HAV and HEV RNA and transfusion transmitted virus (TTV) DNA. As the treatment plant was nonfunctional for almost

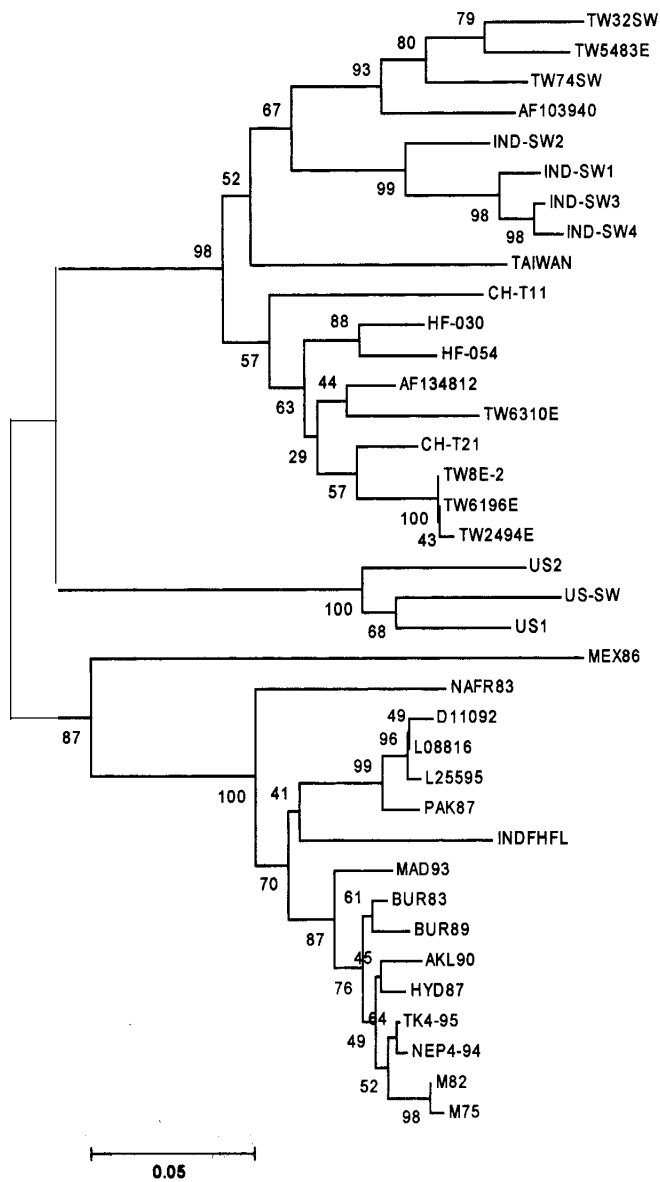


Fig.8 Phylogenetic analysis of Indian swine HEV isolates.

six months, post-treatment samples could not be collected. The overall prevalence in raw sewage was estimated to be 24.42 % for HAV, 10.98% for HEV and 12.70% for TTV. A comparison of PCR positivity among the raw and treated sewage samples during the six month period when the plant was functional, showed a significant reduction in HAV RNA positivity. The prevalence of HEV RNA and TTV DNA did not reduce significantly. Phylogenetic analyses placed sewage-derived HAV and HEV isolates in genotypes 1b and 1a respectively.

Exposure of the Primitive Tribes of Andaman and Nicobar Islands to HAV and HEV

In collaboration with RMRC, Port Blair, a study was conducted by NIV, Pune during 1989-1999 to assess the prevalence of anti-HAV and anti-HEV antibodies among four accessible primitive tribes in Andaman and Nicobar Islands *i.e.* Nicobarese, *Shompens*, *Onges* and Great Andamanese. Earlier studies carried out among these tribes had revealed very high rates of HBV infection. In addition, 240 serum samples collected a decade earlier from age-stratified Nicobarese tribe were also screened. HAV infection was found to be highly endemic among all the tribes whereas HEV infection was common among Nicobarese and *Shompens*. HEV infection showed significant increase over the last decade among Nicobarese. The age-wise prevalence of anti-HEV antibodies among Nicobarese was distinctly different with high rates among children. Efforts to provide safe drinking water and sanitary facilities are urgently needed in these populations.

Virological/Serological Diagnostics

Eight hundred and twenty nine blood products submitted by the Drug Controller of India were tested for HBsAg and HCV RNA. A total of 344 and 367 patients were tested for the presence of HCV RNA and HBV DNA respectively by PCR. A total of 738, 715 and 268 serum samples were tested for the detection of anti-HAV-IgM, anti-HEV-IgM and HBsAg respectively.

Poliomyelitis

In recognition of the work done by the Enterovirus Research Centre (EVRC), Mumbai in the field of poliomyelitis, the WHO has upgraded its status from a regional reference laboratory to Global Specialized Laboratory for Polio from October 2000.

Virological investigations were carried out at the Centre on all cases of acute flaccid paralysis (AFP) reported from Maharashtra, Madhya Pradesh, Goa and Delhi.

Under AFP surveillance, 615, 623 and 23 cases of AFP from the states of Maharashtra, Madhya Pradesh and Goa respectively were virologically studied. The incidence of AFP was 1.9 and 2.0 per 100,000 population under 15 yr. of age in Maharashtra and Madhya Pradesh respectively. OPV immunization history of AFP cases

revealed that 8.2 and 6.2% cases had not been administered the required 3 doses of OPV. Wild polioviruses were isolated from 8 cases in Maharashtra (2 polio 1 and 6 polio 3) and 1 case (polio 3) in Madhya Pradesh.

Wild Polioviruses

Molecular Epidemiology

A total of 1829 poliovirus strains isolated from 780 cases of AFP were submitted by the National Polio Network Laboratories to EVRC for intratypic differentiation, ELISA, nucleic acid hybridization and/or PCR. A case of AFP is classified as confirmed paralytic poliomyelitis if a wild poliovirus has been isolated from stool specimens collected. A total of 265 cases of paralytic poliomyelitis were identified in the year 2000. Maximum number of cases were from Uttar Pradesh (180) followed by Bihar (50). Along with West Bengal (8), Delhi (3) and Haryana (4) the entire north India (except NE, J&K and Himachal Pradesh) was found to be endemic for poliovirus infection. In addition, wild polioviruses were isolated from AFP cases from Maharashtra (7) and Karnataka (8). Most surprisingly a poliomyelitis case due to wild poliovirus infection was detected in Mallapuram district of Kerala. The state was free from wild poliovirus since 1996. No wild poliovirus was detected in adjacent Tamil Nadu state.

Nucleotide sequence of RNA coding for complete VP1 protein was determined for all wild poliovirus type 1 and 3 isolates except from Uttar Pradesh. A150 nucleotides at VP1/2A junction region of RNA of 98 out of the 106 polio1 isolates from Uttar Pradesh were also sequenced. Sequences were analyzed to identify genetic lineages of wild polioviruses in the country and extent of their transmission.

The poliovirus type 1 isolated from Kerala and Karnataka was genetically of the same lineage as detected in Tamil Nadu in the year 1999. It was seen that silent/undetected transmission of wild poliovirus type 1 was taking place in the region.

The wild poliovirus type 1 isolates from Mumbai (Maharashtra) were of two separate genetic lineages (Fig.9) not detected in the state earlier. The isolates were closely related to strains from North India supporting the epidemiological information that the cases had acquired the infection from contacts in Uttar Pradesh.

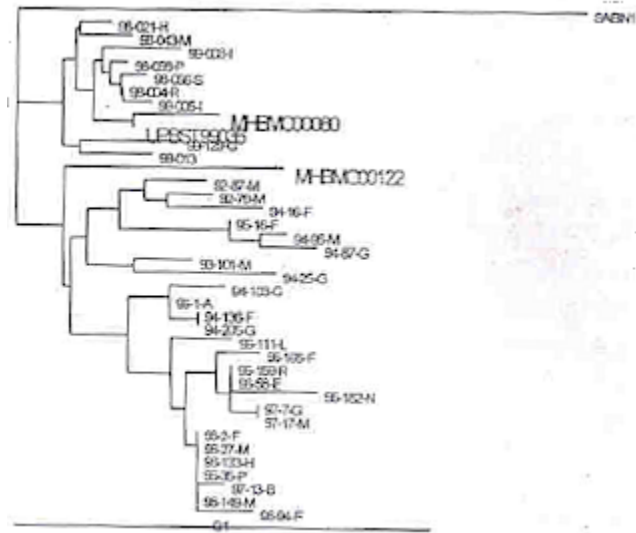


Fig.9 Dendrogram showing recent wild poliovirus 1 isolates from Mumbai are not closely related to those previously isolated in the city.

Six wild poliovirus type 3 isolates were detected from the state of Maharashtra (Fig.10). The 6 viruses formed a tight cluster of related isolates. Two cases from Brigand town in Thane district were reported from hospitals in Mumbai. These isolates belonged to the same lineage of wild poliovirus that was responsible

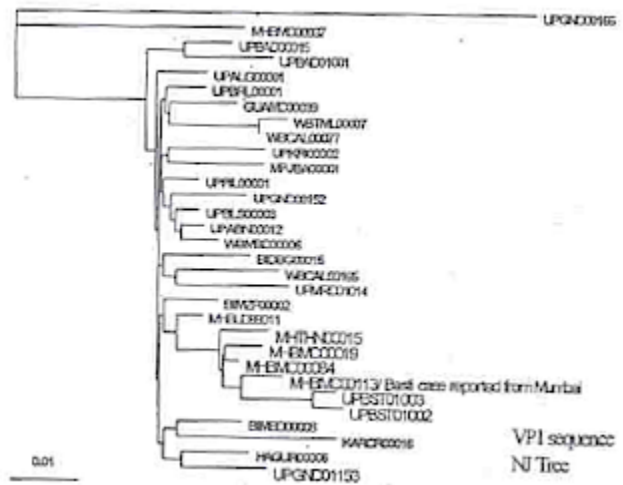


Fig.10 Dendrogram showing genomic relationship of wild poliovirus 3 isolates of the year 2000-2001.

for the epidemic like situation in north India in 1999 and spread to Maharashtra and other states including Gujarat and Karnataka. The genetic relationship of the virus isolate from the Basti district, Uttar Pradesh (reported from Mumbai) with the Bhiwandi isolates confirms that the virus lineage originated in UP.

It was seen that at least 7 lineages of poliovirus type 1 circulated in Uttar Pradesh in the year 2000. The genetic lineages of wild poliovirus 1 strains isolated from UP, Bihar, Delhi and Haryana in year 2001 were traced to related strains isolated in the year 2000. It can be seen that a particular lineage from western Uttar Pradesh (Moradabad - Ghaziabad) has been predominant during early months of the year 2001.

Diagnostic PCR

ELISA using cross-absorbed strain specific antisera (immunological test) and RNA- RNA probe hybridization test (genomic test) are currently employed for routine identification of polioviruses.

Pan-enterovirus, pan-poliovirus (degenerate), Sabin-multiplex and wild poliovirus 3 specific primer pairs were used for amplifying viruses from cell culture harvests.

Out of the 489 virus samples tested, 481 gave correct results of serotyping and poliovirus intratypic differentiation. Of the remaining 8 samples, 3 were identified as NPEV for which the virus neutralization tests failed due to low concentration of virus. In 3 samples, one of the two virus types had failed amplification. In 2 samples discordant results were obtained mainly because PCR was performed using rhabdomyosarcoma (RD) cell harvest and poliovirus identification was done after the RD cell harvest (these cells support growth of polio and NPEV) was further grown in L20B cells (support growth of poliovirus).

446 poliovirus isolates from other laboratories were also tested. Discordant results were obtained for 2 specimens. PCR detected an extra serotype in these samples (a mixture of polio 2 and 3 Sabin vaccine strains). Retesting of the samples by virus neutralization test confirmed the PCR results.

It was concluded that PCR was specific and sensitive for identification of polioviruses. The assay is being routinely used for rapid diagnosis of poliovirus infection.

Supplemental Surveillance System for Wild Poliovirus

It is generally considered adequate to use AFP surveillance for detection of wild poliovirus circulation in communities. Environmental surveillance was initiated in selected sites in Mumbai to provide information about silent/undetected transmission of wild poliovirus in high-risk areas such as urban slums.

During August 1997 to August 1999 the methods of collection of sewage samples, virus concentration and poliovirus isolation were standardized. Also sites were selected for sample collection on the basis of epidemiological data generated over several years.

By the end of 1999, it was clear that wild poliovirus transmission in Mumbai would be minimal if not completely stopped. Molecular sequence data on wild poliovirus isolates from Mumbai strongly suggested importation of wild virus lineages from other areas of the country. Therefore, a third arm to the study *i.e.*, screening apparently healthy children for wild poliovirus excretion was added.

During August 2000 to February 2001, a total of 1681 stool samples collected from healthy children below 5 yr. from slums in F and M wards were studied for poliovirus detection. Additional samples were collected from a locality if a wild poliovirus positive case was detected in the city.

Vaccination coverage with OPV was more than 98%. Sample collection was continued during the pulse polio immunization campaign months. In the month of November 2000, a mop-up round was conducted because of detection of wild poliovirus positive cases. NPEV isolation rate was 53.5%. Vaccine poliovirus strains were isolated in 4% samples. Wild poliovirus type 1 was isolated from stools of 4 children in November 2000. No additional wild poliovirus has been isolated from stool samples till date.

In August 2000, a case of wild poliovirus type 1 was detected in a slum in M ward. In October 2000, a wild polio 3 positive case from Basti (U.P.) was reported from Antop Hill area of F ward. In November 2000, a wild poliovirus type 1 positive case was detected in the Dharavi slum area in G ward of the city.

Wild poliovirus type 1 was isolated from 4 children in Antop Hill area. Wild polio 3 was not isolated from

any child even though the wild polio 3 case was from this area. Inquiries revealed that the slum dwellers from Dharavi and Antop Hill have close social contact. Frequent travel from and to Uttar Pradesh was also reported. Complete VP1 sequence of the poliovirus 1 isolates from the paralytic cases and the healthy children was determined.

For sewage sampling a sewage pumping station in F ward and a big *nullah* carrying domestic waste water from large slum areas in M ward were selected. Every week a 1 litre sample was drawn from each of the two sites. After clarification by centrifugation, virus was concentrated by PEG precipitation. Poliovirus isolation was attempted by inoculation of L20B cells. All poliovirus isolates were further characterized by ELISA and probe hybridization. Complete VP1 protein coding region sequence of wild poliovirus isolates was determined.

From January to March 2001, wild poliovirus 1 was isolated from sewage samples on four occasions (in April and May). Genetic relationship of the wild virus isolates is shown in Fig.11. Polioviruses of two separate genetic lineages were detected in sewage samples. The four poliovirus type 1 isolates from healthy children were genetically identical indicating the same source of infection. They were also of the same genetic lineage as the wild poliovirus 1 strain isolated from the paralytic case from Dharavi slum. Sewage isolates of one lineage were clearly related to the isolate obtained from the

paralytic case from Dharavi slum. Importantly, this virus was genetically distinct from all other wild poliovirus strains so far isolated from Mumbai.

Since November 2000 no wild poliovirus positive paralytic poliomyelitis case has been reported from Mumbai. Results obtained by supplemental surveillance involving environmental sampling clearly show that sewage sample testing from known high-risk areas such as urban slums is sensitive in detecting wild poliovirus transmission in communities.

Identification of Non-polio Enterovirus Types by Molecular Methods

The transgenic mouse cell line (L20B) expresses the human cell receptor for poliovirus. A small number of non-polioviruses were isolated in L20B cells during the past three years while testing stool samples for the presence of poliovirus. Positive amplification of viral RNA in PCR using pan-enterovirus primers proved these to be enteroviruses able to multiply and produce cytopathic effect in L20B cells. Sequence analysis was done for typing these enteroviruses. 19 enteroviruses were identified using sequence information of 350 nucleotides of the 5'end of VP1. These included 14 CA10, 2 CA8, 1 each of CA14 and CA3. One of the isolates could not be typed, as the sequence was unique. It is, therefore, very likely that the isolate represents a new enterovirus.

Nucleotide sequence of the complete VP1 protein gene is being studied. It is proposed that nucleotide sequence encoding complete capsid protein region should be attempted so that unambiguous decision about a new serotype of enterovirus can be taken.

The nucleotide sequence information of nine CA10 isolates was used to determine their genetic relationship. Four separate lineages have been identified.

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

HIV/AIDS is a major problem in the country and measures have been taken to control the epidemic which is supplemented and complemented by a strong basic research component. Socio-behavioural and epidemiological studies and development of an AIDS vaccine are some of the priority areas of research being strengthened to achieve the desired goal. Besides

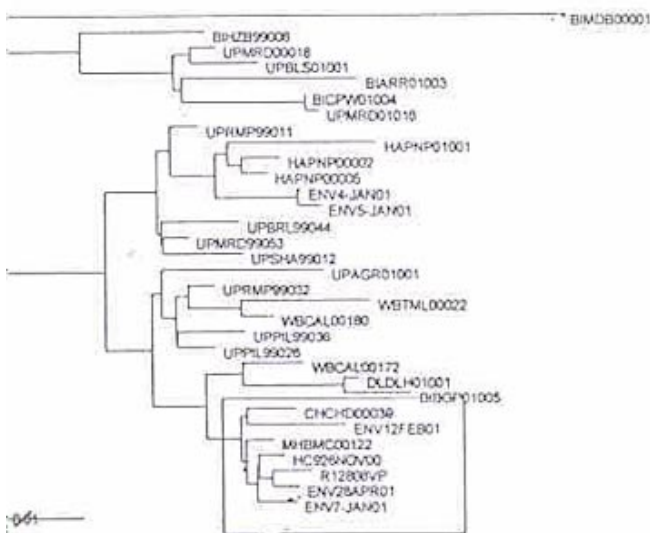


Fig.11 Genetic relationship of wild poliovirus type 1 detected in environmental samples from Mumbai.

these, efforts to understand the molecular aspects of pathogenesis and immunological aspects of the infection are also being pursued actively. The National AIDS Research Institute (NARI), Pune is the flag bearer of the Council's research efforts in the fight to control spread of HIV/AIDS in India.

Epidemiological Studies

In a major prospective cohort study, male and female STD patients and female sex workers attending STD clinics were tested for HIV infection. HIV seronegative patients were also enrolled in the study. This first collaborative cohort study in India, between Johns Hopkins University, USA and NARI was carried out to estimate the prevalence of HIV infection in individuals with high risk behaviour and to study biological and behavioural factors related to HIV acquisition and transmission. Another major objective was to create an infrastructure to undertake HIV prevention trials including vaccine trials in future. This study had clinical, laboratory and data management components. Until the beginning of year 2001, over 12850 patients attending the STD clinics were screened. Of the 6932 patients who returned for collection of report, 2760 were seropositive. Seronegative patients were followed amounting to over 4000 person years.

The HIV epidemic is spreading not only in urban population but also in rural areas. Earlier studies conducted by NARI showed that HIV sero-prevalence in pregnant women in rural areas of Pune district of Maharashtra was 1.2%. A study conducted in rural pregnant women in 34 villages covered by the Comprehensive Rural Health Project (CRHP) in Jamkhed *taluka* of Ahmednagar district (Maharashtra) revealed that the prevalence of HIV infection in them was 0.7 per cent. Sero-prevalence observed in rural women was two and a half times more than expected.

Molecular Virology

The replicative capacity of a virus during primary HIV infection may be an important determinant of subsequent disease course. Subtype B strains isolated immediately after seroconversion have exhibited slow replication kinetics and less cytopathicity. The replicative differences of subtype C isolates from Indian seroconverters were studied

in peripheral blood mononuclear cells (PBMCs) stimulated by anti CD3/IL2, IL2/IL2, PHA/IL-2 and unstimulated cells. Anti CD3/IL-2 source was found to be the best activator for co-cultured cells for propagating HIV-1 strains.

In another study, the spectrum of heterologous neutralizing antibody (NAb) response and its correlation with the laboratory parameters of disease progression was studied in a cohort of subtype C infected seroconverters by using GHOST cell assay. The last available sample from each seroconverter was tested against clade A,B,C and an A/C recombinant from Africa and clade C from India. The response against clade B (86%) was more followed by response against clade C from Africa (67%), clade C from India (58%) and clade A from Africa (24%). Of the 47 seroconverters, 37 demonstrated moderate to strong neutralization activity against one or more viruses tested during the follow up. Out of 37 patients, three demonstrated strong response against all four viruses and one against three viruses. The remaining 10 seroconverters exhibited poor or no neutralization activity.

Study of correlation of neutralizing antibody response with duration of infection demonstrated a steady rise in the antibody response against all viruses suggesting broadening of neutralizing antibody response with the due time course. An increase in the antibody response did not correlate with the increase in absolute CD4 counts and also with decrease in plasma viral load.

HIV 1 & 2 Virus Bank

Subtyping of the HIV-1 isolates was carried out using the heteroduplex mobility assay. The HIV isolates were characterised as syncytium inducing (SI) and non-syncytium inducing (NSI). Co-receptor usage by the HIV isolates was studied using the GHOST cell assay on the flow cytometer. Subtype and genotype analysis of the HIV isolates revealed that more than 85% of the isolates belonged to HIV-1C subtype. However, small percentages of A&B subtypes and HIV-2 genotypes were also encountered.

Among HIV strains tested for SI/NSI phenotyping, 80 were NSI and two SI. Using p 24 antigen results, the ability of the viruses to grow in MT2 cells was studied

in 74 isolates and of these 55 were capable of growing in MT2 cells. Similarly, testing the ability of the isolates to grow in U937 cells revealed that out of 77 isolates only 12 grew in this cell line. The work on the remaining isolates is ongoing.

Sentinel Surveillance

A sentinel surveillance programme under NACO has also been initiated for assessment of the prevalence rate/trend of HIV infection in patients with STD, antenatal cases (ANC), attendants of hospitals and referred cases over a period of time in different groups and places in Bihar. A total of 6069 sera samples have been tested during 1998-2000 in three rounds of sentinel surveillance program. The prevalence of HIV sero-positivity among risk groups like STD, ANC and migrated population was estimated to be around 7.9 per 1000.

In separate studies, for sentinel surveillance for HIV infection in tuberculosis patients, sera from 400 consecutive tuberculosis patients from Sassoon General Hospital, Pune were screened during January-February, 2000. Sentinel surveillance for anti-HIV was also conducted among the consecutive ANC cases. Twenty nine percent TB patients and 1.6% ANC cases were found positive.

Serological and Immunological Studies

Preliminary observations on lymphocyte sub-populations in HIV seropositive and seronegative tuberculosis patients in Pune showed that the CD4 counts in the former group were lower than in the latter while CD8 count was same in both the groups. In HIV seropositive tuberculosis patients with pulmonary cavity, the CD8 counts were significantly higher.

A study is being conducted to carry out lymphocyte subset analysis and to determine plasma viral load, anti-HIV T cell responses and the presence of HIV-1 quasispecies. Reduction in natural killer (NK) and B cells besides decreased CD4 cell counts was seen in early HIV infection. Mean CD8 cell counts were above normal after seroconversion.

Cytotoxic T cell response (CTL) has a very important role in protection against HIV infection. Analysis of CTL in 11 HIV-1 seropositive individuals was done using standard ⁵¹Cr release assay. The response was assessed

against HIV-1 *env* expressing vaccinia (both subtype B and C) after stimulation of PBMCs with either *env* B or *env* C. Five of these 11 cases showed detectable CTL response. Cross-clade CTL response against both subtype B and subtype C *env* was observed in 4 of the 5 individuals while one showed CTL response against subtype B *env* only.

A study carried out to investigate the correlation of HIV-specific T cell responses with plasma viral load and CD4 counts in recent HIV infection showed consistent response against HIV-1 *gagC* peptides in 25% patients. The consistent responders had lower virus load compared to the non-consistent responders.

Opportunistic Infections

A study has been initiated recently at Dr. ALM Postgraduate Institute of Basic Medical Sciences, Chennai to study opportunistic infections particularly aspergillosis in immuno-compromised subjects. An in-house ELISA and IFA have been standardised in addition to CIEP and double diffusion test to detect even minute quantities of specific antibodies. A total of 53 HIV patients with pulmonary infection were screened for isolation of *Aspergillus* and other bacterial and fungal pathogens. The interim results indicate that out of 40 males and 13 females, 5% and 15.3% species respectively were positive for *Aspergillus*. Moreover, out of 4 *Aspergillus* species isolated, 3 were *A. flavus* and one *A. niger*. In 30 patients with pulmonary disease, *A. flavus* was isolated from 4.5%. There was mixed bacterial infection with *Candida* spp in 11 HIV patients whereas in non-HIV patients with pulmonary disease only 5 showed mixed bacterial infection with *Candida*. The study is continuing.

Socio-behavioural Studies

A study designed to assess behavioural factors that could influence the intention of STD patients to inform their partners about their disease or to assess the extent of spousal communication by estimating the rate of return of partners for further investigations and medical management was carried out. The study was carried out in a District Hospital at Nasik from May 2000 to November 2000. It was found that persons from low socio economic status, who had never used a condom with their sexual partners and who continued to have sexual relations with the partner since acquiring

the STD were most likely to inform about their disease, probably because they "felt" or "perceived" the risk of the spread of disease to them. Partners who were more likely to return for health care intervention were those who already knew about the symptoms of their spouses and whose partners (STD index patients) demonstrated concern about "partner notification". Furthermore, they were more likely to be partners of those patients who had come to the STD clinic by themselves. The actual rate of return of partners for further investigations and medical management was observed to be 40.65%.

Vaccine Studies

Development of AIDS vaccine is an unmet social urgency. It is proposed to develop three candidate vaccines based on HIV-1 subtype C Indian isolates. *viz.* vector based vaccine using modified vaccinia Ankara with multiple HIV gene inserts, a DNA vaccine and a vector based or DNA vaccine with multiple immunodominant epitopes. NARI, NIV and NICED will be involved in the development of the vaccine.

Mother to Child Transmission

The NARI is associated with NACO's feasibility study of azidothymidine (AZT) treatment for reduction of mother to child transmission of HIV infection, being carried out in 11 different centres in India. Of these, five centres are located in the western region of India. NARI is the reference laboratory for centres in Sassoon General Hospital, Pune, Mumbai-based J.J.Hospital, Nair Hospital, and K.E.M. Hospital and Civil Hospital, Sangli. Being a reference laboratory, NARI is responsible for quality assurance for serological testing of pregnant women, PCR testing of infants born to HIV mothers at 2 day and 2 months after birth and estimation of plasma virus load before and after AZT treatment. NARI has been providing crucial support for the programme in the form of software development and carrying out PCR with serum samples from HIV-positive women and children.

The first phase of AZT trial has been successfully completed. Results from phase I studies revealed that administration of AZT prevents transmission of virus from mother to child by almost 60-70%.



Reproductive Health

Reproductive health is crucial part of general health and a central feature of human development. Among women of reproductive age (15-44 years), the burden of reproductive ill-health is far greater than the disease burden from tuberculosis, respiratory infections, motor vehicle injuries, homicide and violence. Women run the risks of pregnancy, childbirth and unsafe abortion, take most of the responsibility for fertility regulation and are socially and biologically more vulnerable to reproductive tract infections and sexually transmitted diseases including HIV/AIDS. Men, too, suffer reproductive ill-health, particularly in the form of sexually transmitted diseases and HIV/AIDS. Thus, while recognizing that the main burden falls on women, strategies to improve reproductive health must also take into account men's needs, concerns and roles. The National Population Policy, 2000 affirms the commitment of government towards voluntary and informed choice and consent of citizens while availing of reproductive health care services, and continuation of the target free approach in providing family planning services.

The Council's research activities 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. The researches have been undertaken through 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 including NGOs.

FERTILITY REGULATION

CONTRACEPTION

Basic Research

Biological Action of Octapeptide, a Fragment of FSHBI

A peptide from human ovarian follicular fluid, which inhibits binding of FSH (FSH binding inhibitor) to ovarian

granulosa cells *in vitro*, has earlier been identified at IRR. When injected in rodents and monkeys, FSHBI interfered with follicular maturation and ovulation. N-terminal amino acid sequence of the peptide was deduced, and based on this an octapeptide (OP) was made. Studies were pursued to determine whether OP has FSHBI like antifertility effects. The octapeptide demonstrated a dose related response of FSH binding inhibition to ovarian granulosa cells indicating the inhibiting activity of the native peptide. Further, the low dose of OP when injected in marmosets during the follicular phase interfered with follicular maturation and 50% suppression of fertility was observed. Studies are ongoing with a higher dose to elucidate the role of OP in folliculogenesis and subsequent fertility.

Studies on Mammalian Oviduct Glycoprotein

Recombinant approach was adopted to obtain bonnet monkey oviduct glycoprotein (OGP) in bulk to elucidate its role and mode of action during fertilization and implantation. The partial cDNA for bonnet monkey OGP was cloned and sequenced. Purified OGP as well as antibodies to OGP were characterized. The ability of antibodies to recombinant monkey OGP to inhibit sperm-egg interaction *in vitro* demonstrated the role of OGP in fertilization. Molecular cloning and statement of full length murine oviduct glycoprotein was also achieved successfully. Molecular weight of the expressed recombinant protein agrees with the predicted size. An understanding of the role of OGP during fertilization and implantation will help in the development of an effective immunocontraceptive.

Expression of Functional Markers in Primate Endometrium

Success of implantation depends on the embryo-endometrial cross talk mediated via various molecular factors expressed either by the embryo or the endometrium or both. In order to understand the role

of these molecular factors in implantation in primates, a study was designed (i) to establish a receptivity pattern of selected endometrial markers *i.e.* steroid receptors, cytokines, growth factors, their receptors and other functionally significant proteins and (ii) to identify and characterize the differentially expressed novel endometrial receptivity markers appearing during peri-implantation period in presence and absence of embryonic stimuli in normal ovulatory cycling bonnet monkeys and in monkeys rendered infertile with antiprogesterin ZK 98.299 (onapristone). Studies demonstrated progesterone dependent statement of transforming growth factor 2 (TGF 2) and its receptor (TGF 2R) in receptive and non-receptive endometrial expressions of TGF 2 and its receptor proteins during peri-implantation period in mated as compared to non-mated cycles. However, no change was observed in their transcript levels in the endometria from mated and non-mated animals probably due to the differential rates of transcription and translation in the cell. These

findings, however, suggest the influence of embryonic stimuli on statement of TGF 2 and its receptors in the endometrium. The study may elucidate identity and function of the factors dictating success or failure of implantation in primates.

Lymphocyte Integrins as a Marker to Assess Endometrial Function

10-15% of women in reproductive age group are infertile, 4-5% due to failure of implantation. The biochemical reasons for such defects are not known probably due to lack of definitive information on functional markers for the fertile endometrium. Studies carried out to see whether integrin statement is related to implantation failure in infertile women indicated that $\alpha v \beta 3$ and $\alpha 4 \beta 1$ integrins statement was significantly low/absent in endometrium of infertile women (Fig.12). Further studies also suggested that the pattern of integrin statement was similar in peripheral blood lymphocytes and endometrial stromal cells. The statement of these

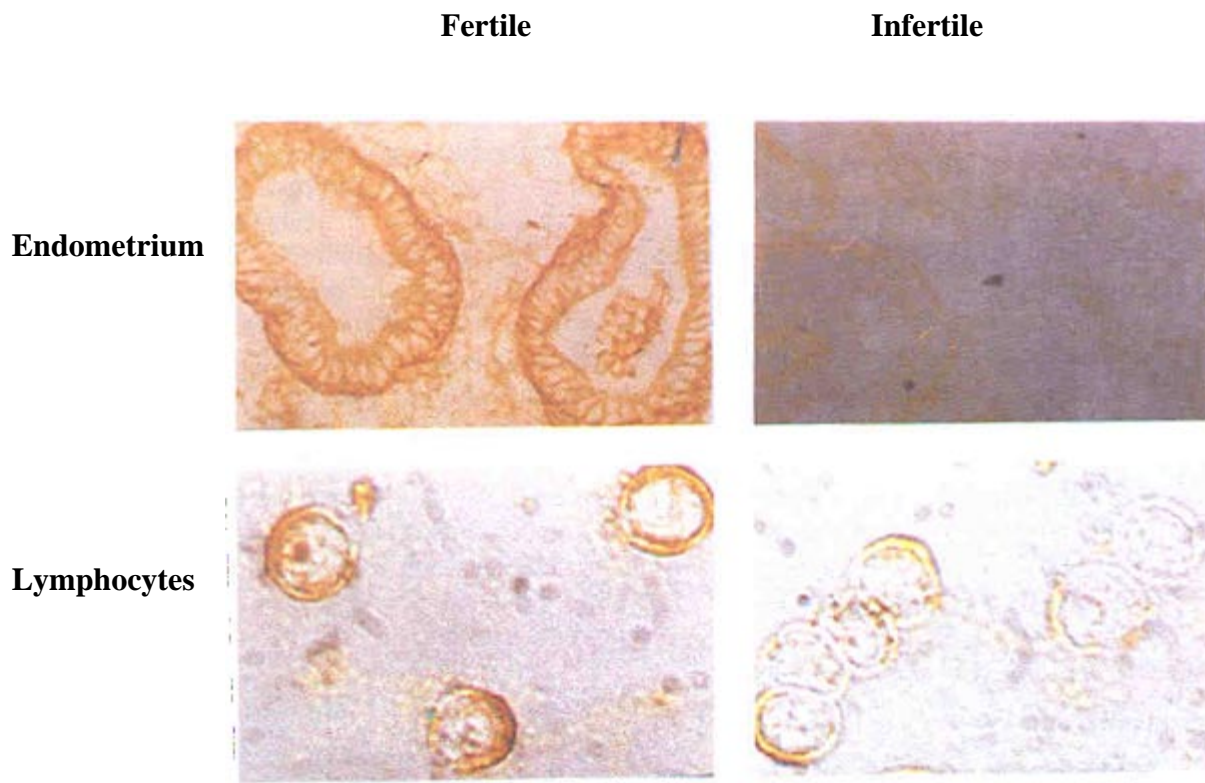


Fig.12 Immunohistochemical localization of $\alpha v \beta 3$ integrin expression in endometrium and lymphocytes of fertile and infertile women during mild-luteal phase.

integrins was found to be estrogen and progesterone dependent. Studies suggest that the statement of integrins on lymphocytes and endometrium can serve as a diagnostic marker for endometrial receptivity.

Human Seminal Plasma Inhibin (hSPI)

hSPI, a 94 amino acid protein of molecular size 10.6 kDa is a sperm coating antigen and antibodies to hSPI agglutinate spermatozoa and impair sperm binding to zona free hamster egg. Since the use of the native protein for immunocontraception has its limitations, surface oriented epitopes of hSPI were identified on the basis of acrophilicity and hydrophilicity of the protein. Two such epitopes, one from the N-terminal 1-17aa (R-17) region and the other from C-terminal region 67-94aa (R-28), were synthesized and both the molecules were found to mimic the immunobiological characteristics of hSPI. In male bonnet monkeys following immunization with synthetic R-17 and conjugated to diphtheria toxoid a rise in antibody titer was observed which caused agglutination of spermatozoa (Fig.13) with decrease in motility. Sperm count and hormone levels remained unaltered. On discontinuation of immunization, antibody titer declined and the sperm function was restored to pre-

immunization levels, suggesting the reversibility of the effect. Further studies to assess the fertility of immunized male monkeys following mating with the female animals are being pursued.

Sperm Maturation Antigens

Studies have shown that when female Balb/c neonates were tolerized against crude testicular sperm proteins, followed by immunization with epididymal sperm extract, it resulted in immune response only to the epididymal sperm proteins. Using sera from these tolerized-immunized mice a 30kDa protein was identified against which polyclonal antibody was raised. The antibody localized antigens on the acrosome and midpiece regions of the spermatozoa and brought about agglutination of spermatozoa in a dose-dependent manner. The polyclonal antibody localized the proteins specifically in the corpus epididymis. Castration and androgen replacement studies indicated that the protein was androgen regulated, appeared to be developmentally regulated appearing from day 40 of birth. Biochemical characterization studies showed that it was not a glycoprotein. Further characterization and sequencing of this protein is being done to study its functional role in fertility.

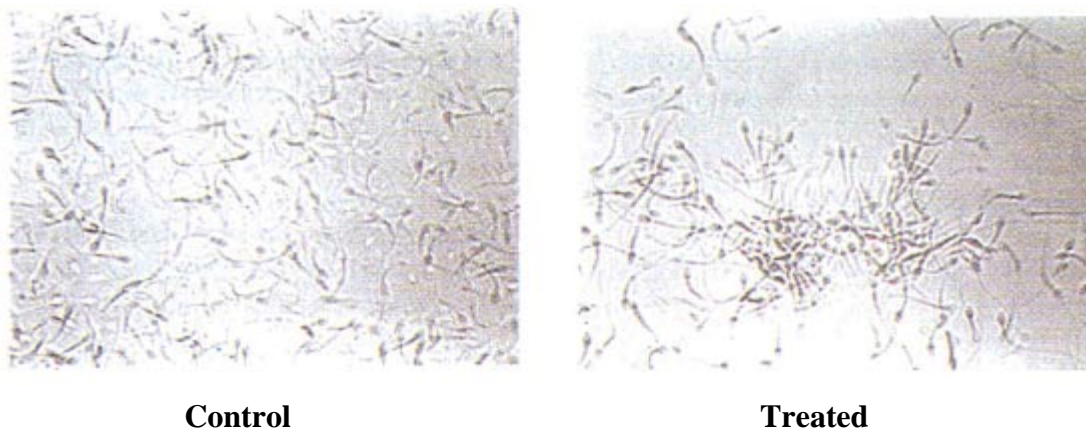


Fig.13 Immunization with synthetic N-terminal 1-17(R-17) of human seminal plasma inhibin (hSPI) conjugated to diphtheria toxoid caused agglutination of monkey spermatozoa.

Development of Kits for Quantitation of Hormones

IRR has developed four kits for the estimation of LH, FSH, estrone glucuronide and pregnanediol glucuronide in urine. These kits utilize indigenously prepared reagents. Since urine samples are used for quantitation, a better compliance is obtained from patients undergoing assessment or treatment of infertility. The technology developed for these kits has been transferred to Zydus Cadila Healthcare Ltd. through Biotech Consortium India Ltd.

Clinical/Operational Research

Phase III Clinical Trial with Subdermal Implant Norplant[®]

Norplant[®] (6 capsules) was offered as one of the contraceptive choices at the Council's 31 HRRCs in an ongoing clinical trial. A total of 2048 Norplant[®] acceptors have been observed for 70,744 woman months of use, 154 women have completed 5 years of use so far. Only one method failure has been reported after 5 years of use. The interim results indicated high efficacy and good continuation of the method upto 5 years of use. The main reasons for discontinuation were (i) menstrual irregularities in the initial 3 years and (ii) planning pregnancy after 3 years of use. One of the concerns about the device is the possible difficulties during removal of the six capsules. The data on 1100 removals indicated that in 86% there was no difficulty but in 14% removal was difficult due to migration of capsules to deeper layer, encapsulation or broken capsules. In 14 cases one of the six capsules could not be located and hence could not be removed.

Emergency Contraception

A study has been carried out at 31 HRRCs to assess the awareness about the emergency contraception (EC) among the providers and beneficiaries of FW services. Interim analysis on 1100 beneficiaries indicated that although awareness about planning method was universal, the knowledge about their efficacy, side effects and duration was lacking. About 60-80% of current users, ever users and never users of contraceptives were not aware of concept of spacing and permanent methods of contraception. About 68% knew about medical termination of pregnancy. Only 14% current/ever users

and 32% never users indicated that they should continue pregnancy if contraceptive fails.

61% current users, 54% ever users and 47% never users felt that they would opt for emergency contraception in case of risk of pregnancy due to unprotected sex. About 29% women had faced such situation in the past. Of these 42% waited for periods, 50% had got MTP done and 6% took some treatment. Only 2% continued with pregnancy. 76% women indicated that couples should know about emergency contraception and 55% felt that it should be made available to adolescent girls.

Mechanism for Providing Emergency Contraception

The primary objective of the study carried out at IRR, Mumbai was to compare the use of the hormonal method of EC among women, relying on condoms as their primary method of contraception, when EC pills were already available with them for use as and when required in comparison to those who had to get the pills from the clinic, within 72 h of as and when required. The data shows that 61/200 women required EC pills for 88 unprotected coital acts. 32 women in the advance provision group (n=100) reported 47 unprotected coital acts during the study period, of which 12.8% unprotected acts were not followed by EC pills; in 27.6% intake was incorrect and in 59.6% it was correct. Similarly, 29 women in as-needed provision group (n=100) reported 41 unprotected coital acts, 43.9% of which were not followed by EC pills (did not come to collect). The intake was correct in all the 100% who collected the EC pills. Thus there was no incorrect intake among this group.

Contraceptive Knowledge and Practices of Women Requesting Medical Termination of Pregnancy

Study was conducted to assess the contraceptive knowledge and practices among abortion seekers in an urban hospital set up; and to identify the determinants of unwanted and mistimed pregnancies in them. Interim analysis of 56 women revealed that nearly 75% abortion seekers were between 21-30 yr of age, over 48% did not anticipate the risk of pregnancy due to recent delivery *i.e.* young child,

infrequent sex, breast feeding status. Among women who felt the need for family planning, fear of side effects of the methods and family opposition were the major reasons for unwanted pregnancy. Over 35% reported use of FP methods to prevent current pregnancy; withdrawal and condoms were most commonly used. Though over 90% were aware of condoms and IUD pills, majority of them had incomplete knowledge. Nearly half of the study subjects deferred using Cu-T or contraceptive pills due to negative or indifferent attitude towards the method. None of the women were aware about emergency contraception or lactation amenorrhoea.

Fertility Intentions and Family Planning Practices of Tribal Men

A survey was undertaken to study the family size preference and to understand the contraceptive knowledge, attitude and practices of tribal men including reasons for not accepting male methods of birth control. Data was obtained through a semi-structured interview schedule from 973 married men aged 18-40 y from Kaman PHC in Thane district of Maharashtra during 1998. Of the 47 tribes in this community, *Varli, Katkari, Mahadeo Koli, Malhar Koli* and *Banjara* were most common. 57% men were illiterate and 91% were unskilled. Half of them (52.5%) had income of less than Rs.1500/- per month. 70% desired three or more children, 60% felt three children as an ideal family size, 55% had a strong preference for two or more sons, 40% preferred that girls should get married before attaining the age of 18 yr and 51.8% preferred that boys should get married before attaining 21 yr of age. Only 36% and 26% were aware of legal age of marriage for girls and boys respectively. Only 15.8% men had used contraceptives in the past, about half of them were not using any contraceptive at the time of survey. Male participation in contraceptive use was 3.1%. Majority of men had no concept of spacing of births. Men who were aware of contraceptive methods had little knowledge of their correct use. 66.7% men had positive views about their role in family planning while 57.7% stressed the need to improve the acceptance of male methods by providing knowledge and information through door to door campaign, advertisement on TV/radio/group meetings at village level and through

medical staff. The study indicates a pressing need for providing quality information, efficient counselling and indulgent services in remote areas.

INFERTILITY

Male Infertility

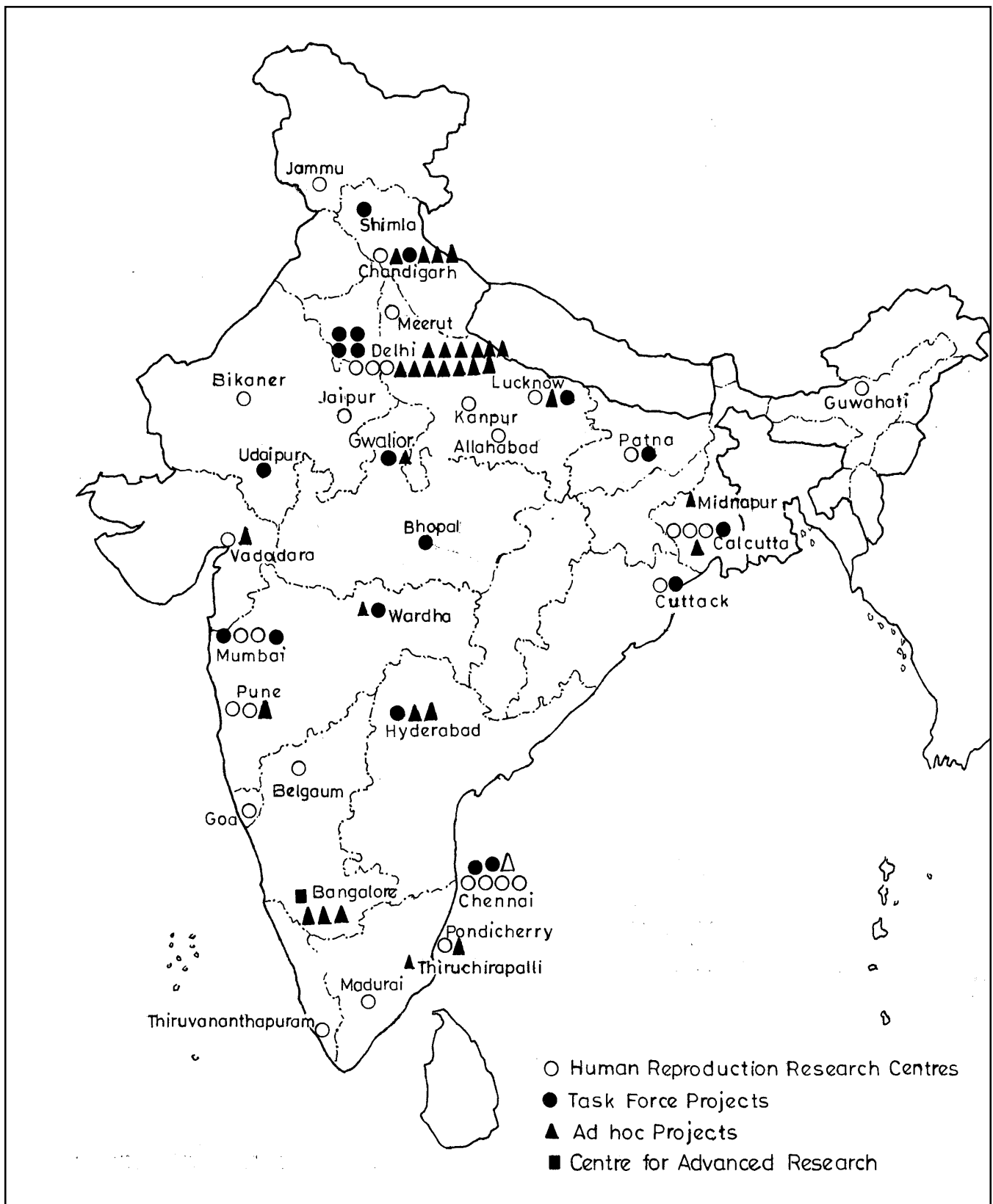
Relevance of Nuclear Vacuoles in Human Spermatozoa

Integrity of the nucleus of human spermatozoa is essential to achieve successful fertilization and embryo development. The presence of nuclear vacuoles in human spermatozoa can affect the homogeneous nature of the chromatin. Therefore evaluation of the size and number of vacuoles present in sperm head is of importance in judging the fertilizing ability of spermatozoa. A retrospective study was conducted on semen samples obtained from 47 fertile and 114 infertile men with the objective of studying the ultrastructural details of sperm head with respect to chromatin integrity and sperm function tests *viz.* nuclear decondensation test (NCD) and acridine orange (AO) test. The percentage of spermatozoa showing nuclear vacuoles was graded as nil, occasional and multiple.

In semen samples from fertile men, 95.1% spermatozoa did not show any vacuole whereas, in the samples from infertile men vacuoles were observed in 92.3% spermatozoa. Ultrastructural studies showed major chromatin abnormalities including large and multiple vacuoles with membrane whorls and displacement of nuclear material from majority of spermatozoa from infertile cases. The percentage of spermatozoa showing normal NCD and AO was significantly decreased in infertile cases as compared to fertile cases.

Localization of Hormone Receptors on Spermatozoa

In studies done at IOP, New Delhi, immuno-chemical localization using specific monoclonal/polyclonal antibodies indicated the presence of membrane bound estrogen, progesterone and androgen receptors in the acrosome and tail regions of the spermatozoa of mice and human.



Major ICMR Research Projects in Reproductive Health

Hormonal Regulation of Spermatogenesis

Pharmacological manipulation of spermatogenesis with the help of agonists and antagonists of sex-steroid receptors was studied. Studies with tamoxifen, an antiestrogen demonstrated a dose-dependent decrease in the fertility of male rats. Change in sperm motility pattern from forward progressive to circular yawing type, disorganization of the seminiferous tubule cytoarchitecture and loss of junctional complex in spermatids was noticed. De-compartmentalization of the seminiferous tubules concomitant with azoospermia was also observed with estradiol treatment. Studies will facilitate understanding the molecular mechanism of neuroendocrine regulation and identification of the causes of idiopathic male infertility.

Female Infertility

Studies on Polycystic Ovarian Syndrome

Polycystic ovarian syndrome (PCOS) is a common and heterogeneous disorder in women of reproductive age, characterized by hyperandrogenemia and chronic anovulation. In view of the known relationship between hyperinsulinemia and hyperandrogenemia and increased risk of atherosclerosis, a study was undertaken to evaluate the association of hyperinsulinemia in obese and non-obese women with PCOS.

Insulinemic response to glucose load was enhanced significantly in 74.1% obese women and 38.4% lean women with PCOS associated with normal or raised testosterone levels as compared to obese women with normal ovaries and testosterone levels. Enhanced LH:FSH ratios were seen in lean women with PCOS and hyperandrogenemia. Induction of ovulation with clomiphene citrate (CC) failed to elicit positive response in 76% women with hyperinsulinemia. Therapy with metformin resulted in normal menstrual cyclicity and weight reduction without restoring ovulation. Simultaneous treatment with CC/hMG/hCG resulted in ovulation in 75% of these women. The study shows that treatment with metformin alone fails to restore ovulation and needs to be coupled with ovulogens.

Endocrine and Metabolic Aspects of PCOS

Study was undertaken to investigate the long-term sequelae of hyperandrogenemia associated with PCOS. Particular emphasis was placed on putative dyslipidemia and its influence on the cardiovascular risk. Study population consisted of women with documented PCOS, along with appropriate controls. Detailed analysis of androgen as well as lipid-lipoprotein profile was carried out with emphasis on the parameters of atherogenic risk. Hyperandrogenemia, in terms of significantly raised total testosterone and decreased sex hormone binding globulin levels was observed in 30% of the PCOS women.

A subclinical but significant deterioration in the apolipoprotein profile was seen among women with PCOS predominantly those with associated obesity. Overall, the study confirmed a trend towards dyslipidemia, indicative of an atherogenic profile in a section of women suggesting an increase in their predisposition to cardiovascular events. The findings emphasize the need for appropriate counseling of these women regarding diet and exercise, reduction in body weight and treatment for reversal of hyperandrogenic condition.

MATERNAL AND CHILD HEALTH

Chlamydia trachomatis

In studies done at IOP, New Delhi, positivity of *Chlamydia trachomatis* infection in 25 genital samples from women with cervicitis/pelvic inflammatory disease was found to be 49.1% by direct fluorescent assay (DFA), 59.3% by culture and 37.2% by PCR. Of the 25 urethral samples from male patients with urethritis, positivity was 31.8% by DFA, 36.3% by culture and 9.09% by PCR while of the 15 samples from conjunctivitis patients, it was 42.8% by DFA, 45.0% by culture and 28.5% by PCR. To know prevalent serovars in patients and for production of serovar - specific monoclonal antibody, 41 clinical isolates (33 from female, 4 from male and 4 from ocular infection) have been isolated in Mc Coy Cell culture for genotyping by PCR and RFLP. A confocal

laser scanning microscope with 488-nm and 543-nm laser excitation line was used to excite fluorescein and Evans blue dyes. Fluorescent green intracytoplasmic structures were interpreted as chlamydial inclusion bodies (Fig.14,15). The method is being tested for sensitivity and specificity.

Study was undertaken at IRR, Mumbai to develop a cost-effective but sensitive technique for diagnosis of *Chlamydia trachomatis*, a sexually transmitted infection. A polymerase chain reaction was optimized

in cervical swab samples for diagnosis of *C. trachomatis*, which is conserved in all the serotypes of *C. trachomatis*. The 144 bp DNA fragment was further confirmed with Eco R₁ digestion, yielding 41 bp and 103 bp DNA fragments. The results obtained by using PCR were also validated using other commercial diagnostics like ELISA and DFA and also with Papanicolaou stain. Validation study showed 100% sensitivity and specificity of the PCR based technique. Analysis of 510 samples collected from cases attending the Gynaecology O.P.D.

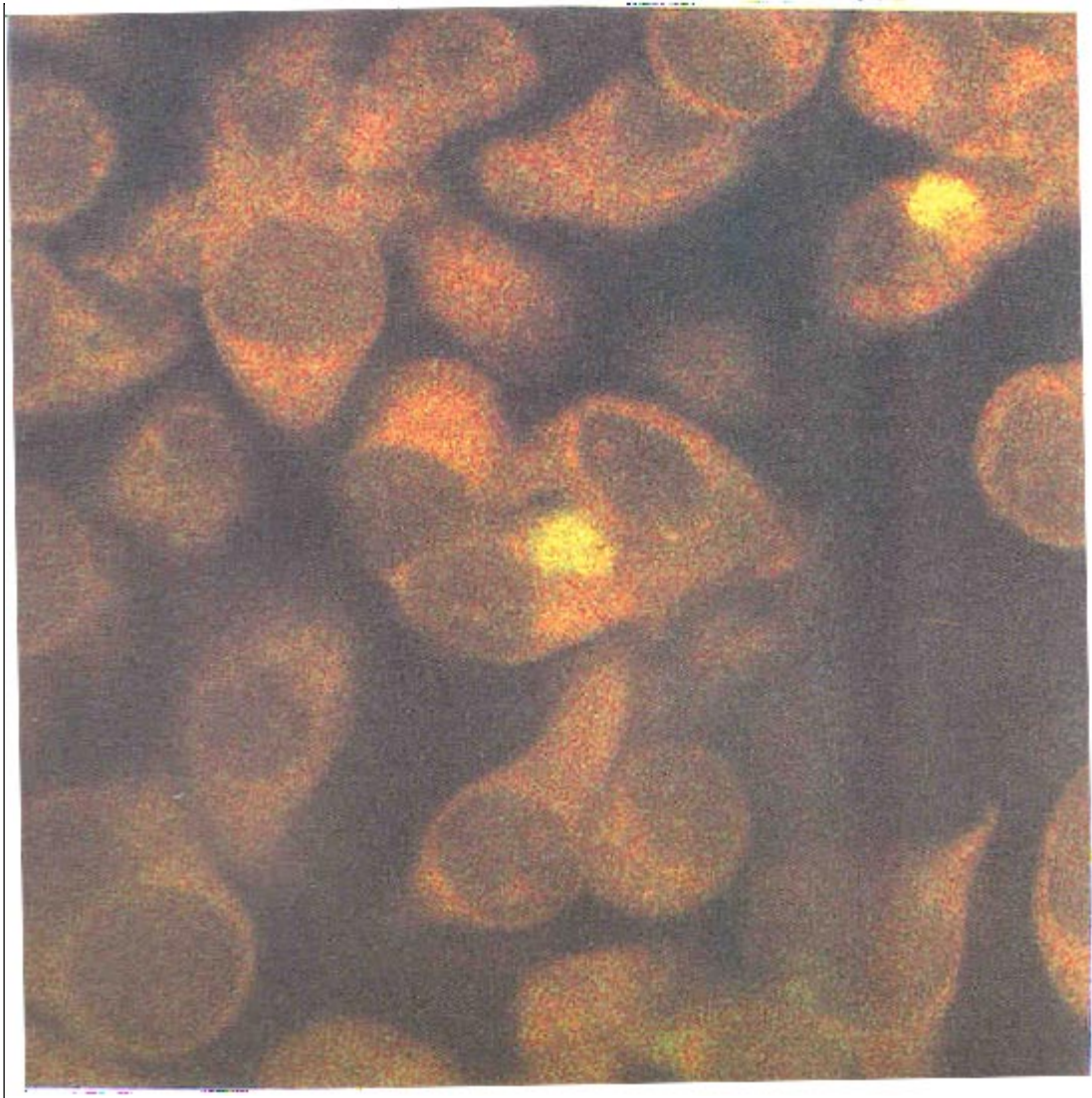


Fig.14 CLSM view of McCoy cell culture using direct fluorescent assay. Intracytoplasmic inclusions (yellow green) of *C. trachomatis* are seen (100x/1.3 oil).

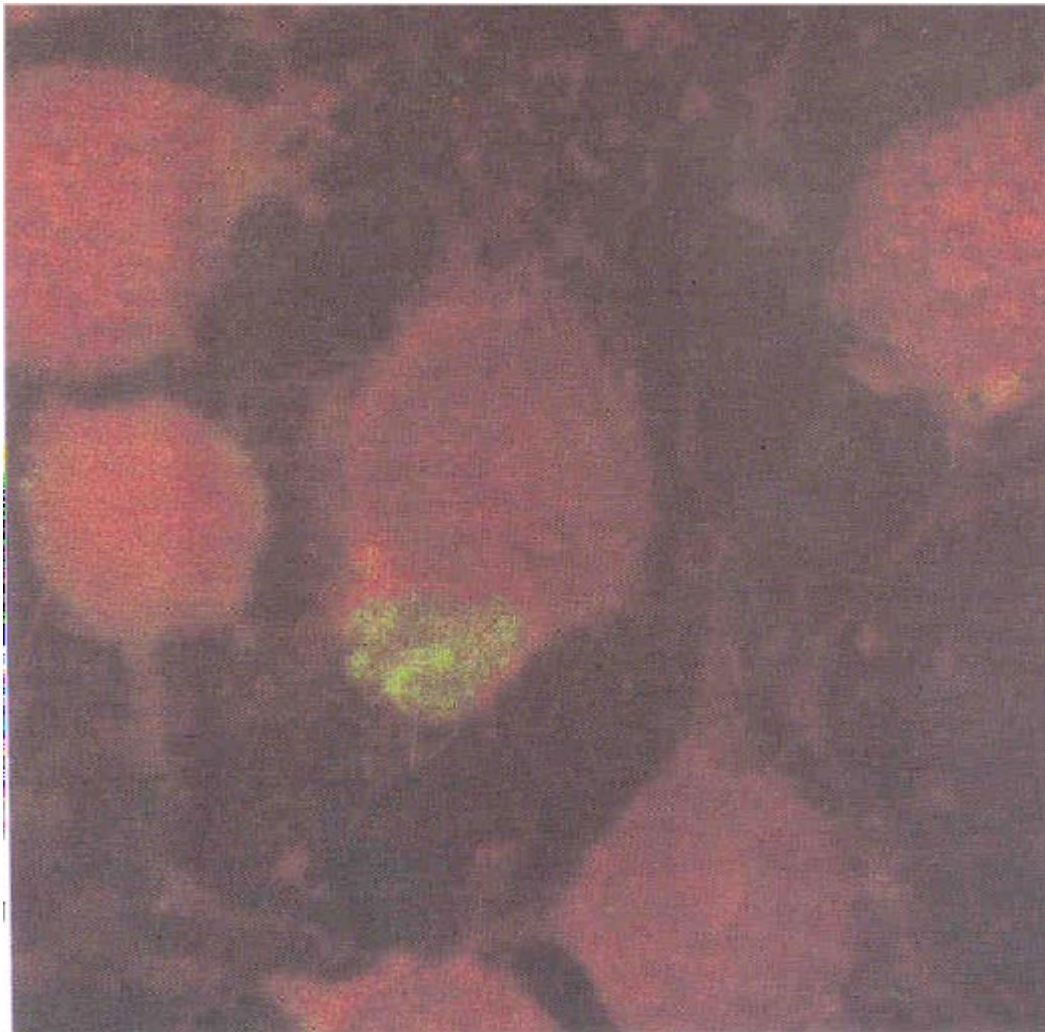


Fig.15 CLSM view of McCoy cell culture using FISH with 16s rRNA probe. Fluorescent green intracytoplasmic hybridization signals are interpreted as chlamydial inclusion bodies (100x/1.3 oil).

of a general hospital showed a prevalence rate of 9.41%. The patients who were positive for *C.trachomatis* infection are being evaluated in detail.

Feasibility of Using Pregnancy Detection Kit at PHC/SC/Village and Urban Slums

Early detection of pregnancy is essential for safe motherhood and reproductive health. There is a need for easy-to-use pregnancy detection kit in NFWP. Reproductive health of women could be improved by offering early MTP services and antenatal care. A study was carried out in two urban slum areas (Delhi and

Calcutta) and two rural areas (Rajasthan and U.P.) covering one lakh population each to study the feasibility of use of pregnancy detection kits at peripheral level. Pregnancy test kits evaluated were: Preg color tube test, Preg color card test (Infar India Ltd.), Easy Preg (Glide chem), Pregnosis (Abacus Technologies, Bangalore) About 150 paramedical and 50 medical staff were trained in conduct of the study including use of these kits, follow up for confirmation of pregnancy and data recording. IEC material, in the form of banners, posters and pamphlets was prepared by the Council and MOH & FW and was used by all the centres for

creating awareness in community so that they come forward for early detection of pregnancy.

Out of the expected number of women requiring early detection of pregnancy, 8-10% in rural area and 18-19% in urban slums availed these services. This is encouraging in view of the fact that this was the first attempt to make the pregnancy test kits available at the peripheral level.

A total of 3794 and 2002 women were enrolled at peripheral centres and HRRCs respectively. Majority (62-70%) of the women had amenorrhoea of more than 42 days *i.e.* they came after 15 days of missed period at both HRRCs as well as peripheral centres. Less than 10% women came for early detection of pregnancy within 7 days of missed period.

The sensitivity of the selected tests ranged from 97% for Pregnosis strip test and Pregcolor card test to 98% for Easypreg strip test and Pregcolor tube test suggesting that all these tests were able to correctly detect early pregnancies in more than 97% pregnant women who had come to these clinics. Specificity ranged from 93% for Pregnosis strip test and Pregcolor card tests to 94% for Pregcolor tube test and Easypreg strip test, indicating that in about 6-7% of non pregnant women, pregnancy was not ruled out by these tests. The results obtained at peripheral centres were as good as those observed at HRRCs for all the test kits.

When asked about their assessment regarding the kits, almost all the paramedical and medical staff indicated that Easypreg strip test was easy to interpret and quick in giving results and ranked first amongst the four tests by 80% of the workers. The second preference was given to pregcolor card test followed by Pregnosis strip test. Pregcolor tube test was least preferred even though it showed high sensitivity and specificity. The procurement cost of Easypreg was the lowest (Rs.19 per test) as compared to that of other kits (Rs.30-32.70 per test).

Psychosocial, Cultural and Service Factors affecting Reproductive Morbidity amongst Rural Women

A study has been initiated to determine the psychological, socio-cultural and service factors which affect reproductive morbidity amongst rural, married women of reproductive age in different regions of the country. The project staff of all the participating centres

has been trained in different methodological aspects of the study and data collection has been initiated.

Management Practices of Meconium Stained Amniotic Fluid and Meconium Aspiration Syndrome

Study was initiated last year at 31 HRRCs with the objectives to assess the management practices of obstetric cases with meconium stained amniotic fluid (MSAF) and to study morbidity and mortality in new born babies with meconium aspiration syndrome (MAS). Interim data on 7181 cases of MSAF indicated that 52.3%, 13.9% and 33.8% cases had thin, moderate and thick meconium stained discharge respectively. As regards management of labour, amnio infusion was given to 7.8 and 16.2% women with thin, and moderate-thick meconium stained discharge respectively. Partogram for foetal monitoring was maintained only in about 1% of cases. Oxytocin drip was given to about 40% women. Oxygen was required by 18.0, 30.8 and 42.0% women with thin, moderate and thick discharge respectively. About 45% women had normal delivery, 47% had caesarian section; the remaining had forceps/vacuum delivery.

7.5% babies born to these women developed meconium aspiration syndrome; 2.2%, 5.2% and 16.5% babies were born to women with thin, moderate and thick discharge respectively. Perinatal mortality was significantly higher (22.6%) in MAS babies as compared to those who did not develop MAS (2.4%). The final analysis is in progress.

Bone Density in Menopausal Women

Postmenopausal women have an accelerated bone loss at the rate of 1 to 5% per year whereby women are at a greater risk of developing osteopenia or osteoporosis as compared to men. Dual energy X-ray absorptiometer (DEXA) is considered the "Gold Standard" for measuring bone density. A study has been initiated to determine bone density in Indian women using ultrasonography (USG) of the foot (calcaneum bone) and DEXA of the hip and spine, so as to develop norms for determining osteoporosis. DEXA could detect osteopenia and osteoporosis more accurately as compared to USG. BMD values of foot, spine and hip are lower in Indian women as compared to women in USA.

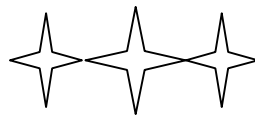
Resuscitation of Asphyxic Newborns

A quasi randomised controlled trial was carried out at three HRRCs to compare the short-term efficacy of room air *versus* 100% oxygen for resuscitation of asphyxic newborns. Asphyxiated babies weighing >1000 gm, with heart rate <100/min and or apnoeic, unresponsive to nasopharyngeal suction and tactile stimuli and having no lethal abnormalities were included in the study. The asphyxiated neonates born on odd dates were given oxygen and on even dates room air for resuscitation. Evaluation indicators were, improvement in apgar score, mortality and abnormal neurological findings. From the asphyxiated babies enrolled for the study, 168 were given room air and 174 hundred per cent oxygen. Both the groups were comparable in terms of maternal and intrapartum parameters. Median apgar scores at 1 min, 5 min and 10 min in the room air and oxygen groups were not found to be statistically different. The improvement in heart rate in both the groups was found to be similar. Median time to first breath (1.4, 1.5 min) time to first cry (2.2, 2.7 min) and median duration of resuscitation (3, 1.7 min) were also similar in the 100% oxygen and room air group. 39.9% babies in the room air and 41.4% in the 100% oxygen group showed neurological abnormality on day 1 of life. Overall mortality in the group resuscitated with room air (12.5%) appeared lower than in the group resuscitated with 100% oxygen (18.9%) but the difference was not statistically significant. Asphyxia related mortality was seen in 16.1% cases in the group resuscitated with 100% oxygen and in 11.3% cases in the room air group. Forty one per cent babies in the room air group and 46% in 100% oxygen group had resuscitation failure. The study concluded that room air oxygen is as good as 100% oxygen for resuscitation of asphyxic newborn babies.

Study of Reproductive Health Awareness and Sex Behaviour among Adolescents

A study was conducted at 7 centres in the country on adolescents from schools and colleges from urban, urban slum and rural areas to understand their awareness level and attitudes towards reproductive health matters including sexual behaviour and the views of parents/teachers about sexual education to them. At each centre, the data of about 2000 adolescents and 200 parents and teachers were collected using structured questionnaires, focus group discussions and case study approach.

The results indicate lack of awareness, misconceptions and risky behaviour of adolescents regarding critical aspects of reproductive health such as safe sex, genital hygiene, STDs, MTP, safe period in the menstrual cycle for pregnancy, HIV transmission and its prevention. Adolescents living in slums followed by rural and female adolescents were particularly poorly informed. A large number of adolescents in all states had exposure to sex and pornographic literature. 22% in slums areas of Tamil Nadu and 51.8% in urban areas of Delhi practiced masturbation. The wet dreams were experienced by 31% in rural areas of Tamil Nadu and 56.3% in slum areas of U.P. The sexual intercourse was reported more by boys than girls. The range of sexual intercourse varied from 2.9% in urban girls to 28.8% in rural boys in Rajasthan and 1.6% urban girls to 14.4% urban boys in Delhi. Most of the adolescents expressed their willingness to know more about these issues in schools and colleges by outside experts. The parents and teachers advocated that adolescents should be imparted sex education by mothers and teachers from 13 to 15 yr of age.



Nutrition

Research investigations carried out during the year at National Institute of Nutrition (NIN), Food and Drug Toxicology Research Centre and National Centre for Laboratory Animal Sciences at Hyderabad and National Nutrition Monitoring Bureau (NNMB) revealed new findings pertaining to several aspects of nutrition science. The NNMB had conducted a series of surveys in different parts of the country. Over 10,000 households were surveyed in 530 villages from nine states to determine the nutritional status of population (as a part of 54th round of consumption-expenditure survey). The data on food and nutrient intakes of individuals analysed during the year indicated that micronutrient intake among people was extremely inadequate and especially children of pre-school age were seen consuming diets bereft of essential micronutrients. However, in comparison with the nutrient intake data of 1975- 79, the data collected in 1996-97 revealed a significant improvement in the fat, energy and vitamin A intake among population groups. Other areas of study included food chemistry, food and drug toxicology, nutrition and infection and nutrition in the elderly.

COMMUNITY STUDIES

Diet and Nutritional Status of Rural Population

The community studies continued to place emphasis on the assessment of diet and nutritional status of the population. This year, the investigations included, (i) monitoring of nutritional status of people in rural areas in 9 States coming under NNMB, (ii) district level nutrition profile surveys in Uttar Pradesh and West Bengal, (iii) drought surveys in the States of Andhra Pradesh, Gujarat and Rajasthan, (iv) micronutrient supplement trials on residential school children to assess the influence on cognitive performance and growth of children, (v) assessment of the current status of Integrated Child Development Services (ICDS) under Andhra Pradesh Economic Restructuring (APER) Programme in tribal and rural areas, and (vi) analysis

of association between nutritional status and development indicators.

Out of the targeted 720 villages in nine states, 14,400 households were selected by NNMB for the assessment of nutritional status of the people. During this year, 10,600 households from 530 villages were surveyed. The rest of the households in the remaining villages will be surveyed during 2001. Analysis of the individual dietary intakes, collected by the NNMB as a part of 2nd repeat survey, using 24-hour recall method revealed that about 13-55% individuals in different ages consumed recommended dietary allowance (RDI) for energy whereas the consumption of micronutrients was woefully inadequate, 50-70% of individuals consumed less than 30% of RDI for vitamin A especially the pre-school children had higher deficits in their diets. A comparison of the median individual intakes between 1975- 79 and 1996-97 indicated that there was significant improvement in the intakes of fat, energy and vitamin A. The consumption was higher in all the age groups except 1-3 yr. old children during 1996-97. However, iron intakes were higher only among adults.

As part of district level nutrition profile survey, a study of diet and nutritional status was conducted in 80 districts in Uttar Pradesh (63) and West Bengal (17) in collaboration with the Institute of Applied Statistics and Development Studies, Lucknow and Child in Need Institute, Kolkata. So far, the Institute has contributed to district level database on diet and nutritional status of 170 districts from Assam, Haryana, Himachal Pradesh, Orissa, Punjab, Uttar Pradesh and West Bengal.

The drought surveys undertaken in Andhra Pradesh, Gujarat and Rajasthan revealed that the impact of drought was more severe in the state of Rajasthan (Fig.16). In general, a large number of households experienced food insecurity. However, no starvation (energy intakes <500 kcal) was reported in any of the households in all the 3 states. The prevalence of

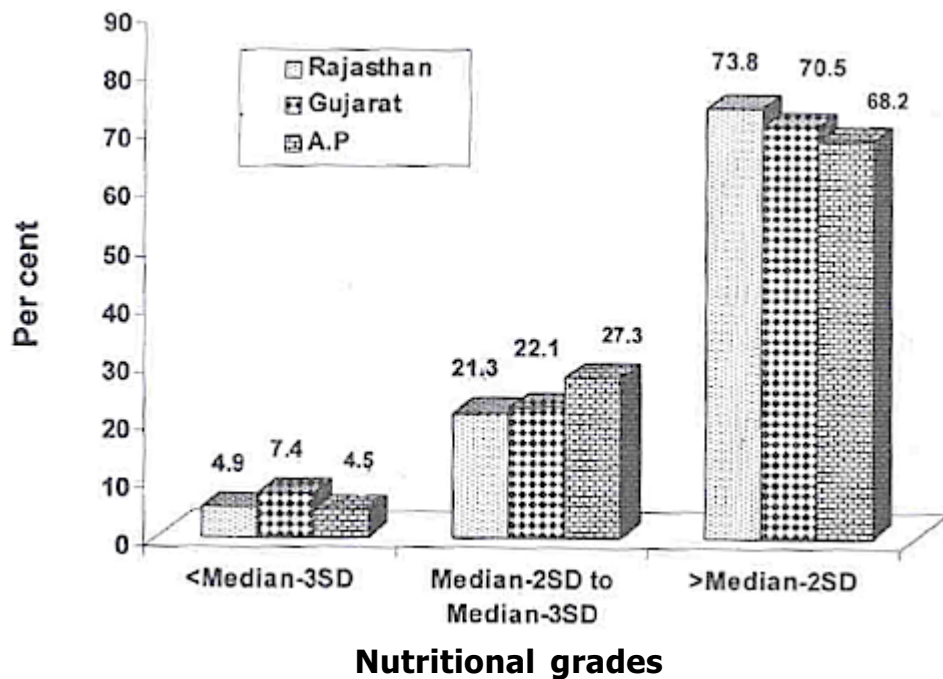


Fig.16 Distribution of preschool children according to weight for height.

undernutrition was by and large comparable to pre-drought surveys. It appeared that relief measures, particularly public distribution system, helped the drought-affected communities to a large extent in the prevention of severe forms of undernutrition.

The survey in ICDS projects in tribal areas of Andhra Pradesh revealed that though more than 75% of the beneficiaries availed the ICDS services, the proportion of 6-35 month old children participating in supplementary feeding was very low (20%) as compared to 48% in older children. Despite better performance with respect to immunisation of children against six childhood diseases or tetanus toxoid immunisation in pregnant women, the coverage under nutrition related services like distribution of iron and folic acid tablets and vitamin A was not adequate. Growth monitoring was not regular. These results point out to the need for strengthening growth monitoring and nutrition services in ICDS.

Repeat surveys carried out by NNMB have shown that though the dietary intakes remain unchanged, the nutritional status (as assessed by nutritional anthropometry) registered a change. Hence, a detailed

statistical analysis was carried out to assess the relationship between data on diet and nutritional status and socio-economic and developmental indicators collected at the village level as part of National Council for Applied Economic Research (NCAER) - NNMB linked surveys. The results indicated that family size of more than six, protected water, SC/ST community status and low vitamin A intake were associated with prevalence of undernutrition.

Operational Evaluation of the Stability of Iodine in Double Fortified Salt

The NIN has successfully developed a formulation of double fortified salt (DFS, containing both iron and iodine) comprising common salt, ferrous salt, potassium iodate and sodium hexametaphosphate. The salt was considered stable at the laboratory and community levels. However, in a recently concluded residential school study at NIN, the iodine stability was found to be very poor in the DFS. It was observed that in some batches the quality of common salt was not up to the mark due to high magnesium content. The distribution of iron and iodine was not uniform

in some batches due to improper mixing at the time of production. An expert committee on DFS constituted by the ICMR has recommended a multicentric study to assess the stability of iodine in DFS using different types of salt for double fortification. Large scale production of the DFS and iodised salt is to be done at a factory in Chennai.

NUTRITION AND INFECTION

Safety and Feasibility of Administering Vitamin A alongwith Oral Polio Vaccine

In view of the persistence of vitamin A deficiency in children as a public health problem, the State Government of Orissa had launched a programme of administering massive oral dose (200,000 IU) of vitamin A alongwith OPV on the first National Immunisation Day of Intensive Pulse Polio Immunisation Programme to children between 12-42 months of age on 24th October, 1999. The feasibility and safety of this strategy was assessed by conducting a rapid post-immunisation survey in 5 randomly selected districts of Orissa on a total of 879 under-5 children, in collaboration with WHO and UNICEF. There was over 90% coverage of the target age group. Not a single infant below the age of 6 months received the dose. Nevertheless, there was a possibility of administering the dose to infants below the age of 12 months. Symptoms of indisposition, observed within 48 h of administration of the dose were not significant suggesting that vitamin A administration along with OPV is safe and feasible. However, training the health functionaries to administer the dose only to the specified age group is suggested.

Nutrition-Infection Interactions in Acute Bacterial Meningitis in Children

Acute bacterial meningitis is one of the major causes of morbidity in young children. The effect of nutritional status, microbial causes and cytokine profile on the outcome was investigated in 140 children hospitalised for acute bacterial meningitis. Malnutrition and presence of tumour necrosis factor (TNF) in cerebrospinal fluid was found to be significantly associated with adverse outcome (survival with permanent neurological sequelae or death).

MICRONUTRIENTS AND TRACE ELEMENTS

Fortification of Sugar with Micronutrients

During this year, stability of fortified sugars -one fortified with single nutrient like iron or iodine and the other fortified with both iron and iodine, was tested. The stability of iodine as well as iron was found to be very good in the sugar fortified with a single nutrient. At the end of 6 months, iodine stability was not uniform with different chemical sources of iron tested. Although the stability of iodine was good with ferrous glycinate, about 50% loss occurred with ferrous sulphate or ferrous fumarate.

Bioavailability of Iron

To answer a query from Human Rights Commission, bioavailability of iron from the pickles commonly consumed in combination with cooked rice and *phulka* or *chapati* was assessed. The total iron content of pickles in combination with rice was 19 mg and that with *phulka* was 103 mg/g. Addition of five pickles to cooked rice decreased the *in vitro* bioavailability of iron in the case of four of them from 32% to 14-23%. However, in combination with wheat-based *phulka*, the bioavailability increased from 4.2% to about 7% with three of the five pickles. With other pickles there was no change in bioavailability.

Iron Availability from Ayurvedic Hematinic

A new hematinic, containing a blend of ayurvedic formulation, was tested for the management of anaemia. Besides iron, this preparation contained herbs presumed to enhance the bioavailability of iron. The relative bioavailability of iron from this preparation was found to be only 66.7% as against one reference preparation used to regenerate haemoglobin in iron depleted rats. The efficacy of this preparation as a hematinic needs to be tested in humans.

Iron Absorption Promoters in Wheat Flour

Fortification of wheat flour with iron and other absorption promoters was attempted to enhance the bioavailability of both exogenous and endogenous dietary iron. Incorporating iron absorption promoters such as ascorbic acid and EDTA in wheat flour at a molar ratio of 1:1 was found to enhance the *in vitro* availability of the endogenous and exogenous iron respectively.

Studies on Selenium

Selenium nutritional status was assessed based on the body mass index, with the cut off level at 18.5. Both plasma selenium and a functional parameter *viz.* the activity of red cell glutathione peroxidase were estimated. While plasma selenium levels were significantly reduced in undernourished and anaemic subjects, activity of glutathione peroxidase was not affected.

Bioavailability of selenium from cereals like rice, wheat, sorghum and pulses was carried out by standard *in vitro* methodology simulating gastric conditions. While initial digestion with pepsin showed the level of available selenium varying between 32% and 72%, it was around 75% after second digestion with intestinal enzymes.

DIET AND NON-COMMUNICABLE DISEASES

Biochemical and Metabolic Studies with Sesame Lignans

The beneficial effects of antioxidants in prevention of diet-related chronic diseases are being increasingly emphasised. Non-glyceride fraction of certain oils contains natural antioxidants, such as tocotrienols and carotenes (palm oil, red palm oil), oryzanol and tocotrienols (rice bran oil) and lignans namely, sesamol (S_1) sesamin (S_2) and sesamol (S_3) (sesame oil). Lignans are known to impart greater stability to sesame oil. Studies were initiated to determine the heat stability of sesame oil in combination with other oils (palm oil and groundnut oil). Heating of single oils (sesame, groundnut and palm) resulted in time-dependent decrease of total tocol content. Percentage retention of total tocols (tocopherols and tocotrienols) at the end of 30 min. (65-69%), 1 h (42-50%) and 2 h (17-20%) of heating was similar in all the three oils. Sesame in combination with palm oil showed higher retention of total tocols as compared to either of the single oils up to 2 h heating. However, sesame oil in combination with groundnut oil did not increase retention of total tocols. The decrease in total tocols in heated oils was associated with increase in peroxide values and TBARS levels. Heating of sesame oil or its blends was associated with decrease in total lignans (30-40%) which was due to decomposition of sesamol. However, sesamol which has higher antioxidant activity than sesamol, increased from negligible levels to ~ 0.04 g/kg oil. These findings suggest that sesame blend with palm oil may be more stable to oxidative deterioration due to heating as compared to single oil.

Effect of Dietary Trans Fatty Acids on Insulin Resistance and Function of Adipocytes

Insulin resistance is an important risk factor associated with type II diabetes, chronic heart disease and obesity. Adipose tissue and skeletal muscle are the major target tissues for insulin action.

Recent studies have shown that there is a positive correlation between skeletal muscle and adipose tissue plasma membrane PUFA composition and insulin action. Since Indian *vanaspati* contains high levels of trans fatty acids, a study was conducted to investigate the effect of dietary trans fatty acids (*vanaspati*) at different levels of linoleic acid on adipocyte and skeletal muscle lipid composition, fluidity and function. The results showed that a casein-based diet, which provided 22 en% fat, 3 en% trans fatty acids, significantly altered the plasma triglyceride and glucose levels, adipose tissue and skeletal PUFA composition and adipose tissue plasma membrane fluidity. These changes were observed at both the levels of linoleic acid (2 en% and 4 en%) in the diet. The results further show that the response to *vanaspati* on PUFA metabolism may vary from tissue to tissue. Studies on the effects of dietary trans fatty acids on functional properties of adipose tissue and skeletal muscle such as glucose transport, insulin binding and lipolytic activity are in progress.

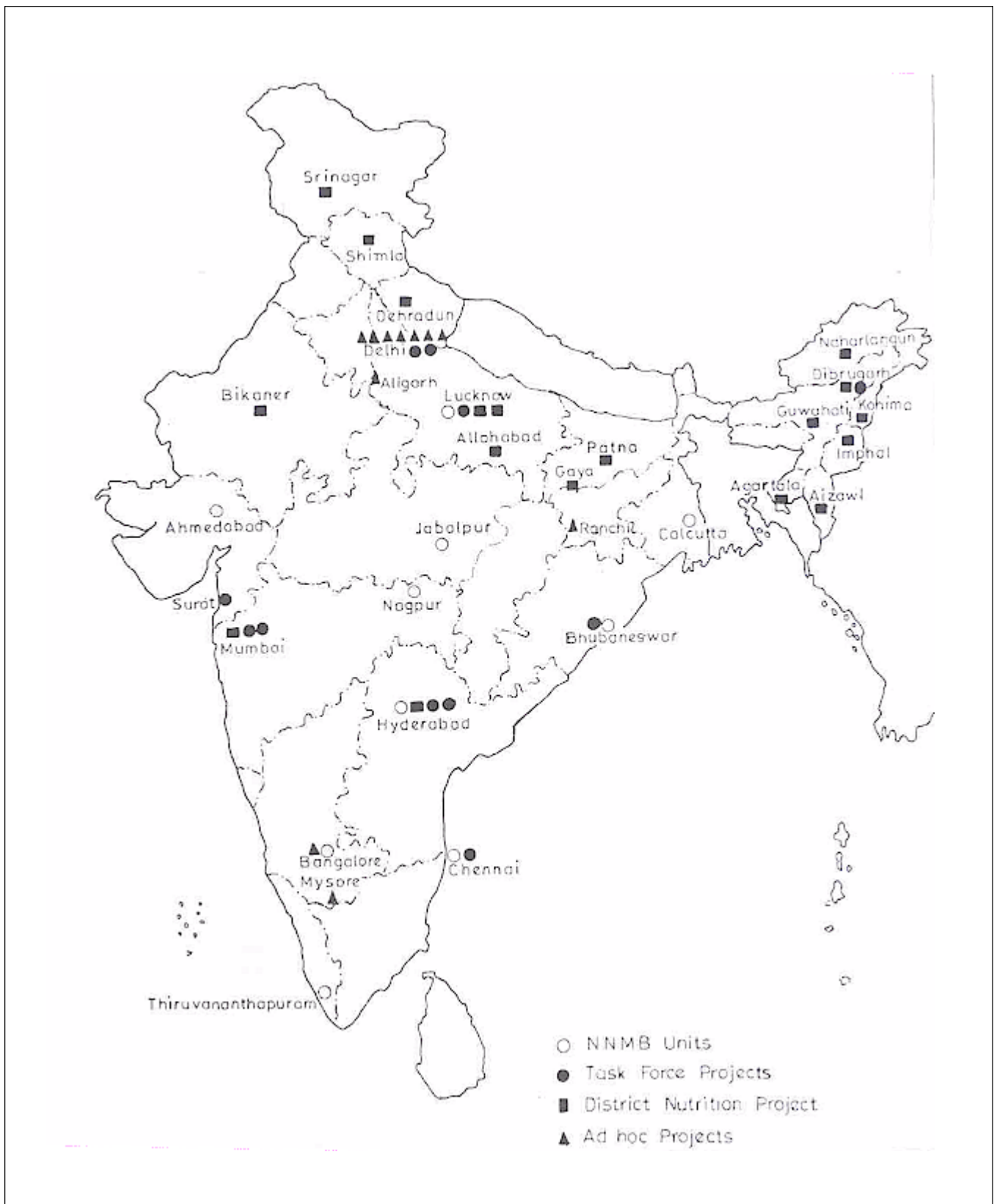
Antioxidant Status in Geriatric Population

Many degenerative diseases occurring in old age have been attributed to free radical associated damage to the tissues and a reduction in antioxidant status. In order to understand the level of lipid peroxidation and the activity of a key antioxidant enzyme, glutathione peroxidase (GSHPx), a study was undertaken in different age groups (40 yr to >60 yr). The study revealed that as age advances, GSHPx tends to decrease with a concomitant elevation in malondialdehyde (MDA) which could be the underlying mechanism for free radical-mediated degenerative diseases in old age.

FOOD CHEMISTRY

Effect of Fly Ash on Nutritional Quality of Foods

Fly ash is a by-product of thermal power stations and its disposal is posing a gigantic problem in recent years. In view of this, on the request of Fly Ash Mission, a detailed study was undertaken on the effects of fly



Major ICMR Research Projects in Nutrition

ash on nutritional quality of foods such as rice, wheat, peas, mustard, groundnuts and vegetables. Proximate composition of these food items grown in soils conditioned with fly ash did not show any definite or specific changes attributable to fly ash. In fact, foods grown on fly ash have shown occasional beneficial effect with respect to protein or fat in some foods. Trace minerals and heavy metal content of foods was essentially similar whether grown on soils with or without fly ash. Similarly, biological evaluation did not show any differences in animals, which were fed foods grown on soils with or without fly ash.

PATHOLOGY

Effect of Food Protein and Vitamin Restriction on Apoptosis in Intestinal Mucosa

The effect of 50% food, vitamin and protein restriction was studied in small intestinal mucosal cell apoptosis in rats for a period of 20 weeks. Body weights, haemoglobin and serum protein levels significantly decreased on 50% diet restriction and 75% protein restriction while apoptotic counts increased in the terminal portions of the villi in 50% vitamin and 75% protein-restricted groups.

FOOD AND DRUG TOXICOLOGY

Dietary Intake of Aflatoxins and Organochlorine Pesticides

A study has been undertaken in a rural area to assess the dietary intake of aflatoxins and organochlorine pesticide residues. Nineteen 24-hour diets, consumed by adult men, were collected from 2 villages near Hyderabad, and analysed for pesticides and aflatoxins. The results of the study indicated that their levels were very low and may not pose a risk to consumer health.

Assessment of Dietary Intake of Synthetic Food Colours

About 315 food items were analysed including sweet meats, vegetables, snacks, *chutneys*, bakery foods, *sherbets*, soups and *biryani* to determine the kind and the quantity of food colours added to them. 95% of these foodstuffs were found to contain permitted food colours while 5% used non-permitted colours. However, 31% food items in the permitted colours category contained colours within the permissible limit of 100 ppm, while 69% had colours above the prescribed limit.

Certain beverages and sweet meats contained as high as 9.4 mg/ml of colours. Pre-schoolers and school-going children were found to be consuming excessive amounts of the permitted colours sunset yellow and tartrazine mainly through *sherbets* and confectionery items.

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

Foods of animal origin pose a risk of transmission of zoonotic and human diseases. Poultry and shrimps were studied to explore the possibility of using HACCP in minimising the risk of disease. All the 34 samples of chicken meat contained aerobic bacteria, the counts ranging from 10^3 to 10^7 cfu/g. In these samples, 88% had coliforms, 76% staphylococcus and 53% salmonella. Nine out of 18 samples of chicken *biryani* also had aerobic bacteria. In addition, all the samples of shrimps sold at 35 outlets in Hyderabad contained aerobic bacteria, the counts ranging from 10^7 to 10^8 cfu/g.

Biotechnological Approach to render Mouldy Sorghum Safe for Consumption

Sorghum is highly susceptible to mouldy damage during unfavourable weather conditions. Such damage affects the yield and the quality of the grain, decreases the nutritive value and favours the production of mycotoxins. A study was carried out using microorganisms like lactic acid bacteria through natural fermentation to detoxify contaminated sorghum and then to convert it into a value-added animal feed ingredient.

NUTRITION AND CANCER

Nitrosamines

Nitrosamines have been postulated to play a role in the etiology of human stomach cancers. Nitrosation of amines *in situ* and identifying the populations at risk was taken up for study this year. In addition, the effect of inhibitors of nitrosation under *in vivo* condition was also studied. The study revealed that ingestion of turmeric could inhibit nitrosation *in situ* to the extent of 60-80%.

Triglycerides, Insulin Resistance and Breast Cancer

Elevation in fasting levels of triglycerides (TG) is associated with increased risk of breast cancer. Since

elevated levels of triglycerides and insulin resistance are closely related. a study was undertaken this year to understand the association of TG, HDL, and insulin resistance. Results indicate higher TG and lower HDL levels in breast cancer cases while there seems to be no relationship of these parameters to insulin levels.

OTHER STUDIES

Studies on Obese Mutant Rats

Research studies, covering both basic and applied aspects, were conducted on obese mutant rats (WNIN/Ob and GR-Ob), isolated and established at the Centre. Molecular analysis of the obese mutant rats concentrated on two aspects, *viz.* to identify the molecular lesion with reference to the known obese gene(s) in rodents and to establish DNA fingerprint specific to these mutants. As regards mutational change(s) in known obese rodent genes, it is now confirmed that the leptin gene in these animals has not altered. This is based on the analysis of the complete leptin gene sequence from (+/+) and (-/-) phenotypes. But, in the obese mutants, there appears to be a difference in its leptin receptor gene. The (-/-) phenotype showed an altered PCR product (devoid of 200 bp) compared to lean control (+/+). This is further confirmed by the leptin receptor binding data of the brain membrane preparations from these rats. A significantly low or decreased binding of ¹²⁵I-labelled leptin was seen in homozygous obese (-/-) animals compared to lean control (+/+) and parental Wistar strain.

With reference to PCR based DNA fingerprinting studies using random primers, a male specific PCR product from obese males was obtained. Efforts are now on to clone this product in a suitable vector and sequence the same.

Accelerated ageing in obese mutant rats as indicated by free radical damage to lipids and protein (as early as 35 days) was reported last year. This year, the study was extended to anti-oxidant enzymes like catalase, glutathione peroxidase, glutathione S-oxidase and superoxide dismutase. These enzymes showed differences in the obese rats, generally around 90 days, but in some cases around 35 days itself (for eg. glutathione peroxidase in kidney and heart). Significant changes in these enzymes reflect decreased antioxidant defence in the mutant rats.

Cogent-db is an herbal drug consisting of nine herbs with *neem*, turmeric, *amla* and *Jamun* as major constituents. This drug was earlier tested by others in alloxan-diabetic rats and diabetic patients, and is currently available in the country across the counter. The anti-diabetic claim of this drug was verified using GR-Ob rats and it was found that the drug was effective at a dosage of 100mg/kg body weight. The drug brought about a significant reduction in cholesterol and triglycerides. These effects continued even one month after the withdrawal of the drug and all the animals in the treated group showed vigorous physical activity.



Environmental and Occupational Health

The National Institute of Occupational Health (NIOH), Ahmedabad and its Regional Centres at Bangalore and Kolkata continued studies on health status of industrial workers, tobacco harvesters and child labour engaged in various industries as well as in the area of environmental pollution.

Health Effects in Manganese Miners

An environmental-cum-epidemiological study was carried out by NIOH to assess the health effects in miners exposed to manganese based on clinical observations, pulmonary function tests (PFT) and neuroendocrine functions. The results of the environmental monitoring of manganese dust in manganese mines were reported last year. During the current year the results of medical examination, PFT and neuroendocrine functions in 476 miners (age 22-57 yr) with duration of exposure ranging from 5-35 yrs are reported.

Major psychological symptoms observed included inability to concentrate, fear without cause, regular insomnia, wide fluctuations in mood, feeling of committing suicide and feeling of killing. Main chronic nervous symptoms observed included headache, vertigo, tinnitus, tremor, tingling and numbness and asthenia. Symptoms related to locomotor system were fatigue, muscle cramps, joint pain and backache and cough and expectoration, haemoptysis, breathlessness and chest pain. 26% had respiratory abnormality – 9% with restrictive, 15.6% obstructive and 1.7% had both types of abnormality. 48% subjects above 47 yr., 28.37% in 35-45 yr. age group and 8.8% subjects aged less than 35 yr. had abnormal PFT. Hypothyroidism (low TSH levels) and elevated prolactin levels were observed in some of the subjects. Other hormones (T_3 , T_4 and cortisol) are under analysis.

The Effect of Lead on Children: A Psychological Evaluation

The health risk with regard to neuro-psychological functions due to lead in blood in children was assessed. A total of 405 children (202 boys and 203 girls), aged 11-15 yr. studying in Vth to VIIth Standards in a school located around lead smelting units was administered the Indian adaptation of WISC (Wechsler Intelligence Scale for Children). Blood was collected from the subjects for estimation of lead in blood. A 2x2 factorial experiment with lead in blood in two levels of low ($10\mu\text{g}/\text{m}^3$) and high ($>10\mu\text{g}/\text{m}^3$) and sex (boys and girls) was applied and Neuman Keuls tests employed. The concentration of lead in ambient air was found to be greater than the recommended value ($0.5\text{gm}/\text{m}^3$ of air). The psychological test scores were corrected for age and converted into scaled scores. High scores indicate better performance. In the verbal scale the scores in general information, mental arithmetic, vocabulary and digit span in boys of the high blood lead group were significantly inferior to the low blood lead counterpart. In the girls of high blood lead group significant performance depressions were observed on general information, general comprehension, similarity and digit span compared to low blood lead group. On the performance sub-tests the performance was significantly adversely affected on picture completion, block design and maze in high blood lead group of boys and on block design, object assembly and coding in high blood lead group of girls compared to their corresponding low blood lead groups. Further, verbal IQ, performance IQ and full scale IQ in high blood lead groups of boys were significantly lower compared to the respective low blood lead groups. The performance IQ was significantly more depressed in boys of high blood lead group compared to girls of corresponding group reflecting that the former group was more sensitive to neurotoxicity of lead.

Health Surveillance of Workers Exposed to Chromium in a Chemical Industry

A study was undertaken on environmental and biological monitoring of chromium to assess the health consequences in 176 workers exposed to chromium in a chemical industry.

Environmental monitoring of chromium at different places in industrial premises revealed that the level of chromium was highest in filtration unit (27.9-82.3 $\mu\text{g}/\text{m}^3$) followed by storage and furnace area. The lowest level of chromium (3.6-4.9 $\mu\text{g}/\text{m}^3$) was found in office premises. The result shows that chromium level in the industry was lower than the prescribed TLV of 500 $\mu\text{g}/\text{m}^3$. The mean blood Cr level in exposed workers (6.41 $\mu\text{g}/100\text{ ml}$) was considerably higher as compared to the control subjects (2.96 $\mu\text{g}/100\text{ ml}$). Nasal perforation was observed in 19 exposed workers.

Silicosis and Silico-tuberculosis among Quartz Grinders

A survey was carried out to determine the prevalence of silicosis and silico-tuberculosis in workers exposed to silica dust in quartz grinding units at Chhotaudepur (Vadodara district).

Detailed clinical examination, chest X-ray and PFT were carried out in 226 workers exposed for around 3 years. Of them 11.6% exposed for one year were found to be suffering from silicosis. Clinical examination reflected respiratory symptoms such as cough in 81.0%, dyspnea in 82.7%, haemoptysis in 16.4% and chest pain in 84.5% workers.

Silicosis was detected in 17.7%, tuberculosis in 5.3% and silico-tuberculosis in 23.0% workers.

The prevalence of restrictive (R) type of functional abnormality was seen in 25.0% males and 17.0% females.

The chest X-ray suggested that both male and female silicotics and silico-tuberculosics exhibited significant loss in functional parameters but it was more pronounced in silico-tuberculosics. This also reflects significantly higher prevalence of 'R' and 'R+O' type of functional abnormality.

The MEFV values (PEF, FEF_{75} , FEF_{50} , FEF_{25}) in both male and female subjects reflected that the site of obstruction was in both larger and smaller airways in silicotics and silico-tuberculosics.

Prevention, Treatment and Control of Silicosis in Agate Workers

An epidemiological study was carried out in and around Khambhat (Gujarat) in order to find out detailed medical history and occupational exposure to silica and exposure-related morbidity among 2049 silica workers, subsequently followed by development and testing of a suitable dust control device. All subjects underwent a detailed medical examination, especially with respect to occupational history, chest X-ray and PFT. In addition, blood was collected for ACE (angiotensin converting enzyme) estimation in 350 randomly selected subjects. An exhaust system was developed and fitted over the agate grinding machine last year. The efficacy of the system for reduction of dust concentration in the work environment was 75.27% for total dust and 60.40% for respirable dust. To improve upon the system further, the design of the bag filter was modified by increasing the filtration area. The dust was collected in a bucket containing water. To reduce the electricity consumption the emery wheel of the grinding machine was rotated with the motor of the exhaust system by attaching it to a pulley. This brought down the electricity consumption. The efficacy testing carried out at two factories showed 93.55% reduction in total dust and 93.80% reduction in respirable dust. Further work is in progress.

Occupational Health Problems in Child Labour in Match Industry

A study was undertaken in a match industry at Sivakasi to assess the occupational morbidity in children (<14 yrs), adolescents (>15 to <18 yrs) and adults (18-30 yrs). An industrial hygiene survey was also carried out to assess the dust levels, heat stress, noise levels and illumination levels at the work place of partially mechanized (A), manual (B) and household (C) categories of match industries.

The concentration of silica dust in the chemical grinding and mixing areas of 'A' and 'B' categories of industries exceeded the TLV, while in 'C' category of industries it was within the TLV. The dust concentration of manganese was as high as 34.91 $\mu\text{g}/\text{m}^3$ in 'A' category exceeding the TLV of 10 $\mu\text{g}/\text{m}^3$, while in 'B' category (11.07 $\mu\text{g}/\text{m}^3$) it was very close to TLV. However, in 'C' category the concentration of manganese dust was negligible. The ambient temperature ranged from 28.3-34.5°C in 'B' and 29.59-37.40°C in 'C' category against the recommended limit of 29.9°C.

Estimation of red phosphorus (striking surface of matchsticks) in serum samples of 509 subjects (392 female and 117 male), and urine samples of 808 subjects (593 female and 215 male) was carried out. It was observed that 30.3% male and 15.32% female subjects (age 15-18 yrs) had >6mg/dl serum phosphorus. In case of urine phosphorus, 12.5% male and 14.4% female subjects of same age group and 19.2% male and 7.84% female subjects in the age group of 19-30 yrs had higher than 0.84 gm/24 h urine phosphorus levels. The study is in progress. The most common findings among the study population were: underweight <20 kg (99.4 to 99.6% in both males and females in the age group \leq 14 yrs), fatigue (13.79%), joint pain (10.34%) and clinical pallor (33.45% among female subjects).

Occupational Health Problems of Cycle Rickshaw Pullers

The main objective of this project was to assess the occupational health problems in this unorganised sector of rickshaw pullers. A group of 400 rickshaw pullers, aged 25-45 yr. with an average exposure of 12 years were examined in Kolkata. The major complaints observed were headache, body ache, backache, joint pain, fatigue, cough, breathlessness and chest pain. The nutritional status of these subjects was poor. The above clinical investigation was supported by biochemical and ergonomic study. The study is in progress.

Studies on Pesticide Formulators with reference to Thyroid Function

Pesticide formulation involves combining active ingredient with the inert substances to yield different forms of the product. During this process, workers were exposed to low and/or high concentration of various toxic chemicals present in working environment. A cross-sectional study was carried out on 35 male pesticide formulators, aged 45-55 yr. exposed to a combination of pesticides for 17-21 years in a formulating unit. Blood samples were collected for the analysis of serum thyroid hormones such as thyroid stimulating hormone (TSH); triiodothyronine (T_3) and thyroxine (T_4) by radioimmunoassay (RIA). The level of TSH was elevated (about 28%) in pesticide formulator group as compared to the reference group. Total T_3 was suppressed significantly in formulators while marginal decrease (about 7%) was noticed in T_4 level. The collected data indicates impact of exposure to pesticides on T_3 levels.

Duration of exposure was found to be one of the causative factors of thyroid function impairment.

Occupational Health Problems of Tobacco Harvesters

Tobacco harvesters are occupationally exposed to nicotine during tobacco cultivation. To detect the chronic health effects of tobacco cultivation a specially designed questionnaire was used which included information on tobacco habits, occupational and reproductive history and detailed medical examination. 685 exposed subjects selected from three villages of Anand district were examined. ECG of subjects indicated sinus tachycardia, in 13.65% men and 32.58% women and T-wave and ST segment changes in 1.32% men and 9.82% women respectively. The reproductive history of exposed women indicated premature delivery (7.45%), abortion (10.08%) and still birth (8.77%). To prevent the absorption of nicotine by dermal route various types of gloves have been provided to the tobacco harvesters and modification in patterns and types is under progress.

Effect of *Pan Masala* on Testicular Tissue and Sperm Morphology of Mice

The habit of chewing *pan masala* is very popular in the Indian sub-continent. A study was carried out on the toxic effects of *pan masala* on mouse testis and sperm morphology after chronic exposure through diet at a dose of 2% in mouse feed for a period of 2,3,9,12 and 13 months. It was observed that both *pan masala* plain (PMP) and one with tobacco (PMT) induced deleterious histological alterations in mouse testis, however, the changes were less pronounced in the PMP treated group as compared to PMT treated animals. A statistically significant elevation of sperm abnormalities (head shape) was observed at autopsy intervals of 12 and 13 months of exposure suggesting deleterious effects of *pan masala* on male reproductive system of mouse.

Toxicity in School Children living on the Vrishabhavathi River Basin

Study was carried out to quantify the levels of environmental lead concentration in air and drinking water and to correlate it with the lead concentration in blood and deciduous teeth of school children located on the banks of Vrishabhavathi river in Bangalore. A group of school children living away from the river was

tested as control. The mean concentration of lead in air was found to be higher in the study area ($0.13 \mu\text{g}/\text{m}^3$) than the control area ($0.007 \mu\text{g}/\text{m}^3$). The drinking water samples collected from the residences in the study area had higher mean lead levels ($31.02 \mu\text{g}/\text{dl}$) compared to those collected from the control area ($22.3 \mu\text{g}/\text{L}$). The mean dentine lead ($18.77 \mu\text{g}/\text{g}$) and blood lead ($16.83 \mu\text{g}/\text{dl}$) levels were found to be significantly higher in the study group.

Acute Poisoning Cases Reported at Poison Information Centre

A total of 395 poisoning cases were reported to the NIOH Poison Information Centre from January-December, 2000. Most of these cases (74.6%) were from the rural areas, the highest being reported from Ahmedabad district (68.9%). Cases were also reported from the neighbouring states like Rajasthan, Madhya Pradesh and Maharashtra. The poisoning was most prevalent in the age group of 20-29 yrs. (52.55%) and was higher in males (66.1%) than in females. A similar

trend was observed during the last five years. The occupation-wise analysis shows that poisoning was most common among individuals employed in different types of odd jobs which included civil employees, rickshaw drivers, office workers, diamond workers, *etc.*, followed by housewives, farmers/farm workers, the unemployed, students and pesticide factory workers. Frequency of poisoning was higher in the month of June, July and March. It was highly prevalent (49.5%) in individuals having secondary education compared to uneducated ones (16.2%). In 90% cases, poisoning was due to suicidal attempts followed by occupational (5.4%) and accidental (4.1%) reasons. Since the suicidal attempts were by ingestion, exposure of poisoning through oral route was found to be the highest (92.2%). Among the compounds encountered, pesticides were the most common (72.5%) followed by other industrial chemicals (6.1%), drugs (4.8%) and household items (2.5%). A few (0.6%) cases reported a mixed exposure involving drug with pesticide or some household items like nail polish, kerosene *etc.* In 13.3% cases the compound involved was unknown.



Non-communicable Diseases

The health care priorities of the country are undergoing a definite change. In the coming years, the three leading causes of lost years of healthy life are likely to be heart disease, depression and road accidents. The burden of disability due to non-communicable diseases is much higher than the disability due to communicable diseases. With an aging population and changing life styles there will be a significant increase in the number of people suffering from these diseases. Planning for health care implementation requires information on the disease prevalence, severity and mortality. Identifying the essential package of cost effective interventions and enabling the primary and secondary health care services to implement these continued to be a major focus of research by the Council during 2000-2001.

ONCOLOGY

Data from National Cancer Registries continued to provide information on cancer incidence and its trends in selected areas. Multidisciplinary research on cervical cancer is expected to provide useful leads on its aetiology and control. Environmental carcinogen testing units have aimed at identifying important substances/chemicals of special importance to India for estimating their permissible limits in the environment. Continuing operational research study on control of cervical cancer would help in identifying cost-effective strategy for its control. Dissemination of results of R&D and their application for cancer control activities has been another area of focus.

National Cancer Registry Programme

The National Cancer Registry Project (NCRP) initiated in 1981-82 continued to collect authentic data on cancer occurrence in the country. The network of seven population based (including two in rural areas) and five hospital based cancer registries aims at generating reliable data on cancer occurrence, conducting

epidemiological studies and developing human resource in the field of cancer epidemiology and registration. The rural population based cancer registry at district Panchmahal, Gujarat has been closed due to operational reasons, and a new rural registry with a smaller population is proposed to be initiated.

The data for the year 1996 from Population Based Cancer Registries (PBCR) showed a crude incidence rate (per 1,00,000 persons) in the five metropolitan cities ranging from 53.7 at Bangalore to 79.6 at Chennai among men and from 68.7 at Bangalore to 93.6 at Chennai among women. The Barshi registry based in rural area had an incidence rate of 36.7 and 44.4 (per 1,00,000) for men and women respectively. The most common forms of major cancers seen were those of lung, stomach, oesophagus, larynx, mouth, hypopharynx among men and of cervix, uterus, breast, oesophagus, ovary, stomach and mouth among women. Stomach cancer was predominant at Chennai and Bangalore whereas lung cancer was predominant at Mumbai, Delhi and Bhopal. Among women, gall bladder cancer also had a high incidence at Delhi. The cancer of cervix and breast are the major cancers among women.

The data from hospital based cancer registries of 1995-96 showed that the extent of microscopic confirmation of cancer diagnosis varied from 77.2% at Chennai to 94.35% at Bangalore in men and 84.7% at Chennai to 96.4% at Bangalore in 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 24.7% (Trivandrum) to 48.7% (Chennai) among men, and from 14.9% (Trivandrum) to 41.2% (Chennai) among women.

Case control studies on cancers of prostate and gall bladder have also been initiated under NCRP. Multicentric study (Bangalore, Delhi and Mumbai) on cancer prostate has been initiated with the objective

of studying the association between vasectomy and cancer prostate. The case series includes all the newly detected cases of prostate cancer registered by the three participating PBCRs. The study of cancer of gall bladder has been initiated by Delhi PBCR with the objective of identifying risk factors for gall bladder cancer. Six hundred newly detected cases from Delhi PBCR area and an equal number of healthy relatives of the patients and neighbours as controls would be studied.

A population based cancer-cum-tobacco survey was undertaken as part of the quality control exercises by the NCRP. The surveys were carried out by the three registries *viz.*, Bangalore, Chennai and Mumbai. This is for the first time that the NCRP has undertaken a systematic exercise for ascertaining the level of coverage of cancer cases by PBCRs. The observed proportion of completeness was found to be 71.8%, 78.0% and 100% in Bangalore, Mumbai and Chennai respectively.

To address the importance of histomorphology in cancer epidemiology, a study on breast cancer was undertaken with the objective to standardise the histopathological reporting of this type of cancer; develop specific guidelines for the same and to have a uniform classification scheme. The cases microscopically diagnosed and registered in the population based cancer registry area of Bangalore from 1982 to 1989 were chosen for the study. Follow up as measured by vital status (dead or alive) as available on 1st January 1993 was for 88% (n=1334 cases) patients diagnosed during this period. The histopathological slides were initially reviewed by one panellist at Kidwai Memorial Institute of Oncology, Bangalore and 2-3 representative blocks were selected for extra sections to be circulated among the panel members. The observed five year overall survival rate was 47.8%. Results of univariate analysis with Cox's proportional hazards model showed that tumour border, grade of mitoses, vascular and or lymphatic invasion, nipple/ areola/ skin involvement and presence of associated benign disease were all statistically significant prognostic factors. Importantly, tumour or nuclear grade did not predict survival; nor did degrees of desmoplasia, elastosis, lymphocyte response or necrosis. Axillary node involvement was not a prognostic indicator.

The human resource development through NCRP was continued. A Workshop for continuing education alongwith quality control exercise was held at Bhopal. Two registry personnel were trained in cancer epidemiology at Tampere, Finland.

Cancer Control Activity

The ICMR helped the Government of National Capital Territory of Delhi in developing a module for training of the medical officers in cancer control activities. Two day training programme was organized by ICMR and the AIIMS, New Delhi.

Indo-German Collaboration

Collaborative cancer research projects between India and Germany are coordinated by ICMR in India and German Science Foundation (GSF) in Germany. During the year, 29 collaborative research projects between India and Germany were identified for future research. Of the thirteen projects received, five have been cleared by Health Ministry's Screening Committee and the remaining are under consideration.

Cervical Cancer

A multidisciplinary study on cervical cancer involving cytological, immunological, genetic and molecular approaches to identify reliable biomarkers and/or risk factors for early identification of this cancer is in progress at Institute of Cytology and Preventive Oncology (ICPO), New Delhi. So far, about 5000 women attending Gynaecology OPD in four major hospitals in Delhi have been screened cytologically using Bethesda System of Classification.

Studies on cervical cancer revealed a central role of human papilloma virus (HPV) and its interaction with cellular genes and transcription factors including certain specific genetic alterations. It has also been shown that expression of HPV transforming genes E6 and E7 can be suppressed by the treatment of a specific antioxidative drug at nontoxic micromolar doses (Fig.17). Studies on transcriptional regulation of HPV oncogene expression in cervical cancer and precancerous cells indicated that an inducible cellular transcription factor AP-1 plays a pivotal role during tumorigenic transformation. One of the dimerization partners of AP-1, c-fos is found to overexpress in cancer while its

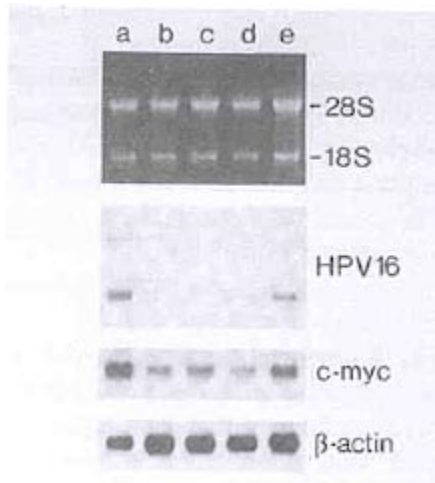


Fig.17 Suppression of HPV expression in a northern blot analysis of RNA extracted from high risk HPV 16 positive cervical cells following treatment with an antioxidant, pyrrolidine dithiocarbamate (PDTC) for different periods. 28S and 18S rRNA are shown in ethidium bromide-stained agarose gel. Lane 'a' is untreated control, lanes 'b to e' overnight, 6hr, 4 hr and 2hr treatment of 100 mM PDTC. While normal genes c-myc and β -actin are not affected, by 4 hr HPV expression is completely abolished.

expression is low in lower grade lesions and controls which instead show a high level of expression of fos-related antigen, fra-1, which is absent in cancers. This indicates that fra-1 might be having tumor suppressor activity in cervical cancer. Interestingly, treatment of cervical cancer cells with an antioxidative agent has been found to completely abolish the expression of HPV but it up-regulates the activity of AP-1 and binding of fra-1 (Fig.18).

A study was carried out in 30 cancer patients, 11 cases with dysplasia of different grades and 15 controls to estimate telomerase activity in precancerous and cancerous lesions of cervix uteri. Preliminary results show that the telomerase activity increases as a function of severity of the cervical lesions. Telomerase activity was not detected in healthy controls (Fig.19).

Considering the need for an alternative strategy for control of cervical cancer, the ICPO organised a National Workshop on Control of Cervical Cancer – Alternative Strategies. Both national and international experts of major organisations involved in the control of cervical cancer participated. The Workshop has come out with some recommendations feasible for Indian situation.

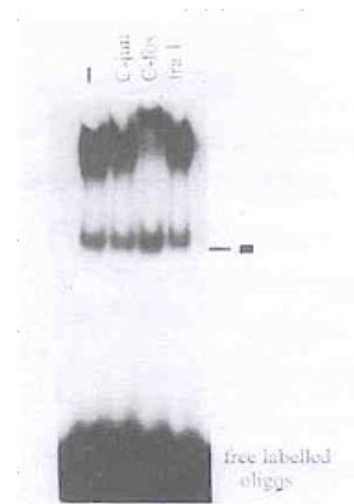


Fig.18 Total cellular protein extracted from HPV 16 positive cervical cancer biopsy specimen shows binding activity of AP-1 family members in a band supershift assay using antibodies against c-jun, c-fos and fra-1. c-fos shows highest DNA binding activity.

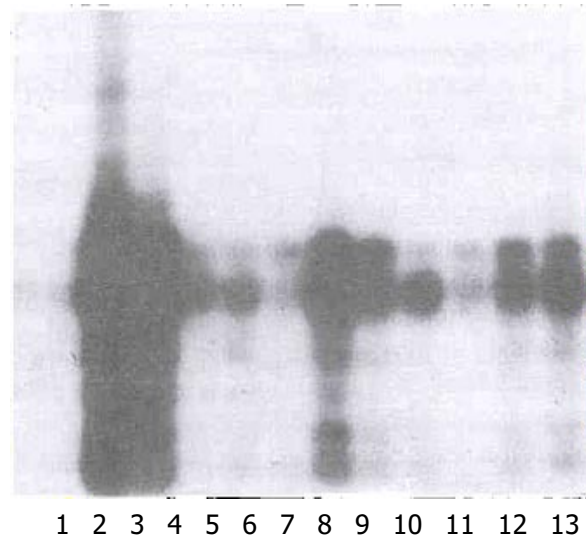
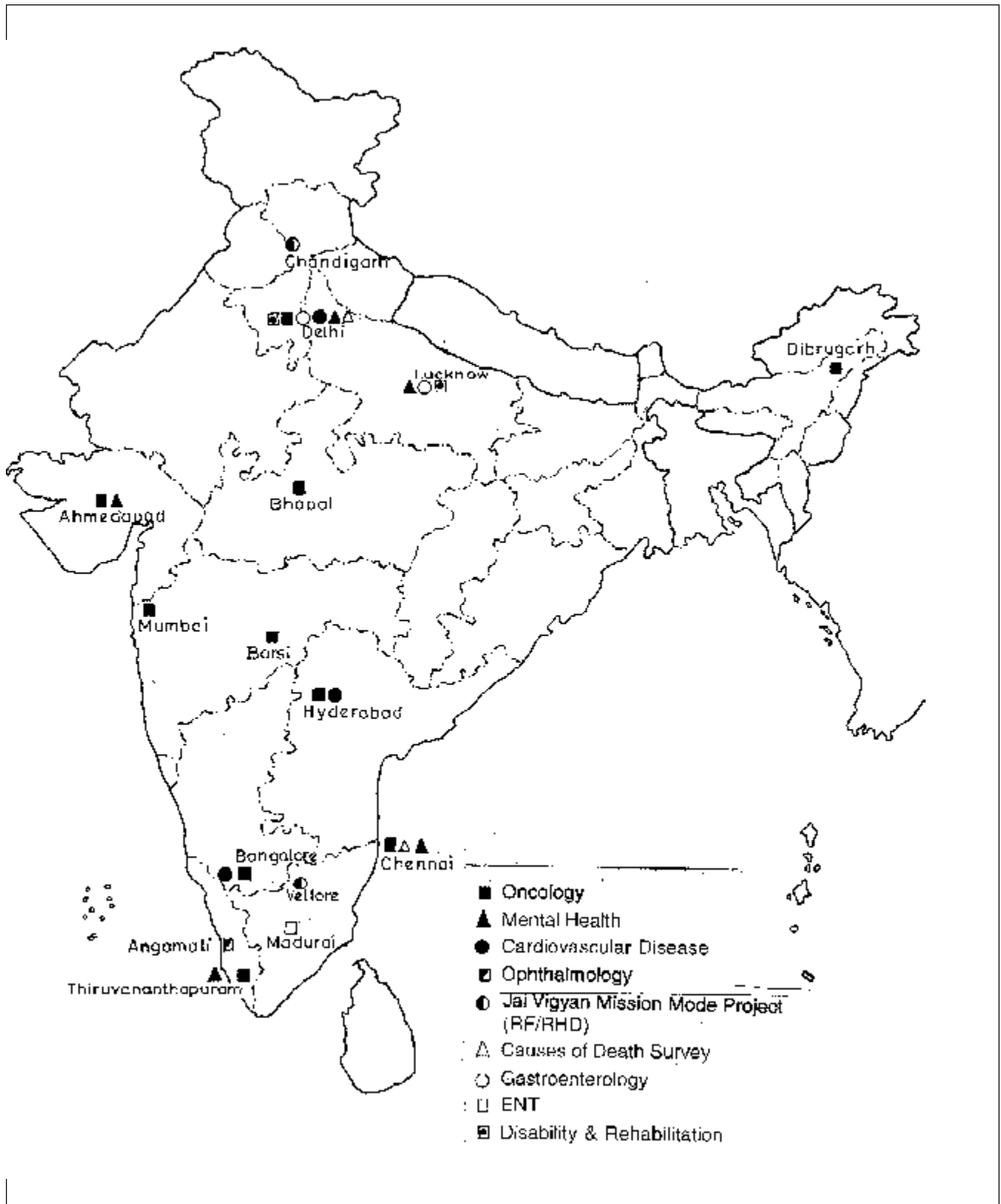


Fig.19 Showing telomerase activity by telomerase repeat amplification protocol (TRAP) assay in different stages of cervical lesions starting from mild dysplasia to invasive cancer of uterine cervix.

Lane 1 healthy women, lane 2, negative control (lysis buffer), lane 3, positive control: oesophageal cancer cell line, lane 4, cervix cancer stage II, lanes 5-7, mild dysplasia, lane 8, severe dysplasia, lane 9-12 moderate dysplasia and lane 13 cervix cancer stage I.



Major ICMR Research Projects in Non-communicable Diseases

Breast Cancer

A multidisciplinary study on breast cancer has been initiated to find out the risk factors, treatment pattern, survival, prognostic factors and susceptibility genes in the families of breast cancer patients. In another study on breast cancer, mutation and expression of breast cancer susceptibility genes BRCA 1 and BRCA 2 along with p53 gene has been investigated to find their role in both sporadic as well as familial breast cancers in India. Studies were conducted for exons 2,11 and 20 of the breast cancer susceptibility genes by both PCR-SSCP and direct sequencing. Preliminary data indicate complete absence of mutation in 9 familial cancers and only 2 mutations each of BRCA 1 and BRCA 2 out of 79 sporadic breast cancer cases investigated.

As the breast cancer is strongly influenced by sex-steroid hormones, a separate study was conducted using paraffin sections from female breast cancer biopsies. Immunohistochemical staining for EGF-R, c-erbB-2 oncoprotein, estrogen (ER) and progesterone (PgR) receptors revealed immunopositivity to EGF-R in 40% cases of breast carcinoma whereas c-erbB-2 oncoprotein was present in 32% cases. Similarly, immunoeexpression of ER was noticed in 36% and PgR in 52% breast cancer patients. The study could not find any interrelation amongst different parameters, except immunopositivity of EGF-R and lymph node involvement. Higher mean level of HDL-cholesterol was observed in ER-positive breast cancer cases compared to ER-negative cases. Overexpression of ER and higher serum level of HDL-cholesterol might be helpful for a better clinical course. Immunohistochemical detection of ACTH peptides in breast cancer revealed 15.2% positivity (Fig.20). The neuroendocrine character of this cancer is a potential area for future research.

Prostate Cancer

There are interesting similarities between breast and prostate cancers, which are mainly adenocarcinomas arising in sexually differentiated organs and dependent on sex hormones. Immunopositivity for EGF-R and c-erbB-2 oncoprotein was observed in 30% and 35% cases of prostate cancer respectively. A statistically significant relationship was noticed between the immunoeexpressions of EGF-R and c-erbB-2 among prostate cancer cases. While the study could not detect immunoeexpression of estrogen receptors in prostate

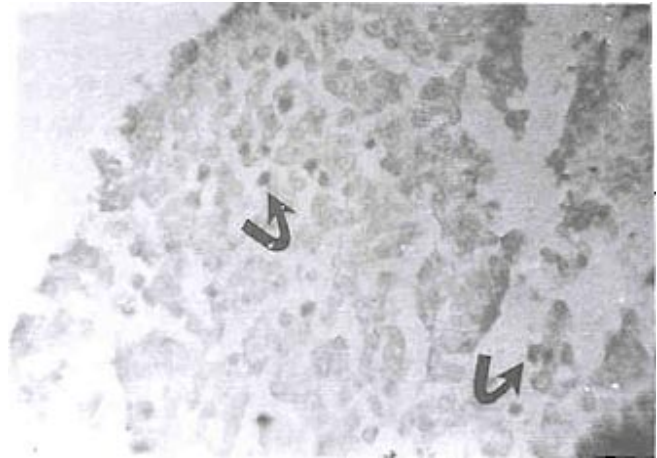


Fig.20 Immunoeexpression of ACTH neuropeptides (arrows) in breast cancer tissue.

cancer cases, 10% cases of prostate cancer were observed to be positive for PgR. Further, in one prostate cancer case, ACTH peptide was detected. The study is in progress on larger number of cases.

In separate studies done at IOP, New Delhi significant increase in P⁵³ expression and apoptotic index was noticed in benign hyperplasia, prostatic intraepithelial neoplasia and prostatic malignancy suggesting significant role of P⁵³ in progression of malignancy from preneoplastic to neoplastic stage.

CARDIOVASCULAR DISEASES

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

The earlier project conducted by the Council on epidemiology of coronary heart disease (CHD) has shown that the conventional risk factors have a role in the occurrence of CHD in our population. A multicentric case control study has been initiated at four centres viz. Bangalore, Delhi, Hyderabad and Lucknow to quantify the association of possible risk factors for acute myocardial infarction (AMI). The study is a hospital based case-control study comprising cases with newly diagnosed ischemic heart disease (IHD). The study will seek to identify factor(s) positively or negatively associated with the risk of IHD. Four different sets of standardized proformae for clinical, biochemical, dietary and stress related factors are required for data collection. During this period, training-cum-workshops for diet and stress proformae, were organised. In addition, Clinical

Coordinating Unit and ICMR Coordinating Unit visited Lucknow and Delhi centres to review the progress of the study. The subject recruitment is being continued, 1308 subjects (436 cases and 872 controls) have so far been recruited at four centres.

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

The *Jai Vigyan* Mission Mode project on community control of RF/RHD in India has been initiated with four main components *viz.* to study the epidemiology of streptococcal sore throat, establish registries for RF/RHD, vaccine development for streptococcal infections and conducting advanced studies on pathological aspects of RF/RHD.

Under the epidemiology component, at the Chandigarh centre, a total of 1192 school age children have been screened and their throat swabs collected. 30% children were diagnosed as sore throat cases clinically and of these 11% were positive on culture. An additional 7% asymptomatic children were also culture positive on throat swabs. Of all the positive throat swabs almost 66% were of group A beta haemolytic streptococci (GABHS), the organism responsible for RF/RHD. In the group of 340 children being followed none of the skin swabs showed any GABHS. The throat swabs have shown a seasonal variance of GABHS positivity with a peak in February during the short follow up undertaken. At the Vellore centre, 570 school age children have already been screened and throat swabs collected. Of these 213 children were culture positive while 150 throat swabs were positive for GABHS. The prevalence is higher than expected since the children who have been screened constitute a high risk group consisting predominantly of boarding school children.

Under the vaccine component of this *Jai Vigyan* Mission Mode project, 50 isolates have been collected and serologically identified. DNA amplification of the amino terminal nucleotide sequence of the M protein has also been completed. Deciphering of the nucleotide sequence of 5 different isolates has been completed and the data shows heterogeneity in their sequences.

It is proposed to start five registries, one in each of the five zones, which would act as the controlling

agency for 3 satellite registries in each zone, to be established as the second phase of the project. The preliminary work has already been undertaken at two of the proposed centres, which includes selection of the study area and contacting the private practitioners and the NGOs active in the region.

Hypertension

A study on hypertension was conducted covering 1015 workers of a tea garden in upper Assam and 812 indigenous Assamese people, aged 30 years and above. In the tea garden population, overall mean systolic blood pressure (SBP) recorded was 145.3 ± 25.9 mm of Hg while mean diastolic blood pressure (DBP) was 87.6 ± 13.7 . In males, mean SBP was 144.4 ± 24.5 and the level of DBP was 87.2 ± 12.8 . In females, on the other hand, mean SBP level was 146.2 ± 27.3 and mean DBP was 88.0 ± 14 . Overall prevalence of hypertension was 42.76% (41.2% in males and in 44.3% females).

OPHTHALMOLOGY

Glaucoma

Glaucoma is one of the important causes of blindness. For determining the prevalence of glaucoma in the Indian population, a project on epidemiology of glaucoma was initiated. The Angamally centre is continuing to collect data on the prevalence of glaucoma using a camp approach. Five thousand seven hundred eligible persons have been screened so far. Preliminary analysis of data has revealed the prevalence of glaucoma to be 4.04% of which 2.02% were primary open angle and 1.01% primary angle closure glaucoma (including acute, subacute and chronic angle closure glaucomas). The remaining 1.01% were other types of glaucoma including secondary glaucoma.

MENTAL HEALTH

Epidemiological Study of Child and Adolescent Psychiatric Disorders

The epidemiological study of child and adolescent psychiatric disorders in urban and rural areas was completed during the year. This was the first large community based study of childhood and adolescent

psychiatric disorders carried out in the country. The project also involved substantial work on methodology. Multi-axial system of classification was used to record diagnostic information on five axes: (i) psychiatric diagnosis, (ii) specific developmental delays, (iii) intellectual level (iv) significant non-psychiatric medical diagnosis, (v) abnormal psychosocial condition. The project also identified the psychosocial situations associated with psychiatric problems in children. The rates of psychiatric disorders among children are shown on the multi-axial system in Fig.21.

individuals with suicidal ideation. A pilot study for the project has been initiated for a period of one year with the objective to develop/adapt and pre-test study instruments. The pilot study will also work out fieldwork logistics and prepare guidelines for training of research staff.

Mental Health Service Needs of the Earthquake affected Population

A study of mental health service needs and service delivery models in earthquake-affected population in

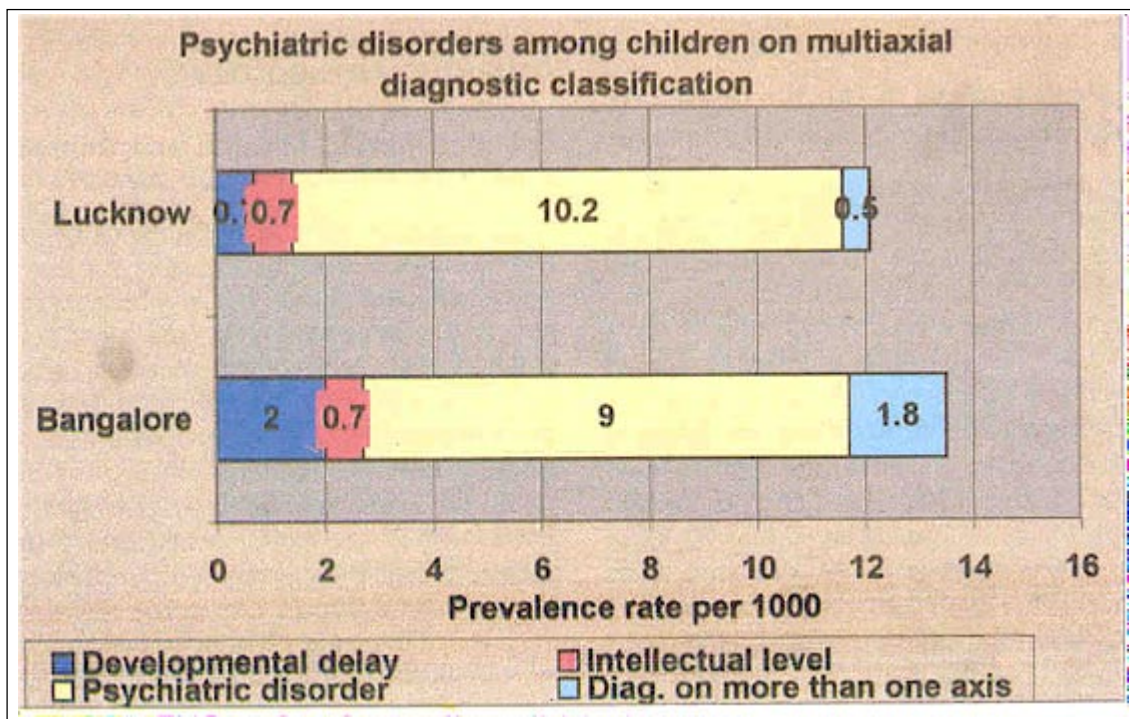


Fig.21 Psychiatric disorders among children on multi-axial diagnostic classification.

Suicide Behaviour

A task force project on suicide behaviour has been initiated at two centres - Delhi and Trivandrum. The project will have two major components - community based study and hospital based study. The specific objectives of the project are: (i) to study the occurrence of suicidal ideation in the community, (ii) to study factors and processes contributing to suicidal ideation and suicidal attempt, (iii) to identify additional diagnoses among suicide attempters as compared to suicide ideators and (iv) to study the course and outcome in

Gujarat has been initiated. A pilot study was carried out by Institute of Human Behaviour and Allied Sciences, Delhi to assess immediate mental health service needs following the earthquake in Gujarat on 26th January, 2001. The pilot study found evidence for definitive need to focus on the emotional and psychological needs of the population in dealing with post disaster situation. It was observed that the mental health service needs of large portions of the affected population can be served by the relief and rescue workers and health care providers, as well as by strengthening and supporting the socio-cultural coping mechanisms of

the local communities. Specialist mental health expertise can be useful and is required for (a) services for a relatively smaller proportion of the population (b) sensitization and training of the rescue/relief workers and health care providers who can take care of the needs of larger proportion of the affected populations. It is proposed to undertake a task force project on mental health service needs of the disaster-affected population of Gujarat. The assessment will include the mental health problems, treatment needs and the existing mental health services available in the affected areas. The project will also develop mental health service delivery models for earthquake-affected communities.

Study of Drug Addicts in the North-Eastern Region

Socio-demographic and behavioural study of drug addicts in the north-eastern region with particular reference to intravenous drug users was continued along the National Highway of Assam and Arunachal Pradesh. During this year a stretch of 70 km on National Highway number 37 (NH-37) from Jagiroad to Guwahati was surveyed and 20 drug addicts were contacted. So far a total distance of 500 km on NH-37, spanning from Doom Dooma to Guwahati has been covered during which 49 drug addicts have been contacted. Overall, majority of drug addicts were in 20-35 yr age group; 51.0% married; 42.9% educated up to matriculate and drug related school drop out rate was 36.7%. 10.2% of drug addicts started taking drugs between 16-20 yr of age and 65.3% addicts were found taking drugs for more than 5 years. About 81.6% addicts were found to be addicted to heroin. Chasing (65.3%) was the preferred route of drug administration next to i.v. (32.7%). More than 77% addicts were referred to hospital by their relatives.

GASTROENTEROLOGY

Hepatitis C is a major health problem in India. In view of the high morbidity and mortality associated with hepatitis C, it is important to find reasons for non-response to existing therapies. Available treatments including interferon therapy have limited impact on the disease progression.

Non-response to Interferon Therapy in Patients with Hepatitis C

Interferon has been used as treatment for hepatitis C (HCV), either alone or in combination with other anti-viral agents. As this therapy is expensive and has to be taken for very long duration, there should be some marker to predict the outcome and non-response. Though high baseline viral load and HCV genotype 1b has been reported to be influenced by the therapy, there is scarcity of data to substantiate this claim in India. A task-force study to determine host and viral factors responsible for non-response to interferon therapy in patients with HCV has been initiated at GB Pant Hospital, New Delhi.

OTORHINOLARYNGOLOGY

Epidemiological, Cultural and Immunological Studies on *Rhinosporidium seeberi*

In spite of several decades of research, the pathogenesis of rhinosporidiosis is still not clear and hence treatment of this disease is neither standardized nor certain. Some researchers claim it to be a disease of fungal origin, while others claim it to be bacterial or protozoal. In view of this and based on the recommendations of an expert group meeting held in the year 1996, a study was initiated at Madurai with the overall objective to isolate, culture and characterize *Rhinosporidium seeberi* for identification of the specific antigen through DNA hybridization, immunological and epidemiological studies. During the year under report the focus of the project was mainly on identification of the pathogen in tissue sample and comparison with pathogen isolated from pond water. The study revealed no homology with *Microcytis aeruginosa*. Genomic DNA amplification using specific primer was carried out. Sequence homology analysis of mitochondrial small rRNA showed a relatively high degree of homology with *Hansenula wingei* and there were no related sequences for elongation factor (EFI and EFII in gcg software). Efforts to grow the organism in axenic culture could not succeed. In pond water almost all stages were observed in the pathogen as that of organism in tissue sample. Major histocompatibility complex (HMC) class II alleles in patients with rhinosporidiosis revealed cent percent concordance in the allele assignment by PCR-SSOP and PCR-SSP method.

DISABILITY AND REHABILITATION

Prevention of Disability among Pre-school Children

A task force project on prevention of disability among pre- school children has been initiated at three centres, namely Delhi, Jaipur, and Lucknow with following objectives: (i) to carry out a study for situational analysis of presently available facilities for prevention of disability among pre-school children, (ii) to review, adapt and develop training material for disability prevention for use in training of health care providers, empowering community for self-care for disability prevention, (iii) to deliver selected interventions, (iv) to study epidemiology of disability prevention through retrospective case study method, (v) to develop basic rehabilitative services at PHC level, (vi) to further develop linkages between various departments and NGOs to strengthen disability prevention among children, and (vii) to evaluate the impact of intervention.

HAEMATOLOGY

The Institute of Immunohaematology (IIH), Mumbai, is carrying out some mission mode programmes besides studies on haemoglobinopathies, disorders of haemostasis and transfusion medicine. Studies on haemoglobinopathies in tribals were undertaken at RMRCs at Bhubaneswar, Jabalpur and Dibrugarh.

Non-invasive Method of Prenatal Diagnosis of β -Thalassaemia

At the IIH, Mumbai, sufficient number of foetal nucleated red cells from blood of pregnant mothers in 10-23 weeks of gestation have been isolated by using magnetic Dynal TM anti-CD71 conjugated beads and by cell sorting for prenatal diagnosis of thalassaemia. The proper PCR reaction using these cells for amplification of DNA is being standardized.

Jai Vigyan Science and Technology Mission Project on Community Control of Thalassaemia Syndrome

This multicentric project aims at identifying, screening, educating and counselling couples at risk

of having thalassaemic children so as to prevent birth of such children. So far, 4111 individuals (2314 college students and 1797 antenatal women) have been screened in 6 states (Maharashtra, Gujarat, Panjab, West Bengal, Karnataka and Assam) and various screening methods have been standardized. Educational, awareness and counselling material has been prepared in regional languages.

Production of Monoclonal Antibodies

Monoclonal antibodies to foetal haemoglobin and factor VIII C have been successfully produced at IIH, Mumbai. The patent has been applied for this.

Cytogenetic Study in Myelodysplastic Syndrome

Out of 25 cases of myelodysplastic syndrome studied by conventional G banding cytogenetic technique and by sister chromatid exchange, 4(16%) showed chromosomal abnormality and the rest showed high frequency of chromosomal breakage and sister chromatid exchange (Fig.22). The frequent chromosomal break points identified were 1 q, 2 p, 9 q, 17 q, 18 q, 3 p *etc.*



Fig.22 Sister chromatid exchange (arrows) in 5-bromo-deoxy-uridine induced cultures in a patient with myelodysplastic syndrome.

Study of HLA-DR in Marathi Speaking Population

The PCR-SSP amplification for the DRB gene and DQB gene have been standardized in Marathi speaking population.

Genetic Diagnosis of Bleeding Disorders

The carrier detection as well as the prenatal diagnosis utilizing DNA technology has also been standardized in cases of von Willebrand disease besides hemophilia A and B at the IIH, Mumbai.

Study of Platelet Specific Antigens in Indian Population and its Association with Neonatal Alloimmune Thrombocytopenic Purpura (NAITAP)

This study being continued at IIH, Mumbai revealed that 1% people in India are HPA 1b homozygous. In Caucasians approximately 98% population carries the platelet antigen allele HPA 1a and the remaining 2% are HPA 1b homozygous. Thus, pregnant women carrying HPA 1b/1b genotype are likely to be sensitized to HPA 1a antigen in the foetus, inherited from the father and produce anti HPA 1b antibodies against the foetal platelets sometimes causing intracranial haemorrhage in the foetus which leads to serious neurological sequel.

Genetic Risk Factors for Coronary Artery Disease in the Young

Investigation of hereditary risk factors has been done in 65 patients <40 yr. old who have had myocardial infarction. Parameters studied include coagulation test, thrombosis like factor V Leiden mutations, prothrombin gene polymorphism, thermolabile methylene tetrahydrofolate reductase variant and polymorphism in fibrinogen -gene.

Haemoglobinopathies/Blood Disorders among Tribals

Haemoglobinopathies among Some Primitive Tribes of India

Multicentric study on intervention programme of nutritional anaemia and other haemoglobinopathies was initiated during 1999-2000 in order to assess their prevalence in various primitive tribal populations of

India. The study is ongoing at five centres (Pune, Yavatmal, Surat, Nilgiris and Bhubaneswar) in four states namely Maharashtra, Gujarat, Orissa and Tamil Nadu. Various tribal groups included in the study were *Kathodi, Kolam, Kotwalia, Kurumba, Irulla, Paniya, Didayi* and *Bondo* and *Madia*.

Of the 947 individuals screened so far anaemia was found to be more common among the *Kurumbas* of Tamil Nadu and *Bondos* of Orissa as compared to the other tribal groups. Iron deficiency anaemia was more common among the *Irulas* followed by *Kurumbas, Madias, Katkaris, Kollas* and *Rotvalias*. Sickle cell gene was present in all the tribal groups except *Bondos* from Orissa. The maximum number of individuals among the *Madias* of Maharashtra and *Irulas* of Tamil Nadu were either sickle cell heterozygotes or homozygotes. G6PD deficiency was found in all the tribal groups studied. Most of the tribals were anaemic.

Haemoglobinopathy and Viral Markers among Primitive Tribes of Tripura

The RMRC, Dibrugarh, one of the four participating centres of this multicentric study, is carrying out the investigations in Reangs in North Tripura and Dhalai districts of Tripura. As per the protocol about 1000 individuals in each district will be screened for sickle cell haemoglobin, thalassaemia syndromes and glucose-6-phosphate dehydrogenase deficiency, hepatitis B and C, HIV and intestinal worms. In addition, their drinking water source will also be tested for potability. Screening of 630 blood samples revealed more than 75% prevalence of HbE and 2.8% prevalence of G6PD deficiency. Screening of drinking water sources of the community and individual households for bacterial contamination revealed that only 10.5% water samples were found potable.

Prevalence of Haemoglobinopathies and G6PD Deficiency among the Tribals of Orissa

The major tribals namely, *Lodha, Bhatta* and *Paraja* were randomly screened for sickle cell haemoglobinopathy, beta-thalassaemia, G6PD deficiency, ABO and Rhesus blood group serology at the RMRC, Bhubaneswar. Sickle cell gene was found in *Bhatta* (18.1%) and *Paraja* (14.8%). Frequency of G6PD enzyme deficiency was high in *Paraja* compared to other tribes. The frequency of Rhesus negative blood group was very low (0.2%) in the three tribes.

Prevalence of Haemoglobinopathies among Gonds and the Scheduled Castes of Seoni and Balaghat

Sickle haemoglobin is the main form of haemoglobinopathy in the study area. In the study done by RMRC, Jabalpur, the prevalence of sickle haemoglobin has been found higher among the scheduled castes than the scheduled tribes. In Seoni district, it was 21.7% among the scheduled castes as compared to 18.9% among the scheduled tribes. In Balaghat district, the prevalence was 18.3% among the scheduled castes and 15.3 among the scheduled tribes. The prevalence of β Thal was less than 2%. The prevalence of G6PD was 1.8% in Seoni and 1.4% in Balaghat respectively. Anaemia was very common in the study area. The prevalence was higher among the Gonds.

Morbidity Profile of Sickle Cell Disease and related Disorders in Central India-A Cohort Study

One hundred patients of sickle cell disease, already diagnosed, have been enrolled by RMRC, Jabalpur. Clinical observations of these patients have been recorded on structured proformae.

All the patients reported bony pain, recurrent fever, abdominal pain *etc.* About half of the patients reported that painful crises were more common in winter and rainy seasons. Splenomegaly was very common (70%) among the patients. The size of spleen varied from 1 to 9 cm. The infection of malarial parasite was ruled out among the patients with fever. The study is in progress.



Basic Medical Sciences

Research in basic medical sciences is carried out both in Council's permanent institutes/centres as well as at various research institutions, medical colleges and universities in the country. The findings of studies carried out in the area of biochemistry, pharmacology, physiology and traditional medicine are highlighted.

BIOCHEMISTRY

Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by the production of anti-DNA antibodies. The origin of antibodies and the etiology of SLE is not yet known. There are many compounds (polyamines, histones and nuclear matrix elements) in the vicinity of DNA which may react upon irradiation. These polybasic molecules found in the cell have a great affinity for acidic constituents such as DNA and their interaction might play a role in the pathogenesis of SLE. A study has been sponsored by the Council at Aligarh Muslim University, Aligarh to characterize the photoconjugates between positively charged amino acids, DNA fragments and polynucleotides respectively. Calf thymus DNA fragments of about 200 base pair (bp) and poly-nucleotides were covalently crosslinked with lysine or arginine under UV light. Both lysine and arginine were found covalently photoconjugated to DNA and poly(dC) respectively, and resulted in the formation of crosslinks. The photoadducts were characterized by various physico-chemical methods. Nearly five lysine residues were found to be in the photobound state between one helical turn of DNA, while one arginine residue was present between four helical turns. Photoaddition of lysine and arginine to 200 bp DNA and to poly (dc) rendered them thermodynamically more stable than their native analogues. After systemic characterization of the 200 bp photoadducts, they were used as antigens for generation of antibodies in experimental animals. Both the lysine and arginine photoadducts of 200 bp were highly immunogenic in rabbits, inducing high titer antibodies. The induced antibodies were found to be non-

precipitating in nature. A strong recognition of DNA - lysine photoadduct was observed with anti-DNA - autoantibodies found in the sera of patients with SLE. Poly(dc) - lysine was recognised more strongly than the DNA-lysine photoadduct. Poly(dC) - lysine appears to provide an immuno-dominant epitope(s) for SLE autoantibody recognition. The result suggests possible involvement of DNA-lysine photoadduct or similar modified structure(s) as a potential trigger for anti-DNA autoantibody production.

PHARMACOLOGY

Nicotine, a major component of cigarette smoke plays an important role in the development of cardiovascular disease and lung cancer in smokers. A study was conducted at University of Kerala, Thiruvananthapuram on the effects of antioxidants isolated from lemons and *Allium* species as compared to α -tocopherol on the damages induced by nicotine in rats. The results showed that the administration of nicotine in rats causes increase in lipid levels as well as lipid peroxidation products in serum and tissues. Simultaneous administration of garlic or onion oil or SACS (S-allylcysteine sulfoxide) from garlic, or SMCS (S-methylcysteine sulfoxide) from onion, or hesperidine (from lemon) effectively counteracted the deleterious effects of nicotine administration. The antioxidant effects of these natural products are comparable to those of α -tocopherol. Administration of these antioxidants improved the natural antioxidant defence mechanisms of the body.

A project aimed to develop novel uterine relaxants by modification of isoxsuprine structure (by structure hybridisation of isoxsuprine with atenolol, metoprolol and acebutol), which would reduce tachycardia was undertaken at IRR, Mumbai. The physico-chemical properties necessary to achieve potent activity were also taken into consideration during the design of the compounds. Thus a series comprising eight compounds

was synthesized. The compounds were evaluated for uterine relaxant activity first in isolated rat uterus (*in vitro*) and then in pregnant rats (*in vivo*). In pregnant rats, delay in onset of labour was used as a measure of uterine relaxant activity. The mechanism of action of these compounds was established by cAMP (3H) assay using homogenized uterine strips. Test compounds exhibited potent uterine relaxant activity both in *in vitro* and *in vivo* methods. No adverse effect on the pregnant rats or their pups was noted. They relaxed the uterus by stimulating α -adrenergic receptors which led to increased production of cAMP. When the compounds were evaluated for cardiac activity in isolated guinea pig atrium and on dog heart, they did not produce tachycardia and thus they were found safe when compared to isoxsuprine hydrochloride.

PRE-CLINICAL TOXICOLOGY

The Council has sanctioned a Pre-Clinical Toxicology Unit at NIN, Hyderabad. The Unit has carried out pre-clinical toxicology studies on alpha interferon of Shanta Biotech and initiated studies on DNA vaccine for rabies developed by IISC, Bangalore.

CLINICAL PHARMACOLOGY

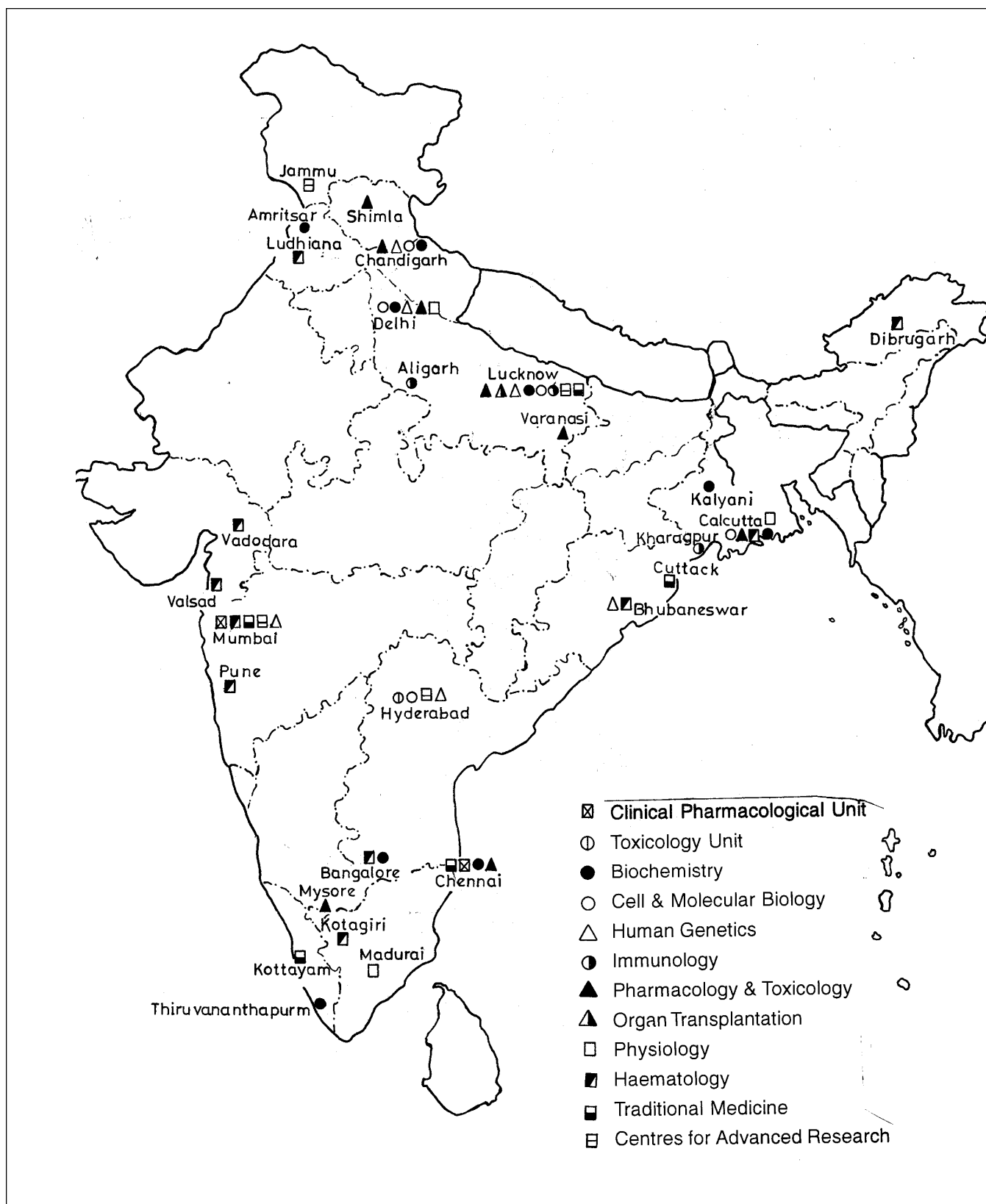
Clinical Pharmacology Unit was set up at TRC, Chennai in collaboration with Institute of Pharmacology, Madras Medical College, Chennai. The Unit carried out dose related pharmacokinetic studies on rifampicin and ofloxacin. HPLC methodology for estimating rifampicin was standardized. Bioavailability studies of rifampicin and ofloxacin in plasma and ofloxacin in saliva are now being undertaken. The methods have been standardized and the Centre is recognised by Drug Controller of India for such studies. The protocols have been approved and already 5 companies have registered. Safety and efficacy studies and adverse drug reaction monitoring when rifampicin, isoniazid and pyrazinamide are administered alone or in combination would be undertaken besides pharmacokinetics of anti-TB drugs in diabetic patients and interactions of anti-TB drugs in children.

PHYSIOLOGY

A study was completed at AIIMS, New Delhi during the year to study the role of angiotensin converting enzyme (ACE) inhibitors in myocardial stunning. In open-

chest pentobarbitone anaesthetised cats, the left anterior descending coronary artery was occluded for a period of 15 min followed by 60 min of reperfusion to produce myocardial stunning (MS). Saline/drug (Catopril, BK₂ receptor antagonist Hoe and Losartan) was administered 5 min before reperfusion. In the vehicle-treated group, the plasma renin activity was enhanced, following ischemia as well as reperfusion, signifying the involvement of renin angiotensin system in MS. Global hemodynamic function (mean arterial pressure, left ventricular-end-diastolic-pressure, peak (+) and (-) dP/dt was also depressed alongwith depletion of myocardial high energy phosphate compounds, rise in both plasma thiobarbituric acid reactive substances and creatine phosphokinase and depletion of endogenous myocardial antioxidants (glutathione, superoxide dismutase and catalase), strongly suggesting the involvement of oxidant stress in MS. The results showed that both Hoe-140 (200 mg/kg/over 2 min. *iv*) and losartan (5 μ g/kg/over 15 min. *iv*) when administered alone effected a complete recovery of hemodynamic functions alongwith significant improvement in the metabolic status. The results of the present study indicated significant role played by the ACE independent pathway in the etiopathogenesis of MS.

To assess the impact of specific nutritional and psychological interventions on the performance of young sports persons, a community based controlled intervention study was undertaken at Sports Medicine Centre, West Bengal on a sample of 65 adolescent (10-14 yr) male, residential trainee footballers selected on the basis of physical, nutritional and sports performance levels and exposed to uniform training in soccer. Random allocation to different predesigned nutritional intervention schedules of high carbohydrate, high-protein, high-fat and balanced diet regimes was done for 17 weeks continuously except in control group. The existing diet was modified and supplemented as required. Half of the subjects in each group also received specific psychotherapeutic interventions. Pre and post-intervention assessment of performance level was done through field tests in physical fitness, motor performance and specific sports skills, along with selected laboratory parameters. Balanced diet had generalized improvement in agility. 35% fat-rich diet in late phase improved motor performance and sports skills. Carbohydrate-rich diet improved pulse rate and cardio-respiratory endurance alongwith other changes. Psychotherapeutic



Major ICMR Research Projects in Basic Medical Sciences

interventions caused improvement in psycho-laboratory and performance parameters, sports skill and motor performance.

TRADITIONAL MEDICINE AND MEDICINAL PLANTS RESEARCH

The multidisciplinary networking for the traditional medicine research programmes continued with central co-ordination. The national task force trials were continued on traditional remedies for diabetes. A Centre on Drug Development from Natural Products at CDRI, Lucknow and the Centre for Clinical Pharmacology in Traditional Medicine at Seth G.S. Medical College and K.E.M.Hospital, Mumbai were continued during the year under report. The Centre for Standardisation, Quality Control and Formulation of Natural Products/Selected Herbal Remedies at RRL, Jammu and Central Biostatistical Monitoring Unit at NIE, Chennai continued to give their support to the Programme. A Unit for Standardisation and Quality Control of Selected Herbal Remedies/Natural Products at National Institute of Pharmaceutical Education and Research, Chandigarh has been initiated.

During the year, a Clinical Pharmacology Unit was established at TRC, Chennai to study herbal immunomodulators and hepatoprotective drugs as adjunct to anti-tuberculosis drugs. A second Centre for Clinical Pharmacology has also been set up for studies on pharmacokinetics, bioavailability and herb-drug interactions at the BYL Nair Hospital, Mumbai. Cultivation of selected medicinal plants and agro-technology for endangered species of *Picrorrhiza kurroa* has been taken up at the Institute of Himalayan Bioresource Technology, Palampur. The programme has an effective networking between institutions and other agencies like CSIR, DBT and Department of Indian Systems of Medicine and Homoeopathy to avoid duplication, strengthen infrastructure and improve expertise.

Traditional Remedies for Diabetes Mellitus

Multicentric, randomised, double blind clinical trials on *Vijaysar* (*Pterocarpus marsupium*) were completed at SCB Medical College, Cuttack, Madras Medical College, Chennai and Medical College, Kottayam. The study validated the findings that *Vijaysar*, although a safe alternative, required a higher dosage as compared to allopathic drug. A new study was initiated at the same

centres to see if it was equally effective in treating patients with uncontrolled diabetics.

Standardisation, Quality Control and Formulation of Natural Products/Selected Herbal Remedies

The Centre for Advanced Research at the Regional Research Laboratory, Jammu continued studies on *Vijaysar*. Stability studies on *Vijaysar* capsules under natural weather conditions were continued. Samples of heartwood and aerial parts, mainly leaves of *P.marsupium* collected from different locations are being studied for active constituents. The LD₅₀ data are being generated in two animal species (rat and mice). Studies on its effect on the cardiovascular system by *i.v.* and intraduodenal routes in anaesthetized animals and isolated tissues are also being undertaken. Modernization, optimisation and upscaling of the process of extraction of *Vijaysar* has commenced. Hypoglycaemic activity of VS-04 and VS-09 was confirmed in fasted and glucose loaded rats and experiments were carried out in the streptozotocin model. An activity patent application on VS-04 has been submitted and work on synthesis of VS-04 initiated. The water insoluble residue remaining at the end of the isolation process is being tested for hypoglycaemic activity.

Varun (*Crataeva nurvala*) is used for the treatment of urolithiasis. General pharmacological, acute and sub-acute toxicity and stability studies and chemical standardisation of its dried aqueous extract are being carried out. Pharmacological activity of marker compounds of aqueous extract against experimentally induced urolithiasis in rats is being studied.

A new mechanical device was developed to manufacture standardised *Kshaarasootra* (medicated) threads to facilitate technology transfer to the pharmaceutical industry.

Drug Development From Natural Products

The work carried out at the Advanced Centre at CDRI, Lucknow pertained to *Picrorrhiza kurroa*, *Terminalia chebula* and *Centella asiatica*.

Dossier on Phase II multicentric trial on Picroliv, a product from *P.kurroa* was submitted to Drug Controller of India for approval to initiate Phase II trial. Stability studies on Sorensen buffer have also been carried out. HPLC fingerprint was developed and 27 compounds were

resolved. Pharmacokinetics with *in situ* absorption studies in recirculation model using rat intestinal loop and intraduodenal infusion were carried out.

Accelerated stability study of alcoholic extract (D003) and pure active marker of *T.chebula* showed that both the samples were stable for more than 2 years. Long-term stability study and chemical fingerprinting of D003 is being done. When compared to *Panax ginseng* it appeared to be superior. Effects on the cardiovascular and gastrointestinal systems and immunomodulatory functions were also studied.

Chemical fingerprinting and long-term stability study of *C.asiatica* is under progress. Wound healing activity was tested by observing the angiogenic effect, antioxidant profile, efficacy in immunocompromised wound and effect on DNA and protein content. Effect on learning and memory and anti-stress activity is being studied. Regulatory pharmacology studies are also being carried out.

Clinical Pharmacology in Traditional Medicine

At the Advanced Centre at Seth G.S. Medical College and K.E.M. Hospital, Mumbai, studies on *neem* oil for wound healing, mechanism of action of *Pterocarpus marsupium* and on a medicated oral rehydration solution were continued.

An in-house *neem* oil (*Vranaropak*) preparation based on Charaka's methodology was standardised and its efficacy was compared to glycerine ichthammol and a commercial *neem* oil preparation. A randomised, observer blind, parallel group clinical trial was designed. Of the 7 patients recruited, 2 have completed the study. The study on angiogenesis using subcutaneous sponge model for blood flow measurement of technetium clearance in Wistar rats has continued.

The ingredients of oral rehydration solution *viz.* Ginger (*Zingiber officinalis*), Cumin (*Cuminum cyminum*) and *Nagarmotha* (*Cyperus rotundus*) strengthen the intestinal mucosal barrier. Standardization of ginger extract is being carried out. Experimental studies were

done using *C.rotundus*. Red kidney beans were used as control which was compared to raw red kidney beans alone and in combination with *C. rotundus*. Bacterial colony count in the intestine and mesenteric lymph nodes came down with the latter. Difference in activity was seen between whole seed and powdered red kidney beans.

Development of Standards of Therapeutically Important Indian Medicinal Plants

Lack of documented evidence about the efficacy, toxicity and non-availability or inadequacy of standards for checking the quality of medicinal plants has been the major lacuna in the wider acceptance of herbal drugs. Despite there being a large number of single drugs and formulations in therapeutic use, very few concerted efforts have been made to develop standards. This has prevented modernization or modification of the methods of their preparation or production, as there is no way to establish the equivalence of the product made by the modified method with the original product. The standardized drugs of well defined consistent quality are needed for reliable clinical trials and therapeutic use.

A programme has been initiated to develop standards for 160 therapeutically important medicinal plants, in a period of 3 years employing sophisticated analytical techniques. It is planned to prepare monographs on them which would focus on phytochemistry, markers, their structure, pharmacology, toxicology, clinical aspects, safety, side effects/contraindications, if any, references and illustrations, besides covering other aspects like general description, synonyms, geographical sources and diagnostic description, *etc.*

The programme has been initiated at five institutions *viz.* Tropical Botanic Garden and Research Institute, Thiruvananthapuram; National Botanical Research Institute, Lucknow; RRL, Jammu; BV Patel Pharmaceutical Education and Research Development Centre, Ahmedabad and National Institute of Pharmaceutical Education and Research, Mohali.



Supporting Facilities

The statistical and epidemiological studies were conducted at Council's National Institute of Epidemiology (NIE), Chennai and Institute for Research in Medical Statistics at New Delhi. A 2-year Master's Programme in Applied Epidemiology has been initiated at NIE, Chennai during the year.

NATIONAL INSTITUTE OF EPIDEMIOLOGY, CHENNAI

With a view to strengthen epidemiological base in the country, National Institute of Epidemiology (NIE), Chennai has started a 2-year field training programme affiliated to Sree Chitra Tirunal Institute of Medical Sciences and Technology, Thiruvananthapuram for award of Master of Applied Epidemiology (MAE) degree. The training methodology consists of 3-month intensive course work at the Institute followed by 21 months of field placement. It would be on-the-job training through a process of learning at the trainee's own field station as well as at selected ICMR Institutes. The trainees will be confronted with the realities of social, economic and managerial problems that directly affect the organization of health care and will thus be trained to consider wide range of diagnostic, analytical and intervention strategies in dealing with health problems. Ten students comprising district level medical/health officers engaged in public health activities from various parts of the country were selected for the Course.

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

The IRMS, New Delhi completed evaluation of the integrated Nutrition and Health Project (INHP) carried out in 7 States (Andhra Pradesh, Bihar, Madhya Pradesh, Orissa, West Bengal, Rajasthan and Uttar Pradesh). In this study four categories of outcome indicators, namely, antenatal care, receipt of supplementary food from *Anganwadi* centres (AWC),

immunization of children and infant feeding practices were considered. It was observed that the percent women receiving 3 + ANC check ups during their pregnancy and percent pregnant women receiving 2+ doses of TT has increased in 5 of the 7 states. However, increase in percent pregnant and lactating women and children in the age group 6-24 months receiving food from AWC was found in all the 7 states, though the degree of increase varied. Five states, except Rajasthan and Uttar Pradesh showed increase in percentages of infants fully immunized by the age 1 year, in the final evaluation survey, as compared to their levels in the baseline survey. There was a general increase in the percentage of infants put on breast milk in the first 8 hours of life in all the 7 States. The states of Madhya Pradesh, Uttar Pradesh and West Bengal had shown higher percentage of children on exclusive breast feeding for first 4 months.

It was found that five of the seven states had achieved targets and Andhra Pradesh and Rajasthan have fallen short of the target.

BIOMEDICAL ETHICS

The Council revised 'Ethical Guidelines on Biomedical Research for Human subjects' prepared by Central Ethics Committee on Human Research under the Chairmanship of Honourable Chief Justice Sh. M.N. Venkatachaliah. It comprises chapters on Specific Principles in the areas of Clinical Research, Human Genetics, Transplantation including Foetal Tissue Transplantation, Epidemiology and Assisted Reproductive Technologies.

A WHO sponsored workshop was conducted at Chennai for sensitisation and dissemination of Council's ethical guidelines. The Central Ethics Committee of the Council will in future handle all ethical issues and matters of national significance and those referred to the Council by the Government of India.

INDO-FOREIGN CELL

The Indo-Foreign Cell (IFC) set up in the early 1980s operating from the Headquarters Office in New Delhi, co-ordinates collaboration in biomedical research between India and other countries/international agencies.

During the year 2000-2001, the IFC facilitated organisation of two Indo-German Workshops, one on RF/RHD in Goa in April 2000 and another on tuberculosis held at Braunschweig, Germany in September, 2000. The IFC also supported the visit of Government of India delegates for Indo-Russian Workshop on Biomedical Technology/Biomolecular and Biomedical Research held in Moscow from 26-29 June, 2000. Several important international visits/meetings were coordinated by IFC during the year 2000-2001. The IFC arranged (with financial support) a number of visits by scientists to and from India under bilateral programmes in the field of biomedical sciences and public health. The ICMR serves as the Secretariat for the Health Ministry's Screening Committee which considers research proposals involving foreign collaboration/assistance.

In keeping with successful trend of Indo-US cooperation in biomedical/health sciences two Indo-US Joint Statements have been signed during the year

by the Ministers of Health of India and USA. These include one on Prevention of STDs/HIV/AIDS and another on Maternal and Child Health and Human Development Research.

INTELLECTUAL PROPERTY RIGHTS

The IPR Cell of the ICMR brought out a document entitled "Contribution of ICMR in the area of Intellectual Property Rights" which provides details of patents obtained/filed, vaccines/diagnostics/kits and products/technologies developed. The IPR Cell is in the process of finalising a panel of patent attorneys for filing applications for patents and also to handle other patent related issues of the ICMR. The scientists of ICMR Hq. and Institutes are being provided technical inputs in terms of advice and assistance on IPR related issues. The IPR cell is being strengthened in terms of manpower as well as infrastructure.

TRAINING PROGRAMMES

The IRMS, Delhi continued to provide training to B.Sc. and M.Sc. students of various universities and to medical records technicians at Safdarjang Hospital. Other ICMR institutes such as NIV, Pune; MRC, Delhi; VCRC, Pondicherry; NIN, Hyderabad; RMRI, Patna; IRR, Mumbai and IOP, Delhi conducted training programmes in their respective areas.



Publication, Information and Communication

The Council continued to bring out periodical publications – the Indian Journal of Medical Research, ICMR Bulletin, ICMR *Patrika* and Annual Reports, both in English and Hindi during the year 2000-2001.

PUBLICATIONS

Periodicals

The Indian Journal of Medical Research (IJMR) continued to be indexed and abstracted by all major global awareness and alerting services. As per the suggestions/recommendations made by the IJMR Expert Group in November 1999, the IJMR is being published with a new lay out from January 2001. A number of articles published in the IJMR have been featured as news items in various newspapers during the period under report.

The ICMR Bulletin continued to publish articles on topics of general interest. The December 2000 issue of the Bulletin featured an article on "A world AIDS campaign where men make a difference: A challenge for the men in the third millennium!", to commemorate the World AIDS Day (December 1, 2000), and the March 2001 issue of the Bulletin published an article on "Directly observed treatment short-course: Tuberculosis, cure for all", to commemorate the World Tuberculosis Day (March 24, 2001). Some of the other interesting topics featured in the Bulletin during the period under report included Japanese encephalitis virus infection in mosquitoes and its epidemiological implications; Need and feasibility of providing assisted technologies for infertility management in resource-poor settings; Ethical guidelines for biomedical research on human subjects; Research achievements of the Central JALMA Institute for Leprosy, Agra, *etc.*

The monthly Hindi publication, the ICMR *Patrika* was brought out regularly during the year. Three articles originally written in Hindi were also published. Some of the articles were reproduced in other popular science magazines. This year the *Patrika* was awarded the *Utkrishta Patrika Samman* during the Millennium World Hindi Conference.

The English and Hindi versions of the Annual Report of the Council for the year 1999-2000 were brought out in an attractive and informative manner with the inclusion of colour photographs, and lists of publications, ICMR aided projects, fellowships, training courses, *etc.*

Other Publications

On popular public demand, the multi-coloured pictorial booklet 'Dietary Guidelines for Indians' was published in Tamil and Kannada.

Monograph on Medicinal Plants of India

Preparation of the Monograph on Medicinal Plants of India is continuing. Multidisciplinary research data on 400 plant species have been collected and compiled; the information on 100 plant species is under computerization.

Monographs on Medicinal Plants for Diseases of Public Health Importance

Preparation of monographs on some plants used for treatment of diseases of public health importance has been initiated. The monographs would incorporate information on the diseases (including etiopathogenesis) and plant drugs as given in the ancient texts (indigenous system of medicine) and research data (pharmacological, toxicological, clinical, phytochemical, pharmacognostic) generated through scientific studies on these plant remedies.

The preparation of these monographs has been initiated in the following thrust areas: Immuno-modulators, kala-azar, malaria, filariasis, diabetes mellitus, liver disorders and anti-inflammatory drugs.

INFORMATICS AND COMMUNICATION

Biomedical Information

The ICMR-NIC Centre for Biomedical Information continued to cater to the biomedical information needs of the medical community. During this period, five medical colleges/organizations registered as MEDLARS User Centres *i.e.* Pravara Medical Trust, Loni; Rangaraya Medical College, Kakinada; Northern Railway Central Hospital, New Delhi; Narayana Medical College, Nellore and Rehabilitation Council of India, New Delhi.

The indexing of journals for the IndMED database was continued. This is a bibliographic database of Indian Biomedical Periodicals developed and maintained at the Centre and at present contains data from 75 journals and can be accessed over Internet. It is proposed to include data from 1986 onwards. The Union Catalogue is being updated and the holdings data for 1999-2000 are being collected.

The Centre has developed a web page giving details of the services being provided. The web page, <http://indmed.nic.in> can be accessed by users within and outside the country. This functions as a portal to the various health/biomedical resources accessible over the Internet; links have been provided to prevalent diseases' web pages. A web enabled BRS/SEARCH training tutorial was developed for the benefit of those who cannot attend the training programmes; the complete training manual has also been made available on the web page.

Workshops on Biomedical Research and the Internet were organized at NIC, New Delhi, Pune and Bhubaneswar for the medical/library professionals. Resource persons were also from the medical and the library fields. These workshops also included extensive hands-on sessions.

A training programme was conducted on Online Searching of Biomedical Databases at NIC, New Delhi. This 5-day programme included lectures on information retrieval techniques and extensive hands-on sessions. The participants were from the User centres as well

as from NIC state and district centres. Similar programmes were conducted online at NIC Centres at Kurnool, Coimbatore and Aurangabad for the district staff. In addition, User Awareness programmes were conducted for doctors at NIMHANS, Bangalore, Government Hospitals in Kurnool, Coimbatore, Pondicherry and Karaikal district (TN).

Scientometrics

Analysis of the 1999 research output of ICMR in terms of publications from all the institutes including RMRCs provides for the first time details on the performance indicators especially average impact factor (IF) per published paper of the Council as a whole and of individual institutes. In addition, the Directory of Journals Publishing Papers from ICMR Institutes is being updated till 1999. The sponsored project "National Mapping of Science – Biomedical Sciences" of the National Information Systems for Science and Technology (NISSAT), Department of Scientific and Industrial Research, is also underway to assess the contributions of Indian researchers in the field of biomedical sciences in two databases *viz.* Tropical Diseases Bulletin and Index Medicus for the disk/calendar year 1998.

A total of 329 papers were published by the ICMR institutes during the calendar year 1999. Among the ICMR institutes, MRC, Delhi contributed the maximum number of publications (36) followed by NICED, Kolkata (34) and NIN, Hyderabad (26). The average number of publications for the Council was 13.71 per institute. Of the 329 papers, 151 (45.90%) were covered by Journal Citation Reports (JCR)-1999. NICED had the maximum share (27) of papers whereas four institutes *viz.* ICMR Genetic Research Centre, Mumbai; EVRC, Mumbai; IRMS, New Delhi and RMRC, Jabalpur did not publish any paper in a JCR covered journal. In 12 institutes, coverage of papers in JCR journals was much below the Council's average *i.e.* 6.29 papers per institute. 151 papers appeared in 81 journals with 51 journals having IF greater than or equal to 1 and 30 journals having IF less than 1. New England Journal of Medicine had the highest IF (28.857) whereas Indian Veterinary Journal had the lowest IF (0.050). Some of the publishing journals having IF in the range of 28.857-5.143 were as follows: New England Journal

of Medicine, (ICPO, New Delhi), Lancet (NIV, Pune; NICED, Kolkata); Journal of Biological Chemistry (NICED, Kolkata), Journal of Immunology (RMRC, Bhubaneswar), Oncogene (ICPO, New Delhi), Journal of Virology (NIV and NARI, Pune), and British Medical Journal (NIN, Hyderabad). The average impact factor per published paper for the Council as a whole was 1.861. A total of 769 authors contributed these 329 papers; 59 different authors contributed 4 or more papers each.

In order to sensitize ICMR institutes about the different aspects and importance of R&D evaluation especially publication-based indicators, a Workshop was conducted at MRC, Delhi. This Workshop provided orientation to scientists to the SCI-based indicators. It is planned to undertake similar exercises at different ICMR institutes in the near future.

In the ongoing project on National Mapping of Science – Biomedical Sciences, screening of Tropical Diseases Bulletin has been completed. The analysis shows that a total of 412 papers (9.64%) have been contributed by Indian scientists out of 4272 papers covered during 1998. These papers appeared in 86 different JCR/non JCR journals. Highest IF journal (28.66) was New England Journal of Medicine followed by Lancet (11.793). Maximum papers (41) appeared in the Indian Journal of Medical Research. The subject category contributing the maximum number of papers was Bacteriology and Bacterial Diseases (198 papers) followed by Virology (48 papers). AIIMS, New Delhi with 22 papers was identified as the most prolific institute followed by CMC, Vellore (19 papers). The analysis of Index Medicus for the disk year 1998 is in progress.

Bioinformatics Centre

The Bioinformatics Centre set up in the Council during 1999, remained fully functional during 2000-2001. The Centre continued its ongoing activity of maintaining databases of extramural projects, scientists associated with ICMR, Management Information System (MIS) of the Indian Journal of Medical Research (IJMR) and seminar/symposia/workshops funded by the Council.

Several new features like abstracts, guidelines for submitting manuscripts and searchable information of IJMR, profiles of ICMR institutes, information on

research projects completed and ongoing in ICMR institutes, biodata and publications of the Council's scientists and other ICMR publications have been added to the ICMR website. All the databases used for the website were shifted from DB2 to Microsoft SQL server. Database search programmes were rewritten using ASPs to increase efficiency and speed of search operations.

The Bioinformatics Centre with assistance from the WHO organized workshops on the Use of Information Technology in Biomedical Research in New Delhi and Mumbai respectively for the benefit of ICMR scientists of the institutes located in northern and western India. The workshops were divided into lectures and practice sessions and provided the participants online exposure of working in a network environment, internet browsing, contemporary research work using bioinformatics techniques, creating websites, etc.

The Council is contemplating creating Bioinformatics Centres of ICMR in leading biomedical education/research institutes in the country under the Genome Research Programme of the Council. The Bioinformatics Centre at ICMR Headquarters will work as the coordinating unit for these centres. These centres are expected to start functioning during 2001.

Work on the networking of 7 ICMR institutes initiated during 1999-2000 was continued during the year.

Dissemination of Information

The Council and its various Institutes/Centres organised various activities for dissemination of biomedical information as also contributions/achievements of the Council to different groups of people including the common man.

On account of *Rajbhasha* Golden Jubilee year and Hindi Day a scientific debate in Hindi on Implications of the Human Genome Study ("*Manav Genome Adhyayan ke Bhavi Prabhav*") was organized at ICMR Hqrs. in September 2000 in which scientists from ICMR Hqrs. and Delhi based Institutes participated.

The ICMR Institutes/Centres celebrated the National Science Day (NSD) in February/March 2001 by

organising lectures/discussions, open houses/question-answer sessions, display/demonstrations/exhibitions, *etc.* for the general public and elocution/debate/essay/drawing/painting/quiz competitions for school children. The theme of the NSD for the year 2001 was Information Technology for Education.

Seven Institutes/Centres *viz.* RMRC, Dibrugarh; NIV, Pune; RMRI, Patna; NARI, Pune; RMRC, Jabalpur; VCRC, Pondicherry and NIE, Chennai organized several programmes in Hindi, such as popular lectures, symposia, demonstrations, debate competitions, audio-visual programmes, health camps *etc.*

Human Resource Development

For human resource development in biomedical communication, workshops on biomedical communication were organized in medical colleges. A workshop on scientific communication was held at Kasturba Medical College, Manipal during December, 2000. Two workshops for the librarians of ICMR institutes on emerging technologies for effective management of library and information services were held in January and February, 2001 at the National Informatics Centres, Hyderabad and Pune respectively.



ICMR Permanent Institutes/Centres

1. National Institute of Nutrition
Jamai-Osmania
Hyderabad-500007.
2. National Institute of Virology
20-A, Dr. Ambedkar Road, Post Box No.11
Pune-411001.
3. Institute for Research in Reproduction
Jehangir Merwanji Street
Parel, Mumbai-400012.
4. Tuberculosis Research Centre
Mayor V.R. Ramanathan Road
Chetput, Chennai-600031.
5. Institute of Immunohaematology
13th Floor, New Multistoreyed Building
KEM Hospital Campus
Parel, Mumbai-400012.
6. National Institute of Cholera and Enteric Diseases
P-33, CIT Road Scheme XM
Post Box No. 177, Beliaghata
Kolkata-700010.
7. Institute of Pathology
Safdarjang Hospital Campus, Post Box No. 4909
New Delhi-110029.
8. National Institute of Occupational Health
Meghani Nagar
Ahmedabad-380016.
9. Vector Control Research Centre
Medical Complex, Indira Nagar
Pondicherry-605006.
10. National Centre for Laboratory Animal Sciences
National Institute of Nutrition
Jamai-Osmania
Hyderabad-500007.
11. Food and Drug Toxicology Research Centre
National Institute of Nutrition
Jamai-Osmania
Hyderabad-500007.

12. Central JALMA Institute for Leprosy
Post Box No. 101, Tajganj
Agra-282001.
13. Malaria Research Centre
22, Sham Nath Marg
Delhi-110054.
14. Institute for Research in Medical Statistics
ICMR Headquarters Campus
Ansari Nagar
New Delhi-110029.
15. National Institute of Epidemiology
1, Sathyamurthi Road
Chetput
Chennai-600031.
16. Institute of Cytology and Preventive Oncology
Maulana Azad Medical College Campus
Bahadur Shah Zafar Marg
New Delhi-110002.
17. Enterovirus Research Centre
Haffkine Institute Compound
Acharya Donde Marg, Parel
Mumbai-400012.
18. Rajendra Memorial Research Institute of Medical Sciences
Agam Kuan
Patna-800007.
19. Centre for Research in Medical Entomology
Post Box No. 11,
4-Sarojini Street, Chinna Chokkikulam
Madurai-625002.
20. ICMR Genetic Research Centre
Jehangir Merwanji Street
Parel
Mumbai-400012.
21. National AIDS Research Institute
Post Box No. 1895,
Plot No.73, Block G, Bhosari Industrial Estate
Pune-411026.

Regional Medical Research Centres

1. Regional Medical Research Centre
Nandankanan Road
Chandrasekharpur
Bhubaneswar-751016.
2. Regional Medical Research Centre
NE Region, Post Box No. 105
Dibrugarh-786001.
3. Regional Medical Research Centre
Post Box No.13, Farzand Ali Market,
Port Blair-744104.
4. Regional Medical Research Centre for Tribals
Nagpur Road
Jabalpur-482003.
5. Desert Medicine Research Centre
Post Box No. 122, New Pali Road
Jodhpur-342005.
6. Regional Medical Research Centre
National Highway No.4
Belgaum-590010.

Appendix III

ICMR Centres for Advanced Research

1. ICMR-NIC Centre for Biomedical Information
National Informatics Centre
Lodi Road
New Delhi-110003.
2. Centre for Advanced Research on Standardisation, Quality Control and Formulation
of Selected Traditional Remedies/Natural Products
Regional Research Laboratory
Canal Road
Jammu-Tawi-180001.
3. Centre for Advanced Research for Health Consequences of
Earthquake Disaster with Special Reference to Mental Health
B.J. Medical College and Sasoon General Hospital
Pune-411001.
4. Centre for Advanced Research for Drug Development from Natural/Plant Products
Central Drug Research Institute
Chattar Manzil Palace
Lucknow -226001.
5. Centre for Advanced Research for Clinical Pharmacology in Traditional Medicine
Seth G.S. Medical College and K.E.M. Municipal Hospital
Parel
Mumbai-400012.
6. Centre for Advanced Research for Pre-Clinical Toxicology
National Institute of Nutrition
Jamai-Osmania
Hyderabad-500007.
7. Advanced Centre for Cellular and Molecular Reproduction
Indian Institute of Science
Sir C.V.Raman Avenue
Bangalore-650012.
8. Centre for Advanced Research on Clinical Pharmacology
T.N. Medical College
Dr. A.L. Nair Road
Mumbai-500008.
9. Centre for Research on Aging and Brain
University of Hyderabad
P.O. Central University
Gachibowli
Hyderabad-500046.

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Training Programmes Conducted by ICMR Institutes during 2000-2001

Diarrhoeal Diseases

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

- JICA/NICED Training Course on Molecular Epidemiology of Diarrhoeal Diseases with special Emphasis on Cholera (November 27 - December 6, 2000).
- In-House Training Programme on Application of Behavioural Sciences in Health Systems Research (March 23, 2001).

Malaria

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

- Reorientation Course in Malariology for PHC Medical Officers of North-Eastern Region of India (January 8-12, 2001).
- Training Course for Malaria Microscopists of Assam (February 12-16, 2001).

Filariasis

At the Vector Control Research Centre, Pondicherry:

- WHO-TDR Workshop on Development and Evaluation of Advocacy Measures for Sustained Compliance with DEC Mass Treatment for the Control of Lymphatic Filariasis (July 15-18, 2000).

Vector-borne Diseases/Entomology

At the Vector Control Research Centre, Pondicherry:

- Regional Course on Comprehensive Vector Control (August - September 2000).
- Postgraduate Diploma in Medical Entomology (July 2000 - May 2001).

Molecular Immunology

At the Vector Control Research Centre, Pondicherry:

- Training Course in Applied Molecular Immunology (July - December 2000).

Reproductive Biology

At the Institute for Research in Reproduction, Mumbai:

- Advanced Workshop in Human Semenology (September 4-16, 2000).
- Training Course in Immunological Techniques and Their Application (December 8-15, 2000).
- Workshop on Dissemination of Use of Resazurin Reduction Test and Sperm Function Test for Infertility (February 5-9, 2001).

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Certificate Course on Endocrinological Techniques and their Application (August 1 - September 15, 2000).

Nutrition

At the National Institute of Nutrition, Hyderabad:

- Training Course on Techniques for Assessment of Nutritional Anaemias (December 1-10, 2000)
- M.Sc. in Applied Nutrition (June 1, 2000 - March 16, 2001).
- Postgraduate Certificate Course in Nutrition (January 3 - March 15, 2001).

Oncology

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

- National Workshop on Early Detection of Cervical Cancer – Alternative Strategies (January 6-8, 2001).

Haematology

At the Institute of Immunohaematology, Mumbai:

- Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 1 - September 23, 2000).
- Training Course in Blood Group Serology and Blood Bank Methodology for Blood Bank Technicians (August 1-31, 2000).

Laboratory Animal Technology

At the National Centre for Laboratory Animal Sciences, Hyderabad:

- Training Course for Laboratory Animal Technicians (June 15 - July 31, 2000).
- Training Course for Laboratory Animal Supervisors (September 4 - November 30, 2000).

ICMR Aided Seminars/Symposia/Conferences/ Workshops

The following ICMR aided Symposia/Seminars/Workshops/Conferences were held during the year 2000-2001:

1. Symposium on Relevance of Environmental Security in the New Millennium organised by National Environmental Science Academy at Pondicherry (April 5-7, 2000).
2. National Symposium on Ethics in Administration of Sciences organised by Society for Scientific Values at Hyderabad (April 8-9, 2000).
3. Young Scientists Workshop on Identification and Diagnosis of Parasites of Biomedical and Zoonotic Importance organised by School of Life Sciences, North-Eastern Hill University, Shillong (April 17 - May 3, 2000)
4. XIV National Congress of Parasitology : Parasitology in the New Millennium organised by Indian Society for Parasitology at New Delhi (April 23-26, 2000).
5. National Seminar on Food Fortification in India : Do We Need It and Why organised by Nutrition Syndicate, New Delhi (April 27-28, 2000).
6. Symposium on Stress : Manifestations and Management organised by Institute of Medical Sciences, Banaras Hindu University, Varanasi (April 29, 2000).
7. Workshop on Proposed Postgraduate Research Medicine Programme organised by Indian Institute of Technology, Kharagpur at New Delhi (May 9, 2000).
8. Workshop on Biomedical Communication and Research Methodology and Symposium on Drugs for the New Millennium organised by St. John's Medical College, Bangalore (June 15-17, 2000).
9. XXX National Seminar on Crystallography – NSC-2K organised by Sri Venkateswara University, Tirupati (June 28-30, 2000).
10. National Seminar on Indian Science : Vision for the New Century organised by Prajna Bharti, Hyderabad (July 7-9, 2000).
11. International Conference on Microbial Biotechnology, Trade and Public Policy organised by Osmania University, Hyderabad (July 15-17, 2000).
12. Seminar on Recent Advances in Biological Sciences : Biospectrum 2000 organised by Association of Microbiologists of India, Sree Sankara College, Kalady (July 19-20, 2000).
13. International Conference on Vector Borne Disease Control in the New Era : Science, Policy and Action organised by Vector Control Research Centre, Pondicherry (July 19-21, 2000).
14. CME on New Drug Developments in Neuropsychiatric Disorders: Relevance in Clinical Practice organised by Institute of Human Behaviour and Allied Sciences, Delhi (September 5-7, 2000).
15. Workshop on Priority Settings in Health Research organised by All India Institute of Medical Sciences, New Delhi (September 10-11, 2000).
16. Symposium on Recent Advances in Nuclear Medicine organised by Indian Institute of Chemical Biology, Jadavpur, Kolkata (September 12-13, 2000).

17. National Seminar on Frontiers of Research and Development in Medicinal Plants organised by Central Institute of Medicinal and Aromatic Plants, Lucknow (September 16-18, 2000).
18. Symposium on Clinical Research in India – The Road Ahead organised by All India Institute of Medical Sciences, New Delhi (September 17, 2000).
19. XXXIV Annual Convention of the Indian College of Allergy and Applied Immunology organised by K.Gs' Medical College, Lucknow (September 29 - October 1, 2000).
20. Joint Conference of Geriatric Society of India organised by Government Medical College and Rajendra Hospital, Patiala (September 30 - October 1, 2000).
21. Single Theme Conference on Hepatic Encephalopathy organised by Postgraduate Institute of Medical Education and Research, Chandigarh (October 2, 2000).
22. National Symposium on Recent Trends in Combating Mosquitoes organised by Department of Zoology, Loyola College, Chennai (October 3-4, 2000).
23. XI Regional Meeting of International Union Against Sexually Transmitted Infections : STDs and HIV Break the Chain organised by Postgraduate Institute of Medical Education and Research, Chandigarh (October 13-15, 2000).
24. II International Congress and CME on Hypertension, Atherosclerosis and Coronary Artery Disease organised by Institute of Medical Sciences, Banaras Hindu University, Varanasi (October 14-16, 2000).
25. National Symposium on Microbes and Human Welfare organised by Department of Microbiology, Chaudhary Charan Singh University, Meerut (October 14-16, 2000).
26. XXXV National Conference of the Association of Plastic Surgeons of India and Hands on Workshop on Ear Reconstruction organised by K.G's Medical College, Lucknow (October 16-19, 2000).
27. National Symposium on Cellular and Molecular Biology of Ageing organised by School of Life Sciences, Jawaharlal Nehru University, New Delhi (October 20-21, 2000).
28. X Symposium on Urolithiasis organised by Panjab University, Chandigarh (October 31 - November 2, 2000).
29. International Conference on Adolescent Reproductive Health : Evidence and Programme Implications for South Asia organised by Institute for Research in Reproduction, Mumbai (November 1-4, 2000).
30. Symposium on Advanced Neonatal Care organised by Lokmanya Tilak Municipal Medical College and L.T.M.G. Hospital, Mumbai (November 3, 2000).
31. National Symposium on Harnessing Science and Technology for the New Millennium : A Vision organised by National Academy of Sciences, Allahabad (November 3-6, 2000).
32. International Congress on Fertilization, Embryo Development and Implantation organised by National Institute of Immunology, New Delhi (November 6-9, 2000).
33. International Symposium on Tropical Diseases : From Genome to Drugs and Vaccines organised by Central Drug Research Institute, Lucknow (November 7-9, 2000).
34. Seminar on HIV/AIDS and Traditional Medicine organised by National Institute of Immunology, New Delhi (November 9-10, 2000).
35. II Symposium on Current Advances in Molecular Biochemistry : Applications in Health, Environment and Agriculture organised by Lucknow University, Lucknow (November 9-11, 2000).
36. International Symposium on Ageing : A Challenge in the New Millennium organised by Baranas Hindu University, Varanasi (November 10-12, 2000)

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37. National Symposium on Male Reproduction : Andrology Update in the New Millennium organised by Bharathiar University, Coimbatore (November 10-12, 2000).
 38. XXV National Conference of Indian Society of Blood Transfusion and Immunohaematology organised by S.V. Institute of Medical Sciences, Tirupati (November 10-12, 2000).
 39. XXXII Annual Conference of the Society of Nuclear Medicine – Millennium Conference organised by Radiation Medicine Centre, BARC Hospital, Mumbai (November 15-18, 2000).
 40. International Child Neurology Education Conference - 2000 organised by All India Institute of Medical Sciences, New Delhi (November 17-19, 2000).
 41. XVIII Annual Conference of the Indian Society for Medical Statistics : Challenges and Opportunities in the New Millennium organised by Central JALMA Institute for Leprosy, Agra (November 18-20, 2000).
 42. III Congress of Federation of Indian Physiological Societies organised by University College of Science and Technology, Kolkata (November 24-26, 2000).
 43. Microbiotech – 2000 : XLI Annual Conference of the Association of Microbiologists of India organised by Birla Institute of Scientific Research, Jaipur (November 25-27, 2000).
 44. Symposia: 1. Current Status and Future Prospects of GM Foods in India. 2. Implementation of National Programmes – A Way Ahead organised by National Institute of Nutrition, Hyderabad (December 1-2, 2000).
 45. National Symposium on Medicinal Plants and Industrial Biotechnology organised by Cochin University of Science and Technology, Kochi (December 1-2, 2000).
 46. National Conference on Substance Dependence, HIV/AIDS and Mental Health organised by TRADA De-addiction and Rehabilitation Centre, Kottayam (December 1-3, 2000).
 47. I Annual Conference of Indian Society of Veterinary Pharmacology and Toxicology organised by College of Veterinary Science, Ludhiana (December 6-8, 2000).
 48. IV International Conference of South Asian Society for Atherosclerosis and Thrombosis organised by Institute of Immunohaematology, Mumbai (December 10-13, 2000).
 49. XXVII Annual Conference of the Indian Immunology Society and Symposium on Immunology of Infectious Diseases in the Millennium organised by Central JALMA Institute for Leprosy, Agra (December 10-13, 2000).
 50. GUHA Research Conference – 2000 organised by National Centre for Cell Science, Pune (December 13-16, 2000).
 51. National Symposium on New Frontiers in the Field of Medical Sciences and Management of Cardiac Problems organised by National Academy of Medical Sciences (Rajasthan Chapter) at Jaipur (December 17, 2000).
 52. XII Annual Conference of Physiological Society of India organised by Regional Occupational Health Centre (Eastern), Kolkata (December 22-23, 2000).
 53. Workshop on Disaster Medicine (Medical Rescue and Resuscitation) organised by National Association of Critical Care Medicine at New Delhi (December 23-24, 2000).
 54. National Conference on *Swadeshi Vigyan* : Traditional and Modern organised by Netaji Subhash Institute of Technology, New Delhi (December 26-28, 2000).
 55. XXIV Indian Social Science Congress : Prospective of Development of India in the Twenty First Century organised by Indian Academy of Social Sciences, Chandigarh (December 26-30, 2000).
 56. International Seminar on Haemoglobinopathies in South Asia : Problems and Prevention organised by Ramakrishna Mission *Seva Pratishthan*, Kolkata (December 27-29, 2000).

57. XXXIII Annual Conference of Indian Pharmacological Society organised by K.B. Institute of Pharmaceutical Education and Research, Gandhinagar (December 28-30, 2000).
58. Joint Statistical Meeting on Recent Developments in Statistics and Probability and Their Applications organised by University of Delhi, Delhi (December 30 - January 3, 2001).
59. XII National Endoscopic Sinus Surgery Course organised by Metro Multispeciality Hospital, NOIDA (January 1-3, 2001).
60. Seminar on History of Medicine and Health in India and LXI Annual Session of the Indian History Congress organised by Aligarh Muslim University, Aligarh (January 2-4, 2001).
61. Workshop on Mathematical and Computational Biology organised by Centre for Cellular and Molecular Biology, Hyderabad (January 8-13, 2001).
62. International Symposium on Mycobacterial Diseases : Pathogenesis, Protection and Control organised by Bose Institute, Kolkata (January 9-11, 2001).
63. XXVII Annual Conference of the Association of Clinical Biochemists of India organised by Indira Gandhi Medical College, Nagpur (January 12-14, 2001).
64. National Symposium on Biophysics organised by Indian Institute of Chemical Biology, Kolkata (January 15-17, 2001).
65. Symposium on Neuro-AIDS organised by National Institute of Mental Health and Neurosciences, Bangalore (January 16, 2001).
66. XX Annual Convention of Indian Association for Cancer Research organised by The Gujarat Cancer and Research Institute, Ahmedabad (January 19-21, 2001).
67. International Symposium on Quality of Life in Children with Chronic Diseases : Evaluation and Clinical Applications organised by Mahatma Gandhi Institute of Medical Sciences, Sevagram (January 21, 2001).
68. International Conference on Pathophysiology and Drug Therapy of Cardiovascular Disorders organised by Punjabi University, Patiala (January 22-26, 2001).
69. VIII All India Conference on Cytology and Genetics : Genetics and Better Life for All organised by Bangalore University, Bangalore (January 23-25, 2001).
70. International Conference on Biomedical Engineering – 2001 organised by Guindy Engineering College, Chennai (January 24-26, 2001).
71. XI Biennial Conference of the Indian Society of Medical and Paediatric Oncology organised by The Nizam's Institute of Medical Sciences, Hyderabad (January 27-29, 2001).
72. Annual Conference of the Indian Section of International Society of Heart Research organised by All India Institute of Medical Sciences, New Delhi (January 27-29, 2001).
73. Workshop on Ethical Issues in Health Research in South Asia organised by Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram (January 29 - February 1, 2001).
74. LI National Conference of Indian Association of Occupational Health organised by ESI Hospital, Delhi (February 1-4, 2001).
75. International Symposium on Critical Care in Obstetrics organised by University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi (February 3-4, 2001).
76. National Seminar on Emerging Methodologies of Data Analysis and Related Inferences organised by Banaras Hindu University, Varanasi (February 5-7, 2001).
77. Training Workshop on the Production of Transgenics and Gene Knockout Animals organised by National Institute of Immunology, New Delhi (February 15 - March 1, 2001).

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78. Symposium on Statistical and Mathematical Techniques and Radiation Safety in Nuclear Medicine organised by All India Institute of Medical Sciences, New Delhi (February 16-17, 2001).
 79. IX Annual Meeting of Molecular Immunology Forum organised by Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow (February 17-19, 2001).
 80. International Workshop on Seabuck Thorn : A Resource for Health and Environment in the 21st Century organised by Himachal Pradesh Krishi Vishvavidyalaya, Palampur (February 18-21, 2001).
 81. International Conference on Radiation Protection Measurements and Dosimetry – Current Practices and Future Trends organised by Bhabha Atomic Research Centre, Mumbai (February 20-23, 2001).
 82. VIII Annual Conference of Indian Association for the Advancement of Veterinary Research organised by College of Veterinary Science, Ludhiana (February 22-23, 2001).
 83. Symposium on Perspectives in Genome Analysis organised by Centre for Cellular and Molecular Biology, Hyderabad (February 23-24, 2001).
 84. Inaugural Scientific Meeting of the Indian Society for Histocompatibility and Immunogenetics organised by All India Institute of Medical Sciences, New Delhi (March 1-4, 2001).
 85. National Conference on Challenges of Care Giving organised by Heritage Educational and Research Society, New Delhi (March 2-3, 2001).
 86. XXVI Annual Conference of Environmental Mutagen Society of India and International Symposium on Environmental Health Science in 21st Century organised by All India Institute of Medical Sciences, New Delhi (March 5-7, 2001).
 87. FIMSA-IIS Advanced Course on Basic and Molecular Immunology organised by All India Institute of Medical Sciences, New Delhi (March 5-9, 2001).
 88. Liver Update-cum-Hepatology Workshop organised by Maulana Azad Medical College, New Delhi (March 13-14, 2001).
 89. National Symposium on Stability and Stabilization of Biomolecules organised by Aligarh Muslim University, Aligarh (March 13-14, 2001).
 90. VI International CME and Update on Surgical Pathology organised by Postgraduate Institute of Medical Education and Research, Chandigarh (March 15-17, 2001).

Appendix VII

List of Research Schemes Funded During 2000-2001

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
Epidemiology and Communicable Diseases			
1	Characterization of the human B and T cell immune response to the membrane capsid, NS1, NS2B and NS5 proteins of Japanese encephalitis virus	Dr. S. Vijaya Indian Institute of Science Bangalore	9.19
2	Vector immunity to filarial parasites : molecular studies in mosquito vectors with reference to development of <i>B.malayi</i> and <i>w.bancrofti</i>	Dr. A.P. Dash Institute of Life Sciences Bhubaneswar	1.82
3	Intervention for hereditary common haemolytic disorders among the major tribals of Sundargarh district of Orissa	Dr. R.S. Balgir Regional Medical Research Centre Bhubaneswar	1.82
4	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	4.58
5	Intervention programme for cholera, intestinal parasitism, vitamin - A deficiency disorders and scabies amongst some primitive tribal populations of Orissa - A pilot study	Dr. G.P. Chhotray Regional Medical Research Centre Bhubaneswar	4.58
6	Assessment of disease burden due to leptospirosis	Dr. S.K. Kar Regional Medical Research Centre Bhubaneswar	0.48
7	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
8	Potential of polysaccharide - cholera toxin B subunit conjugate for respiratory mucosal immunity	Dr. Sanjay Chibber Panjab University Chandigarh	0.60

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
9	Studies on mutation of TGF β and IFN γ genes in the pathogenesis of pulmonary fibrosis	Dr. Digamber Behera Postgraduate Institute of Medical Education and Research Chandigarh	1.05
10	Serodiagnosis of invasive zygomycosis	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	2.68
11	Natural habitat of <i>Cryptococcus neoformans var. gattii</i> strains in the environment of north India and north Karnataka	Dr. Arunaloke Chakrabarti Postgraduate Institute of Medical Education and Research Chandigarh	6.72
12	Molecular characterization of group A streptococcus	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	2.31
13	Molecular cloning, sequencing and expression of adhesin gene of enteroaggregative <i>E.coli</i> (EAggEC) towards development of a specific probe	Dr. Anuradha Chakraborti Postgraduate Institute of Medical Education and Research Chandigarh	4.17
14	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	2.78
15	Development of IFN ELISA and immuno-PCR based on <i>Mycobacterium tuberculosis</i> complex specific antigen (s) for early and specific diagnosis of tuberculosis	Dr. G.K. Khuller Postgraduate Institute of Medical Education and Research Chandigarh	1.75
16	Molecular mechanism of malabsorption in <i>Shigella</i> induced diarrhoea in rabbit as experimental model	Dr. Safrun Mahmood Postgraduate Institute of Medical Education and Research Chandigarh	1.01
17	Study on the pathophysiology of <i>V. cholerae</i> induced diarrhoea : At transcriptional level and at translational level	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.23
18	Study on the cellular responses by a galactose specific adhesin of enteroaggregative <i>Escherichia coli</i>	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	2.48

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
19	Study on the mechanism of action of a biologically active excretory secretory product of <i>G.lambli</i> a in mice enterocytes	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	1.84
20	Study on the cellular responses by a mannose sensitive adhesin of <i>Salmonella typhimurium</i>	Dr. Siddhartha Majumdar Postgraduate Institute of Medical Education and Research Chandigarh	2.08
21	Detection of <i>Leishmania donovani</i> "axenic" amastigote specific antigen by patients' sera through immunoblotting for diagnosis of kala-azar	Dr. Nancy Malla Postgraduate Institute of Medical Education and Research Chandigarh	2.60
22	Human filariasis : immunological (immunoglobulin and cytokine) responses in <i>W.bancrofti</i> and <i>B.malayi</i> infections in endemic areas in India	Dr. Nancy Malla Postgraduate Institute of Medical Education and Research Chandigarh	1.31
23	Association of genital mycoplasma and <i>Chlamydia trachomatis</i> in neonatal infections	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	3.49
24	Assessment of disease burden due to leptospirosis	Dr. Meera Sharma Postgraduate Institute of Medical Education and Research Chandigarh	1.58
25	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	0.92
26	A study of possible mechanism(s) for T cell anergy in lepromatous leprosy	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	1.47
27	Interactions of galactose- binding lectin of <i>Entamoeba histolytica</i> with immune-competent cells	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	0.89
28	Studies on regulation of apoptosis in leprosy patients	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	1.60

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
29	Mechanism of target cell death induced by gal/galnac lectin of <i>E.histolytica</i>	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	2.34
30	Evaluation of newer diagnostic methods for detection and differentiation of <i>Entamoeba histolytica</i> and <i>E.dispar</i>	Dr. Harpreet Vohra Postgraduate Institute of Medical Education and Research Chandigarh	1.00
31	Study of clinical utility and effect of a tumour necrosis factor inhibitor (pentoxifylline) on immune profile in patients with HIV infection	Dr. Ajay Wanchu Postgraduate Institute of Medical Education and Research Chandigarh	0.77
32	Studies on pulmonary opportunistic mycotic infection in immunocompromised patients	Dr. Usha Ananda Rao Dr.A.L. Mudaliar P.G. Institute of Basic Medical Sciences Chennai	1.59
33	A study on the transmission pattern(s) of hepatitis B virus (HBV) / hepatitis c virus (HCV) in symptomatic /asymptomatic pregnant women and their impact on pregnancy outcome and on children born to them	Dr. S.P. Thyagarajan Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences Chennai	8.61
34	Polymerase chain reaction for detection and genotyping of <i>Chlamydia trachomatis</i> in conjunctivitis	Dr. H.N. Madhavan Vision Research Foundation Chennai	2.95
35	Detection and molecular characterisation of mycobacteria by polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP) and DNA sequencing technique from ocular and other clinical specimens	Dr. K.Lily Therese Vision Research Foundation Chennai	5.00
36	Integrated Vector Control of malaria, filaria and other vector-borne diseases	Dr. Sarala K. Subbarao Malaria Research Centre Delhi	24.43
37	Delineation of breeding habitats and landscape features suitable for <i>Anopheles culicifacies</i> abundance using satellite remote sensing	Dr. R.C. Dhiman Malaria Research Centre Delhi	1.05
38	The role of proinflammatory cytokines in the induction of nitric oxide from human mononuclear phagocytes of patients suffering from pulmonary tuberculosis	Dr. Mridula Bose Vallabhbai Patel Chest Institute Delhi	1.06

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
39	Assessment of disease burden due to leptospirosis	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	1.55
40	Assessment of disease burden due to leptospirosis	Dr. V. Lakshmi The Nizam's Institute of Medical Sciences Hyderabad	0.48
41	Strengthening of health care delivery services in primitive tribes of Madhya Pradesh	Dr. K. Madan Gopal Regional Medical Research Centre for Tribals Jabalpur	2.52
42	Assessment of disease burden due to leptospirosis	Dr. B.K. Tyagi Desert Medicine Research Centre Jodhpur	1.49
43	Lactoferrin and antibodies to lactoferrin in tears of leprosy patients	Dr. Ebenezer Daniel Schieffelin Leprosy Research and Training Centre Karigiri	1.12
44	Viability of <i>Mycobacterium leprae</i> in leptomatous patients after completion of 12 month and 24 month multidrug therapy	Dr. Gigi J. Ebenezer Schieffelin Leprosy Research and Training Centre Karigiri	1.61
45	Assessment of disease burden due to leptospirosis	Dr. C.K. Eapen Malankara Orthodox Syrian Church Medical Mission Hospital Kolenchery	0.80
46	Assessment of disease burden due to leptospirosis	Dr. Debaprasad Pal All India Institute of Hygiene and Public Health Kolkata	0.48
47	Generation of peptide mimics against the immunodominant lipoglycan/lipopolysaccharide antigens of <i>Mycobacterium tuberculosis</i> and <i>Vibrio cholerae</i> using phage display libraries and their evaluation as diagnostic and prophylactic agents	Dr. Sujoy K. Das Gupta Bose Institute (New campus) Kolkata	0.48
48	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 Kolkata	1.47

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
49	Optimization of dendritic cell-based vaccination / therapy against murine visceral leishmaniasis induced by antimony-resistant and -sensitive strains of <i>Leishmania donovani</i>	Dr. Santu Bandyopadhyay Indian Institute of Chemical Biology Kolkata	3.26
50	An approach to develop DNA vaccine against experimental visceral leishmaniasis	Dr. Syamal Roy Indian Institute of Chemical Biology Kolkata	1.94
51	Impact of domestic animals and food derived from animals on the epidemiology of enterohaemorrhagic <i>Escherichia coli</i> (EHEC) and shiga - toxin producing <i>E.coli</i> (STEC)	Dr. S.C. Das Indian Veterinary Research Institute Kolkata	7.47
52	Natural history of <i>Helicobacter pylori</i> infection and its outcome in India	Dr. Abhijit Chowdhury Institute of Postgraduate Medical Education and Research and S.S.K.M. Hospital Kolkata	1.50
53	Studies on HIV/AIDS and drug abuse in eastern and north eastern part of India	Dr. S.K. Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	13.81
54	Studies on HIV/AIDS and drug abuse in Dimapur, Nagaland	Dr. S.K. Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	11.96
55	Studies on HIV/aids and drug abuse in Aizwal, Mizoram	Dr. S.K. Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	11.96
56	Studies on HIV/AIDS and drug abuse in Imphal, Manipur	Dr. S.K. Bhattacharya National Institute of Cholera and Enteric Diseases Kolkata	13.69
57	Identification and characterization of multiple genes in <i>Entamoeba histolytica</i> during human collagen type I and ca ²⁺ interaction : use of mRNA differential display	Dr. Pradeep Das National Institute of Cholera and Enteric Diseases Kolkata	4.80
58	Detection of <i>Entamoeba histolytica</i> , <i>Giardia lamblia</i> and <i>Cryptosporidium parvum</i> by molecular biological tools	Dr. Pradeep Das National Institute of Cholera and Enteric Diseases Kolkata	0.96

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
59	Monitoring of multiple antibiotic resistance among clinical strains of enteric pathogens	Dr. Thandanarayan Ramamurthy National Institute of Cholera and Enteric Diseases Kolkata	1.55
60	A correlative study of the prevalence of IgM immunoglobulins against torch infections in pregnancy, with congenital malformations	Dr. K. F. Zuhara University of Calicut Kozhikode	3.76
61	Herpes simplex encephalitis in children	Dr. Rashmi Kumar K.G's Medical College Lucknow	1.26
62	Study of T-cell epitopes of human hepatitis E virus	Dr. Rakesh Aggarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	4.22
63	Development of an animal model for Indian strains of <i>Helicobacter pylori</i>	Dr. Archana Ayyagari Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	4.97
64	Assessment of disease burden due to leptospirosis	Dr. Archana Ayyagari Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	1.55
65	<i>Campylobacter</i> infection and Guillain - Barre syndrome	Dr. K.N. Prasad Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	0.69
66	Establishment of a field station in South Arcot district, Tamil Nadu for control trials of Japanese encephalitis	Dr. K. Satyanarayana Centre for Research in Medical Entomology Madurai	12.61
67	Study on impact of health programmes in Bihar state	Dr. Chakradhar Sinha B.R. Ambedkar Bihar University Muzaffarpur	2.89
68	A prospective evaluation of clinical profile and natural course of waterborne viral hepatitis in adults and seroepidemiology of HAV in children in India	Dr. S.K. Acharya All India Institute of Medical Sciences New Delhi	1.95

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
69	Multicentric study of interferon - glycyrrhizin combination therapy and interferon - ribavirin combination therapy in the management of chronic hepatitis C - Clinical Coordinating Centre	Dr. S.K. Acharya All India Institute of Medical Sciences New Delhi	43.32
70	Natural history of <i>Helicobacter pylori</i> infection in a birth cohort in an urban slum setting : risk factors, rates of clearance and re-infection, immune response to first infection, impact of infection on physical growth	Dr. Rajiv Bahl All India Institute of Medical Sciences New Delhi	6.00
71	Monitoring of poliovirus strains for inter and intratypic variability by restriction pattern analysis and sequencing	Dr. Shobha Broor All India Institute of Medical Sciences New Delhi	3.96
72	Molecular typing of <i>Acinetobacter</i> sp. isolated in AIIMS hospital	Dr. Arti Kapil All India Institute of Medical Sciences New Delhi	1.54
73	Characterisation of <i>Pseudomonas aeruginosa</i> isolated from cystic fibrosis patients	Dr. Arti Kapil All India Institute of Medical Sciences New Delhi	4.13
74	Diagnosis of malaria by detection of <i>Plasmodium falciparum</i> HRP-2 antigen using antigen capture assay	Dr. D. Nageswara Rao All India Institute of Medical Sciences New Delhi	1.29
75	Protective efficacy of peptide immunogens between B and T cell epitopes of F ₁ antigen <i>Y.pestis</i>	Dr. D. Nageswara Rao All India Institute of Medical Sciences New Delhi	1.60
76	Phenotypic and molecular characterisation of ocular isolates of coagulase negative staphylococci : implications in colonization and virulence	Dr. Niranjana Nayak All India Institute of Medical Sciences New Delhi	1.60
77	Hepatitis B virus mutants in acute non A to E hepatitis patients	Dr. S.K. Panda All India Institute of Medical Sciences New Delhi	3.00
78	Role of genomic instability due to alterations of recombination factors p53 and BRCA1 in the pathogenesis of breast cancer	Dr. Ranju Ralhan All India Institute of Medical Sciences New Delhi	18.00
79	Molecular characterization of VP3 gene of human rotavirus strains associated with severe diarrhoea and without diarrhoea in children	Dr. Pratima Ray All India Institute of Medical Sciences New Delhi	2.01

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
80	Surveillance of anti -tuberculosis drug resistance	Dr. Pradeep Seth All India Institute of Medical Sciences New Delhi	5.69
81	PCR and cytokine assays for diagnosing latent infection of <i>Leishmania</i> in asymptomatic family members of kala-azar patients of Bihar	Dr. Sarman Singh All India Institute of Medical Sciences New Delhi	1.06
82	Generation and <i>in vitro</i> characterisation of recombinant phage display antibodies to hepatitis B surface antigen	Dr. Subrata Sinha All India Institute of Medical Sciences New Delhi	4.58
83	Identification of target genes of the DEVR-DEVS two-component system of <i>M.tuberculosis</i> and development of rapid assays to measure its activity	Dr. Jaya Sivaswami Tyagi All India Institute of Medical Sciences New Delhi	3.63
84	To study the role of host genetic factors in hepatitis B viral infection in family contacts of HBVC related liver disease patients	Dr. S.K. Sarin G.B. Pant Hospital New Delhi	3.74
85	Anti-POL II anti-TBP antibodies as markers for scleroderma and mixed connective tissue diseases (MCTD)	Dr. Uttam Pati Jawaharlal Nehru University New Delhi	2.65
86	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
87	Role of polyketide syntheses in the biology of <i>Mycobacterium tuberculosis</i>	Dr. Rajesh S. Gokhale National Institute of Immunology New Delhi	7.62
88	Intracellular trafficking of salmonella in macrophages to understand the mechanism of bacterial survival	Dr. Amitava Mukhopadhyay National Institute of Immunology New Delhi	2.28
89	Mechanistic studies on the defensive mechanisms of <i>Leishmania donovani</i> against oxidative stress : role of phase I and phase II defensive enzymes of the parasite	Dr. Chandrima Shaha National Institute of Immunology New Delhi	3.48
90	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	3.85

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
91	Molecular epidemiology and genomics of filariasis - a national network for molecular typing	Dr. S.I. Hoti Vector Control Research Centre Pondicherry	1.32
92	Operational feasibility and impact of co-administration of albendazole and DEC in controlling lymphatic filariasis	Dr. S.P. Pani Vector Control Research Centre Pondicherry	18.25
93	Prevalence of haemoglobinopathies and G6PD deficiency among the primitive tribal population of Andaman and Nicobar	Dr. K.M. Murhekar Regional Medical Research Centre Port Blair	0.25
94	Studies on transmission dynamics of diurnally sub-periodic <i>W.bancrofti</i> infection in Nancowry group of islands	Dr. S.C. Sehgal Regional Medical Research Centre Port Blair	0.80
95	Estimate of disease burden due to shigellosis in rural community in the Andamans	Dr. S.C. Sehgal Regional Medical Research Centre Port Blair	2.21
96	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	19.46
97	Assessment of disease burden due to leptospirosis - Co-ordinating Centre	Dr. S.C. Sehgal Regional Medical Research Centre Port Blair	17.06
98	Assessment of disease burden due to leptospirosis	Dr. Renu Bhardwaj B.J. Medical College and Sasoon General Hospital Pune	0.48
99	Virological studies in relation to assessment of efficacy of drug therapies for chronic hepatitis B and C	Dr. Vidya A. Arankalle National Institute of Virology Pune	18.00
100	Assessment of disease burden due to leptospirosis	Dr. Pratibha Narang Mahatma Gandhi Institute of Medical Sciences Sevagram	1.44
101	Study of different immunological factors across the clinical spectrum of filariasis in an endemic area	Dr. M.V.R. Reddy Mahatma Gandhi Institute of Medical Sciences Sevagram	0.87

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
102	Assessment of disease burden due to leptospirosis	Dr. Azra Shah Sher-I-Kashmir Institute of Medical Sciences Srinagar	0.48
103	Studies on mosquitoes of southern Rajasthan	Dr. P.N. Sharma M. L. Sukhadia University Udaipur	0.07
104	Assessment of disease burden due to leptospirosis	Dr. K.K. Tripathi Institute of Medical Sciences Banaras Hindu University Varanasi	0.48
105	A molecular approach to the detection of enteroviruses in acute and chronic neurological illnesses	Dr. Gopalan Sridharan Christian Medical College and Hospital Vellore	1.40
Reproductive Health and Nutrition			
106	District Nutrition Project for prevention and control of micronutrients deficiency disorders - phase II	Dr. K. Ropari Directorate of Health Services Aizwal	4.92
107	Alpha-2 macroglobulin in type- I, type-II and experimental diabetes: correlation of plasma vascular endothelium levels with severity of the disease	Dr. Jamal Ahmad Jawaharlal Nehru Medical College Aligarh	2.21
108	Human Reproduction Research Centre	Dr. Krishna Mukherjee Motilal Nehru Medical College Allahabad	10.91
109	Pilot study on emergency contraception with CuT 200B and 0.75mg levonorgestrel (2 doses)	Dr. Krishna Mukherjee Motilal Nehru Medical College Allahabad	0.78
110	National Nutrition Monitoring Bureau	Dr. J. Sundaram Directorate of Health and Family Welfare Services Bangalore	8.90
111	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	0.84

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
112	Identification of estrogen regulated epididymal factor(s) involved in sperm maturation	Dr. A. Jagannadha Rao Indian Institute of Science Bangalore	4.26
113	Advanced Centre for Cellular and Molecular Reproduction	Dr. A. Jagannadha Rao Indian Institute of Science Bangalore	33.92
114	Human Reproduction Research Centre	Dr. B.S. Kodkany Jawaharlal Nehru Medical College Belgaum	9.00
115	Role of IEC/counselling in facilitating couples' informed choice between conventional and no-scalpel vasectomy procedures	Dr. Yogiraj Sharma Directorate of Health Services Government of Madhya Pradesh Bhopal	3.48
116	Operational evaluation of the stability of iodine in double fortified salt	Dr. S.K. Kar Regional Medical Research Centre Bhubaneswar	0.67
117	National Nutrition Monitoring Bureau	Dr. K. Satyanarayana Regional Medical Research Centre Bhubaneswar	8.90
118	Human Reproduction Research Centre	Dr. Durga Gehlot S.P. Medical College and Associated Group of Hospitals Bikaner	9.00
119	Human Reproduction Research Centre	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	9.00
120	Profile of women with polycystic ovaries	Dr. Sarala Gopalan Postgraduate Institute of Medical Education and Research Chandigarh	6.84
121	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	2.76
122	Reactive oxygen intermediates and reactive nitrogen intermediates with microbiological studies in copper intrauterine device users	Dr. Indu Gupta Postgraduate Institute of Medical Education and Research Chandigarh	2.76

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
123	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	1.98
124	Quantitative changes in body water contents, occurrence of syndrome of inappropriate antidiurectic hormone secretion (SIADH) and their significance in children with acute bacterial meningitis	Dr. Sunit C. Singhi Postgraduate Institute of Medical Education and Research Chandigarh	1.78
125	National Nutrition Monitoring Bureau	Dr. K.C. Viswanathan Directorate of Public Health and Preventive Medicine Chennai	8.90
126	Assessing the sexual and psychological health of HIV+ and HIV- women in India	Dr. C.N. Deivanayagam Government Hospital of Thoracic Medicine Chennai	1.00
127	Human Reproduction Research Centre	Dr. Bhuvneshwari Government Kasturba Gandhi Hospital for Women and Children Chennai	11.08
128	Human Reproduction Research Centre	Dr. A. Sundaravalli Government Kilpauk Medical College and Hospital Chennai	11.58
129	Human Reproduction Research Centre	Dr. R. Thirupurasundari Government R.S.R.M. Hospital Chennai	9.00
130	Human Reproduction Research Centre - Regional Centre for Clinical Research	Dr. M. Kuppulakshmi Institute of Obstetrics and Gynaecology and Government Hospital for Women and Children Chennai	15.88
131	Profile of women with polycystic ovaries	Dr. Gajalakshmi Subramanyam Institute of Obstetrics and Gynaecology and Government Hospital for Women and Children Chennai	0.59

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
132	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. Catherine Barnard Service & Research Foundation of Asia on Family & Culture Chennai	1.98
133	Operational evaluation of the stability of iodine in double fortified salt	Dr. P.R. Narayanan Tuberculosis Research Centre Chennai	0.67
134	Assessing the sexual and psychological health of HIV+ and HIV- women in India	Dr. Soumya Swaminathan Tuberculosis Research Centre Chennai	2.35
135	Human Reproduction Research Centre	Dr. S.K. Mishra S.C.B. Medical College Cuttack	9.00
136	District Nutrition Project for prevention and control of micronutrients deficiency disorders - phase II	Dr. V.B. Prakash V.C. Prakash Cancer Research Foundation Dehradun	1.45
137	Human Reproduction Research Centre	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	14.47
138	Pilot study on emergency contraception with CuT 200B and 0.75mg levonorgestrel (2 doses)	Dr. Pushpa Bhatia Kasturba Gandhi Hospital Delhi	0.78
139	Operational evaluation of the stability of iodine in double fortified salt	Dr. Sarala K. Subbarao Malaria Research Centre Delhi	0.67
140	District Nutrition Project for prevention and control of micronutrients deficiency disorders - phase I	Dr. F.U. Ahmed Assam Medical College Dibrugarh	3.49
141	Operational evaluation of the stability of iodine in double fortified salt	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	0.67
142	National Nutrition Monitoring Bureau	Dr. Nargis Naseem Directorate of Health, Medical Services and Medical Education Gandhinagar	8.90

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
143	District Nutrition Project for prevention and control of micronutrients deficiency disorders - phase I	Dr. Motilal A.N. Magadh Medical College Gaya	3.01
144	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. P.K. Sharma Gauhati Medical College Guwahati	14.55
145	Evaluation of the role of environmental hazards in the etiology of male reproductive failure : a comparison with normal fertile men (controls)	Dr. Roya Rozati Bhagvan Mahavir Hospital Medical Research Centre Hyderabad	4.84
146	Operational evaluation of the stability of iodine in double fortified salt	Dr. Kamala Krishnaswamy National Institute of Nutrition Hyderabad	7.39
147	Central Reference Laboratory of the National Nutrition Monitoring Bureau	Dr. K. Vijayaraghavan National Institute of Nutrition Hyderabad	8.90
148	National Nutrition Monitoring Bureau	Dr. K. Vijayaraghavan National Institute of Nutrition Hyderabad	8.90
149	Survey of <i>khesari</i> dal consuming populations in India and Bangla Desh for detoxification of ODAP and metabolic derangements	Dr. M.P. Pratap Rudra Osmania University Hyderabad	1.47
150	Purification and characterization of LTC ₄ synthase from sheep uterus	Dr. P. Reddanna University of Hyderabad Hyderabad	1.91
151	District Nutrition Project for prevention and control of micronutrients deficiency disorders - phase II	Dr. E.Yaima Singh Regional Institute of Medical Sciences Imphal	1.50
152	National Nutrition Monitoring Bureau	Dr. Tapas Chakma Regional Medical Research Centre for Tribals Jabalpur	8.90
153	Human Reproduction Research Centre	Dr. Anju Taly S.M.S. Medical College and Hospital Jaipur	13.80
154	Human Reproduction Research Centre	Dr. Sadhna Sharma Government Medical College and S.M.G.S. Hospital Jammu	11.35

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
155	Efficacy of some herbal medicines used by the tribal people and their impact in the control of fertility	Dr. C.K. Manna University of Kalyani Kalyani	1.04
156	Human Reproduction Research Centre	Dr. V.K. Singh G.S.V.M. Medical College Kanpur	10.46
157	Human Reproduction Research Centre - Regional Centre for Clinical Research	Dr. Abha Sarkar Institute of Postgraduate Medical Education and Research Kolkata	12.31
158	Human Reproduction Research Centre	Dr. M. Sangthamita Medical College and Eden Hospital Kolkata	15.55
159	Human Reproduction Research Centre	Dr. A.K.Mondal R.G.Kar Medical College and Hospital Kolkata	13.63
160	Pilot study on emergency contraception with CuT 200B and 0.75mg levonorgestrel (2 doses)	Dr. A.K. Mondal R.G.Kar Medical College and Hospital Kolkata	0.78
161	National Nutrition Monitoring Bureau	Dr. A. Roy Chowdhury Regional Occupational Health Centre(Eastern) Kolkata	8.90
162	Human proacrosin-acrosin system and sperm-egg interaction	Dr. A.K. Bhattacharya University College of Science Kolkata	2.65
163	Human Reproduction Research Centre	Dr. Sushma Pandey K.G's Medical College Lucknow	9.00
164	Evaluation of the effects of immunotherapy with husband's lymphocytes on prevention of recurrent spontaneous abortion : a double blind randomized trial	Dr. Suraksha Devi Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	2.54
165	Human Reproduction Research Centre	Dr. P. Meenambal Madurai Medical College and Government Rajaji Hospital Madurai	13.40

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
166	Human Reproduction Research Centre	Dr. Usha Sharma L.L.R.M. Medical College Meerut	9.00
167	Role of leaf extract of <i>Stephania hernandifolia</i> (<i>aknadi</i>) on fertility regulation in male : an evaluation for male pill of plant origin for 21st century	Dr. Debidas Ghosh Vidyasagar University Midnapore	0.92
168	Human Reproduction Research Centre	Dr. Rekha G. Dever Grant Medical College and Sir J.J.Group of Hospitals Mumbai	9.00
169	Operational evaluation of the stability of iodine in double fortified salt	Dr. C.P. Puri Institute for Research in Reproduction Mumbai	0.67
170	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in India	Dr. Ravi Verma International Institute for Population Sciences Mumbai	1.98
171	Human Reproduction Research Centre-Regional Centre for Clinical Research	Dr. Mina Bhattacharya Seth G.S. Medical College and K.E.M. Municipal Hospital Mumbai	9.00
172	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	0.88
173	Studies on antioxidant properties and hypocholesterolemic effect of sesame oil	Dr. K. Sambaiah Central Food Technological Research Institute Mysore	0.29
174	National Nutrition Monitoring Bureau	Dr. N.R Khan Public Health Institute Building Nagpur	8.90
175	Prevalence of testosterone biosynthetic defects among male hypogonads	Dr. A.C. Ammini All India Institute of Medical Sciences New Delhi	2.37
176	Role of cytokines in premature ovarian failure	Dr. Anand Kumar All India Institute of Medical Sciences New Delhi	0.38

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
177	The effect of egg on serum lipid profile	Dr. R.L. Bijlani All India Institute of Medical Sciences New Delhi	0.92
178	The effects of <i>ghee</i> (clarified butter) on the serum lipid profile	Dr. R.L. Bijlani All India Institute of Medical Sciences New Delhi	0.87
179	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	2.86
180	Prevalence of multiple micronutrient deficiencies amongst pregnant and newly married non-pregnant women in a rural block, Haryana state	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	3.92
181	Human Reproduction Research Centre	Dr. Deepa Takkar All India Institute of Medical Sciences New Delhi	12.00
182	Profile of women with polycystic ovaries	Dr. Deepa Takkar All India Institute of Medical Sciences New Delhi	5.96
183	Mechanism of antiprogestin interaction with experimental animal and human target tissues	Dr. Urmila Vj All India Institute of Medical Sciences New Delhi	3.27
184	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. Gulshanjit Singh Deen Dyal Upadhyay Hospital New Delhi	0.34
185	Assessing the sexual and psychological health of HIV+ and HIV- women in India	Dr. B.B. Riwari Dr. Ram Manohar Lohia Hospital New Delhi	1.00
186	Feasibility studies on the use of indigenous ELISA kits of cortisol and testosterone	Dr. G. Lakshmi Kumari Hormone Research Foundation New Delhi	2.75
187	Development of simple, sensitive and rapid low cost pregnancy test for early detection of pregnancy	Dr. G. Lakshmi Kumari Hormone Research Foundation New Delhi	3.22
188	Assessing the sexual and psychological health of HIV+ and HIV- women in india - Co-ordinating Unit	Dr. R.N. Gupta Indian Council of Medical Research New Delhi	3.14

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
189	Central Co-ordinating Unit for Contraception Research	Sh. N.C. Saxena Indian Council of Medical Research New Delhi	13.00
190	Pilot study on emergency contraception with CuT 200B and 0.75mg levonorgestrel (2 doses) - Co-ordinating Unit	Sh. N.C. Saxena Indian Council of Medical Research New Delhi	13.00
191	Development of indigenous thread to be used for the production of CuT 200B	Dr. B.L. Deopura Indian Institute of Technology New Delhi	0.54
192	National Nutrition Monitoring Bureau	Dr. Padam Singh Institute for Research in Medical Statistics New Delhi	8.90
193	Lipid profile, blood glucose and insulin levels of adolescents from affluent families	Dr. Santosh Jain Passi Institute of Home Economics New Delhi	2.48
194	Long term management of retinal and renal complications in experimental diabetes by vanadate and antidiabetic compounds	Dr. Najma Zaheer Baquer Jawaharlal Nehru University New Delhi	1.44
195	Morphological changes of placenta in tobacco users and non tobacco users	Dr. Gayatri Rath Lady Hardinge Medical College and Associated Hospitals New Delhi	3.15
196	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. H.C. Das Lok Nayak Jaiprakash Narayan Hospital New Delhi	4.50
197	Identification and characterization of spermatozoa surface proteins involved in binding to zona pellucida glycoproteins	Dr. S.K. Gupta National Institute of Immunology New Delhi	3.49
198	Nutritional status of affluent school going children in Delhi	Dr. C. Gopalan Nutrition Foundation of India New Delhi	2.64
199	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	4.73
200	Phase III clinical trial of an injectable intravasal contraceptive for the male	Dr. S.K. Basu Rural Hospital New Delhi	0.34

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
201	Assessing the sexual and psychological health of HIV+ and HIV- women in India	Dr. Virendar Dhir Safdarjang Hospital New Delhi	1.00
202	Human Reproduction Research Centre	Dr. Sudha Salhan Safdarjang Hospital New Delhi	14.78
203	Human Reproduction Research Centre	Dr. Prasad Neurencar Goa Medical College Panaji	9.00
204	Pilot study on emergency contraception with CuT 200B and 0.75mg levonorgestrel (2 doses)	Dr. Prasad Neurencar Goa Medical College Panaji	2.03
205	Human Reproduction Research Centre	Dr. Sushma Pande Patna Medical College and Hospital Patna	10.69
206	Human Reproduction Research Centre	Dr. Syed Habeebullah Jawaharlal Institute of Postgraduate Medical Education Pondicherry	12.45
207	Profile of women with polycystic ovaries	Dr. Asha Oumachigui Jawaharlal Institute of Postgraduate Medical Education and Research Pondicherry	0.59
208	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	4.35
209	Human Reproduction Research Centre	Dr. Aparna Shrotri B.J. Medical College and Sasoon General Hospital Pune	10.31
210	Cognitive problems in children who were "high risk" at birth- an eleven year follow up	Dr. Sudha Chaudhari King Edward Memorial Hospital Research Centre Pune	2.45
211	Human Reproduction Research Centre	Dr. K. Coyaji King Edward Memorial Hospital Research Centre Pune	6.58

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
212	Profile of women with polycystic ovaries	Dr. K. Coyaji King Edward Memorial Hospital Research Centre Pune	0.59
213	Health-disease-nutritional status of tribal and non-tribal pre-school children and their mothers : a study in the Jharkhand region of south Bihar Chhotanagpur plateau	Dr. M.R. Chakravartti Centre for Environmental and Developmental Research Ranchi	3.45
214	A prospective study on reproductive health and disease among the tribal and non-tribal women belonging to the Jharkhand-Vananchal region of south Bihar plateau	Dr. M.R. Chakravartti Centre for Environmental and Developmental Research Ranchi	3.48
215	Role of IEC/counselling in facilitating couples' informed choice between conventional and no-scalpel vasectomy procedures	Dr. S.K. Gupta State Health and Family Welfare Shimla	3.45
216	Operational evaluation of the stability of iodine in double fortified salt	Dr. Vikas Desai Government Medical College and New Civil Hospital Surat	0.67
217	Reproductive health problems of women among the fishing communities in Kerala	Dr. V. Gopalakrishnan Central Institute of Development Research and Environmental Management Thiruvananthapuram	3.39
218	Human Reproduction Research Centre	Dr. P.K. Syamala Devi Medical College and SAT Hospital for Women & Children Thiruvananthapuram	10.59
219	Pilot study on emergency contraception with CuT 200B and 0.75mg levonorgestrel (2 doses)	Dr. P.K. Syamala Devi Medical College and SAT Hospital for Women & Children Thiruvananthapuram	0.78
220	National Nutrition Monitoring Bureau	Dr. K.A. George State Nutrition Bureau Nutrition Research Centre Thiruvananthapuram	8.90
221	Screening of marine cyanobacteria for male antifertility property	Dr. M.A. Akbarsha Bharathidasan University Tiruchirapalli	3.15

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
222	Promotion of vasectomy by training the providers and community education	Dr. R.K. Baxi Medical College and S.S.G. Hospital Vadodara	2.79
223	Human Reproduction Research Centre	Dr. L.N. Chauhan Medical College and S.S.G. Hospital Vadodara	14.10
224	Study of altered cell biology and signal transduction in platelets in pregnancy toxemia	Dr. Debabrata Dash Institute of Medical Sciences Banaras Hindu University Varanasi	0.75
225	A study of psychosocial, cultural and service factors affecting reproductive morbidity amongst rural women in india	Dr. S.K. Mishra Child in Need Trust 24-Parganas	1.98
Non-communicable Diseases			
226	Study of TGF beta system in advanced human breast tumors	Dr. Sunil Trivedi The Gujarat Cancer and Research Institute Ahmedabad	8.25
227	Epidemiology of glaucoma	Dr. S.T. Fernandez Little Flower Hospital and Research Centre Angamally	14.18
228	National Cancer Registry Co-ordinating Unit (Technical Wing)	Dr. A. Nandakumar Kidwai Memorial Institute of Oncology Bangalore	7.70
229	Vasectomy and cancer of prostate : a multicentric case control study - Co-ordinating Unit	Dr. A. Nandakumar Kidwai Memorial Institute of Oncology Bangalore	0.95
230	National Cancer Registry - Hospital Based	Dr. P.S. Prabhakaran Kidwai Memorial Institute of Oncology Bangalore	0.70
231	National Cancer Registry - Population Based	Dr. P.S. Prabhakaran Kidwai Memorial Institute of Oncology Bangalore	4.00
232	Vasectomy and cancer of prostate : a multicentric case control study	Dr. P.S. Prabhakaran Kidwai Memorial Institute of Oncology Bangalore	0.80

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
233	Diagnostic potential of p67 (MUNC-18) in neurological disorders	Dr. K.Taranath Shetty National Institute of Mental Health and Neurosciences Bangalore	1.19
234	Urban hospital-based case- control study to identify risk factors for acute myocardial infarction - Control Data Unit	Dr. Prem Pais St.John's Medical College Bangalore	3.29
235	Urban hospital-based case- control study to identify risk factors for acute myocardial infarction (Participating Centre)	Dr. Prem Pais St.John's Medical College Bangalore	1.67
236	Bhopal Cancer Registry	Dr. Shiela Kanhere Gandhi Medical College and Associated Hospitals Bhopal	8.00
237	Operational feasibility and impact of co-administration of albendazole and DEC in controlling lymphatic filariasis	Dr. G.P. Chhotray Regional Medical Research Centre Bhubaneswar	4.68
238	Orbital blood flow studies in glaucoma	Dr. V.P. Munjal Government Medical College and Hospital Chandigarh	0.53
239	HLA typing in Vogt Koyanagi Harada (VKH) syndrome in Indian population	Dr. Amod Gupta Postgraduate Institute of Medical Education and Research Chandigarh	1.81
240	A study of factors affecting bacterial adherence to various intraocular lens materials (polymethyl methacrylate and foldable intraocular lenses)	Dr. Jagat Ram Postgraduate Institute of Medical Education and Research Chandigarh	0.82
241	Role of resveratrol in colon and lung carcinogenesis	Dr. K.L. Khanduja Postgraduate Institute of Medical Education and Research Chandigarh	2.09
242	Molecular genetics of essential hypertension : role of genetic determinants in essential hypertension in Indian subjects	Dr. Madhu Khuller Postgraduate Institute of Medical Education and Research Chandigarh	2.50

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
243	Community-based follow up and treatment of children identified to have psychiatric disorders	Dr. Savita Malhotra Postgraduate Institute of Medical Education and Research Chandigarh	s3.45
244	<i>Jai vigyan</i> mission mode project on community control of RF/RHD in India	Dr. Rajesh Kumar Postgraduate Institute of Medical Education and Research Chandigarh	69.21
245	Comparative study of growth index of adenomatous hyperplasia of liver with those of cirrhotic nodules and hepatocellular carcinoma	Dr. Kim Vaiphei Postgraduate Institute of Medical Education and Research Chandigarh	2.73
246	National Cancer Registry - Hospital Based	Dr. V. Shanta Cancer Institute Chennai	0.60
247	National Cancer Registry - Population based	Dr. V. Shanta Cancer Institute Chennai	2.77
248	Causes of death by verbal autopsy - a pilot study	Dr. M.D. Gupte National Institute of Epidemiology Chennai	7.78
249	Operational feasibility and impact of co-administration of albendazole and DEC in controlling lymphatic filariasis	Dr. V. Kumaraswami Tuberculosis Research Centre Chennai	16.00
250	Development and evaluation of bioactive ceramic coating	Dr. S. Rajeswari University of Madras Chennai	1.63
251	Molecular biological and virological study of intraocular fluids from patients with viral retinitis and choroiditis - correlation with clinical features and visual outcome	Dr. H.N. Madhavan Vision Research Foundation Chennai	3.52
252	Mental health consequences and service needs of a disaster (fire) affected community in an urban slum	Dr. N.G. Desai Institute of Human Behaviour and Allied Sciences Delhi	9.27
253	Studies on suicide behaviour	Dr. N.G. Desai Institute of Human Behaviour and Allied Sciences Delhi	4.93

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
254	To develop the technology for the production of bone cement and bone substitute	Dr. R.K. Diwan Shriram Institute for Industrial Research Delhi	3.95
255	Development of a simple regime of play therapy and to assess the impact of this on growth and development of institutionalized children in an orphanage setting	Dr. Jacob M. Puliye St.Stephen's Hospital Delhi	0.34
256	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	0.98
257	National Cancer Registry - Hospital Based	Dr. F.U. Ahmed Assam Medical College Dibrugarh	2.80
258	Etiology of endemic goitre in North-East India : Role of environmental goitrogen	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	1.67
259	Cancer chemopreventive potential of certain vegetables, fruits and medicinal plants of the north eastern region of India	Dr. Rupjyoti Bharali Gauhati University Guwahati	6.47
260	Role of growth factors and receptors in cataract	Dr. Yogendra Sharma Centre for Cellular and Molecular Biology Hyderabad	6.91
261	Differentiation of embryonal carcinoma cells with curcumin and identification of differentially expressed genes that trigger differentiation	Dr. Usha K. Srinivas Centre for Cellular and Molecular Biology Hyderabad	6.37
262	Role of apoptosis in tissue damage and wound healing in corneal infections	Dr. K.V. Geeta L.V. Prasad Eye Institute Hyderabad	2.51
263	Etiology of endemic goitre in north eastern India : Role of environmental goitrogen	Dr. Kamala Krishnaswamy National Institute of Nutrition Hyderabad	2.23
264	Urban hospital based case control study to identify risk factors for acute myocardial infarction (Participating Centre)	Dr. P. Krishnam Raju Osmania Medical College and Associated Hospitals Hyderabad	1.49

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
265	Prevention of disability among pre- school children	Dr. M.K. Mathur S.M.S. Medical College and Hospital Jaipur	10.39
266	Role of integrin and lectin cell surface molecules in tumor metastasis	Dr. Amitava Chatterjee Chittaranjan National Cancer Institute Kolkata	4.00
267	Studies on human papillomavirus infection during pregnancy, perinatal infection and its persistence	Dr. Ramdas Chatterjee Chittaranjan National Cancer Institute Kolkata	3.76
268	Evaluation of dopamine as a potential protective agent against cytotoxic drug- induced myelosuppression	Dr. M.R. Ray Chittaranjan National Cancer Institute Kolkata	1.90
269	Mode of action of calcium glutarate in skin tumorigenesis	Dr. K.P. Gupta Industrial Toxicology Research Centre Lucknow	1.33
270	Role of reactive oxygen radicals and herbal preparations in anterior uveitis	Dr. Basant Lal K.G's Medical College Lucknow	0.32
271	Urban hospital-based case-control study to identify risk factors for acute myocardial infarction	Dr. V.K. Puri K.G's Medical College Lucknow	2.08
272	Prevention of disability among pre - school children	Dr. J.V. Singh K.G's Medical College Lucknow	10.39
273	Recidivism : a study to identify risk factors to formulate preventive and rehabilitative strategies	Dr. S.C. Tiwari K.G's Medical College Lucknow	2.02
274	Study with human retinal S-antigen : epitope mapping in uveitis patients	Dr. V.K. Singh Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	4.82
275	Value of culture and serology in ophthalmic complications of leptospirosis	Dr. P. Namper Umalsamy Aravind Eye Hospital and Postgraduate Institute Madurai	4.23

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
276	Studies on epidemiology, culture, immunology and molecular biology of <i>Rhinosporidium seeberi</i>	Dr. C. Rajamanickam Madurai Kamaraj University Madurai	4.36
277	The role of HPV, p53 alterations, ras mutations and Bcl-2 expression in cervical cancers in India	Dr. D. Saranath Cancer Research Institute Mumbai	4.03
278	National Cancer Registry - Population based	Dr. M.R. Kamat Indian Cancer Society Mumbai	6.82
279	Vasectomy and cancer of prostate : a multicentric case control study under NCRP	Dr. M.R. Kamat Indian Cancer Society Mumbai	0.80
280	National Cancer Registry -Hospital based	Dr. K.A. Dinshaw Tata Memorial Hospital Mumbai	0.98
281	National Cancer Registry - Rural Cancer Registry	Dr. K.A. Dinshaw Tata Memorial Hospital Mumbai	3.46
282	Alternating triple therapy regimen in aggressive lymphomas (B - cell type) : correlation with distinct biologic entities	Dr. R. Gopal Tata Memorial Hospital Mumbai	8.81
283	Study of P ₁₅ and P ₁₆ in acute lymphoblastic leukemia	Dr. Purvish M. Parikh Tata Memorial Hospital Mumbai	1.94
284	Mechanisms of protein phosphorylation and signalling pathways during tumour promotion by two new liver tumour promoters in primary cultures of normal and preneoplastic rat hepatocytes	Dr. K.V.K. Rao Tata Memorial Hospital Mumbai	0.95
285	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	1.99
286	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	0.22

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
287	Study of risk factors in adult onset focal dystonia	Dr. Madhuri Behari All India Institute of Medical Sciences New Delhi	2.48
288	Evaluation of iatrogenic nerve injuries following orthopedic procedures and role of nerve stimulation in their management	Dr. Surya Bhan All India Institute of Medical Sciences New Delhi	4.14
289	Incremental predictive accuracy of transcranial magnetic stimulation (TMS) as prognostic indicators for motor recovery in patients with acute stroke	Dr. Manvir Bhatia All India Institute of Medical Sciences New Delhi	3.79
290	Assessment of human cardiac allograft rejection using light microscopy, electron microscopy and immunohistochemistry	Dr. Prem Chopra All India Institute of Medical Sciences New Delhi	0.53
291	Studies on the immunomodulation by insecticides : effects of DDT, BHC and aldrin on the serum complement and complement macrophage interactions	Dr. Nibhriti Das All India Institute of Medical Sciences New Delhi	1.54
292	Urinary screening of school children of Delhi : a preliminary study	Dr. A.K. Dinda All India Institute of Medical Sciences New Delhi	1.38
293	Urban hospital-based case- control study to identify risk factors for acute myocardial infarction	Dr. B.L. Jaiikhani All India Institute of Medical Sciences New Delhi	7.58
294	Estimation of serum sialic acid - glycosaminoglycans in patients of ankylosing spondylitis - development of a possible new laboratory test for diagnosis of early ankylosing spondylitis	Dr. Arvind Jayaswal All India Institute of Medical Sciences New Delhi	3.00
295	Role of nutritional factors in laryngeal cancers in India	Dr. Umesh Kapil All India Institute of Medical Sciences New Delhi	4.28
296	A study of proliferative index, apoptotic index and galectin expression pattern in thyroid lesions presenting as solitary thyroid nodule	Dr. A.K. Karak All India Institute of Medical Sciences New Delhi	2.23
297	Stress in children	Dr. Manju Mehta All India Institute of Medical Sciences New Delhi	0.20

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
298	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	2.19
299	Molecular alterations in human esophageal cancer : potential prognostic implications	Dr. Ranju Ralhan All India Institute of Medical Sciences New Delhi	6.76
300	Evaluation of external fixation and internal fixation in fractures of distal radius in Indian patients	Dr. S. Rastogi All India Institute of Medical Sciences New Delhi	5.16
301	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	1.81
302	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	1.40
303	Medulloblastoma in children and adults : a comparative study with special reference to clinicopathological features as well as cell proliferation , apoptosis and their regulatory proteins	Dr. Chitra Sarkar All India Institute of Medical Sciences New Delhi	2.89
304	<i>C.pneumoniae</i> and coronary artery disease : use of polymerase chain reaction assay (PCR), agent detection and serology in investigating the association	Dr. Gita Satpathy All India Institute of Medical Sciences New Delhi	3.19
305	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	1.69
306	Telomerase activity in carcinoma cervix - role of HPV	Dr. Neeta Singh All India Institute of Medical Sciences New Delhi	1.75
307	Prevalence, etiological factors and treatment of malnutrition by dietary intervention in patients with chronic pancreatitis	Dr. R.K. Tandon All India Institute of Medical Sciences New Delhi	3.80
308	National Cancer Registry- Population based	Dr. Kusum Verma All India Institute of Medical Sciences New Delhi	5.78

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
309	Vasectomy and cancer of prostate : a multicentric case control study	Dr. Kusum Verma All India Institute of Medical Sciences New Delhi	1.96
310	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	3.63
311	Antioxidant status in Parkinson's disease	Sh. S. Vivekanandhan All India Institute of Medical Sciences New Delhi	2.30
312	National Cancer Registry- Co-ordinating Unit (Operational Wing)	Dr. Bela Shah Indian Council of Medical Research New Delhi	10.25
313	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	2.50
314	Prevention of disability among pre - school children (Technical Wing)	Dr. Bela Shah Indian Council of Medical Research New Delhi	0.25
315	Causes of death by verbal autopsy - a pilot study	Dr. Arvind Pandey Institute for Research in Medical Statistics New Delhi	7.78
316	The role of pentanucleotide repeat (PNR) and kringle IV polymorphism in atherosclerosis	Dr. Uttam Pati Jawaharlal Nehru University New Delhi	4.97
317	Studies on the association of chronic infection with coronary artery disease (CAD) with special reference to <i>Chlamydia pneumoniae</i>	Dr. S. Padmavati National Heart Institute New Delhi	4.46
318	<i>In vitro</i> cultivation of differentiated epidermis from human keratinocytes suitable for autologous grafting in burns patients	Dr. S.P. Bajaj Safdarjang Hospital New Delhi	9.18
319	Prevention of disability among pre - school children	Dr. H.C. Goyal Safdarjang Hospital New Delhi	12.25
320	Clinical and radiological assessment of patients of severe arthritis of hip joint by hybrid total hip arthroplasty and comparative analysis of results with cemented THR and cementless THR arthroplasty	Dr. Awadesh Kumar Singh Safdarjang Hospital New Delhi	3.10

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
321	Relevance and significance of proteins S100 - A2, A4, A6 and B in CNS neoplasms and development of cell lines from clinical specimens	Dr. Anjali S. Shiras National Centre for Cell Science Pune	4.29
322	Studies on suicide behaviour	Dr. K.A. Kumar Medical College and SAT Hospital for Women & Children Thiruvananthapuram	2.93
323	Recent trends in role of diet and drinking water in urolithiasis	Dr. Y.M.Fazil Marickar Medical College and SAT Hospital for Women & Children Thiruvananthapuram	2.92
324	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	1.75
325	Biological prognostic markers in oral squamous cell carcinoma	Dr. S. Kannan Regional Cancer Centre Thiruvananthapuram	0.84
326	National Cancer Registry - Hospital Based	Dr. M. Krishnan Nair Regional Cancer Centre Thiruvananthapuram	3.02
327	Metalloproteinase gene activation during tumor progression in the oral mucosa	Dr. M. Radhakrishna Pillai Regional Cancer Centre Thiruvananthapuram	6.21
328	Studies on energy deficiency in an animal model of hepatic microvesicular steatosis produced by inhibition of fatty acid oxidation	Dr. K.A. Balasubramanian Christian Medical College and Hospital Vellore	1.01
329	The value of intravesical oxybutynin, probanthine and capsaicin in the management of neuropathic bladders	Dr. Suranjan Bhattacharji Christian Medical College and Hospital Vellore	5.12
330	<i>Jai vigyan</i> mission mode project on community control of RF/RHD in India	Dr. A. Abraham Joseph Christian Medical College and Hospital Vellore	10.68
Basic Medical Sciences			
331	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. M. Rajani BV Patel Pharmaceutical Education and Research Centre Ahmedabad	4.75

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
332	Medicinal plant monographs on diseases of public health importance - Filariasis	Dr. R.K. Shenoy T.D. Medical College and Hospital Alappuzha	0.34
333	Studies on the reactive oxygen species damaged DNA : implications in the etiopathogenesis of SLE	Sh. Moinuddin Jawaharlal Nehru Medical College Aligarh	1.00
334	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	1.47
335	Characterization of <i>Plasmodium falciparum</i> inosine monophosphate dehydrogenase (IMPDH) as a drug target	Dr. Hemalatha Balaram Jawaharlal Nehru Centre for Advanced Scientific Research Bangalore	4.20
336	Alpha adrenergic receptor linked second messenger response to antidepressants in rat brain	Dr. M.N. Subhash National Institute of Mental Health and Neurosciences Bangalore	0.96
337	<i>Jai vigyan</i> mission project on community control of thalassaemia syndromes - awareness, screening, genetic counselling and prevention	Dr. Cecil R Ross St. John's Medical College Bangalore	6.73
338	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. G.P. Chhotray Regional Medical Research Centre Bhubaneswar	2.60
339	Effect of prenatal exposure of ethanol on the functional development of intestine in rats	Dr. Akhtar Mahmood Panjab University Chandigarh	0.76
340	Biochemical mechanisms of aluminium induced neurotoxicity and its role in neurodegenerative diseases	Dr. Kiran Dip Gill Postgraduate Institute of Medical Education and Research Chandigarh	2.48
341	Phase II study of transcriptional regulation of human LDL-receptor gene by cholesterol	Dr. Deepak Kaul Postgraduate Institute of Medical Education and Research Chandigarh	2.21
342	Molecular mechanisms responsible for the defective allele of human hepatic cytochrome p450 2c19	Dr. K.K. Kohli Postgraduate Institute of Medical Education and Research Chandigarh	1.39

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
343	Medicinal plant monographs on disease of public health importance - Kala-azar	Dr. R.C. Mahajan Postgraduate Institute of Medical Education and Research Chandigarh	0.34
344	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	2.25
345	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	2.55
346	Flexible dose open trial on <i>Vijayasar</i> for known diabetes	Dr. R.S. Hariharan Chennai Medical College and Government General Hospital Chennai	2.80
347	Effect of vitamin-E supplementation on the function of RBC anionic binding protein in uraemic patients	Dr. R. Selvam Dr.A.L. Mudaliar P.G. Institute of Basic Medical Sciences Chennai	1.56
348	Central Biostatistical Monitoring Unit for Epidemiology	Dr. M.D. Gupte National Institute of Traditional Medicine Research Chennai	15.72
349	Clinical Pharmacology Unit	Dr. V. Kumaraswami Tuberculosis Research Centre Chennai	33.99
350	Flexible dose open trial on <i>Vjayasar</i> for known diabetes	Dr. P.K. Mishra S.C.B. Medical College Cuttack	2.75
351	Medicinal plant monographs on diseases of public health importance - Malaria	Dr. S. Pattanayak B-91, Swasthya Vihar Delhi	0.34
352	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	1.00

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
353	Role of lipoprotein(a) and its phenotypes as a risk factor for premature coronary artery disease in Indian subjects	Dr. Jasvinder K. Gambhir University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	1.19
354	Investigations on the hypoglycaemic activity of <i>Eugenia jambolana</i> in rabbits	Dr. Suman Bala Sharma University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	0.37
355	Biochemical investigations on the mechanism of action of hypoglycaemic compound from the water extract of the bark of <i>Ficus bengalensis</i>	Dr. Rimi Shukla University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi	1.93
356	Determinants of genetic and sociocultural aspects of health <i>vis-a-vis</i> the role of health providers among the tribes of coastal, desert and Himalayan regions	Dr. G.K Khatriya University of Delhi Delhi	0.50
357	Behaviour of pulmonary vagal sensory receptors on opening of an arteriovenous shunt in dogs	Dr. K. Ravi Vallabhbhai Patel Chest Institute Delhi	0.48
358	<i>Jai vigyan</i> mission project on community control of thalassaemia syndromes - awareness, screening, genetic counselling and prevention	Dr. J. Mahanta Regional Medical Research Centre Dibrugarh	6.73
359	Study on genetic diversity in tribal populations of Andaman and Nicobar Islands and creation of immortalised cell lines of vanishing tribes	Dr. Lalji Singh Centre for Cellular and Molecular Biology Hyderabad	7.05
360	Genetic causes of male infertility in India	Dr. K. Thangaraj Centre for Cellular and Molecular Biology Hyderabad	4.75
361	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	0.82
362	Centre for Research on Aging and Brain	Dr. K. Subba Rao University of Hyderabad Hyderabad	34.00

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
363	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	29.66
364	Application of primary monolayer cultures of rat hepatocytes in the development of hepatoprotectives from medicinal plants	Dr. R.K. Johri Regional Research Laboratory Jammu Tawi	2.02
365	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. B.K. Kapahi Regional Research Laboratory Jammu Tawi	1.41
366	Optimization of lead molecule from <i>Boerhaavia diffusa</i> as anti-osteoporosis agent	Dr. Rakesh Maurya Regional Research Laboratory Jammu Tawi	1.25
367	Studies on oxidant-mediated activation of ca ²⁺ dependent proteases in pulmonary vascular smooth muscle membrane	Dr. Sajal Chakraborti University of Kalyani Kalyani	2.28
368	Rapid diagnostic test for c-reactive protein (CRP) based on whole blood agglutination by a conjugated protein of monovalent lectin and fab fragment of anti human c-reactive immunoglobulin	Dr. T.K. Maiti Indian Institute of Technology Kharagpur	1.16
369	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 Kolkata	0.51
370	Pharmacological aspects of gastrointestinal motility with special reference to development of prokinetic drugs	Dr. Lalima Chaudhury Indian Institute of Chemical Biology Kolkata	1.67
371	Antibody - mediated drug delivery in visceral leishmaniasis	Dr. P. K. Das Indian Institute of Chemical Biology Kolkata	3.49
372	Evaluation of naturally occurring indole alkaloids from <i>Tabernaemontana coronaria</i> for the treatment of opioid tolerance and dependence	Dr. Sumantra Das Indian Institute of Chemical Biology Kolkata	2.31
373	Production of a functional antimicrobial peptide in order to study the potential bacterial resistance it may encounter	Dr. S.K. Pal Jadavpur University Kolkata	0.80

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
374	<i>Jai vigyan</i> mission project on community control of thalassaemia syndromes - awareness, screening, genetic counselling and prevention	Dr. M.K. Ghosh N.R.S. Medical College and Hospital Kolkata	7.04
375	Neuropharmacological studies in rats having d - galactosamine - induced hepatitis	Dr. Dipankar Bhattacharyya University College of Medicine Kolkata	0.92
376	Further studies on the snake venom neutralizing factor from <i>Hemidesmus indicus</i> and <i>Pluchea indica</i>	Dr. Antony Gomes University College of Science and Technology Kolkata	2.22
377	Nicotine and hypertension : role of kidney	Dr. Juthika Koley University College of Science and Technology Kolkata	1.74
378	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 Kolkata	4.03
379	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. K.S. Suresh Kumar Nilgiris Adivasi Welfare Association Kotagiri	4.21
380	Flexible dose open trial on <i>Vijayasar</i> for known diabetes	Dr. R.V. Jaya Kumar Medical College and Hospital Kottayam	2.80
381	Centre for Advanced Research for Drug Development from Natural/Plant Products	Dr. C.M. Gupta Central Drug Research Institute Lucknow	45.71
382	<i>Plasmodium falciparum</i> ORF 470: investigation of structure- function relationship	Dr. Saman Habib Central Drug Research Institute Lucknow	1.00
383	Rational approach to new remedies for mycotic infections	Dr. Vishnu Ji Ram Central Drug Research Institute Lucknow	2.04
384	Development of new antimalarial agents based on leads from natural products	Dr. Chandan Singh Central Drug Research Institute Lucknow	2.56
385	Cellular and functional recovery of Parkinsonian rats after intrastriatal transplantation of para neural cells : carotid body and olfactory ensheathing cell transplantation	Dr. A.K. Agrawal Industrial Toxicology Research Centre Lucknow	2.31

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
386	Reactive metabolites of benzene with the ability to induce oxidative stress as component of the mechanism of benzene toxicity	Dr. Alok Dhawal Industrial Toxicology Research Centre Lucknow	1.41
387	Traditional remedies for diabetes mellitus - toxicity study for <i>Vijayasar</i>	Dr. K.K. Gupta Industrial Toxicology Research Centre Lucknow	2.75
388	Mechanism of tumour suppression by nicotinamide	Dr. K.P. Gupta Industrial Toxicology Research Centre Lucknow	2.79
389	Ameliorative potential of <i>Picrorhiza kurroa</i> in cadmium induced hepato - and renal toxicity in rat model	Dr. Shashi Khandelwal Industrial Toxicology Research Centre Lucknow	0.55
390	Neurochemical, reproductive and immunotoxicological evaluation of the pyrethroid based mosquito repellents exposed during developmental period	Dr. P.K. Seth Industrial Toxicology Research Centre Lucknow	1.00
391	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. Shanta Mehrotra National Botanical Research Institute Lucknow	5.36
392	Handigodu disease - phase II	Dr. S.S. Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	8.62
393	Medicinal plant monographs on diseases of public health importance - Immunomodulators	Dr. S.S. Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	0.34
394	Prevalence and molecular characterization of alpha-thalassaemia in Uttar Pradesh	Dr. Sarita Agarwal Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow	0.91
395	Medicinal plant monographs on diseases of public health importance - Diabetes mellitus	Dr. B.N. Dhawan 3, Ramakrishna Marg Lucknow	0.34
396	<i>Jai vigyan</i> mission project on community control of thalassaemia syndromes -awareness,screening, genetic counselling and prevention	Dr. Sheila Das Christian Medical College and Brown Memorial Hospital Ludhiana	6.73

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
397	Physiological and behavioural aspects of human circadian rhythms under prolonged socio-temporal isolation	Dr. G. Marimuthu Madurai Kamaraj University Madurai	0.90
398	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. K.K. Bhutani National Institute of Pharmaceutical Education and Research Mohali	6.19
399	ICMR Unit on Standardisation, Quality Control and Formulation of Traditional Medicine	Dr. K.K. Bhutani National Institute of Traditional Medicine Research Mohali	2.76
400	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 Research Society Mumbai	0.68
401	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Dipika Mohanty B.J. Medical College and Sasoon General Hospital Pune	3.62
402	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	11.03
403	Centre for Advanced Research on Clinical Pharmacology	Dr. Nilima A. Kshirsagar Topiwala National Medical College and B.Y.L. Nair Charitable Hospital Mumbai	34.91
404	Circumvention of drug resistance by phenoxazine MDR modulators in antibacterial chemotherapy	Dr. K.N. Thimmaiah University of Mysore Mysore	1.79
405	Development of enriched /cocktail antivenin to the toxic principles of <i>Vipera russelli</i> venom of different regions of India	Dr. T. Veerabasappa Gowda University of Mysore Mysore	1.19
406	Simultaneous electroencephalography (EEG) and MRI studies of sleep- wakefulness in rat brain	Dr. N.R. Jagannathan All India Institute of Medical Sciences New Delhi	4.13

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
407	Endocrinological effects of 50 hz electromagnetic fields of moderately high intensity in rats	Dr. P. Jha All India Institute of Medical Sciences New Delhi	2.70
408	Quinolone binding to DNA : spectroscopic and computer modelling studies	Dr. M.R. Rajeswari All India Institute of Medical Sciences New Delhi	1.96
409	Medicinal plant monographs on diseases of public health importance - Liver diseases	Dr. S.S. Handa F/7, Lajpat Nagar III New Delhi	1.96
410	Monographs on medicinal plants of India	Dr. Ashok Gupta Indian Council of Medical Research New Delhi	1.96
411	Medicinal plant monographs on diseases of public health importance - Co-ordinating Unit	Dr. Ashok Gupta Indian Council of Medical Research New Delhi	1.87
412	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Vasantha Muthuswamy Indian Council of Medical Research New Delhi	2.27
413	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	1.64
414	Domestication and cultivation of characterized population of <i>Picrorhiza kurroa royle</i> ex.benth. in Indian western Himalaya	Dr. Virendra Singh Institute of Himalayan Bioresource Technology Palampur	2.35
415	New natural products as human immuno-deficiency virus reverse transcriptase (NHRT) inhibitors from the genus <i>Calophyllum</i>	Dr. Debashis Mitra National Centre for Cell Science Pune	0.50
416	New natural products as human immuno-deficiency virus reverse transcriptase (NHRT) inhibitors from the genus <i>Calophyllum</i>	Dr. M.K. Gurjar National Chemical Laboratory Pune	1.55
417	Mechanism of amelioration of denervation - induced atrophy in rat skeletal muscle by β -adrenergic agonists, clenbuterol and isoprenaline	Dr. S.S. Katoch H.P. University Shimla	2.01
418	Indigenous plant lectins and their use as reagents in immunology and pathology	Dr. P. Remani Regional Cancer Centre Thiruvananthapuram	1.06

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Investigator/Institution</i>	<i>Grant released during the yr. (Rs. in lakhs)</i>
419	Development of standards of selected therapeutically important medicinal plants and preparation of monographs thereof	Dr. G. Sreekandan Nair Tropical Botanic Garden and Research Institute Thiruvananthapuram	4.03
420	<i>Jai vigyan</i> 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	3.98
421	Intervention programme for nutritional anaemia and haemoglobinopathies amongst some primitive tribal populations of India	Dr. Y.M. Italia Valsad Raktadan Kendra Valsad	2.65
422	Experimental evaluation of some ayurvedic rasayanas on peptic ulcer and gastric muscosal offensive and defensive factors	Dr. R.K. Goel Institute of Medical Sciences Banaras Hindu University Varanasi	2.61
423	Behavioural teratology of some centrally acting drugs	Dr. Mandavi Singh Institute of Medical Sciences Banaras Hindu University Varanasi	0.95
424	Medicinal plant monographs on diseases of public health importance - Anti-inflammatory Drugs	Dr. R.H. Singh Institute of Medical Sciences Banaras Hindu University Varanasi	0.95
Publication and Information			
425	Scientometric studies on ICMR- sponsored research	Dr. K. Satyanarayana Indian Council of Medical Research New Delhi	0.99
426	ICMR-NIC Centre for Biomedical Information	Smt. Naina Pandita National Informatics Centre New Delhi	10.18

Appendix VIII

List of Fellowships Funded During 2000-2001

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
Epidemiology and Communicable 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	A study of polymorphic regions of the genes encoding protective antigens of <i>P.vivax</i> and <i>P.falciparum</i> strains prevalent in north-western regions of india	Sh. Umar Farooq Gaur Postgraduate Institute of Medical Education and Research Chandigarh
3	Antibody mediated selective targeting of isonicotinic acid hydrazide (INH) entrapped in PLG microparticles specifically to <i>Mycobacterium tuberculosis</i> infected macrophages	Smt. Indu Mehta Postgraduate Institute of Medical Education and Research Chandigarh
4	Role of anaerobic stress proteins in pathophysiology of <i>Salmonella typhimurium</i> infection	Sh. Raman Deep Singh Postgraduate Institute of Medical Education and Research Chandigarh
5	Protective efficacy and immunogenicity of iron regulated outer membrane proteins (IROMPs) of <i>Salmonella typhi</i>	Km. Shaloo Sood Postgraduate Institute of Medical Education and Research Chandigarh
6	To study the protective efficacy of antioxidants and Indian herbal antidiarrhoeals in rotavirus diarrhoea	Sh. Ranjan Katyal Postgraduate Institute of Medical Education and Research Chandigarh
7	To study the immune response against lipopolysaccharide and outer membrane proteins and role of free radicals during experimental <i>H.influenzae</i> infection in mice	Km. Jaya Sahni Postgraduate Institute of Medical Education and Research Chandigarh
8	Rapid diagnosis of tuberculosis using purified antigens	Km. K.R. Uma Devi Tuberculosis Research Centre Chennai

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
9	Immunomodulatory effect of immune complexes in experimental tuberculous infections	Dr. H. Shakila Tuberculosis Research Centre Chennai
10	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
11	HLA - DR2 and granulysin producing potential of CD8+ and CD4+ cells in pulmonary tuberculosis	Dr. Anila Anna Mathan Tuberculosis Research Centre Chennai
12	HIV seroprevalence in primary opioid dependence	Dr. Shubhangi Bedi Institute of Human Behaviour and Allied Sciences Delhi
13	Awareness of HIV/AIDS and risk behaviour pattern in patients of primary opioid dependence	Dr. Versha E. Millicans Institute of Human Behaviour and Allied Sciences Delhi
14	Restriction analysis and cloning of plasmid from a clinical isolate of <i>Mycobacterium avium - intracellulare</i>	Km. Divya Venugopal Vallabhbhai Patel Chest Institute Delhi
15	Identification and pathogenesis of influenza virus in acute exacerbation asthma	Sh. Pankaj Kumar Vallabhbhai Patel Chest Institute Delhi
16	Natural habitats of <i>Cryptococcus neoformans</i> var. <i>gattii</i> and var. <i>neoformans</i> and their serotypes	Sh. S.R. Nawange Rani Durgawati Vishwavidyalaya Jabalpur
17	An intervention study among certain categories of health personnel in the medical colleges & teaching institutes in Calcutta, on their knowledge, attitude and practice with regard to HIV infection, AIDS and its control measures	Dr. Dipanjan Sujit Roy All India Institute of Hygiene and Public Health Kolkata
18	Molecular mechanism of bile induced changes in <i>Vibrio cholerae</i> and their physiological relevance	Sh. Nilanjan Sengupta Indian Institute of Chemical Biology Kolkata
19	Characterization of fumarate reductase mediated succinate formation from <i>Leishmania donovani</i> promastigotes for potential target of chemotherapy	Sh. Gautam Datta Jadavpur University Kolkata

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
20	Evaluation of newer laboratory techniques for early diagnosis of extra pulmonary tuberculosis	Smt. Vandana Tiwari K.G's Medical College Lucknow
21	Is leptospiral infection a significant public health problem in north India	Smt. M.Martha Prem Latha All India Institute of Medical Sciences New Delhi
22	Prevalence and molecular typing of enterotoxigenic <i>Bacteroides fragilis</i> (ETBF) in diarrhoeal diseases	Dr. Nidhi Sharma All India Institute of Medical Sciences New Delhi
23	Monitoring vancomycin resistant enterococci (VRE) amongst leukemia patients	Dr. Rachna Chandra All India Institute of Medical Sciences New Delhi
24	Molecular fingerprinting of clinical isolates of <i>Mycobacterium tuberculosis</i> by IS 6110 - based restriction fragment length polymorphism (RFLP)	Smt. N.Vijaya Bhanu All India Institute of Medical Sciences New Delhi
25	Characterization of DEVR - DEVS and DEVS homologue (RV2027C gene product) of <i>Mycobacterium tuberculosis</i> with special reference to their phosphorylation	Sh. S.Chakravorty All India Institute of Medical Sciences New Delhi
26	A comparative study of the role of flexible fiberoptic bronchoscopy and sputum examination in diagnosis of pulmonary infections in iatrogenic immunocompromised patients	Dr. Nitin Sood Army Hospital (Research & Referral) New Delhi
27	Neurological manifestation of HIV infection	Dr. Shibashish Bhattacharyya Army Hospital (Research & Referral) New Delhi
28	Phenotypic and genotypic characterisation of methicillin resistant <i>Staphylococcus aureus</i> and its role in epidemiological typing	Sh. N.P.Mohapatra Lady Hardinge Medical College and Associated Hospitals New Delhi
29	Genital infection with human papilloma virus : correlation with pregnancy and neonatal outcome	Dr. Garima Chauhan Maulana Azad Medical College and Associated Hospitals New Delhi
30	Role of hepatitis E virus (HEV) infection in acute viral hepatitis and fulminant hepatitis during pregnancy	Km. Nishat Jilani Maulana Azad Medical College and Associated Hospitals New Delhi

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
31	Pathogenicity of <i>Yersinia enterocolitica</i> of human and animal origin	Sh. Itender Singh University of Delhi South Campus New Delhi
Reproductive Health and Nutrition		
32	Biodegradable polymeric implants for the controlled release of contraceptive agents	Sh. D. Selvaraj Central Leather Research Institute Chennai
33	Characterization of cadherin and catenin expressed during implantation and establishment of its role in embryonic attachment	Km. Deeksha Saxena Devi Ahilya Vishwavidyalaya Indore
34	Antifertility investigations on the partially purified fractions of the seeds of <i>Carica papaya</i> with particular emphasis on mode of action in male albino rats	Dr. Neelam Pathak University of Rajasthan Jaipur
35	Development of an improved cryopreservation technology for human ejaculated spermatozoa	Sh. C.N. Kundu Indian Institute of Chemical Biology Kolkata
36	Fertility failure in intrauterine insemination : its causes with special reference to oxidative damage	Dr. Anuradha Chakrabarty Indian Institute of Chemical Biology Kolkata
37	A study of health and nutritional status in relation to some biosocial factors among the Kora and Mahali tribes of West Bengal	Dr. Bechuram Mondal Indian Statistical Institute Kolkata
38	Studies on further development of progesterone releasing intrauterine device (IUD) to enhance its duration of release	Dr. A.K.Ghosh Jadavpur University Kolkata
39	Studies on protein-fat interaction and its influence on serum and tissue lipid profile	Smt. Malabika Sen University College of Science & Technology Kolkata
40	Studies on molybdenum in tissues and interaction with other trace elements	Km. Ratna Pandey Lucknow University Lucknow
41	The effect of administration of low, non-lethal doses of methyl parathion, phorate and monocrotophos on reproduction of male rats	Dr. Vijay Kumar Verma Punjab Agricultural University Ludhiana

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
42	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
43	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
44	Modulation of intergrin and cytokine expression in mouse blastocysts by steroid hormones : mechanisms of embryo implantation	Km. Sayantani Basak All India Institute of Medical Sciences New Delhi
45	Effect of food flavor cinnamaldehyde on kidney - a molecular approach	Dr. J.T. Sivakumar All India Institute of Medical Sciences New Delhi
46	Nutritional status of diabetics	Dr. Sneh Arora 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	Estimation of losses of iodine in foods prepared with iodized salt during different cooking procedures	Dr. Anita Nath All India Institute of Medical Sciences New Delhi
49	Trans-vaginal colour doppler assessment of high risk pregnancies	Dr. Ranjit Manchanda All India Institute of Medical Sciences New Delhi
50	Role of assisted conception in management of infertile couples	Dr. Shalini Singh All India Institute of Medical Sciences New Delhi
51	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
52	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
53	Nutrition knowledge of medical practitioners in hospitals : an assessment, intervention and impact	Km. Charu Institute of Home Economics New Delhi

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
54	The effect of ethinyl estradiol in clomiphene induced cycles on endometrial thickness and pregnancy outcome	Dr. Shalini Pal Maulana Azad Medical College and Associated Hospitals New Delhi
55	A study of socio-demographic and medical variables as predictors of severe acute maternal morbidity and mortality in a tertiary care hospital	Dr. Babita Sharma Maulana Azad Medical College and Associated Hospitals New Delhi
56	Antioxidative effects of melatonin to counter damage induced by lipid peroxidation during pregnancy and post delivery : studies in rats	Dr. Kanchan Upreti National Institute of Health and Family Welfare New Delhi
57	Evaluation of the effects of estrogenic environmental contaminants in male reproduction of adult rats	Sh. C. Latchoumycandane University of Pondicherry Pondicherry
58	Potential of antioxidants in fruits and vegetables in prevention of oxidation stress related disorders prevalent in Indians with special reference to cataract	Smt. Kirtan Vilas Tarwadi Agharkar Research Institute Pune
59	Role of micronutrients (vitamins and W-3 fatty acids) in foetal adaptations to undernutrition and implications for adult health using rat model	Dr. Sadhana Ramachandra Joshi Agharkar Research Institute Pune
60	Gender discrimination and child mortality : a sociological study in Salem district of Tamil Nadu	Sh. P. Murugan Bharathidasan University Tiruchirapalli
61	Assessment of the status of iodine deficiency disorders in urban area of Udaipur district, Rajasthan	Km. Ritu Pradhan College of Home Science Udaipur
62	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		
63	Effect of nephrotoxic agents on kidney	Km. Sabiha Fatima Aligarh Muslim University Aligarh
64	Study of mucin in the blood of cancer stomach patients	Smt. R. Deepti Bala University of Madras Chennai

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
65	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
66	A study of oxidative state and immunological status in experimental animals and human cases exposed to some common pesticides	Km. Vandana Seth University College of Medical Sciences and Guru Teg Bahadur Hospital Delhi
67	Improving mental health of high school students with psychotherapeutic interventions in relation to examination anxiety	Dr. Anita Gupta University of Delhi Delhi
68	Biochemical and molecular genetics of homocysteine metabolism in coronary artery disease	Sh. Vinukonda Govindaiah Centre for DNA Fingerprinting and Diagnostics Hyderabad
69	Comparative study on tobacco consumption among medical and non-medical male college students in Calcutta	Dr. Manas Kumar Barua All India Institute of Hygiene and Public Health Kolkata
70	Studies on ceramide in relevance to synovial cell and fluid of rheumatoid arthritis to find a basis for recovery	Dr. Aditi Banerjee Indian Institute of Chemical Biology Kolkata
71	Antitumour potential of 1 alpha, 25- dihydroxyvitamin D3 in N-nitrosodiethanolamine induced rat liver carcinogenesis : a mechanistic approach	Sh. Ranjan Basak Jadavpur University Kolkata
72	Studies on correlation of chlorinated pesticide and heavy metal lead and cadmium residues with human semen quality	Km. Niraj Pant Industrial Toxicology Research Centre Lucknow
73	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
74	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
75	MIB-1 immunocytochemical expression in normal and neoplastic epithelium of human uterine cervix	Dr. Anju Mehrotra K.G's Medical College Lucknow

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
76	Rehabilitation surgery for lower limb deformities due to poliomyelitis	Dr. Rahul Khare K.G's Medical College Lucknow
77	Effect of timing of palatal repair on dento-facial growth and speech development : a retrospective study in South India	Dr. Yukti Nautiyal College of Dental Surgery Manipal
78	Evaluation of the antineoplastic and radiosensitizing activities agents in cultured HELA cells	Sh. Shrinath M. Baliga Kasturba Medical College and Hospital Manipal
79	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
80	Comparison of white on white and blue on yellow automated perimetry in ocular hypertension and primary open angle glaucoma	Dr. Vikas Gulati All India Institute of Medical Sciences New Delhi
81	Generation of domain specific antibodies against HIC-1,a putative tumour suppressor protein, with a long term perspective to study its expression in various grades of human glial and other tumours and cell lines	Sh. Abdul Matin Mondal All India Institute of Medical Sciences New Delhi
82	Studies on the interaction of endosulfan and malathion with serum complement and macrophages	Km. Sadia Ayub All India Institute of Medical Sciences New Delhi
83	Studies on BRCA1 and BRCA 2 gene mutations in breast cancer patients	Dr. T.M. Valarmathi All India Institute of Medical Sciences New Delhi
84	Cytokine profiles of peripheral blood lymphocytes in patients with oral cancer	Km. Abhilasha Agarwal All India Institute of Medical Sciences New Delhi
85	To assess the response of chemotherapy and radiotherapy in high grade malignant glioma and estimation of micronuclei in these radio-chemo exposed human population	Dr. Dilip Kumar Parida All India Institute of Medical Sciences New Delhi
86	Correlation of polymorphism of apolipoprotein E gene with dyslipidemia and body composition of North Indian subjects : a case-control study	Km. Manjari Dwivedi All India Institute of Medical Sciences New Delhi
87	Study of retinoic acid receptors in human oral premalignant and malignant lesions	Sh. Nitin Chakravarti All India Institute of Medical Sciences New Delhi

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
88	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
89	A study of genetic alterations overriding the cell arrest effect of normal p53 overexpression in an <i>in vitro</i> glial tumour model	Sh. S. Ilanchezhian All India Institute of Medical Sciences New Delhi
90	A critical study of clinicopathological features with ultrasound of neck in malignant neck masses	Dr. Nirupam Adlakha Army Hospital (Research & Referral) New Delhi
91	A comparative study of solid silicone tire versus silicone sponge application in inferior retinal detachment surgery	Dr. A.K. Rastogi Army Hospital (Research & Referral) New Delhi
92	Histopathological examination study of host cornea undergoing keratoplasty and its correlation with the preoperative diagnosis of the corneal disease	Dr. Radha Vasan Army Hospital (Research & Referral) New Delhi
93	Study of inflammatory response to normothermic cardiopulmonary bypass	Dr. S.N. Naresh Army Hospital (Research & Referral) New Delhi
94	Serum estimation of carcinoembryonic antigen (CEA) in head and neck neoplasms	Dr. Rahul Sharma Army Hospital (Research & Referral) New Delhi
95	The merits and techniques of ossiculoplasty	Sh. Debajyoti Roy Army Hospital (Research & Referral) New Delhi
96	An evaluation of hearing in new born children of high risk group as compared to normal new born children to find out the incidence of congenital and early acquired sensori neural hearing loss	Dr. Shilpi Arora Army Hospital (Research & Referral) New Delhi
97	Study of transient evoked otoacoustic emissions as a screening technique of hearing in neonates	Dr. B.S.Pandey Army Hospital (Research & Referral) New Delhi

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
98	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
99	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
100	Comparison of combination of epidural buprenorphine and neostigmine with combination of epidural buprenorphine and ketamine for postoperative analgesia	Dr. Sanjay Choubey Army Hospital (Research & Referral) New Delhi
101	Study of continuous epidural blockade using bupivacaine and bupivacaine with fentanyl for labour analgesia	Dr. Reshma Tewari Army Hospital (Research & Referral) New Delhi
102	Comparison of ossicular destruction by atticoantral disease in adults and children	Dr. Nimesh Kumar Gupta Safdrjang Hospital New Delhi
103	Rehabilitation of patients of severe arthritis of hip joint by hybrid total hip arthroplasty	Dr. Naval Bhatia Safdrjang Hospital New Delhi
104	A clinical study of postoperative glaucoma in cases following penetrating keratoplasty with posterior chamber intraocular lens implantation	Dr. Aradhana Singh Armed Forces Medical College and Command Hospital Pune
105	Role of aspiration biopsy reverse transcriptase PCR (ABRP) for the objective diagnosis of thyroid malignancies	Km. T.T. Sreelekha Regional Cancer Centre Thiruvananthapuram
106	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

107	Investigation into the role of dopamine and 5-hydroxytryptamine in glycemic control and central effects of hypoglycemia-induced convulsions	Sh. D.N. Umrani L.M. College of Pharmacy Ahmedabad
108	Antihyperglycaemic effect of <i>Phaseolus vulgaris</i> L.(kidney bean) and <i>Coccinia indica</i> W.and A. (little gourd) in experimental diabetes: effects compared with troglitazone, a new oral antidiabetic agent	Sh. S. Venkateswaran Annamalai University Annamalai Nagar

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
109	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
110	Identification and role of intestinal lactase gene in hypolactasia in adult rats	Km. Jaspreet Kaur Panjab University Chandigarh
111	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
112	Therapeutic efficacy of <i>Tinospora cordifolia</i> stem extract along with paclitaxel on 7,12-dimethyl benz(a) anthracene induced breast cancer in albino rats	Km. M. Sarumathi Dr. A.L. Mudaliar P.G. Institute of Basic Medical Sciences Chennai
113	Search for antidiabetic agents from arid zone plants	Dr. Rekha Arora University of Rajasthan Jaipur
114	Anti-thyroid action of phenylhydrazine: studies on the hypothalamopituitary - thyroid axis in juvenile and adult male rats	Dr. Mitali Pramanik Bose Institute (New Campus) Kolkata
115	Detection of specific snake envenomation : a non-instrumental approach	Sh. Parthasarathi Mitra Indian Institute of Chemical Biology Kolkata
116	Studies on growth and melanization of epidermal cells by selected ceramides and cerebrosides to compare the action of ceramides present in a human placental extract meant for vitiligo therapy	Km. Shampa Mallick Indian Institute of Chemical Biology Kolkata
117	Influence of black tea polyphenols on secretory and motor activity of gastrointestinal system	Dr. Saujen Basu Indian Institute of Chemical Biology Kolkata
118	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 Kolkata
119	9-O-acetyl sialoglycoconjugate (9-O-AC-SG), a novel biomarker on the surface of leukemic blasts-specific target molecule for drug targeting in childhood acute lymphoblastic leukemia (ALL) using an unique lectin and specific antibodies	Sh. Satyabrata Biswas Indian Institute of Chemical Biology Kolkata

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
120	Involvement of calcium in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine - induced neurotoxicity	Dr. Supriti Samanta Ray Indian Institute of Chemical Biology Kolkata
121	Ischaemic myocardial damage and red blood cells : role of antiarrhythmic drugs	Smt. Aiandriila Chattopadhyay Jadavpur University Kolkata
122	<i>In vitro</i> model for evaluation of medical devices for biological hazards	Dr. A.B. Pant Industrial Toxicology Research Centre Lucknow
123	Study of longitudinal growth and bone radiography in relation to oral iron chelator deferiprone (kelfer)	Dr. Anita Saxena Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
124	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
125	Development of antibodies against human sodium/iodide symporter (HNIS) and development of assay procedures for NIS	Dr. Amita Mehrotra Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow
126	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 Medical College and Hospital Manipal
127	Pre-clinical studies on the radio- and chemoprotective potential of the <i>Ocimum</i> flavonoids orientin and vicenin	Km. B. Vrinda Kasturba Medical College and Hospital Manipal
128	Apoptosis during immune response	Sh. C.P. Winston Kasturba Medical College and Hospital Manipal
129	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
130	Molecular genetic studies in glaucoma	Km. R. Vijaya All India Institute of Medical Sciences New Delhi

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
131	The septal noradrenergic mechanism for elaboration of male sexual behaviour in rats	Dr. Kamlesh Kumari Gulia All India Institute of Medical Sciences New Delhi
132	Cardioprotective effect of <i>Hibiscus rosa sinensis</i> : a biochemical study	Sh. K. Gauthaman All India Institute of Medical Sciences New Delhi
133	Role of the medial 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
134	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
135	Effects of arsenic on cell growth and development of <i>Dictyostelium discoideum</i>	Dr. Sampati Mukhopadhyay Jawaharlal Nehru University New Delhi
136	Heparin from the seaweed <i>Grateloupia filicina</i>	Sh. A. Muruganantham Centre of Advanced Study in Marine Biology Parangipettai
137	Patent anti- microbial substance from the marine mollusc <i>Aplysia</i> sp. (Gastropoda; Anaspidea; Aplysiidae)	Sh. J. Rajaganapathi Centre of Advanced Study in Marine Biology Parangipettai
138	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
139	Antineoplastic evaluation of alkaloidal principles of <i>Amoora rohituka</i> based on flow cytometry	Dr. T. Rabi Regional Cancer Centre Thiruvananthapuram
140	Studies on the metabolism of extra cellular matrix components by hepatic non-parenchymal cells	Km. P. Pranitha University of Kerala Thiruvananthapuram
141	Biochemical investigations on the flavonoids from <i>Emblica officinalis</i> and <i>Mangifera indica</i>	Km. L. Anila University of Kerala Thiruvananthapuram

<i>Sl.No.</i>	<i>Title of the Project</i>	<i>Name of the Fellow and Institution</i>
142	Effect of algal toxins (<i>Ptychodiscus brevis</i>) on the spinal monosynaptic transmission <i>in vitro</i>	Sh. J.N. Singh Institute of Medical Sciences Banaras Hindu University Varanasi
143	Search for <i>Brahmi</i> – a comparative study of <i>Bacopa monnieri</i> and <i>Centella</i> species	Dr. Deepa Arora Institute of Medical Sciences Banaras Hindu University Varanasi
144	Evaluation of biochemical changes of bile juice under the influence of a compound indigenous drug in biliary stone diseases	Dr. Pankaj Srivastava Institute of Medical Sciences Banaras Hindu University Varanasi
145	Neuropsychopharmacological studies on Indian <i>Hypericum perforatum</i> Linn	Sh. Vikas Kumar Institute of Technology Varanasi

Expenditure on Fellowships during the year Rs.108.00 lakhs