INTRODUCTION

The President notified the creation of the Department of Health Research under the Ministry of Health & Family Welfare through an amendment to the Government of India (Allocation of Business) Rules, 1961 on the 17th September, 2007.

The Department of Health Research was formally launched on 5th October, 2007 by the Minister for Science & Technology and Earth Science in a function presided over by the Minister for Health & Family Welfare, in the presence of the Minister of State for Health & Family Welfare.

The first Secretary of the Department who is also the Director General of the Indian Council of Medical Research, was appointed in November, 2008.

The following work has been allocated to the Department of Health Research:

- Promotion and co-ordination of basic, applied and clinical research including clinical trials and operational research in areas related to medical, health, biomedical and medical profession and education through development of infrastructure, manpower and skills in cutting edge areas and management of related information thereto.
- Promote and provide guidance on research governance issues, including ethical issues in medical and health research.
- Inter-sectoral coordination and promotion of public-private partnership in medical, bio-medical and health research related areas.
- Advanced training in research areas concerning medicine and health including grant of fellowships for such training in India and abroad.
- International cooperation in medical and health research including work related to international conferences in related areas in India and abroad.
- Technical support for dealing with epidemics and natural calamities.
- Investigation of outbreaks due to new and exotic agents and development of tools for prevention.
- Matters relating to scientific societies and associations, charitable and religious endowments in medicine and health research areas.
- Coordination between organizations and institutes under the Central and State Governments in areas related to the subjects entrusted to the Department and for the promotion of special studies in medicine and health.
- Indian Council of Medical Research (ICMR).

After the creation of the new Department, the only ongoing scheme transferred to the Department was that relating to the ICMR. Although the responsibilities entrusted to the new Department are multiple, there were no matching mechanisms, processes or schemes to undertake these schemes.

In view of the above, and in order to finalise the road map for the Department, new schemes have been formulated over the last year so as to fulfil the mandate and work entrusted to the Department.

These new initiatives are in various stages of finalisation, and the process has commenced for securing mandatory clearances to commence the scheme. It is anticipated that most of these will be launched in the next financial year, in case necessary outlays are made available.

The major thrust areas that have been identified and where work has been initiated include the following:

To promote health research governance through:

- The enactment of an Ethics Bill and the establishment of the National Biomedical Research Authority
- Creation of National Health Research Forum
- Establishing mechanisms for mapping and accreditation of health research institutions,

To promote the Development of basic, applied and clinical research through the finalisation of three major initiatives for:

- Promotion of medical research in medical colleges through establishment of advanced centres, special training programmes, research fellowships, grants etc.
- The establishment of model rural health research units which should serve as model units to transfer the technology to the state system by showing its applicability and feasibility in the rural settings; and
- The Establishment of a Network of Virus Diagnostic Laboratories in the Country, which would enable a quick response for diagnosis of viral diseases by develop expertise for diagnosis of specific viruses circulating in their geographic area
- Programme for gender and health
- Advanced training in Medicine & Health

Apart from the above, the Department is also establishing mechanisms for coordination and networking among different institutions and partners in health research like academia, industry, government departments, authorities like NDMA and State Governments, scientific societies etc. including mechanisms for promotion of research, technology management, start up support, joint funding mechanisms etc. in order to coordinate and promote health research initiatives. In this context, a group of Secretaries within MOHFW has been established for coordination within the Ministry. Expert groups and coordinating mechanisms have been put in place in order to operationalize the above activities. Modules for training of manpower for handling medical aspects of natural and man made disasters are being prepared. DHR played important role in strengthening infrastructure & capabilities for development, application of diagnostics as well as vaccines during recent H1Ni1 pandemic.

Since the Department was created after the commencement of the 11th Plan, there is no separate plan allocation of DHR, apart from the allocation made for ICMR, which was transferred to the new Department. The Plan allocation and expenditure has been as follows:

Scheme Wise Break Up of Outlay & Expenditure for the Department of Health Research

Rs. in crores

SN	Scheme	11th Plan	2008-09 Expenditure		2009-10 Expenditure*	
		Outlay	Plan	Non Plan	Plan	Non Plan
1	Promotion & Coordination of basic, applied & clinical research	-	-	-	-	-
2	Promotion of Research governance issues including ethical issues	-	-	-	-	-
3	Inter- sectoral coordination & promotion of PPP in medical, bio-medical & health research related areas	-	-	-	-	-
4	Advanced training in research areas	-	0.09	-	-	-
5	International cooperation including international conferences	-	0.29	-	0.25	-
6	Technical support for dealing with epidemics & natural calamities	-	-	-	-	-
7	Investigation of outbreaks due to new & exotic agents & development of tools for prevention	-	-	-	-	-
8	Matters relating to scientific societies and associations, charitable and religious endowments in medicine & health research areas	-	-	-	-	-
9	Secretariat	-	-	-	-	0.07
10	Direction and Administration	-	-	-	-	-
11	Coordination with Govern-ment/organisations/ institutions	-	-	-	0.10	-
12	ICMR	4496.08	390.18	174.00	399.50	184.00
	ICMR & IRR	200.00	-	-	-	-
	TOTAL	4696.08	390.60	174.00	399.85	184.07

*Till February 2010

COMMUNICABLE DISEASES

2009 was an exceptionally challenging year for communicable diseases control, management and research.

Influenza A (H1N1) 2009, pandemic flew into India and tested the capacity and capabilities of several institutes of ICMR, but more so of the NIV. Overnight the entire institute got converted from a research laboratory to a public health laboratory, providing diagnosis for each sample sent to it, with a turn around time of less than 24 hours. It provided training and reagents not only to scientists/technologist deputed from 14 Institutes/Centres of ICMR but to others as well. It did full gene sequence H1N1 of viruses isolated (5), monitored drug sensitivity (114 isolates), investigated out break in a closed community, conducted community based studies to document exposure to H1N1 in various categories of persons belonging to different socio economic class, profession and within health care settings. The Council was also directed to spearhead development of indigenous vaccines as well as diagnostic tests for H1N1. The Council encouraged, facilitated fast-track approvals and placement of advance purchase orders with Indian vaccine manufacturers. By mid February 2010, permission to conduct Phase I clinical trials have been given by DCGI for five vaccines – live, attenuated (1), killed, egg based (3); and killed, cell based (1). Similarly 4 indigenous tests (3 based on PCR and 1 on lamp technology) are in process of revalidation, and for another one funds have been provided for development and validation of a point-of-care micro PCR test.

Studies to find the cause of acute encephalitis syndrome in Uttar Pradesh were intensified through national and international collaborations. Follow-up of some leads have not resulted in a definitive answers so far. Ecology and behaviour of *Aedes* mosquitoes have been studied for development of site specific integrated vector management strategy to prevent *Aedes* borne arboviral diseases in rubber plantation areas of Kerala.

A cohort of 200 cases of chikungunya is being followed at Port Blair for development of sequlae especially joint pains. Preliminary results indicate development of chronic inflammatory erosive arthritis as the most severe outcome. Efforts to produce a vaccine for chikungunya and chandipura virus are progressing along the expected lines.

High rates of Hepatitis B and C were detected amongst primitive tribes of Orissa. Statistical analysis of data indicates that body piercing and sharing of razor are risk factors. The control strategies are being worked out. In a similar study in tribal population of Madhya Pradesh, the prevalences of HBsAg ranged between 0.6% and 10%, anti HBs 5-33% and anti HCV1-14%. HBV isolates were predominantly of genotype D.

NIV provided 1536 MAC ELISA kits for laboratory diagnosis of JE, Dengue, and Chikungunya. JE MAC ELISA kit was evaluated by WHO at CDC and showed 95.8% concordance with anti IgM test in CSF (accepted gold standard).

A phase-III clinical trial in Kolkata of a Vi polysaccharide vaccine against typhoid fever indicated a protective efficacy of 61% in all age-groups (higher in children under 5 years) at the end of 2 years post-vaccination. The potential for combined direct and herd immunity by Vi vaccine will be very attractive for introducing this vaccine in public health programmes. Another phase-III trial of a bivalent whole cell killed oral cholera vaccine by IVI Korea produced a protective efficacy of 67% in all age groups at the end of two years post vaccination. This study led to licensing of the new cholera vaccine in March 2009. India now has an effective, cheap, safe and produced in GMP compliant facility which can be used prophylactically in cholera prone area and/or for combating epidemics.

A Phase I HIV vaccine trial using prime and boost strategy of using a DNA vaccine (ADVAX) followed by a MVA vaccine (TBC-MA) has been completed in Chennai (TRC) and Pune (NARI). Greater interest in this trial has been ignited by encouraging results in a trial in Thailand using prime-boost strategy. NARI has also successfully modified a 99 item Mental Health Needs Scale to a 20 item one and is being used in a multi centre study. Genotyping of HIV-1 strains among injecting drug users in Darjeeling hints at emergence of new recombinant strains is West Bengal.

Three to five years of follow-up of cases of leprosy at Model Health Research Unit, Ghatampur, who have completed treatment indicated that the reactions as well as relapses were low and were observed to have occurred in the first 3 years of post treatment follow up. ASHAs have been trained and successfully used to detect, diagnose and treat cases of leprosy in Kanpur *dehat*. Facilities for culture and drug sensitivity testing for tuberculosis have been established at RMRC, Port Blair.

The protocols developed (TRC) for assessing the Annual Risk of Tuberculosis infection have been adopted by the programme and a module for establishment of national data base for TB has been created (NJILOMD). Modules on integrated vector management for programme managers have been developed.

A study of fixed dose combination of artesunate/amodiaquin combination in treatment of uncomplicated falciparum malaria showed a cure rate of over 95% as compared to amodiaquin monotherapy. Based on these results the fixed dose combination has been registered in India Similarly another fixed dose combination of Artesunate-mefloquin in treatment of uncomplicated falciparum malaria had an efficacy of above 95%. Artesunate + Sulfadoxine + Pyrimethamine was found to be 98-100% for *P.falciparum* infection. Pharmaco-vigilance studies have been initiated to monitor side effects of artemisinin based combination therapies.

Knock down resistance domain of Indian *An. culicifacies* was sequenced for the first time and the nucleotide sequence has been deposited in the Gene Bank. In order to reduce the risks of complications of malaria in pregnancy a prospective study to see the effect of chloroquin prophylaxis given to pregnant women has been started. Using PCR, a higher prevalence of *P.malariae* (about 45%) and co infections with *P.falciparum, P.vivax and P.malariae* have been detected in Orissa. Studies to see if these co-infections have any link to severity of malaria are being planned. A site is being prepared for a malaria vaccine trial(s) in Jabalpur. Two biomarkers (sTNF-RI, sTNF-R2) have been identified to be associated with cerebral malaria severity and mortality. Their usefulness in predicting prognosis is being investigated.

More data has been generated to show that 2 drug strategy (DEC+ albendazole) showed a greater reduction and significant advantage over DEC alone in reducing lymphatic filariasis infection in community. Studies are being conducted to generate evidence about the number of rounds of

mass drug administration that would be required to bring down transmission to zero level. Studies have also shown that when this is supplemented by vector control operations it is possible to sustain the gains for longer periods. To help decide on the number of rounds of mass drug administration in control of filariasis, epidemiological evaluation was carried out in 7 districts, the data is being analysed. Different dosages and combination of DEC and albendazole given at varying periodicity are being examined to enhance compliance and have better impact on mf load, density and transmission indices. The VCRC has transferred the technology for commercial production of a mosquito larvicide *Bacillus thuringiensis var. israelensis* (as earlier arrangements have not worked out) to another firm. A mosquitocidal metabolite of *Bacillus subtilis sub sp. subtilis* isolated from soil samples was found to have novel properties which could be used in dehairing process in leather industry. Thymol, a terpene with phenolic property, isolated from the fruit extracts of *Trachyspermum ammi* was found to exhibit promising macrofilaricidal activity against *B.malayi*. Extracts of two plants have exhibited promising results on leishmania promastigotes.

To evaluate combination therapy in visceral leishmaniasis, a trial has been completed which compares standard amphotericin B with combination treatments using two drugs : single dose of LAMB with either Paromomycin or miltefosine; and combination of miltefosine plus paromomycin. All three combinations showed a safety profile better than standard amphotericin B. The cure rates for all patients were about 93% for Amphotericin B and over 98% for the three combination treatments. Final results are being compiled. A sputum test for diagnosis of kala azar has been developed by RMRI and it has also confirmed that use of PCR for diagnosis of visceral and post kala-azar dermal leishmaniasis gives better results as compared to microscopy of bone marrow/ splenic aspirate and slit skin biopsy.

Preliminary results of genetic studies on leptospirae isolated from patients with varying severity at various points of time indicate presence of some novel genes which could be responsible for severe pulmonary complications in the Andaman Islands.

Poliovirus antibody zero prevalence study in Moradabad showed very low antibody prevalence for type 2 and type 3. High risk of poliomyelitis cases due to type 2 vaccine derived polio virus was predicted by EVRC, Mumbai in 2007. In 2009 16 cases due to type 2 VDPV were detected. This is a strong evidence to strengthen routine immunization programme. EVRC also provided the technical laboratory expertise for testing and analysis of samples of a clinical trial which evaluated usefulness of a bivalent (type 1 + type 3) OPV. On the basis of trial results bivalent vaccine has been used for first time in January 2010.

Investigation of an outbreak of jaundice, caused by unsafe injection practice with high mortality in Modasa, Gujarat lead to identification of a new mutant virus of Hepatitis B causing fulminant hepatic failure and high mortality. An outbreak of hand, foot and mouth disease (HFMD) in Mumbai and adjoining areas was investigated. Coxsackie virus A was the predominant virus type isolated. Internationally too, this is emerging as the main cause of HFMD. Outbreaks of dengue like fever (in South Andamans), influenza-like illness (in Port Blair, Car Nicobar, and Chowra islands) were investigated and confirmed as dengue and pandemic influenza A (2009).

A time series model for prediction of cholera and diarrhea using atmospheric temperature, relative humidity, rain fall and El Nino effect in Kolkata has been established for evaluation of impact of climate change on the occurrence of diarrhoeal diseases. A generic protocol is being prepared which would be used as a template to develop specific protocols for countries in South

East Asia. Studies on impact of climate change on malaria have shown an increase in transmission windows by almost 3 months.

The WHO recognized the measles lab of NIV as the Reference Measles laboratory and also declared it as GCLP compliant laboratory for vaccine trial. The drug resistance laboratory at NARI has been accredited by the WHO and the NIH, USA. NJILOMD has been recognized as one of National Reference laboratory for drug resistance surveillance in leprosy. RMRI has been identified as a WHO Reference Centre for Leishmania parasite and sera bank.

Through the extramural research programme financial support was provided to conduct 283 projects. 191 projects were investigator initiated (*adhoc*) ; 89 were Task Force oriented; and 3 Centres for Advanced Research were funded. 93 projects completed their planned duration. In addition, 110 post-graduate students (Sr Research Fellowship) and one post doctoral student (Research Associate) were given grant-in-aid.

A new initiative to create a network of viral diseases diagnostic laboratories across the country was launched. In the first phase, four labs are expected to be funded by March 2010. The ICMR-ICAR joint-panel has been revived to give an impetus to research on zoonotic diseases. Efforts to generate interest in developing vaccine(s) and anti-sera against gram negative bacteria has resulted in expression of interest by eight investigators.

INTRAMURAL RESEARCH

CENTRE FOR RESEARCH IN MEDICAL ENTOMOLOGY, MADURAI

ACHIEVEMENTS

Japanese Encephalitis

Longitudinal study on JE vector abundance in index villages of Cuddalore district showed that both *Cx. gelidus* and *Cx. tritaeniorhynchus* were prevalent with relatively higher densities throughout the year indicating that the *Cx. gelidus* may also play role of a secondary vector. Prospective study is needed to confirm this phenomenon. However, JEV infection rate in wild caught vectors, which was very low, is recorded for the first time in this area. Silent JE virus transmission study continued in Thanjavur district to define the mode of JEV transmission in non-endemic area and to develop appropriate forecasting tool and to avoid on set of future outbreaks. In non-endemic area (Thanjavur) the paddy cultivation scenario correlates with the abundance of *Cx. vishnui* subgroup species where mainly three paddy crops per year are cultivated IN the increasing number of paddy fields, whereas in both the endemic areas 1 –2 crops are grown. Screening (300 serum samples) of school children (5-15yr. age) showed that 27% population had flavivirus infection ranging from 4 - 52% indicating that lower level of JEV infection is prevalent in this non-endemic zone. In collaboration with the Directorate of Public Health, TN, the JE surveillance network using desiccated vector mosquitoes was continued and for the first time the JEV infection was recorded from Dindigul zone. Results of positive pools were intimated regularly to TN state health dept. for taking appropriate control strategies. A study on population genetics of the predominant Japanese encephalitis vector *Culex tritaeniorhynchus* is in progress.

Filariasis

The impact of mass drug administration (MDA) under filariasis elimination campaign on entomological and parasitological aspects of filariasis were continued during this year. Perceived benefits of worm expulsion in DEC+ALB arm have enhanced the drug compliance rate. It was clear from the available data that the 2-drug strategy (DEC+ALB) showed a greater reduction and significant advantage over DEC alone arm in reducing filarial infection load in the community and also in the vector population. Additional rounds of MDA is required to bring down the transmission to nil, as even during post MDA V the AGP level in 2-5 years was 2.47% in DEC+ALB arm.

The long-term impact of the vector control operation on the sustainability of the gains achieved by the earlier intervention strategies was determined. The vector control villages (MDA+VC) continued to demonstrate negligible vector density with nil transmission. Assessment of added impact of VC for augmentation of MDA to eliminate LF in S.India at a larger scale was initiated.

Dengue

A research proposal on Eco-Bio-Social aspects of dengue in urban and peri-urban ecosystems in Tamil Nadu, India was developed with a multi-country effort with a core protocol. The Phase I was completed and Phase II, designed on the basis of the initial situation analysis of Phase I findings clearly defined and described, the intervention will be implemented. Measurement of key breeding habitats and windows were carried out to introduce vector control tools to design lids (wooden frames with insecticide treated polyester nets to cover properly cement cisterns / tanks, and chemical tools – Insecticide impregnated window curtains) to reduce dengue vector density.

The studies on population genetic analysis of dengue vectors, *Aedes aegypti* and *Aedes albopictus* using biochemical markers is in progress. Dengue virus serotype 3 (DENV- 3) was isolated from human blood samples collected from the rural villages near Madurai and confirmed the circulation of DENV-3 in Madurai, TN, India.

Chikungunya

Chikungunya virus outbreak investigation in Lakshadweep showed that the isolates were closely related to the Central/East African genotype of CHIKV. Attempts were made to analyze the full-length genome of the CHIKV isolates by RT-PCR followed by nucleotide sequencing.

Patents

Some patentable materials have been developed in the Centre, particularly for morphological taxonomical work and modified ovitrap used for the control of *Aedes albopictus.*

ENTEROVIRUS RESEARCH CENTRE, MUMBAI

Achievements

Vaccine Derived Polioviruses (VDPV) outbreak in India

A poliovirus antibody sero-prevalence study was undertaken in Moradabad district, Uttar Pradesh at the end of 2007. Antibody prevalence in children between 3 to 5 years was 99.6, 93.3 and 85.3% for poliovirus type 1, 2 and 3. In age group of 6 to 24 months the antibody prevalence was 85.4, 65.2 and 72,6% for the three poliovirus types. Immunity gap towards poliovirus type 2 infection was greatest followed by type 3. High risk of poliomyelitis cases due to type 2 VDPV was predicted. The reasons for low population immunity to poliovirus type 2 and type 3 was due to the very low

routine immunization coverage in Uttar Pradesh and the compelling urgency of wild poliovirus type 1 eradication. Multiple rounds of supplementary immunizations with monovalent type 1 poliovirus vaccine (mOPV1) were conducted during 2006 and 2007 in western UP. By extrapolation the same situation was expected to prevail in Bihar also.

In 2009, two paralytic poliomyelitis cases due to type 1 VDPV were identified through the AFP surveillance. The first case, poliovirus type 1 VDPV was, however, reported from Assam in June 2009. The second case, reported in September 2009, was a known immunodeficient child from Delhi receiving i.v. immunoglobulin therapy. Serial stool samples collected from the child were positive for VDPV indicating that is a long term excerptor of VDPV. A total of 19 cases due to type 2 VDPV, 3 from Bihar and 16 from UP were reported in 2009. The most recent type 2 VDPV case was reported in January 2010 in UP. VDPVs were also isolated from healthy children in Bihar. VP1 sequence analysis revealed multiple chains of type 2 VDPV transmission. Environmental surveillance in Mumbai detected type 1 and 3 VDPV in Mumbai sewage.

Detection and characterization of VDPVs led to changes in vaccine type used in NIDs in the affected districts to stop spread of VDPV. Trivalent OPV was used in place of mOPV1 recommended by IEAG in October 2009.

Clinical trial on comparative evaluation of immunogenicity of monovalent and bi-valent type 1 and 3 (b-OPV) oral poliovirus vaccines

Considering that there is no risk of wild poliovirus type 2 and adverse effect type 2 poliovirus on immune response to type 1 and 3 in the trivalent OPV, a bivalent combination of type 1 and 3 (b-OPV) was investigated in a clinical trial. The trial was conducted by the WHO at three sites in India and ERC provided the technical laboratory expertise for testing and analysis of the samples. On the basis of the trial results, a recommendation has been made to use b-OPV in UP and Bihar.

Detection of differential expression of TLRs and cytoplasmic helicases in cultured cells infected with wild versus attenuated type 1 Sabin OPV strain

Sabin (OPV) strains do not replicate efficiently in neurons as compared to the wild type polioviruses. The expression of TLRs and cytoplasmic RNA helicases in human neuronal and muscle cells infected with wild type 1 and Sabin vaccine strain was studied. In neuronal cells, Sabin virus induced TLR -3, -7 and MDA-5 and type 1 interferon at the beginning of the infection (up to 4 h). Whereas in wild type1 infected neuronal cells such up regulation was observed 16h post infection. These results suggest that attenuated poliovirus is recognized by TLRs and cytoplasmic helicases early in the infection cycle leading to release of cytokines that restrict progress of infection in neuronal cells. Further studies may help better understanding of the attenuated phenotype of poliovirus.

Development of a novel assay for detection of specific mutations in Sabin OPV strains

A new/ novel assay was designed and evaluated for detection of mutations (reversion) at attenuating sites in genomes of Sabin vaccine viruses. The assay is capable of detecting the nucleotide substitutions at all the known attenuating sites in a single multiplexed run.

Development of a PCR/ sequencing method for detecting mutation in human poliovirus receptor gene CD155

Recently, a single amino acid substitution in the human poliovirus receptor gene has been suggested to confer increased risk of paralytic disease. A sequencing based assay has been developed to identify the amino acid position Ala67Thr mutation in CD155 in human subjects.

Determining CVA24v importation from China and Taiwan as the cause of an outbreak of acute hemorrhagic conjunctivitis in Mumbai in 2007

Mumbai experienced an outbreak of acute hemorrhagic conjunctivitis (AHC) during September –November 2007. Coxsackievirus A24 variant was isolated from 14 out of 31 patients tested. Full VP1 and 3C proteinase region sequencing was used for phylogenetic analysis. Two distinct genetic lineages were found. Close genetic linkage with Taiwanese and Chinese strains indicate strong possibility of importation of CVA24v from these countries as the cause of the outbreak.

Human CVA6 caused outbreak of hand foot and mouth disease in India

Hand foot and mouth disease (HFMD) was not reported in India until very recently (2006). Epidemics of HFMD are caused mainly by EV 71 and CVA16 viruses. Of these increased virulence, neurological and pulmonary involvement with fatality has been recorded during EV71 HFMD outbreaks. An outbreak of HFMD was reported from Mumbai and Thane area in October 2009. The disease was characterized by fever, rash, sore throat, vesicles in oral cavity, around mouth, hands, feet and buttock. Human Enteroviruses were detected from throat swabs, vesicles and stool samples of 62/ 113 cases investigated. Coxsackievirus A6 was the predominant virus type isolated (32/55). This is the first virologically confirmed large outbreak of HFMD in India. In 2008, an outbreak of HFMD due to CVA6 was reported in Finland. Thus this Enterovirus type is becoming an emerging pathogen causing HFMD.

ICMR VIRUS UNIT, KOLKATA

Achievements

Viral Hepatitis

The study present work attempted to evaluate the prevalence of HBV DNA in the PBL of HBV infected general population, specially among HBsAg negative subjects, to determine the replicative status of this HBV DNA by means of cccDNA detection, characterize HBV genotypes from the peripheral blood leukocytes (PBL) of a large set of subjects Results showed that compared to HBsAg +ve subjects; HBV DNA was present in significantly higher percentage of HBsAg –ve/antiHBc positive subjects, clearly indicating peripheral blood leukocytes (PBL) as an important extra hepatic site of HBV persistence. In a number of samples, the replicative intermediate and template of transcription, the cccDNA was also detected, supporting the hypothesis that PBL serve as a site of active viral replication and persistence, independent of the status of serological markers. This study also revealed the selective dominance of genotype A, in the PBL, in contrast to the serum ($P<0.001$).

A study on 109 genotype D infected individuals, revealed that HBV/D1 was significantly associated with chronic liver disease ($P = 0.01$), and in this subgenotype A1896 (PreC mutations) were most common. BCP mutations (T1762/A1764) were frequently associated with HBV/D2 (33% and 33%) and D5 (47% and 59%), without apparent clinical correlation, On the other hand, HBV/D3 was significantly associated with occult HBV infection, along with low level of BCP and PreC mutations and several non-synonymous substitutions in the catalytic reverse transcriptase (RT) domain of polymerase gene.

During a study on Cloning Major Genotype Variant of Hepatitis C Virus, Full-length HCV cDNA was synthesized successfully in presence of two RT enzymes mix, Superscript III, and AMV. A nested RT-PCR amplified product above 9.2kb was observed from a genotype 3b serum sample out of five samples studied.

Arbovirus Infection

A total of 392 acute samples, from the suspected Dengue cases, were referred for the detection of Dengue IgM antibody, among them 68 samples were positive for IgM antibody. Among the 204 acute samples available from the suspected cases of chikungunya like illness, only 42 samples were positive. 142 blood samples were collected from the patients, admitted in the different District hospitals and in the different medical colleges in West Bengal, to screen for IgM antibody to JE and Dengue viruses. Out of these21 samples were positive for JE IgM antibody and all of them were negative to Dengue IgM antibody. Attempts were made to isolate the viral RNA followed by RT-PCR testing, with 8 IgM positive samples. Only 5 samples yielded distinct band. To isolate the virus, tissue culture system and IC route of mice brain were employed. Only one sample produced mice illness and CPE in the tissue culture system.

Herpes simplex

A study on 442 inmates from two major Jails of West Bengal revealed that HIV-1, HBV, HSV-2 and HCV positivity rate is 3.70%, 7.69%, 13.88% and 5.88% respectively, while the VDRL positivity is 16.44%. The maximum infection is observed in age group of 18-35 years. Among them co-infection of HIV & HSV-2 IgG was 37.5%, HIV & HSV-2 IgM was 75%, HIV & HSV-2 (IgG and IgM) was 25%; and 50% samples showed HIV and VDRL positivity. Out of 442 inmates VDRL positivity was 16.44%, HSV-2 IgG positivity was 13.88% and HSV-2 IgM positivity was 16.96% and the maximum number of infections was recorded in the age group of 18-35.

Out of 79 HIV positive samples collected for the study on Seroprevalence of HSV-1 and HSV-2 and their relation with HIV infection among STD Clinic Attendees of Medical College & Hospitals, Kolkata, 53 (67.08%) were HSV-2 (IgG) sero-reactive.

Opportunistic infections among AIDS patients

A rapid immuno chromatographic assay for the detection of Mycobacterium tuberculosis antigens in pulmonary samples from HIV seropositive patients and its comparison with conventional methods revealed that the rapid method called rapid immunochromatographic assay (RICA) for cocktail-based diagnosis was superior to conventional methods. Six antigenic fractions of pathogenic Mycobacterium tuberculosis were used in combination as the capture antigens in the control line of the flow-through assay. Antigen detection of 200 sputum samples from HIV seropositive patients by RICA assay gave a sensitivity of 97.9%, specificity of 99.0%, positive predictive value of 98.9%, negative predictive value of 98.0%, false positive rate of 0.9%, false negative rate of 2.0%, prevalence rate of 49%, likelihood ratio for positive results 97 and likelihood ratio for negative results 0.02. The combination of RICA and AFB staining gave a sensitivity of 100%, specificity of 100%, positive predictive value of 100%, negative predictive value of 100%, false positive rate of 0%, false negative rate of 0%, likelihood ratio for negative results 0. The assay was simple, rapid and economical for the detection of M. tuberculosis infection and suitable for large scale screening of samples in endemic areas without any sophisticated equipment.

NATIONAL AIDS RESEARCH INSTITUTE, PUNE

Achievements

Prevention of HIV Infection

HIV Vaccine Trial POO1: NARI initiated preparatory activities for phase-1 HIV vaccine trial using prime and boost strategy to be tested among 16 volunteers to evaluate the safety and

Immunogenicity of ADVAX(DNA vaccine) followed by TBC-M4(MVA vaccine). Enrolment of volunteers and the follow up have been completed in December 2010. There were no vaccine related serious adverse events reported.

Vaccine Development:Evaluation of HIV-1 subtype C based DNA vaccine candidate and Multi-epitope vaccine candidate developed by NARI are being tested for immunogenicity in mice.

Microbicide Acceptability Study: A socio-behavioural study to understand the familial and socio-cultural factors influencing initial acceptance and long term use of vaginal microbicides was completed. The important findings include need of appropriate introduction strategies that avoid associations with infidelity, need to emphasize positive product attributes and the potential to enhance couple harmony, interventions that strengthen women's self-efficacy, health-seeking, and sexual negotiation skills. Microbicide introduction strategies should also meaningfully involve men.

Prevention of Cervical Cancer: A clinical epidemiology research program has been initiated with an overall goal of evaluating prevention options for HPV-associated cervical cancer in HIV-infected women.

Care and Support for HIV Infected Persons

Adherence to Treatment: A Qualitative study is being carried out to understand non-adherence to ART among defaulting patients at three NACO ART Centres in Maharashtra, GMC Nagpur, GMC Yavatmal and Ambejogai. In the preliminary analysis of data following factors appeared to be associated with non-adherence in preliminary analysis; fear, side effects, complex regimens, difficulty in transport to ART Centre, ART Centre timing, stigma etc.

ARV Drug Resistance: Drug Resistance laboratory at NARI is accredited by WHO and National Institutes of Health, USA. A threshold survey among newly infected ART naive persons was conducted in Mumbai and Kakinada and both the surveys reported less than 5% ARV drug resistant strains. A monitoring survey to study emergence of drug resistance among those on ART in National ART Rollout programme is ongoing.

Psychosocial needs and stressors: A study was conducted to test a psycho-educational intervention package consisting of eight modules to reduce anxiety and depression among PLHAs and to increase quality communications between HIV individual and his/her significant other. There was a statistically significant difference between the Anxiety-Depression scores between pre-intervention and the Post-intervention evaluations ($p<0.001$). As depression is known to be associated with ART non adherence, the training module for the significant other of PLHA can be utilized to reduce anxiety and depression among the patients in the ART roll out program.

NARI Mental Health Needs Scale [NMHS]: A 99 item instrument using 5 point Likert scale was used for survey among 680 HIV infected individuals. Using Principal Component Analysis (PCA) and Varimax Rotation methods the 99 items were reduced to 20 items. This tool has been shared with NACO and is currently being used in a multi-centric study sponsored by NACO.

ACTG 5175 Study: In a controlled clinical trial for comparing gold standard twice daily regimen (2 NRTIs + NNRTI) with two once daily regimens (2 NRTIs + PI and 2NRTIs + NNRTI) it was found that unboosted Atazanavir containing regimen was inferior to gold standard regimen and FTC+TDF+EFV regimen was found to be as good as gold standard. Patients initially enrolled in unboosted atazanavir containing regimen were shifted to gold standard regimen as per recommendation of Data Safety Monitoring Board. The study will be closed in March 2010.

Biology of HIV Infection

Genetic Diversity and Evolutionary Trend in HIV-1 circulating in India: Made molecular near full length clones from 75 HIV infected individuals from different stages of infection and isolates from recent infections over a decade. The clones are being assessed for their comprehensive genetic properties. Also standardized TaqMan based Real Time PCR for 7 distinct genes that are prone to mutations. This approach provides a rapid dissemination of identification of recombinants in a high throughput assay platform. This area of research is highly relevant for rapid screening of viral strains circulating in different geographic areas.

Regulation of nuclear export of unspliced HIV RNA: The role of RNA helicase, DDX3X in nuclear export of HIV-1 unspliced RNA was studied by evolutionary and computational approaches. Found key residues in phosphorylation site that are under evolutionary constraints. *In silico* analysis revealed key residues both in RNA binding domain and helicase domain of DDX3X that are potentially regulating rev-exportin 1 interaction crucial for nuclear export of unspliced HIV RNA. This could lead to new attractive target for intervention.

***Role of DCs in HIV infection*:** Preliminary findings suggest that there is depletion of pDCs and mDCs during AIDS stage. While mDC populations revert to normal level after ART, the pDC population remains depleted. PDCs are also depleted during early HIV infection. While the delpletion of pDCs can be attributed to apoptosis migration to lymphoid organs is also responsible for depletion of mDCs. The drop in pDCs in early HIV infection may be irreversible and also may down regulate innate immunity. The DC functions, expression of co-stimulatory molecules and involvement of transcription factors is under study.

Integrated Behavioural and Biological Assessment Survey

Round 1 was completed in early part of the year. The data from round 1 has been published as a supplement in international journal 'AIDS' with eight papers from NARI and collaborating Institutes. IBBA Round II has been completed in the same survey groups in the districts as in Round I. The initial analysis indicates increase in condom use with occasional clients and increase in the percentage of those tested for HIV. The detailed analysis of the data is underway.

NATIONAL INSTITUTE OF CHOLERA AND ENTRIC DISEASES, KOLKATA

Achievements

Vibrio cholerae

Detection, distribution and expression of virulence factor(s) among clinical *V. cholerae* non-O1, non-O139 strains were performed by PCR-based screening demonstrated that non-O1, non-O139 strains possessed virulence genes *hlyA* and *rtxA*.

The mechanism of initial adherence of *V. cholerae* to the intestine involved a coordinated interaction between *V. cholerae* chitin-binding protein GbpA and intestinal mucin. The results highlight the possibility of inhibiting colonization by use of agents that block the proposed interaction and this mechanism can be used as a useful intervention strategy.

In a nationwide screening of phage types of *V. cholerae*, 88.8% strains were confirmed as *V. cholerae* O1 biotype ElTor. N-4 ϕ, a lytic bacteriophage of ElTor O1 typing scheme was sequenced.

The pro-inflammatory potential of the flagellar proteins of *Vibrio cholerae* has been established.

Role of two forms of Hemagglutinin Protease (HAP) towards the pathogenic mechanism of non O1, non O139 *Vibrio cholerae* was established. The results have suggested that HAP is an important virulence factor of these strains.

A phase II trial was conducted in Kolkata among healthy volunteers aged 1 year and above, which showed the vaccine to be safe and immunogenic. A Phase III randomized double blind placebo controlled trial with the bivalent whole cell killed oral cholera vaccine among 110,000 urban slum populations in Kolkata. The protective efficacy (PE) of all age group was 67% at the end of two years post vaccination.

Other enteric pathogens

A method was developed to characterize *Salmonella enterica* serovar *typhi* isolated from blood of clinically suspected typhoid fever cases in children was found to be highly sensitive compared to conventional culture methods.

A randomized controlled evaluation of protection by the Vi polysaccharide vaccine against typhoid fever in eastern Kolkata, was conducted among 60, 000 urban slum population in 2004 in collaboration with International Vaccine Institute (IVI). Protective efficacy (PE) at the end of 2 years post-vaccination in all age groups was 61%, being higher in children under 5 years of age.

The potential antibacterial activity of curcumin against *H. pylori* in vitro was demonstrated. Curcumin showed immense therapeutic potential by inhibiting *H. pylori* growth as well as in restoration of *H. pylori*-induced gastric damage in mice.

Surveillance data showed that rotavirus, adenovirus and sapovirus were more closely associated with acute watery diarrhea among children below five years whereas Norovirus and Astrovirus affected children above five years and adults.

A hospital based surveillance system has been established in Infectious disease hospital for diarrhoeal disease. Through a systematic sampling, 1485 patients were enrolled during the last 1 year period, 76% of the cases presented with acute watery diarrhoea. 32% of the diarrhoea pathogens were *V. cholera*e O1, and among the viral pathogen, rotavirus was the leading pathogen with an isolation rate of 14%. Parasitic pathogens include *Giardia lamblia*, *Cryptosporidium* species and *Entamoeba histolytica*. *V. cholerae* and Rotavirus were the main causative diarrhoeagenic organisms for under five children. Antimicrobial susceptibility assay on toxigenic *V. cholerae* showed more than 40% resistance to Tetracycline.

A multiplex PCR-based method was developed to detect common colonization factors of enterotoxigenic *Escherichia coli* (ETEC) for quicker typing purpose.

Impact of climate change

A time series model study for prediction of cholera and diarrhoea using atmospheric temperature, relative humidity, rainfall and El Niño effect in Kolkata, India has been established. Evaluation of the impact of climate change on the occurrence of diarrhoeal diseases with emphasis on cholera is also being done as a part of preparing a generic protocol for WHO SEARO.

HIV

Genetic characterization of full-length *gag* gene of HIV-1 from India revealed that there were subtype specific divergences between the C and B strains.

The 1.5 kb full length gag gene of subtype C strain was cloned in vaccinia expression vector. This could prove to be useful for the studies of antigenic properties of HIV-1 Gag proteins.

Genotyping of HIV-1 strains based on *env*, *gag* and *tat* genes among Injecting Drug Users (IDU) from West Bengal indicated that IDU sequences from Darjeeling were again found to be more close to the C-strains from Manipur, which is linked to the Golden Triangle via Manipur-Myanmar border, rather than the IDU C-sequences from Nepal. The study implied that there might be emergence of new recombinant strains in West Bengal.

A community based cross-sectional study to understand genetic susceptibility to HIV infection, indicated that north-eastern IDUs were susceptible to HIV infection genetically apart from vulnerabilities caused by behavioral and other relevant factors.

Seasonal Influenza

Surveillance and molecular characterization of seasonal Influenza Virus strains circulating in Eastern India is on-going.

NATIONAL INSTITUTE OF EPIDEMIOLOGY, CHENNAI

Achievements

The Institute offers two post graduate courses, namely, Master of Applied Epidemiology (MAE) and Master of Public Health (MPH) in collaboration with Sree Tirunal Institute of Medical Sciences and Technology. In 2009, 25 MAE scholars were graduated and 51 (MAE and MPH) scholars are currently pursuing the courses. Sree Tirunal Institute of Medical Sciences and Technology has extended their affliation to MAE course for 3 more years. During the above period, several outbreaks that occurred in various states of the country were investigated and the reports shared with the respective State health authorities. The scholars participated in National (Epi days, jointly organized by NICD and NIE at New Delhi) and International conferences (TEPHINET at Seoul, Korea – 21 abstracts accepted, EIS at Atlanta, USA – 4 abstracts accepted and Global Health forum – 1 abstract accepted) and won best presentation awards.

- Two research studies were completed and 13 studies were initiated and progressing.
- Twenty four papers were published in peer-reviewed journals and three others are under review.
- Six workshops were organised during 2009-10.
- Signed MoUs with Tufts University, USA; Swiss Tropical Institute, Basel; Boston School of Public Health, USA; Sri Ramachandra Medical University and Hopers' Foundation, Chennai.

The details of the completed and on-going research studies are :

Completed studies

- A study on the married couples seeking STD care at the Govt. General Hospital, Chennai, Tamil Nadu, India.
- Reverse Tracking: A method of size estimation of HIV high-risk populations

On-going studies

- Integrated Behavioral and Biological Assessment: Round – II (IBBA – R II) in Tamil Nadu• Nutrition status of HIV-positive and HIV-negative injection drug users in Chennai, India - A longitudinal study

- Prevalence of HIV/STI and associated risk factors among wives of truck drivers in Namakkal, Tamil Nadu
- HIV Sentinel Surveillance in eight southern states of India
- Molecular Epidemiology of HIV
- HIV-Cervical Cancer Prevention Research Project
- Disability status in pauci-bacillary leprosy patients after release from treatment
- Progress of the WHO/TDR multicentric trial on 'Uniform MDT regimen for all types of leprosy patients', November 2009
- Cardiovascular risk factors in a rural population in Tamil Nadu: A cohort study
- Multiple micronutrient deficiencies and adverse pregnancy outcomes –A Hospital Based Pilot Study – A Collaborative study between NIE, NIN and HRRC field Unit at Kasturba Gandhi Hospital, Chennai.
- National nutrition monitoring bureau – Tamil Nadu unit
- Tuberculosis and RNTCP - DOTS - awareness, treatment satisfaction and patients' out of pocket expenses: A study of selected districts in Tamil Nadu
- Study on the prevalence of Rickettsial infections in a rural population near Chennai.

NATIONAL INSTITUTE OF MALARIA RESEARCH, NEW DELHI

ACHIEVEMENTS

Clinical Management of Malaria

Therapeutic Efficacy of antimalarials aimed at regular assessment of the efficacy of the antimalarials being used in the national programme. It was found that the efficacy of Artesunate+ Sulfadoxine Pyrimethamine combination ranged from 98 to 100%, while as that of Chloroquine for treatment of vivax malaria was 100%. *In vitro* and molecular studies on drug resistance also continued. *In vitro* studies showed widespread resistance to chloroquine in *falciparum* malaria. Institute continued testing the *in vitro* antimalarial activity of various molecules three different molecules and extracts from three plants show promise.

Based on the results of the phase III clinical trial conducted by NIMR, a fixed dose combination of artesunate+amodiaquine was registered in India. Evaluation of ACTs was continued this year also. The institute also initiated a phase III trial of arterolane, a synthetic analogue of artemisinin and piperaquine. Artemisinin monotherapy has been banned by the World Health Organisation. NIMR conducted a study to know the extent of monotherapy use in India, and it was revealed that it was being prescribed and sold rampantly. Based on the results, artemisinin monotherapy was banned in the country by the Drugs Controller General of India.

Pharmacovigilance

Pharmacovigilance of antimalarials was initiated with an aim to study the side effects of the antimalarials, artemisinin based combination therapy in particular. NIMR has been recognized as the National Pharmacovigilance Centre for malaria by the Central Drugs Standard Control Organisation in this regard.

Initiated an ambitious project on malaria elimination in Goa state. In this connection, a memorandum of understanding was signed with the Government of Goa and the National Programme. The project aims at zero transmission in the state by the year 2012, sustainability for 3 years, followed by subnational stratification.

Malaria and Environment

Continued climate change studies, which gave projections of temperatures over time at different intervals. The study shows that with increase in temperature over the years, there is reduction in transmission windows where they are open for 9-12 months, and increase in 3-6 month TW open category areas. Also carried out a study to categorise villages into low and high malarious areas in Karnataka by satellite images. It was observed that presence of irrigation tanks, vegetation cover; low barren areas etc. were associated with high malaria endemicity.

GIS Mapping was done in malaria endemic districts to formulate malaria control strategy at national level in collaboration with NVBDCP.

The technology was also used for monitoring and controlling dengue in Delhi.

Studies on Plasmodium

Developed an Immunodiagnostic reagent for detection of *P. vivax.* Patent has been filed in relation to this product. Also started a project on Quality Assurance of rapid diagnostic tests for malaria being used in the programme. A study on subtypes of *P. vivax* showed that old and new world sub types belong to same gene pool, and are not separate species. The *P. vivax* isolates show global population structure and the species has ancient origin in India. Studies on evolutionary genomics of parasite continued.

Biology of Anophelines

Surveys in malaria endemic districts in tribal dominated states revealed the presence of highly anthropophagic Fluviatilis S in Orissa and Chhattisgarh. The salivary gland proteomes of *An. stephensi* were characterized using mass spectrometry, the study may provide valuable information for control of disease transmission. Trials of various insecticides, insecticide treated nets, and other vector control products continued. Promising results were seen with an adulticide chlorphenapyr that can be used for management of multiple insecticide resistant vectors. Trials with long lasting insecticide nets showed that they have a good future ahead.

Insecticide resistance

A project on monitoring of insecticide resistance in 13 states. The study shows that *An. culicifacies* was resistant to multiple insecticides in Chhattisgarh, Andhra Pradesh and Madhya Pradesh while in Orissa it is still susceptible to Deltamethrin. Another study showed Knockdown resistance (*kdr*)-like mutations in vgsc gene of *An. culicifacies* complex. PCR-based assays were also developed for monitoring of kdr resistance in field populations.

NATIONAL INSTITUTE OF MEDICAL STATISTICS, NEW DELHI

Achievements

Major Research Achievements

- Having collaborated with National Institute of Health & Family Welfare (NIHFW) for the NACO's HIV Sentinel Surveillance, and estimates HIV burden in the country since 2003 in

conjunction with WHO and UNAIDS, the Institute provided major breakthrough in revising the methodology to estimate HIV burden in the country in 2006. The scientific contents are published as "Improved Estimate of India's HIV Burden in 2006 : IJMR, January 2009".

- Institute acted as the nodal agency for the conduct of the IDSP-NCD Risk factor Survey in all the States of the Country under the Stewardship of MOHFW (NICD & ICMR). NIMS developed the survey design, data management mechanism, design weights and analysis. Reports for individual States (7) as well as combined have been prepared and submitted for dissemination.
- Clinical Trial Registry – India (CTRI) has been functioning at NIMS. The CTRI was launched on 20th of July 2007, and has its HQs at the National Institute of Medical Statistics, ICMR, New Delhi. The CTRI is an online public record system for registration of all clinical trials being conducted in our country. The CTRI (www.ctri.in) is a Primary Registry of International Clinical Trials Registration Platform) (ICTRP) and all trials registered in CTRI is searchable from the ICTRP.
- The results of IBBA-NH first round survey are being used by NACO in its programme.
- The findings of the Survey Methodology to Estimate Disease Burden of Leprosy - A Pilot Study in Bareilly District, U.P. are used to finalize the national sample survey to estimate the disease burden of leprosy in India.
- The Institute collaborates in a randomized control intervention trial for the Prevention of HIV/STI among urban poor Married Women in Mumbai slums.

Training Programmes

- On Medical Statistics to the M.Sc. Students of different universities, viz. Banaras Hindu University - PG students of Health Statistics, Institute of Medical Sciences, and Statistics, Faculty of Sciences (Number trained during 2009-10 = 15 students from the University and 35 personnel working in projects).
- On Clinical Trial Registry – India (CTRI) organized at NICED Kolkata and Kidwai Memorial Institute of Oncology, Bangalore, the Annual Conference of Indian Society for Medical Statistics (ISMS) held at Institute of Medical Sciences, BHU, Varanasi.
- Organized a series of capacity building and dissemination regional workshops on modelling and estimation of HIV/AIDS in India at National Institute of Epidemiology, National Institute of Enteric and Cholera Diseases, Kolkata, Regional Medical research Centre, Dibrugarh, International Institute for Population Sciences, Mumbai, National AIDS Research Institute, Pune, Post Graduate Institute of Medical Sciences, Chandigarh, All India Institute of Medical Sciences, New Delhi, and All India Institute of Hygiene & Public Health (Over 300 participants attended the above workshops).
- Organized capacity building workshops on multilevel modelling at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow (There were 25 participants).
- Collaborated in organizing Annual Conferences of the Indian Association for the Study of Population (Varanasi: 2007; Bangalore: 2008; Tirupati: 2009) and Indian Society for Medical Statistics (Institute of Medical Sciences, B.H.U.: 2009).

NATIONAL INSTITUTE OF VIROLOGY, PUNE

ACHIEVEMENTS

Pandemic Influenza A H1N1(2009)

Provided rapid diagnosis to patients from all over the country. For 6 months the lab worked 24-hours a day. Of the 22348 clinical samples tested by real-time PCR 4694 (21%) and 2068 (9.5%) were pandemic Influenza A(H1N1-2009) and seasonal influenza A positive respectively. All 14 ICMR centers were trained for diagnosis and reagents are being supplied to all centers. Of the 724 specimens, including 107 from fatal cases tried for virus isolation, 122 isolates (22 from fatal cases) were obtained. Whole genome analysis was done for 5 isolates and Indian isolates were genetically close to A/California-04 /2009 (99- 100% identity at amino acid level). All 114 isolates were found to be Tamiflu sensitive. An outbreak of Influenza A (H1N1), 2009 was investigated in a residential school at Panchgani, Maharashtra. An extensive serosurvey was conducted to assess the magnitude of the viral spread in different populations. NIV played an active role in collaboration with the state and central governments in laying down policies for pandemic mitigation.

Real time PCR for the quantitation of pandemic H1N1-09 influenza viral RNA and ELISA for the detection of IgG and IgA antibodies employing recombinant HA protein were standardized. To understand the basis for differential outcome of pandemic H1N1-09 influenza, several parameters were compared among mild-self-recovering cases and patients requiring mechanical ventilation support, yielding crucial information.

A mouse model was used to assess the efficacy of the recombinant pandemic H1N1-09-HA protein as vaccine candidate employing different approaches. Vaccine prepared by Serum Institute of India was assessed in mice at NIV for immunogenicity and efficacy.

Seasonal and Avian Influenza

Multi-Site Epidemiological and Virological Surveillance in India was continued. Characterized a novel avian influenza (H11N1) isolated from the Indian subcontinent from a Eurasian spoonbill and H9N2 virus from wet markets of Pune.

Encephalitis outbreak in Gorakhpur

Despite extensive efforts and screening of over 800 CSF samples, etiology of the outbreak could not be established. A small proportion of patients had acute HAV infection. Fecal shedding of multiple enterovirus serotypes from human enterovirus genogroups A, B and C was noted in AES cases from Gorakhpur.

Japanese encephalitis

Molecular characterization of newly isolated JE and WN virus strains from India highlighted the introduction of newer JEV strains close to Chinese genotype 1 strains. Real time RT-PCR assay for the detection and quatitation of WN virus was developed.

Dengue

2009 witnessed a large outbreak of Dengue in Maharashtra. Multiple serotypes (DENV-1 to 4) were co-circulating; DENV-4 detected for the first time in almost 20 years in Pune.

Higher levels of IL-6 and IL-8 early in course of infection could be prognostic markers for progression to DHF. Comparison of viral loads in DF and DHF cases showed significantly higher

viremia in DHF cases within first 5 days post onset of symptoms. The viral load was also higher in primary infections compared to secondary infections. Analysis of inter outbreak variations in the genome indicated that DENV-2 and DENV-3 were more conserved and evolved at a lower rate when compared to DENV-1. Comparison of intra host nucleotide diversity revealed that DHF cases of DENV-1 and DENV-2 showed significantly higher diversity when compared to DF cases ($p<0.001$).

Chikungunya

Attempts to develop both killed and recombinant chikungunya vaccines have given promising results in mice. An excellent mouse model was developed for chikungunya infection and mechanism(s) for disease progression were dissected out.

Chandipura

High IgG-anti-CHP titres were maintained in mice immunized with candidate recombinant protein vaccine. Outbreaks of fatal encephalitis in western Maharashtra and Gujarat were attributed to Chandipura.

Entroviruses

Group-A rotavirus was present in 39% of the children <5 years, and 22% of adolescent and adults cases hospitalized for diarrhea in Pune. Generation of full-length genomes of 3 noroviruses highlighted genetic drift in NoV strains that may be linked to the evolution, sustenance and spread of NoVs in the population.

Investigations of outbreaks of HFMD in Kerala, Orissa and West Bengal during 2009-2010 indicated circulation of CA-6, CA-16, Echo-9 and EV-71 types as etiological agents.

Hepatitis

In collaboration with an industry four novel adjuvants were evaluated in mice for the development of hepatitis vaccines for E, combination of hepatitis E and B and hepatitis C viruses. Efficacy of the adjuvants was antigen-dependent. The best combinations are being evaluated in rhesus monkeys, the challenge model for HEV.

A new genotype "genotype-I" of Hepatitis B virus(HBV), earlier thought to be a recombinant was identified in the Midu Ishmi primitive tribe of Arunachal Pradesh. In February 2009, an outbreak of HBV with high mortality (456 cases with 89 deaths) was reported from Modasa town of Sabarkantha district, Gujarat. Sequence analysis of the virus showed clear association of the mutant virus (Pre-C and BCP mutants) with FHF and mortality and wild HBV with uneventful recovery.

A new subgenotype of HCV "3i" was identified was characterized at full genome level.

NATIONAL JALMA INSTITUTE FOR LEPROSY AND OTHER MYCOBACTERIAL DISEASES, AGRA

Achievements

Leprosy

- Phase II of the field programme on the epidemiological studies in leprosy has been completed at the Model Rural Health Research Unit, Ghatampur. 3-5 years follow-up of the cases who have completed treatment indicated that the reactions as well as relapses were low and

observed to have occurred during the first 3 years of post treatment follow-up (RFT). In the re-survey the number of was about 1/5th of what was detected earlier and in these also about half the cases had been diagnosed of having leprosy earlier but had not taken, or completed the treatment earlier. The majority of cases belonged to the borderline group (BT and BB). The number of childhood cases (i.e. <15 years) was decreasing, cases were observed in all groups including those above 50 years. Slit skin smear examination indicated a decline in smear positivity as compared to the previous survey. *M fortttuium, M chelonae, M phlei, M vaccae, M terrae and, M flavescein were* the non tuberculous mycobacteria (NTM) isolated from the soil and water samples of the area in the decreasing order of frequency. In the UMDT multicentric study of 300 PB and MB patients (funded by WHO) there were 4 episodes of late reaction (2MB cases and 2 PB cases) and 2 relapses (1 MB and 1 PB) during the follow-up of 3 to 5 years after stoppage of MDT.

- The study on post elimination leprosy scenario was undertaken in the Kanpur dehat district with collaboration of The Leprosy Mission. A population proportional survey was carried out in the 6 tehsils of the area which included both urban and rural clusters to identify and treat the leprosy cases identified. The ASHAs of the selected clusters were first trained in detection, diagnosis and treatment of leprosy. The doubtful cases were confirmed by a medical doctor and patients treated by the ASHAs as per the NLEP guidelines. A total of 186 cases were diagnosed as suffering from leprosy which included 137 PB cases and 49 MB cases and were put on treatment.
- Studies on mechanisms of granuloma formation continued using experimental model as well as human biopsies by immuno-histochemistry.
- Recognized as one of the National Reference Laboratory for drug resistance surveillance in leprosy using molecular methods. Training for collection of clinical samples has been initiated in 5 districts of UP for this purpose. Linkages were established with state health services and with STDC, Agra and a joint study on conducting drug resistance surveillance (DRS) of tuberculosis in 35 districts of Bundelkhand region and western Uttar Pradesh. After completing a pilot study in 10 districts the main study has been initiated in 22 districts.
- Animal experiments were conducted in BSL-3 facility for vaccine development, Th1-Th2 response by SMAR1 and protective efficacy of live Mw. A new BSL-3 laboratory for drug susceptibility testing has been commissioned.

Tuberculosis

- The survey on detecting the prevalence of tuberculosis in Kanpur Nagar district was completed (multi-centric study funded by Central TB Div, Government of India). Briefly the survey covered a population of about 49,766 aged 15 years and more belonging to both rural and urban clusters using the population proportional cluster sampling method. Three thousand chest symptomatics were identified of which 236 patients were confirmed to be suffering from TB (both by sputum microscopy and or culture positivity) with a prevalence of 4.74 in this area.
- Proteome analysis of aminoglycoside resistance of *Mtb* isolates is also progressing (DBT funded).

- Using micro array analysis 562 differentially regulated genes have been identified. Microarray experiment by hybridizing cDNA of RNA obtained from guinea pig lung tissue and *in- vitro* grown *M.tb* H37Rv for expression analysis of potentially relevant genes involved in virulence, persistence and pathogenesis was done. Expression of these genes had been analyzed and compared with *in vitro* grown H37Rv standard strain of *M.tb*, as well as from human isolates . In these experiments 12 genes had been found to be differentially expressed. Out of these, 11 genes were found over expressed and one gene repressed in the tubercular granuloma. These are being further analysed. Studies on genotyping of *Mtb* continued and Real Time PCR assay for detection of mutations in inhA gene was standardized.
- A Module has been developed for establishment of National Database for TB with networking of five Institutes.

REGIONAL MEDICAL RESEARCH CENTRE, BHUBANESWAR

ACHIEVEMENTS

Filariasis

Current Mass drug Administration (MDA) programme against filariasis is targeted with divided doses ranging from 100 – 300mg in three age groups, given annually to eliminate transmission. A 5-year study is comparing a lower dose of DEC (100mg) in uniform dosage to all age groups with 200 or 300 mg uniform doses in three defined matched communities. The preliminary results at end of three years are indicative of significant improvement in community compliance, and comparable reduction in vector transmission. The study would continue to evaluate the effect on mf load, density and transmission indices.

A randomized open clinical trial is being undertaken comparing DEC (300 mg) plus Albendazole (800 mg) given biannually and annual standard doses among eligible microfilarimics. Current study recruiting 78 subjects where thirty subjects completed six months follow up indicated significant result in disappearance of adult parasite through ultrasonography in cases receiving double strength of Albendazole (33 %) compared to cases receiving usual strength of Albendazole (11%).

Risk map has been developed in two blocks in two districts of Orissa identifying the ecological factors that are the risk factors for growth of filaria vector and spread of infection by comparing remote sensing satellite image, topographic maps with ground truth and epidemiological data from the districts. Bivariate analysis showed positive association of mf rate with Culex quinquifasciatus and of vector density with soil moisture index, Normal Differential Vegetation Index (NDVI) and infectivity rate and soil pH values. This study will be extended to other districts of Orissa.

Malaria

Prospective evaluation of 501 pregnant mothers from endemic area, followed in each trimester from Nayagarh district indicated 40 % compliance to CQ throughout the pregnancy and 60 % with irregular or no compliance to CQ chemoprophylaxis. Risk of developing disease (malaria) was high (OR 2.51, P= 0.005) among non compliant mothers, so also the chance of low birth weight babies (OR – 4.75, P<.001).

A study has shown high level of CD36 receptors on the platelet surface that triggers adhesion phenomenon and demonstrated the association of endothelial and platelet microparticles with decreased

platelet count that is observed in progression to cerebral malaria. Also demonstrated that increased production of NOx from endothelial cells inhibits the progression to severe pathology and curtails further endothelial damage. Angiotensin II has shown protective role and increased production of NOx through AT2 pathway in individuals who demonstrated polymorphic genes. Further work is underway to understand other protective pathways.

Blood slides (n=242) collected from eight highly endemic districts of Orissa, examined by both standard microscopy and PCR, indicated significantly higher detection of parasite by PCR (81.4%)as compared to microscopy (43.4%). Detection of *P malariae*, which was not reported to be commonly prevalent in the region was detected in 44.6% by PCR as compared to microscopy (8.3%). While co-infection with *P malariae* was detected in 49.6% with *P falciparum*, 12.1% was observed with *P vivax*. Besides, the co-infection could also be detected with *P falciparum* and *P vivax* in 2.3% of subjects by PCR. Studies to demonstrate association of severe malaria with co-infection are being planned.

Hepatitis

Prevalence study undertaken amongst five primitive tribes indicate high prevalence of Hepatitis B (HBsAg 1-5%) and Hepatitis C (Anti HCV 1-14%) viral infection in the population where risk of infection peaks at 30-45 years age group accompanied by HBV viral load ranging from 3.3 $X10^5$ to 2.6 $X10^8$. All the HBVDNA isolated belonged to Genotype D. Regression analysis of prevalent risk factors indicated body piercing and sharing of razor as the major risk factors for spread of infection. Control strategy to prevent spread is being attempted amongst two tribes exhibiting anti body to Hepatitis C (Mankidia-9%, Juanga-14).

Nutrition

Association of vitamin A levels compared with hemoglobin level in 50 randomly selected girls proportionate decline in retinal level with the severity of anemia. Children with sickle cell trait, sickle cell disease, thalasemia trait and disease also exhibitted similar association of Hb level with retinol.

Influenza A (HINI) 2009

A BSL-II laboratory was established at the Centre for diagnosis of influenza H1N1 infection by Real Time PCR technique. 65 samples from districts were tested showing 30 cases positive for influenza A of which 21cases were H1N1 (Swine flu) positive.

REGIONAL MEDICAL RESEARCH CENTRE FOR TRIBALS, JABALPUR

Achievements

Sickle Cell Disease

At Sickle Cell Clinic of RMRCT, situated at NSCB Medical College, till March 2009, 470 sickle cell disease patients were registered of which 279 patients did not report for the follow-up regularly. Out of these, 218 patients were contacted at their residence and among them 74 (33.9%) were not alive. Of the 144 surviving patients the most common reason for loss to follow up was long distance (87.5%) to the clinic.The most common illness reported was fever (95.8%), joint pain (87.5%), anaemia (15.3%), jaundice (16.7%) and others (9.7%). More than one-fourth patients (27.8%) were seeking medical intervention two or less times a year and 53.5% patients required medical treatment 3 times a year. Among those who died the most common cause of death was

hepatic failure or complications and splenic sequestration i.e. 27% eachThe mean age at death of the patients is 13.3± 8.0 years.

Viral Hepatitis

A total of 1223 subjects were screened for viral hepatitis. Serology for HAV, HBV and HCV was conducted by using commercial ELISA kits. HBV genotyping was carried out at National Institute of Virology, Pune. Polymerase Chain Reaction (PCR) was employed to detect HBV DNA and for genotyping.The prevalence of hepatitis B was higher in males (80.5%) as compared to females (19.5%). The prevalence of hepatitis C was higher in females (53%) as compared to males (47%). The overall HBV prevalence was found in the range of 3 -4 % in all the age groups. The anti-HCV prevalence was higher in the age group of 20-50 yrs (8%). The prevalence of HBsAg varies between 0.6% - 10% in these tribes. The prevalence of Anti HBs and Anti HCV has been found to be ranging between 5-33% and 1-14.4% respectively. High Anti HCV prevalence was found in Bharia tribe (14.4%). Molecular studies of HBV isolates indicated a predominance of genotype D in the region.

Tuberculois

In a cross sectional study to be conducted among 90,000 adults aged ≥15 years in urban and rural population of Jabalpur district of Madhya Pradesh, the survey in the rural population has been completed. Of 55278 eligible individuals covered so far, 4734 (8.56%) were found symptomatic. Sputum was tested of 4548 (96.07%) and 136 cases (smear/culture positive) have been identified and were referred to the nearest DOTS centre for anti-TB treatment as per the RNTCP guidelines.

Malaria

A project on "Preparation of a field site for malaria vaccine trial in and around Jabalpur" was undertaken to develop a field site where immune response to malaria antigen and parasite diversity are well understood for any intervention trial/ future malaria vaccine trial. Laboratory facilities for DNA sequencing, culture and drug susceptibility testing for malaria, lymphocyte proliferation assay against different malarial antigen using radioactivity measurement (β counter), Sporozoite ELISA to determine sporozoite of *Plasmodium falciparum* and *Plasmodium vivax*, PCR for sibling speciation of *An. fluviatilis,* and FACS to sort cells of interest tagged with fluorescent antibodies have been established.

Identified key biomarkers associated with cerebral malaria severity and mortality outcome of the disease. The plasma levels of sTNF-R1, sTNF-R2, showed increase with disease severity and expression of the apoptotic markers Fas-L and sFas also increased with disease severity. Their usefulness in predicting prognosis is being in investigated

Evaluated the sensitivity, specificity of rapid diagnostic method (malaria Pf/Pv kit), in comparison with microscopy and polymerase chain reaction (PCR) for diagnostis of *Plasmodium falciparum* and non falciparum malaria and found that RDT gives slightly higher positivity rate (51%) compared to microscopy (44%). At higher levels of prasitaemia, the sensitivity of the test increases.

H1N1 Influenza

Established H1N1 testing facility following the ICMR guidelines. As on 15th January 2010 the centre has received and tested 262 samples and 21.3 % are found to be positive. The samples were received from Indore, Bhopal and Jabalpur.

Links with State Government

Established close linkages with Tribal Welfare Department for evaluation and monitoring their

programme particularly among the primitive tribes – Bharia, Saharia and Baiga. Tribal Welfare Department also provides financial support for the studies undertaken by RMRCT. Alsi initiated studies on Health and nutritional status among primitive tribes in different districts of MP (Dept. of Tribal Welfare, Govt. of MP).Two social and behavioural studies have also been initiated with the support from Tribal Welfare Department, Govt. of MP.

RAJENDRA MEMORIAL RESEARCH INSTITUTE OF MEDICAL SCIENCES, PATNA

ACHIEVEMENTS

Clinical Studies

- Various clinical drug trails for treatment of VL, PKDL and co-infection were undertaken; few of them completed and some are still ongoing.
  - Dose finding study of Miltefosine in treatment of PKDL (WHO/TDR) – Completed
  - Paromomycin Phase IV study (iOWH) – Completed
  - Combination therapy of Ambisome, Miltefosine and Paromomycin for treatment of VL (DNDi) – Completed
  - Combination therapy of Miltefosine and Ambisome for treatment of VL (WHO/TDR) – Completed
  - Single low dose of ambisome for treatment of VL (MSF-Spain) – Ongoing
  - Treatment of Kala-azar co-infected with HIV/ Tuberculosis (MSF-Spain) – Ongoing
  - Amphomul Phase III study (Bharat Serum Pvt. Ltd.) – Ongoing
- Role of nutritional factors in relation to severity of VL revealed that zinc and albumin level was down regulated and magnesium up-regulated with increase in severity of malnourishment

Studies on Parasite

- It has been observed that TGF-btriggers apoptotic death of lymphocytes through up-regulation of tyrosine phosphatase activity and the use of sodium orthovanadate (NaOVa, a tyrosine phosphatase inhibitor) reduces the apoptotic frequency.
- Trypanothione Reductase (TR), Tryparedoxin (PXN) and tryparedoxin peroxidase (CTP) showed up-regulation in resistant strain, compared to sensitive indicating involvement of thiol metabolic Pathway genes in conferring resistance. ABC Transporter PgPA showed ~ 3 fold up-regulation in the resistant strain in comparison to sensitive, but MDR expression is almost similar. Drug efflux rather sequestration is involved in drug resistance.
- It was observed that natural T- regulatory cells which are a source of IL-10 and TGF-β expands in response to *Leishmania* antigen. Comparatively a higher % of CD4 Natural T-regulatory cells were observed in active cases of VL. It was decreased in absence of compatible antigen presenting cells and increased in presence of *Leishmania* impregnated macrophages in *in vitro* experiments.

Diagnosis

- A non-invasive test for diagnosis of kala-azar using sputum has been developed.

- Application of PCR as diagnostic test for Kala-azar and PKDL has shown better results than conventional microscopy of bone marrow/ splenic aspirate and slits kin/ biopsy.

Studies on Vector

- It was observed that vector salivary gland homogenate (SGH) exhibits dual mode of action as it helps in providing immunity as well as infection to the host.
- CDC light trap was found to be an efficient method for monitoring *P. argentipes* population.
- Cluster-wide provision of Long lasting nets (LN) significantly reduced the GM LT total *P. argentipes*/house by 24.9%.
- Application of Remote Sensing and GIS for validation of sandfly distribution and Kala-azar prevalence revealed strong relationship between NDVI and total sandfly density as well as density of *P. argentipes* in both endemic and non endemic foci.

New candidates

- *In-vitro* study to assess the significance of KMP-11 molecule in protection from VL revealed that the primed T-lymphocytes responded to KMP-11 resulting in release of IFN-γ but not IL-4 in healthy donors together with the induction of super-oxide radicals in macrophages of the patients. The findings suggest that the KMP-11 molecule can be examined further as vaccine candidate for Kala-azar.
- Structural models of twelve different proteins of various *Leishmania* strains have been developed and tested for its ligand protein interaction. Anticancer drug sulforaphane has been indicated for leishmaniasis by *in-silico* ligand protein interaction studies of a surface protein of *Leishmania* i.e. KMP11. Three compounds have shown best fit score to act as potential drug candidates against P-glycoprotein of *Leishmania donovani.*
- Two plants' extract exhibiting lethal effect on promastigotes have been explored.

Repository and Data bases

- Identified by WHO as reference centre for Leishmania parasite and Sera Bank. The repository has 89 isolates of different categories of leishmania isolate and 443 sera samples from kala-azar and control subjects.
- LEISHPROT, a web based repository database for all known *Leishmania donovani* proteins, was developed to provide easy access to voluminous data related to sequences and annotation with linkage facility to other data source.
- *LeishMICROSATdb*, a database of di to hexa nucleotide repeats of three Leishmania species i.e. *L. major, L. infantum* and *L. braziliensis*, has been developed using genome sequence data available in NCBI. This user-friendly database helps in retrieving precised need based microsatellites data and clustering information of different microsatellites in the genome

REGIONAL MEDICAL RESEARCH CENTRE, PORT BLAIR

Achievements

Leptosplrosis

Studies were undertaken to understand genetic makeup of the lepstospiral isolates recovered from patients with variable severity at different points of time, genetic difference if any with that of

strains of pathogenic, non pathogenic and intermediate phenotypic characters and geographic genomics, genetic changes in the genome as a repertoire of gene acquisition and loss on an evolutionary time scale. Four strains *viz*., CH31 (isolated from a patient during common source outbreak in 1928 at Andaman islands, belonging to group Akiami A, phenotypically pathogenic and associated with mild illness), CH 11 (isolated from a patent during common source outbreak in 1928 at Andaman islands, belonging to group Andamans A, phenotypically with intermediate characters and associated with severe illness), DS 15 and DS 18 (isolated from patients during outbreaks in 1997 at Andaman islands belonging to sero-group Grippothyposa, phenotypically pathogenic associated with pulmonary leptospirosis and mild illness respectively) were sequenced. Several novel genes were identified, which could be responsible for severe pulmonary complications of the disease in these islands. However, comprehensive analyses of whole genome of these strains are required to conclude the findings.

Dengue Fever in South Andaman

From June through July 2009, we observed an increase in the number of dengue like febrile patients was observed. Laboratory investigations to confirm the diagnosis of the suspected case patient was under taken. Concurrently, entomological survey was carried out in one of the locality reporting suspected cases. A total of 83 patients were admitted to the hospital/child care/health centers in Port Blair. Dengue virus specific IgM was detected in 26 patients. There were 12 cases of classical dengue fever while 7 cases each were with DHF and DSS respectively. DHF/DSS group of patients had clinical evidence of capillary leak syndrome including hypoalbuminaemia, thrombocytopenia, pleural effusion, ascitis, oedema and hypotension. There were no deaths. Entomological survey indicated high density *Aedes aegypti*, with evidence of widespread domestic/ peri- domestic breeding of *Aedes aegypti*.

Chikungunya

A cohort of 203 confirmed patients of CHIKV infection was followed longitudinally. In majority of the patients most of the symptoms resolve within initial 15 days, then the disease progresses into a second month with chronic arthropathy (75%) and fatigue (30%) as major feature. During the tenth month of follow up the symptoms/signs observed were joint pain+/-swelling (46%), fatigue (13%), and neuritis (6%). The cure rate at the end of a month was 23% and the same was 51% at tenth month. The MRI findings were joint effusion, bony erosion, marrow oedema, synovial thickening, tendinitis, and tenosynovitis. The study shows with relative certainty that CHIK arthritis is chronic inflammatory erosive arthritis.Destructive arthropathy and possible role of CHIKV infection has been postulated.

H1N1 influenza

Facilities for the diagnosis of the infection was set up in the Centre. An outbreak of influenza like illness was observed among the NCC cadets at the annual naval NCC training camp held on September 24 2009. Out of the 319 participants/officials of the camp, 107 suffered influenza like illness giving an attack rate of 33.5%. Throat swabs were collected from 11 patients with ILI and seven (63.6%) were positive for novel H1N1 Influenza A. All the patients recovered with Oseltamivir therapy.

A rapid survey was conducted among the household and immediate neighbourhood contacts of the participant of the NCC Camp who returned to Car Nicobar. The patients with ILI were investigated. Out 18 patients screened 6 were found to be positive for novel H1N1 Influenza A

During early November an upsurge in the number of cases of ILI was also observed among the Nicobarese inhabitants of Chowra Islands. A total of 391 cases of influenza like illness occurred among the population giving an attack rate of 26.3%. Throat swabs were collected from three patients and one of the samples was positive for novel influenza A H1N1.

Drug susceptibility pattern of *Mycobacterium tuberculosis* isolates from Andaman and Nicobar islands

Facilities for culture of *M. tuberculosis* and drug sensitivity testing were established in the Centre. Drug sensitivity testing was done on 29 isolates and five (17.2%) were found to be multi-drug resistant (MDR).

Human papillomavirus

A total of 78 cases were screened,for human papillomavirus type 16 and 18, 43 were the tribal patients attending the OPD of District Hospital of Car Nicobar and rest of the 35 cases were the patients attending the OPD of G.B.Pant Hospital and PHC Garacharma. One of the samples was positive by L1 consensus PCR. Further HPV typing was done by using type specific primers for the same sample. The sample was positive for HPV 16.

Non-communicable diseases

The overall prevalence of hypertension among the studied subjects population of Andaman and Nicobar Islands was 15.4% (95% CI: 13.9, 17.0), with the males having a higher prevalence of 17.1% as compared to 13.6% in females. Prevalence of alcohol consumption among males was 28.1% with a slightly higher prevalence of 28.8% in urban areas as compared to the prevalence of 27.4% in the rural areas. The survey is in its last stage with a few hundred more people to be surveyed. Data entry and analysis is in progress.

TUBERCULOSIS RESEARCH CENTRE, CHENNAI

ACHIEVEMENTS

Tuberculosis Clinical trials

In the ongoing trial which evaluates the ability of Moxifloxacin containing regimens to shorten the duration of treatment to 3-4 months, 270 patients have been enrolled. Preliminary results indicate that a significantly higher proportion of patients treated with Moxifloxacin-containing regimens became sputum negative at first and second month of treatment as compared to patients on standard regimens. The Centre is also recruiting patients to a study that assesses the feasibility, effectiveness and profile of adverse reactions of DOTS plus regimen compared to modified DOTS plus regimen in patients who fail to Category-II regimen and have MDR-TB. The Centre has completed intake to the study to assess the cure rate in Category-II PTB patients after the addition of *Mycobacterium w* vaccine to standard anti-TB drugs in which patients were randomly chosen to receive either the vaccine or placebo along with the standard Category-II RNTCP regimen. Four patients developed serious adverse events – 2 renal and 2 hepatic. Six patients required change of chemotherapy – 4 for multi-drug resistance, one for clinical complication, and one for pregnancy.

Epidemiological studies

Three surveys have been conducted to assess the epidemiological impact of DOTS and in addition a one time prevalence survey to measure the impact of DOTS alone is nearing completion.

Coverages in all the surveys have been in excess of 90%. Spoligotyping of over 1700 samples obtained from Tiruvallur district were completed and analyzed. It showed a predominance of EAI 3 and EAI 5 spoligotypes.

Basic studies

A model structure of AccD6 developed by the Centre suggests that AccD6 could also be the target for activated INH in addition to InhA and KasA. Another completed study showed that the yield of AFB positive smears in sputum smear positive patients was similar in mucoid and salivary samples, high in samples containing >4ml volume, and in samples collected in the morning.

Immunogenetic studies completed at the Centre have shown that patients with pulmonary tuberculosis have increased plasma 1,25(OH)2D3 levels which might lead to downregulation of VDR and could cause defective VDR signalling which may influence the down stream process that triggers innate immunity against *M. tuberculosis* infection. Other completed studies showed that a) Phagebiotics supplemented with lysin can be used to control the overgrowth of normal flora in liquid media without compromising on the viability of M. tuberculosis, b) cinnamaldehyde has good anti-mycobacterial activity and c) the relative lytic efficacy of mycobacteriophages. Molecular docking studies along with development of a drug resistance database are the focus of the ongoing bioinformatics studies.

In an another study it was shown that a combination of factors such as young age, and CYP2B6 GG/GT genotype and stunting could result in sub-therapeutic NVP levels in children suggesting the need for higher doses for malnourished (stunted) children and those below three years of age.

Ongoing laboratory studies are exploring more HLA and non HLA polymorphisms associations with various forms of tuberculosis, the immunological basis of latent tuberculosis and the role of interferon gamma and chemokines and dendritic cells in TB and HIV-TB.

HIV and Tuberculosis

The efficacy of two different preventive therapy regimens in HIV-infected persons in reducing the incidence of TB and overall mortality is being studied using either Ethambutol (EMB) (800 mg) and INH (300 mg) daily for six months, self-administered, collected once in fifteen days or INH (300 mg) daily for 3 years (in lieu of lifelong prophylaxis) self administered, collected once in fifteen days. The interim findings suggest that 6 months of EMB/INH is as effective as 3 years of INH in preventing TB among HIV-infected persons. In another randomized clinical trial the efficacy of a once-daily regimen of didanosine (ddI) and lamivudine (3TC) with either efavirenz (EFV) or nevirapine (NVP) when given along with standard ATT in patients with HIV and TB with CD4 < 250 cells/mm3 was compared. After the second interim analysis, the DSMB recommended that intake to the study can be stopped, as the primary outcome had been determined to be significantly different between the two regimens.

A qualitative research study provided the first evidence from India that routine, provider-initiated voluntary HIV testing of TB patients can be achieved with very high efficiency under programmatic conditions.

HIV vaccine trial

In a phase I HIV vaccine trial using a prime-boost regimen involving a DNA vaccine (ADVAX) to prime and the MVA vaccine to boost the recruitment was completed as planned.

VECTOR CONTROL RESEARCH CENTRE, PUDUCHERRY

ACHIEVEMENTS

Development of vector control agents

Fifty five-fold enhancement in the yield of mosquito pupicidal metabolite of *Pseudomonas fluorescens* (VCRC B426) was achieved through redesigning of the culture medium.

The technology for production of mosquito larvicide, *Bacillus thuringiensis* var. *israelensis* was transferred to another firm M/s Amit Biotech Private Limited, Kolkata (7th firm). With this, the total fund generated so far from all the firms is to the tune of Rs. 58.80 lakhs.

An enzyme useful for dehairing process in leather industries was identified as a byproduct from a biocontrol agent and the patent on the process for its pilot scale product has been filed.

The novel mosquitocidal metabolite of *Bacillus subtilis* sub sp. *subtilis* (VCRC B471) isolated from soil samples was purified, characterized and identified as 'Surfactin'.

A process for preparing WDP and slow release formulations of *Bacillus thuringiensis* var. *israelensis* utilizing Flyash, a waste product from lignite industry, as a carrier material has been developed and the bioefficacy of the formulations evaluated.

Parasite diagnosis and genomics

Polymorphism analysis of the *FtsZ* gene controlling cell division, and *Wsp* gene coding for surface antigen of endosymbiont, *Wolbachia* of *Wuchereria bancrofti* from country-wide samples has shown that the genes are highly conserved and hence could be an ideal drug target.

An epitope of collagen of *Wuchereria bancrofti* expressed specifically in infective (L3) stage of *Wuchereria bancrofti* that reacted with the monoclonal antibody (VCRC B5) and having potential in the xenomonitoring of lymphatic filariasis (LF) was identified.

Development of macrofilaricidal drug

Thymol, a terpene with phenolic property, isolated from the fruit extracts of *Trachyspermum ammi* was found to exhibit promising macrofilaricidal activity against *Brugia malayi* in *Mastomys coucha.*

Vector research for strategy development

Ecology and behavior of *Aedes* mosquitoes have been studied for development of site specific IVM strategy to prevent *Aedes* borne arboviral diseases in rubber plantation areas in Kerala.

61 species of mosquitoes belonging to 10 genera collected from parts of the country have been bar-coded, additionally.

Knock down resistance (kdr) domain of Indian *An. culicifacies* was sequenced for the first time and the nucleotide sequence (183 bp) has been deposited in the GenBank (Accession No. FJ968792).

Gravid trap has been standardized to collect gravid females of *Cx. quinquefasciatus* for xenomonitoring in LF elimination programme.

Contribution to LF elimination programme

The risk map of India for LF transmission, created using Geo-environmental risk model (GERM)

for delimiting areas for programme implementation is under validation based on field surveys in 64 sites across the country.

The methodology to assess Health Related Quality of Life of filariasis patients has been validated for its application as a tool to monitor the impact of Morbidity management intervention towards Filariasis Elimination.

Epidemiological evaluation was carried out in seven districts in India for decision making on stopping or continuing MDA.

Independent assessment of MDA programme implementation was carried out in six districts in Tamil Nadu and four districts in Pondicherry and the results were useful for feedback to improve programme performance.

Human Resource Development

Modules on Integrated Vector Management for a Regional Training course for programme managers have been developed with the support of WHO/SEARO.

Short term training programme on epidemiology and control of vector borne diseases was conducted in collaboration with WHO/SEARO/Universities in which 40 public health personnel/ faculty/students from India/abroad were trained.

EXTRAMURAL RESEARCH

Several out breaks of H5N1 outbreaks in West Bengal, Manipur, Tripura and Assam. All isolates belonged to Clade-2.2, but were caused by three different introductions. Extensive influenza virus surveillance network (9 centres in different geographical areas) has been established for undertaking epidemiological and virological monitoring of human influenza viruses in India. As a part of the Ist phase of the surveillance programme in India, the network has, during the reported period, antigenically characterized 115 influenza viruses (~5.4%) of which about 46% belonged to type B (53), followed by the remaining type A (21 H1N1 and 41 H3N2). The role of the network centres, which have been strengthened for the use of RT-PCR and developed adequate surveillance capacity through molecular diagnosis, has been reflected during outbreak situations of avian H5N1 in the Eastern and Northeastern India, and particularly during the current influenza A H1N1 (2009) pandemic situation, i.e., in conducting rapid testing of all suspected cases of swine influenza

The ICMR is coordinating efforts to encourage indigenous production of H1N1 vaccines. Four vaccine manufacturers are working on schedule to start the human clinical trials in early 2010. It is expected that the vaccines would be available in the second quarter of 2010 for public health use. For the interim period a limited amount of pandemic influenza A vaccine is being imported. The Council is providing technical assistance for conduct of bridging studies which would enable their use for priority categories of persons as decided by the Ministry of Health & family Welfare.

The Council is also assisting in indigenous production of diagnostic tests for pandemic influenza A. Expression of interest from ten companies have been received and examined. Three of these are in advanced stage of evaluation, three are undergoing internal validation, while four are in various stages of development.

Investigation of Acute Encephalitis syndrome in Eastern Uttar Pradesh, Gorakhpur area show JE as cause in less than 20% of cases. Enterovirus as causative agent is being investigated. An

outbreak of acute haemorrhagic conjunctivitis occurred in Mumbai and coxsackie virus variant A24v was incriminated as the cause. Chikungunya outbreaks were investigated in several states viz. Kerala, Tamil Nadu, Andaman Islands etc

NARI has been accredited by WHO to carry out anti-retroviral drug resistance testing – (the only one in South East Asia). Post graduate diploma in Medical Entomology was revived at NIV, Pune. Units of NIV were established at Gorakhpur, Uttar Pradesh and Allapuzzha, Kerala to address Arboviral infections especially Japanese Encephalitis (JE). Combination therapies for visceral leishmaniasis have been evaluated (Ambisome, Miltofosine and Paramomycin). A recombinant protein-based vaccine for Chandipura was developed, and combination of this vaccine with DPT was found to be stable in animal experiments.

A multicentric Hospital Based Rotavirus Surveillance conducted in various geographical region revealed Rotavirus infection in more than 40% of stool samples by ELISA in children >5 years admitted with severe diarrhoea with G1P(8) and G2 (P4) strains found predominantly. Thus indicating that rotavirus is a major cause of morbidity and mortality due to diarrhoea in children less than 5 yrs of age. A 10-centre study on epidemiology of viral hepatitis in Tribals of Orissa, Madhya Pradesh/ Chattisgarh and Jharkhand India being conducted in 10 primitive tribes to assess the prevalence of HAV, HBC,HCV and HEV infections. The HAV of HEV infections was found to be rampant and were coinciding with National figures. HBV genotype D is circulating on mainland primitive tribes. A study on prevalence of common Hb-pathies among the STs and SCs of Damoh district of Madhya Pradesh revealed that HbS & b-thalassaemia trait was common and G6PD deficiency - high (9%) in Scheduled Tribes . The prevalence of Anaemia was high in ST (71%) and lower (32%) in SC.

A phase I HIV vaccine trial using the prime boost approach was initiated in NARI, Pune and TRC, Chennai. The enrollment for the trial has been completed and the volunteers are now being followed. A study carried out in Mumbai identified significant differences among cases or AIDS Related Lymphomas(ARL) from India from what is seen in other counties. In particular, India has a higher proportion of PBL, which are very aggressive EBV-associated lymphomas, frequently occurring in the oral cavity. This study has documented that PBL, while extremely rare in the US and Europe, may be more common health problem in India, and warrants further attention with hope for better treatment approaches.

REPRODUCTIVE HEALTH

INTRAMURAL RESARCH

NATIONAL INSTITUTE FOR RESEARCH IN REPRODUCTIVE HEALTH, MUMBAI

The NIRRH had its humble beginning as a Family Planning Unit, attached to the Directorate General of Health Services, at the Indian Cancer Research Center in 1954. The unit was reorganized in 1956, as the Contraceptive Testing Unit. The two sections were formalized in 1959 with the birth of the Reproductive Physiology Unit, headed by Dr Shanta Rao and the Contraceptive Testing Unit headed by Dr Katayun Virkar. The two units moved to the Seth G S Medical College premises in 1963. Concomitant with this physical transfer was a vital administrative transfer from the Directorate of Health Services to the Indian Council of Medical Research. The Institute moved to its present premises as the Institute for Research in Reproduction on 21st February 1970, later renamed in July 2002 as the National Institute for Research in Reproductive Health with its expanded mandate.

NIRRH is dedicated to research in reproductive health, with a focus on basic, clinical and operational research, contraceptive research and genetic diagnosis and testing, together with support facilities including an animal house, a dedicated library and plans for a primate colony centre for primate breeding and research.

More recently, the mandate of the institute has further been expanded covering research on all aspects of reproductive health. The emphasis of research is on integrating biomedical, clinical, socio and behavioral sciences addressing various aspects of reproductive health rather than addressing them in isolation. The main area of research is focused on developing more effective and safer fertility regulating technologies, developing safer medical methods for pregnancy termination, detection, diagnosis and treatment of reproductive tract infections including sexually transmitted diseases, making pregnancy safer, reproductive adolescent health and development, menopause, infertility and male responsibilities for reproductive health care.

ACHIEVEMENTS

- Evaluation of a number of contraceptives such as oral pills, injectables, transdermal devices, vaginal rings, intrauterine devices and emergency contraceptives for their safety, efficacy and acceptability. The data generated helped the government to introduce some of these methods in the national family welfare programme.
- The Institute has identified several novel molecules which have a role in fertility regulation, both in the male and the female. Some of these molecules are being tested for their safety and efficacy so that clinical evaluation could be initiated.
- The studies carried out by the Institute have shown that oral administration of an antiprogestin (RU 486) followed by a prostaglandin analogue (Misoprostol) provides a safe and effective

method for early pregnancy termination. Availability of such noninvasive methods has made pregnancy termination much safer and affordable.

- Studies in the area of infertility management have resulted in establishing assisted reproductive technologies in the country. The birth of our country's first scientifically documented test tube baby through the research endeavors at this Institute and the KEM Hospital is a testimony of this achievement.
- Identification of some novel molecules which have the potential for further development as microbicides.
- The development of simple, cost-effective and highly accurate methods for diagnosis of fertility status and reproductive tract infections. Some of the technologies have been transferred to industry for developing appropriate kits for wider use.
- In the area of adolescent health, an operational research study conducted in schools recommended that medical examination of reproductive system of adolescents needs to be included in the existing school health programme. Adolescent friendly health services were successfully operationalized at two health posts of Muncipal Corporation of Greater Mumbai. The model has been accepted and upscaled at other health facilities in Mumbai by the corporation.
- National guidelines on prevention, management and control of reproductive tract infections including sexually transmitted Infections were developed for RCH-2 and NACP-3, following which training models (trainer's guide and trainee manuals) on delivery of RTI/STI services was developed for doctors, nurses and laboratory technicians. The material will be used in the national programme.
- A community based study on prevalence of chronic obstetric morbidities among women assessed the magnitude of reproductive morbidities in a district and recommended inclusion of genital fistula in the National Rapid Household Survey of RCH. Based on the recommendation, the survey has measured the prevalence of genital fistula in the country.
- Operational studies carried out in urban slums for enhancing participation of men in reproductive health in collaboration with Municipal Corporation of Greater Mumbai (MCGM) illustrated the benefits of involving men in enhancing their as well as spouses' reproductive health. The model has been handed over to the MCGM and is being sustained in the study area.
- Studies carried out at the Institute have revealed that BMD measurements at the hip, spine and foot are approximately 15% lower in Indian women as compared to age matched Caucasian women (Hologic database). Of the bone turnover markers, c-terminal telopeptide and deoxy-pyridinoline(bone resorption markers) in comparison to osteocalcin (bone formation marker) are more sensitive markers for the prediction of bone health. Age wise data base for bone turnover markers for Indian women has been established.
- The Institute is in the process of establishing a primate centre which would serve as a national resource for undertaking research on human health-related problems where non-human primates serve as the most appropriate animal model.
- The Institute has established a centre for evaluation of reproductive and genetic toxicology of new products, devices and vaccines. This centre caters to the needs of the Institute as well as of other institutions and pharma industries in the country.

GENETIC RESEARCH CENTRE, MUMBAI

The Genetic Research Centre at Mumbai is dedicated to research in genetics catering to the needs of families having children with mental retardation, birth defects and reproductive loss. The Centre aims to reduce fetal mortality and under-five mortality by appropriate genetic counseling and prenatal diagnosis of common genetic and chromosomal disorders. It also focuses on the reproductive health of adults and adolescents. The Centre runs an effective genetic clinic where couples are counseled regarding recurrent risk of genetic disorders.

Screening for β Thalassaemia by an in-house ELISA for HbA_2 quantitation

The Centre developed a simple ELISA for quantitation of HbA_2. The ELISA is simple, accurate, precise and inexpensive and several samples can be processed simultaneously.

Screening for Mental Retardation

A common cause of mental retardation in males is fragile X syndrome. The Centre undertook a screening survey for this syndrome in 18 special schools of Municipal Corporation of Mumbai as well as some other selected schools in Maharashtra state. A simple in-house immunocytochemical technique was used for the screening. Fragile X syndrome was found to be positive in one tenth of the cases screened.

Studies on Neural Tube Defects (NTD)

Neural tube defects (NTD) are common severely disabling central nervous system malformations occurring worldwide. Genetic variations in MTHFR gene are reported to be associated with NTD. In a study at the Centre, the gene was screened in a cohort of couples with a history of child with NTD. A substantial number (≈20%) of these cases was found to have variations in the MTHFR gene.

Additionally, as a part of the reproductive health program of the Centre, individuals with ambiguous sexual development (XX males and XY females) are being screened for variations in the SRY gene.

Genetic Clinic Services

The Centre offers services in clinical genetics by providing genetic counseling, genetic screening and prenatal diagnosis for common genetic disorders. Cases are referred from all over the country.

EXTRAMURAL RESEARCH

The Extramural research programmes in reproductive health are largely being conducted through a nation-wide network of Human Reproduction Research Centres (HRRCs) and other non ICMR collaborating institutions/medical colleges and NGOs. The network of 31 HRRCs, established in different parts of the country in 1980s, have been engaged in conducting nationally relevant multicentre research projects which include clinical evaluation of newer contraceptive technologies for safety, efficacy and accept-ability, evaluation of medical methods for elective termination of pregnancy and intervention studies on maternal and child health, RTIs/STDs; pre-programme introduction studies of newer contraceptives and cost-effective diagnostics. Besides this, research is being carried out on micronutrient deficiencies, obesity, consumption patterns of cold drinks and junk foods, health of tribals and people of north-eastern regions of the country. Grant-in-aid is also

provided for open-ended basic, clinical, operational and health system research submitted by individual researchers of non-ICMR institutes including setting up of centres for advanced research in chosen areas.

Phase-III Clinical Trial with an Intravasal Injectable Male Contraceptive – RISUG®

The development of safe, effective, reversible and acceptable method of male contraception is one of the priorities of Government of India. A new molecule [i.e. styrene maleic anhydride (SMA)] has been developed for male contraception. The registered name of this contraceptive is reversible inhibition of sperm under guidance (RISUG). RISUG has undergone various pre-clinical efficacy, safety and toxicological studies on various species of animals. After successful completion of limited phase-III studies the RISUG is undergoing extended Phase III clinical trials.

The trial has been initiated at 4 centres in the Country and around 64 subjects have received the RISUG injection. Because of some internal problems M/s Marksans Pharma Pvt. Ltd., assigned to manufacture the test batches for the ongoing phase-III informed the Council of their inability to continue supply of the test batches. An expert committee has now identified IIT, Kharagpur as a site for manufacturing RISUG test batches for the ongoing clinical trail.

Comparative Long-term Retrospective Follow up Study of RISUG Injected and Vasectomized (NSV) Subjects

To study the long-term safety and efficacy of RISUG injection in comparison to vasectomy the Council is conducting a study entitled "Comparative long-term retrospective follow up study of RISUG injected and vasectomized (NSV) subjects" at one centre in Delhi. Under this study subjects who received RISUG injection during restricted phase–III clinical trial at three centres in Delhi are being followed up for a period of three years. Simultaneously, efforts are going on to enroll almost similar number of vasectomized subjects of similar characteristics based on specific criteria. Both husband and wife are being followed up whereas in vasectomied subjects only males are being followed up. Out of 139 subjects who received RISUG injection during 2000-02 around 69 have been identified and followed up for detailed examinations. No serious adverse clinical symptoms have been noticed in them after 6 to 8 years post RISUG injection.

The Assisted Reproductive Technologies (ART) Bill & Regulations - 2009

The draft ART Bill & Rules–2008 developed by the Council were subject to public debate by placing the draft ART Bill & Rules – 2008 on the website of Council & MOHFW, Govt. of India with the request for comments from the public. The comments received from various stakeholders including various international agencies and organizations were compiled and after detailed discussion with the experts the draft bill has been modified. The revised draft of Assisted Reproductive Technology (Regulation) Bill 2009 has been sent to the Ministry of Health & Family Welfare, Govt. of India for further necessary action.

When the ART (Regulation) Bill & Rules - 2009 is passed by the Parliament it will become mandatory for all the ART Clinics in India to be accredited and to maintain all the records as per the Bill and submit to a Central database. Based on the recommendations of Department. of Family Welfare, MOHFW, GOI, the Council has developed a detailed proposal to establish the National Registry of ART Clinics in India at ICMR Hqrs., New Delhi.

Expanding Contraceptive Choices

In order to decrease the unmet need and improve the contraceptive prevalence the Council initiated a Phase III clinical trial with subdermal contraceptive single rod implant 'Implanon' as task force study. This is an open labeled multricentre clinical trial being carried out at 22 Human Reproduction Research Centres (HRRCs) of ICMR located in the OBGY departments of medical colleges and hospitals. A total of 3158 women have been enrolled in the study so far. These women have been observed for a total of 84, 482 months of use. Majority of the acceptors are from urban (67.6%) and urban slum (15.0%) areas and only 17.4 % women are from rural areas. 85.2% of the women are housewives and 85.7% are literate. 73.0 % of the acceptors are interval cases and 27.0% accepted the method concurrently with elective termination of pregnancy. The method is efficacious as no method failure (pregnancy) has been reported till date. Since the study ensured regular follow-up of acceptors by scheduled or unscheduled clinic or home visit, the lost to follow-up is low (four women) till date and efforts are ongoing to trace them. The cumulative continuation rate is 90.0, 76.5, 70.2 and 64.1 per 100 users at 12 and 24, 30 and 36 months of use. 1426 women have completed 36 months of use. The cumulative discontinuation due to medical reasons is 4.2 per 100 users and due to personal reasons it is 3.2 per 100 users at 36 months of use. The predominant reason for discontinuation of the method is menstrual disruptions. Cumulative discontinuation rate for this reason at 36 months is 19.0 per 100 users, mainly for prolonged bleeding/frequent bleeding (12.9 per 100 users). This is because women experiencing prolonged or heavy bleeding discontinue the method immediately, whereas those experiencing irregular bleeding or amenorrhoea tend to continue with the method. This is also indicated by the analysis of menstrual pattern of the women using Implanon wherein, although majority of the women have a reduced / infrequent menstrual bleeding pattern cumulative discontinuation due to this reason (3.8 per 100 users) or discontinuation due to amenorrhoea is low (3.0 per 100 users) at 36 months of use.

Celiac Disease in Reproductive Performance of Women

Celiac disease earlier considered to be a disease of the West, is rising in Indian women as well. Most women with celiac disease are undiagnosed because they are asymptomatic . Undiagnosed celiac disease can increase the risk of an unfavorable outcome of pregnancy. Serological testing is the first step in pursuing a diagnosis of celiac disease and the best available tests are IgA anti-human tissue trans-glutaminase (tTG) and anti-endomysial IgA antibodies (EMA). A total of 685 women were recruited (230 cases of infertility, 150 pregnant women with IUGR, 230 non-pregnant control & 75 pregnant control) and screened for the presence of antigliadin IgA (IgA AGA), antigliadin IgG (IgG AGA), anti tissue transglutaminase IgA (IgA tTG) by ELISA and IgA anti endomysium antibody (EMA) by indirect immunofluorescence microscopy. On the basis of IgA tTG alone, latent celiac disease was found to be 4.53 and 7.62 times more likely to occur in infertility and IUGR groups respectively. Thus women having unexplained infertility or intrauterine growth retardation could have subclinical coeliac disease, which can be detected by serological markers. Therefore, consideration should be given to add serological screening for celiac disease in the battery of tests while investigating women with poor reproductive performance.

Diagnosis of Genital Tuberculosis in Infertile Women and the Effect of Anti-tubercular Therapy

To evaluate rate of diagnosis of female genital-tuberculosis(GTB) by various diagnostic modalities and to evaluate fertility outcome after treatment, a prospective study was carried out on infertile women subjected to infertility-workup including laboratory tests: endometrial aspiration(EA) and peritoneal fluid/wash(PW) for histopathology(HPE), DNA-PCR, AFB, bactec sampling;

laparoscopy and hysteroscopy. The study revealed that no single test can pick-up all cases of GTB, hence, whole battery of tests is needed to increase pick-up. Treatment given solely on basis of positive DNA-PCR also results in conception.

Estimation of Oxidative Stress (OS) during Oral Iron Supplementation among Pregnant Mothers

A hospital based randomized controlled trial is ongoing at 2 HRRCs and one central coordinating lab 1) to estimate the oxidative stress status during pregnancy in normal pregnant women and women with mild anemia 2) to study the status of oxidative stress while supplementing iron in daily and weekly doses in normal and mild anemic pregnant women. Micronutrient profile, oxidative stress, diet, placenta are being evaluated in 600 participants for 3 visits. A total of 471 samples from AIIMS and 282 from PGIMER have been received. Preliminary analysis on 51 samples showed raised thiobarbituric acid reactive substances (TBARS) and reduced catalase in control when compared with anemic pregnant women.

CHILD HEALTH

Under child health initiatives of ICMR the major focus of research is on perinatal and neonatal health including childhood cancers and pediatric HIV, operational research and public health related to child health.

Impact of Daily Zinc Supplementation to Infants born with Low Birth Weight on Mortality and Severe Disease requiring Hospitalization

Zinc supplementation prevents diarrhea and pneumonia in 6 months to 3 yr old children. A double blind randomized placebo controlled trial was undertaken in 2012 hospital born infants with birth weight < 2500g. They were randomly assigned to receive zinc or placebo for 6 months. Zinc group received 5mg of elemental zinc as acetate daily from 4 weeks of age. Cause specific hospitalization deaths , episodes of diarrhea, acute respiratory infections , other illnesses, were recorded at 3 months and 6 months of age. The number of infants with one or more diarrhea episodes was less by 17% in zinc group but the number of children with acute respiration infection (ARI) was similar in the two groups. The hospitalization rates for all causes or diarrhea or ARI were also similar in the two groups. The study revealed that hospital born low birth weight infants did not derive worthwhile benefits from daily zinc supplementation.

Pune Low Birth Weight Study – Birth to Adulthood

A cohort of low birth weight babies weighing < 2.00kg at birth were followed up to 18 yr of life. They were assessed for the cognitive problems, scholastic performance, aptitude, the biological risk factors at birth which contributed to the IQ. They were also measured for final height, head circumference and weight on reaching adulthood, (especially those who were small for gestational age (SGA). Low birth weight children (birth weight <2000g) were found to have lower IQs on attaining 18 yr of age compared to normal controls. The socio-economic status had a great impact on IQ and children from, upper - middle and higher socio-economic class had better IQs than those from the lower classes. Mothers‘s education and birth weight greatly influenced the IQ. All low birth weight children showed poor speed on differential aptitude test. Preterm SGA children had low scores in mechanical reasoning while full term SGA children were poor in space relation. Preterm SGA males and VLBW children were remarkably short at 18 yr. Preterm females had a smaller head circumference, so also all VLBW children. The results indicate —that the SGA males need to be watched closely in future for they may develop the “metabolic syndrome’

NUTRITION

INTRAMURAL RESEARCH

NATIONAL INSTITUTE OF NUTRITION, HYDERABAD

The National Institute of Nutrition (NIN) is one of the permanent research Institutes of the Indian Council of Medical Research located in Hyderabad. NIN was founded in 1918 at Conoor, Tamilnadu and the institute was relocated in 1958 to Hyderabad. In addition three more Centres *viz*. Food and Drug Toxicology Research Centre (FDTRC), National Nutrition Monitoring Bureau (NNMB) and National Centre for Laboratory Animal Sciences (NCLAS) and a Pre-Clinical Toxicology Unit (PCT) are located on the same campus. NIN is devoted to research, training, monitoring and consultancy in nutrition related problems of the people at the national as well as regional levels. The institute conducts research in the area of food and nutrition. FDTRC carries out research in areas of food safety, food toxicology, drug-nutrient interactions, mycotoxins, heavy metal contaminants and fluorosis. NCLAS develops breeds and supplies various animal models and feeds for experimental purposes.The PCT carries out short term and long term toxicological evaluations of candidate molecules. NNMB, an extramural project of NIN operating in 10 states, generates information on food and nutrient intakes, nutritional status, prevalence of chronic degenerative disorders such as overweight/obesity, hypertension, type 2 diabetes, micronutrients deficiency disorders *etc*. among rural communities on a continuous basis.

ACHIEVEMENTS

Among the major achievements of NIN are the following :-

- Exploded the protein myth and highlighted the calorie gap as a major bottleneck in protein energy malnutrition (PEM). Based on this finding, several community based feeding programmes were started in different parts of the country, including ICDS.
- Institute's research formed the basis for formulation and implementation of national nutrition intervention programmes for the control and prevention of iron deficiency anaemia, vitamin A deficiency and iodine deficiency. Developed kits to detect iodine content in salt and food adulterants in foods.
- Determined nutritive value of over 650 Indian foods.
- Established recommended dietary allowances (RDA) for different age/gender/ physiological and occupational groups in India.
- Generated data on diet and nutritional status of populations at different time points that formed the basis for development of nutrition policies and intervention programmes.
- Developed technology of double fortification of cooking salt with iron and iodine to tackle the twin problems of anaemia and iodine deficiency.

- Established anti-cancer properties of traditional Indian spices such as turmeric and ginger.
- Developed simple and sensitive method for assessment of blood vitamin A levels using dried blood spot technique.
- Established molecular link for degenerative disorders such as diabetes, cardiovascular diseases and obesity.
- Developed different animal models for studying various nutrition related disorders.
- In the area of pre-clinical toxicology, toxicological and safety evaluation of efficacy of various products including biotech formulations, traditional medicines, neutraceuticals etc.

FOOD AND DRUG TOXICOLOGY RESEARCH CENTRE, HYDERABAD

ACHIEVEMENTS

i. Out of 376 street food samples (including chicken fired rice, chicken noodles, boiled noodles/ rice) analysed for microbiological contamination, *Bacillus aureus* and *Staphylococus aureus* were found to be the major pathogens. *Salmonella* was present in salads and handwashings of the food handlers. Enteric pathogens were found in drinking water provided by street food vendours. Out of 217 consumers of street foods, 18% experienced symptoms of food borne infections. As per the study, there is a need to emphasize risk evaluation and identification of risk factors. At present, PCR and RT-PCR based diagnostic kits to detect food and water borne human pathogens are being developed.

ii. In a total diet study, food samples were analysed for pesticide residues, toxic metals, mycotoxins and fluoride. Out of 70 samples, 60 had pesticide residues, 100 out of 155 samples had either lead or cadmium or both, 35 out of 40 samples had aflatoxins B1 in the range of 0.1-13.1 ppm. All the 26 samples of water analysed for fluoride (from flurotic and non-flurotic areas) had detectable concentration of fluoride and highest was 0.17 ppm. Three out of eight samples had more than 1.0 ppm.

iii. In a study to assess the problem of hydrofluorosis in Uchapalli village of Nellore district in Andhra Pradesh, it was found that levels of silica (Si) and Strontium (Sr) were very high in drinking water (Sr is known to increase bone density and Si increase Fluoride deposition)

iv. Nutrient like vitamin B and C are known to reduce lead toxicity by mobilizing lead from the body. In our invitro experiment, Thiamin has been found to possess antichelating property and hence had therapeutic potential.

v. Having established the chemopreventive potential of turmeric, transplacental antigenotoxic effect of this spice was studied in experimental animals. Inhibitory potential of turmeric on invitro nitrosation under simulated gastric condition was investigated. Dose dependent inhibition of nitrosamine formation with turmeric was observed. Efficacy of turmeric and garlic powder administration during treatment in the course of H pylori eradication was also studied as both turmeric and garlic are known for their anti-microbial activity.

vi. A collaborative study with National Research Centre for Sorghum was done to popularize consumption of millet based foods. Studies are in progress to assess the efficacy of these foods on diabetes and on growth patterns of children.

vii. As a part of pre-clinical toxicity studies, safety evaluation of ABFNO2, an antiosteoarthritic medicine, shea olein, DAG oil and new chemical entity (NCE) meant for treatment of cancer has been completed.

EXTRAMURAL RESEARCH

HEALTH PROFILE OF POPULATION OF NELLORE (A.P.)

Under the study information has been collected on utilization and accessibility of health facilities and assessment of nutritional deficiencies in population by measuring blood serum levels for vitamin A, E, zinc, copper, B_{12}, folic acid, ferritin, calcium, phosphorus, lipid profile *etc.* Data are being analyzed.

HEALTH PROFILE OF POPULATION OF DHAR (M.P.)

The study is being carried out in Badwani block of Dhar district tribal (with 90% tribal population) for assessment of micronutrient deficiency based on biochemical markers like ferritin, B_{12}, folic acid, zinc and selenium. Information is also being collected on utilization and accessibility of health facilities.

Consumption Pattern of Carbonated Soft Drinks of Indian Population

The study was carried out with the objective to assess the consumption pattern of carbonated soft drinks (organized and unorganized sectors), fruit juice, milk and frequency of consumption of junk food. The data was collected from 16 locations across the country including four metropolitan cities, four medium sized cities (urban), areas adjoining the medium sized cities (rural) and one district each of hilly and tribal areas. The information was collected monthly and throughout the year hence capturing the seasonal variations in the consumption pattern on the basis of both preceding day and weekly information. Around 9178 households and 44435 subjects were covered under the study. The study was completed in 2008 and the data is being analyzed.

ENVIRONMENTAL AND OCCUPATIONAL HEALTH

NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH, AHMEDABAD

National Institute of Occupational Health, Ahmedabad and its regional centres at Bangalore and Kolkata are India's specialist research organizations engaged in intensive research in the field of occupational health. The research initiatives of the institute include epidemiological studies, environmental pollution and toxicology, ergonomics and intervention studies, and national surveillance programmes.

ACHIEVEMENTS

The institute installed a facility in an industrial unit at Beawar, Rajasthan resulting in 85-90% reduction in silica exposure in the premises.

Study of haemolytic profile of arsenic exposed population in West Bengal revealed Bowen's disease and hyperpigmentation with severe keratosis of palm and sole in exposed population.

Studies are continuing on workers in handloom and power loom weaving garment, incense stick (agarbatti) and bidi making, fish processing, sheep breeding and wool cottage industries. The male weavers aged 25 yr of age were found to have increased relative risk of respiratory symptoms in comparison to those <25 yr of age. Female weavers having 5 yr of job tenure and raised level of chronic fatigue and somatic anxiety had increased risk to respiratory problems. Incense stick (agarbatti) making involves large number of female workers. The females having job tenure over 5 yr and working more than 8 hr a day and having the habits of chewing and snuffing tobacco had increased relative risk to the occurrence of general health problems.

In a study on 209 iron workers, 65% workers reported chronic fatigue with significant relative risk in the occurrence of respiratory and eye problems. Male and female workers engaged in *bidi* making were found to have increased prevalence of pulmonary function impairment due to their exposure to tobacco dust. Predominant complaints among the workers were cough, chronic bronchitis and breathlessness. Study undertaken among brick making workers showed potential risk to musculo-skeletal stress and strain and exposure to brick kiln emitted toxic fumes containing suspended particulate matter.

Efforts are ongoing for developing biophysical model to simulate heat exchange phenomena across the multiple body segments and layers, numerically define the human vulnerability to heat stress, predict heat susceptibility limits, apply geo-spatial mapping of heat related effects and disorders, and identify warning and danger zones.

Epidemiological as well as experimental studies were conducted to study the effect of exposure of pesticides, heavy metals, solvents, and *panmasala* on male reproductive system in workers of the printing press, industrial solvents and welding industries. Toxicity study of CS_2 showed decrease in sperm count and increased sperm shape abnormalities. Study on toxic effect of *panmasala* with

and without tobacco revealed deleterious histological alterations in mouse testis and sperm morphology.

The NIOH has embarked on a large scale multicentric research initiative to study toy toxicity due to presence of heavy metals and other compounds used in toys.

The NIOH runs an ENVIS centre, with the objective to collect, collate, storage, retrieve and disseminate information related to occupational and environmental health.

NON-COMMUNICABLE DISEASES

INTRAMURAL RESEARCH

Over the past few decades research has clearly shown that chronic noncommunicable diseases have their roots in unhealthy lifestyles or adverse physical and social environments. Risk factors like unhealthy nutrition over a prolonged period, tobacco use, physical inactivity, excessive use of alcohol, and psychosocial stress are among the major lifestyle issues. (WHO, '09). The research at ICMR has aimed to respond to the non-communicable diseases (NCD) epidemic by providing technical support and appropriate guidance in assessing the research needs, developing effective projects and towards capacity building and training. NCD related policies have found a substantial place during the 11th plan proposal of the Ministry of Health. Policy for tobacco, cancer, CVD, diabetes & stoke, mental health, and food & nutrition are being facilitated through ICMR's researches. The implementation of the Integrated Disease Surveillance Programme was facilitated through strategies evolved by the Council, and its implementation in 7 states, which have information on the major NCD risk factors and a national surveillance system for major NCDs has been included in the National Programme.

INSTITUTE OF CYTOLOGY AND PREVENTIVE ONCOLOGY, NOIDA

ACHIEVEMENTS

ICPO has been involved in conducting multidisciplinary studies for control of cervical cancer since inception. During the year 2009-10 this work was continued along the leads that were obtained in the past. ICPO pioneered the strategy of visual inspection for early detection of cervical cancer. The test characteristics of this modality were compared with that of cytology and HPV screening in the past in a hospital setting.

ICPO has been selected as one of the sites for carrying out the HPV vaccine trial (Gardasil trial, MERC). During the year under report different formalities for the site selection and site preparation were undertaken including the approval of the project for ethical clearance. The Institute was also involved in carrying out a randomized, multicentric trial for clearance of HPV infection in uterine cervix by Basant (a polyherbal cream) and curcumin soft gelatine capsules in females infected with HPV. The main areas of research is molecular genetics and biochemistry focussed on studying SNP profling of immunomodulatory genes in cancer. The Institute was also engaged in the development of DNA vaccines against HPV and SNP analysis of cell cycle regulatory genes in cancer. The Institute also carried out studies on expression profiling and identification of genes associated with development of cervical cancer, analysis of promoter methylation of E-cadherin gene in cervical cancer among Indian women, role of AP-1 and NF-kB in regulation of telomerase activity in cervical cancer cells, transcriptional targeting of human papillomavirus gene expression by herbal derivatives, role of transcription factors, signal

transducer and activator of transcription 3 (stat 3 in cervical carcinogenesis). ICPO has been identified as one of the regional HPV laboratories for monitoring HPV vaccine programme in South East Asia region under global HPV laboratory network (HPV labnet of WHO). Currently ICPO has developed the capability of performing in-house qualitative and quantitative PCR for HPV 16 and 18. During the year under report ICPO initiated many new areas of research such as breast cancer, oral cancer, esophageal cancer, gastric and lung cancer. Most of these studies are laboratory based.

REGIONAL MEDICAL RESEARCH CENTRE, DIBRUGARH

Regional Medical Research Centre, Dibrugarh, was established on 12th July, 1982 with the mission to promote bio-medical research in north-eastern states of India using multidisciplinary approach and build up scientific manpower. The current areas of research are cancer, cardiovascular diseases and hypertension, mosquito borne diseases, HIV and drug abuse, trematode infections, haemoglobinopathies, and medicinal plants of NE India

The prevalence of CHD and hypertension among Mizos, Assamese and Tea garden population showed large variation hence genetic aspects of essential hypertension in north-east region using 3 markers *viz.* ACE polymorphism, SNPs in hypertensive families, and angiotensin receptor polymorphism were studied across these populations.

Status of haemoglobinopathies in various ethnic groups of north-eastern region was documented. The prevalence of thalassaemia carrier state and haemoglobinopathy in Assam was studied among college students and expectant mothers for the community control of thalassaemia syndromes**.** Incidence of G-6-PD deficiency and its molecular characterization in north-east India (Assam and Mizoram states) was also determined.

The risk factors of nasopharyngeal carcinoma in Nagaland, oesophageal cancer in Assam and stomach cancer in Mizoram were analyzed. Significant association of consumption of smoked meat and use of herbal nasal drops was found in cancer nasopharynx. Higher risk of developing stomach cancer was seen in tobacco users, especially for Meizol (a local cigarette) smokers and Tuibur (tobacco smoke-infused water) consumers.

Among dietary habits, frequent consumption of sa-um (fermented pork fat, a traditional fat) and smoked dried salted meat and fish were found the risk factors for stomach cancer in Mizoram. Betel nut chewing and consumption of water extract of charred banana stem, known as 'kalakhar' in Assamese, emerged as significant risk factors.

Screening of local plants resulted in identification of two plants *i.e.* one possessing good antimalarial activity and the other having mosquito larvicidal activity for which Indian patents have been filed. A module of malaria control for organized sector(s) located in forest/forest fringed areas was developed and technology transferred through contract research.

Paragonimiasis, also known as lung fluke disease or endemic haemoptysis, is caused by trematodes belonging to the genus *Paragonimus*. Studies done at RMRC established that a majority of cases of pulmonary paragonimiasis are being confused with that of pulmonary tuberculosis by treating physicians in north-east India, especially in Arunachal Pradesh where both diseases co-exist, and are being treated without success with anti tubercular drugs. ELISA kit was developed for identification of paragonimiasis

DESERT MEDICINE RESEARCH CENTRE, JODHPUR

Achievements

The major areas of research at DMRC are dengue and dengue hemorrhagic fever (DHF), malaria and tuberculosis diabetes, RF & RHD and muscular-skeletal disorders, nutritional morbidities of desert population; immunization coverage, disease burden and vector biology. Main emphasis has been given on the result oriented research to be utilized under various national health programmes at community level.

The dengue & DHF research has been directed to disclose different intricacies through developing predictors and determinants of dengue for designing surveillance mechanisms and molecular and genetic markers of virus transmission competence of dengue vectors, zoonotic cycles of dengue virus in maintaining endemic DF and causing DHF. Tuberculosis research revolved round the rapid culture of *M. tuberculosis* from sputum samples and suitable interventional methods for early detection of new PTB cases. Mapping of insecticide resistance in vectors of malaria has been another attempt to make the malaria control programme more effective and specific. Exploration of indigenous plants S. *xanthocarpum* and *C. procera* for their mosquito larvicidal and anti-virus activities respectively has also been another line of research.

Studies on epidemiology of musculoskeletal conditions, control of rheumatic fever and rheumatic heart disease and dermatoglyphic patterns in diabetes mellitus patients were continued during the year. Nutrition morbidity surveys on NNMB pattern, meta-analysis of NDDs and nutritional status and morbidity patterns of neonates are some of the studies representing nutrition and MCH disciplines.

Evaluation of immunization coverage and estimation of disease burden by DALY measurement and its distribution at household levels are some more field oriented research endevours in the current year.

EXTRAMURAL RESEARCH

Some of the most significant contributions of the Council during 2009-10 include the setting-up of the first NCD risk factor surveillance system, and first Centre for Advanced Research on Diabetes and study of the role of health workers in the detection and management of chronic diseases. Some noteworthy achievements include bringing out consolidated reports of the research investigations of the Bhopal gas tragedy, investigating mental health issues in urban areas and disaster situations, expansion of the national cancer registry programme, study of new vaccine for cervical cancer, setting up satellite centres for management of RF and RHD, understanding foetal origins of heart disease, and translational research in diabetes. Important epidemiologic information has been collected on the prevalence and risk factors for asthma, stroke, and on the functional status of elderly. More recently, the Council has undertaken setting up of web based data capture for diabetes and acute myocardial infarction, and road traffic injuries. Investigating new areas such as musculo-skeletal diseases, breast cancer and addressing obesity as an important determinant of chronic diseases to further address the growing NCD epidemic.

The Council has undertaken broad range of basic research aimed at expanding understanding of the role of gene environment interactions in foetal origin of coronary artery disease, maturity onset diabetes of the young (MODY) and early onset type 1 and type 2 diabetes, salt sensitive

hypertension, Parkinson's disease, molecular basis of genesis of breast and cervical cancer and gene therapeutics in cancer. Recognizing that development of biomarkers for cardiovascular diseases will depend critically on large sets of well annotated biological specimens, a disease specific Biobank on acute coronary events is being initiated with French collaboration.

The Council has also contributed to virtually all the national disease control programmes like cancer, blindness, mental health, and to the new programme activites of the Government such as IDSP, trauma and accidents, geriatrics, environmental health and climate change. The Council also brought out national guidelines on management of site specific cancers and diabetes in the young. Published reports on road traffic injuries, urban mental health, mental health needs of earthquake affected population in Gujarat, etc have helped to disseminate the research findings.

North Eastern region continues to be in focus for facilitation and augmentation of research activities. Expansion of the Cancer registry now includes 8 registries covering 6 states in the north east, and Cancer Atlas continues in two states. Study of hypertension and gene environment interactions, and focus on communicable diseases, especially paragonomiasis in Assam has helped to suggest strategies for their prevention and management .

The Council has been actively supporting partnerships and networking among international partners committed to NCD prevention and control. Collaborations with CDC, Atlanta, USA on environment and occupational health having been renewed for the next 5 years, continues to actively support training workshops, consultancy meetings and projects. French collaboration has resulted in 3 projects completed under neurosciences. Cancer research continues to be jointly undertaken with German collaboration. Renewal of Canadian collaboration with Canadian Institute of Health Research has addressed the problem of obesity. New areas for collaborations with University of Minnesota, USA, Research Triangle Institute, USA, George University, Australia, and Medical Research Council, UK have been planned.

BASIC MEDICAL SCIENCES

INTRAMURAL RESEARCH

NATIONAL INSTITUTE OF IMMUNOHAEMATOLOGY, MUMBAI

National Institute of Immunohaematology was started in 1957 as Blood Group Reference Centre (BGRC) under ICMR at the KEM Hospital Campus, Mumbai and renamed as Institute of Immunohaematology on its 25th anniversary. In view of its expanded activities and the only institute in the country working in the area of immunohaematology it was rechristened as National Institute of Immunohaematology in 2008.

The institute is known for many achievements in the area of immunohaematology which include: i) discovery of Bombay & In blood group system; ii) development of prenatal diagnosis for thalasaemmia, sickle cell anemia, haemophilia, vonWillebrand disease, rare coagulation factor deficiencies, immunodeficiency and other haemoglobinopathies; iii) describing several new and rare mutations in haemoglobinopathies; iii) describing several new and rare mutations in haemophilia, Glanzmann's thrombasthenia and in rare coagulation disorders; iv) developing cost effective ways of managing congenital bleeding disorders; v) several new HLA antigens were described; vi) association of HLA- B27 with haemophic synovitis; v) association of factor V Leiden with Budd-chiari Syndrome in the Indian sub continent; vi) several new G-6PD variants from India; vii) salutary influence of thrombophilic genes on congenital bleeding disorders; viii) molecular biology techniques were improved for diagnosis of mutations in thalassaemias and other haemoglobinopathies; ix) technique for prenatal diagnosis from mother's blood for haemoglobinopathies was developed; x) RhD typing of foetus for mother's blood was perfected; xi) demonstrated the usefulness of EACA for management of haemophilia;

INSTITUTE OF PATHOLOGY, NEW DELHI

The thrust area for research at IOP are tumour biology, infections diseases and stem cell biology.

TUMOUR BIOLOGY

Breast Cancer

One breast cancer cell line (PCB20) has been established from an early onset breast cancer case as an important tool to study molecular carcinogenesis.

Gene expression profile has been studied in ten cases and role of promoter hypermethylation in five cases of early onset breast cancer using microarray technology to understand its molecular pathogenesis.

Correlation of expression of type 1 growth factor receptor genes EGFR, c-erbB-2, c-erbB-3 and MDR1 and AR genes in locally advanced breast cancer cases with response to neo-adjuvant chemotherapy showed that AR gene carries independent predictive role.

Urogenital Malignancies

Study to identify CAG microsatellite repeats in androgen receptor gene, (TTTA) repeat analysis in *CYP19* gene, polymorphism in prostate specific antigen (PSA) gene and MLH1 gene in prostate cancer and their correlation with genetic susceptibility and progression of carcinoma showed protective role of GG genotype of PSA gene, slight association of genotype A2A2 of *CYP19* [TTTA] repeat with cancer prostate (CaP) cases and significant association of CC genotype at -93 position of the core promoter region of *MLH1* gene with risk of prostate carcinoma.

Study on role of effector function of cyclooxygenases (Cox-1 and Cox-2) and associated cytokines in peripheral blood mononuclear cells (PBMCs) in invasive and non invasive transitional cell carcinoma (TCC) of urinary bladder showed increased Cox-2 expression in invasive cancer patients. Significant variation in IL-1B and IL-6 level was observed in patients in comparison to normal group. The expression of CD74 was also found high in cancerous patients compared to controls.

Cancer in North-East Region of India

A comprehensive study on oesophageal carcinoma to investigate genetic factors associated with tobacco and familial association has been completed. On the basis of gene ontology, four molecular functional pathways (MAPK, G-protein coupled receptor family, ion transport activity and serine or threonine kinase activity) were upregulated and six pathways (structural constituent of ribosome, endopeptidase inhibitor activity, structural constituents of cytoskeleton, antioxidant activity, acyl group transferase activity, eukaryotic translation elongation factor activity) were downregulated in tobacco associated oesophageal cancer. Genes involved in humoral immune response, extracellular matrix organization, metabolism of xenobiotics, TGF-ß signaling and calcium signaling pathways were down-regulated and genes involved in regulation of actin cytoskeleton, neuroactive ligand receptor interaction, toll-like receptors, B-cell receptors and insulin signaling pathways were up-regulated.Validation of differential expression of subset of genes by PCR and tissue microarray in familial and non-familial cases showed no significant difference in expression of these genes in two groups.

No significant contribution of GSTM1 and GSTT1 null polymorphisms was found in oral and gastric cancers. Polymorphism in codon 72 of p53 gene showed that genotype pro/arg may act as a risk factor for gastric cancer while genotype pro/pro acts as protective factor for lung cancer. Gene expression studies have been initiated in oral, gastric and lung cancers and copy number analysis has been done in oesophageal cancer using 10K array.

In pesticide associated cancers no significant contribution of mutations in BRCA1 and 2 genes, CYP17 and p53 gene and codon 72 polymorphisms have been found, however, GSTP1 null polymorphisms show significant contribution to risk of breast cancer. Copy number analysis by microarray is being done to identify genes associated with risk and progression of breast cancer.

Hematopoietic-Lymphoid Malignancies

Study on prevalence and prognostic value of gene mutations in acute myeloid leukaemia (AML) done at IOP showed alterations in FLT3 gene in 23% patients, however, there was no significant difference in response to induction therapy in patients with or without FLT3/ITD mutation. Significant difference in expression of IkB-α, IKK-B, P53, cIAP-2 and survivin was seen in samples of AML and acute lymphoid leukaemia (ALL). Significanly low expression of p53 was found in non-responder group of AML patients which correlated with IKK-alpha gene expression. Expression level of cIAP-2 was significantly lower in non-responder group of ALL patients.

Brain Tumours

A high-throughput tissue microarray (TMA) chip containing 300 brain tumours from archival paraffin blocks has been constructed and used to study the protein expression of differentially expressed genes.

PATHOLOGY OF INFECTIOUS DISEASES

Chlamydiasis

Study on role of chlamydial heat shock proteins in pathogenesis of genital tract infection in women showed that in cervical epithelial cells, cHSP60 and cHSP10 had a different pattern of expression in infertile compared to fertile women. The results strongly support their involvement in immunopathological conditions associated with infertility .

Study on correlation of chlamydial infectious load with immune factors showed significantly higher inclusion counts in chlamydia-positive fertile women compared to women with fertility disorders with lower recovery of chlamydia from the cervix of these women . Further, chlamydial inclusion forming units (IFUs) correlated positively with CD8, pDC, IL-8, c-reactive protein (CRP) and IFN-γ in women with mucopurulent cervicitis (MPC). In women with fertility disorders, chlamydial IFUs correlated positively with plasmacytoid dendritic cells (pDC), IL-10 and estradiol and negatively with CD4 and IFN-γ levels. The data suggest that clinical condition presented is decided by interplay of infectious load and host immune responses.

Significant decrease in levels of IL-8, interferon-gamma (IFN-γ) and tumour necrosis factor-alpha (TNF-α) was observed in cervical secretions of *Chlamydia* positive women with and without infertility after administration of azithromycin as compared to levels before therapy suggesting that azithromycin modulates the production of cytokines in eradication of infection.

In the study on role of iron on pathogenesis of *C. trachomatis,* expression of transferrin receptor (TfR) was found down-regulated whereas that of ferritin heavy chain (FHC) was up-regulated in *C. trachomatis* infected HeLa 229 cells. Expression of TfR in infected cells did not change upon addition of iron chelator deferoxamine (DFX) and iron source ferric ammonium citrate. Expression of iron regulatory protein (IRP)-1 predominated over IRP-2 in infected cells. Attenuation in binding activity of iron-responsive proteins and elements was observed in electrophoresis mobility shift assay of infected cells and is central to iron homeostasis.

Leishmaniasis

Identification of a novel ubiquitin-like system in the protozoan parasite *L. donovani* in infected bone marrow samples from leishmaniasis patients suggested its role in the disease pathogenesis.

Transcriptome profiling for identification of antimony resistance determinants in *L. donovani* isolated from Indian patients of kala-azar showed genes coding for protein surface antigen 2 (PSA2), histone (H1), histone 2A (H2A), histone 4 (H4) and MAP-kinase. Two hypothetical proteins were transcribed more abundantly in antimony resistant in comparison to sensitive parasites.

In vitro susceptibility of isolates to antileishmanial drugs (miltefosine, amphotericin B, paromomycin and sitamaquine) significantly correlated with one another raising the possibility of cross- resistance. The data indicated paromomycin be more effective treatment option.

Evaluation of host immuno-determinants involved in pathogenesis of kala-azar and PKDL implicated the presence of effector and regulatory molecules together with apoptosis and chemokine related genes.

Analysis of intralesional cytokine gene expression in PKDL and kala-azar revealed significant down-regulation of TNFR1 transcript. Investigation of matrix metalloproteinases provided evidence for role of TIMP-1 and TIMP-3 in pathogenesis of PKDL.

IL-8 was found to be an effective immuno-determinant in pathogenesis of cutaneous leishmaniases caused by *L. tropica.*

Studies on multilocus microsatellite typing revealed genetic homogeneity of *L. donovani* strains in the Indian subcontinent including Bangladesh, India and Nepal.

STEM CELL BIOLOGY

Pancreatic Progenitor Stem Cells

Studies done at NIN, Hyderabad on the role of nutrients in characterization and proliferation of pancreatic progenitor cells/stem cells to insulin secreting cells indicated that nestin, a class VI intermediate filament protein, could be participating in the cytoskeletal formation as well as in cell migration and mitosis.

Studies for Finding Optional Attenuation Conditions for Fibroblasts

Studies were done at IOP, New Delhi for finding optimal attenuation conditions for 3T3 fibroblasts for use as feeder cells. The results indicated that successful attenuation is dependent on numerical dosing with concomitant optimization in the stimulation of keratinocyte cell proliferation. Investigation of the utility of a patented synthetic thermo-reversible hydrogel polymer (TGP) as supportive matrix for development of 3-D composite skin showed that TGP specifically stimulates only those keratinocytes that have inherent stemness.

Derivation of Human Embryonic Stem Cell Lines in Xeno-free Environment

Research efforts at NIRRH are aimed to realize clinical potential of human embryonic stem cells (hES). In order to achieve this, two cell lines have been derived and characterized. To elucidate factors secreted by fibroblasts, differential proteome and genome analysis of feeder fibroblasts, derived from D13.5 (supportive) and D18.5 (non-supportive) mouse embryos was carried out. Correlation of data generated in microarray study with the published proteome data of supportive feeder fibroblasts enabled identification of proteins – which may be the likely candidates in supporting the undifferentiated expansion of ES cells *in vitro.* Results indicate that TGFβ and its associated signaling molecules facilitate undifferentiated proliferation of hES cells *in vitro.*

Cryopreservation and Maturation of Germ Stem Cells for Fertility Conservation of Individuals with Gonadal Insufficiency

Gonadal tissue cryopreservation protocols and culture conditions for *in vitro* maturation of germ cells is being standardized at NIRRH with the aim to preserve fertility of individuals with gonadal insufficiency. The c-kit receptor and its ligand, Sertoli cell factor (SCF), represent one of the key regulators of testicular formation, development and function and have been extensively studied in various animal models. Cellular localization of c-kit receptor has demonstrated, for the first time, a stage specific expression in normal adult human testis. *In situ* hybridization revealed that the transcripts of the gene were also localized in a similar pattern . The results will help in expanding current knowledge about the c-kit/SCF system in human spermatogenesis.

Stem Cell Therapy

A pilot study was conducted to evaluate the safety and feasibility of autologous olfactory mucosal transplantation in chronic spinal cord injury at Indian Spinal Injury Centre, New Delhi. The results revealed that procedure was tolerated well by all American Spinal Injury Association (ASIA) Impairment Scale (AIS) A participants. MRI evaluation revealed a syrinx in one participant and increase in length of myelomalacia in four participants. There were no other adverse findings on MRI evaluation. There was no significant improvement in any of the neurological, electrophysiological or urodynamic efficacy variables. Statistically significant improvement was seen in functional scores but this could not be attributed to the procedure. Overall the procedure was relatively safe and feasible in participants with thoracic level injuries at 18 month follow up.

REGIONAL MEDICAL RESEARCH CENTRE, BELGAUM

Regional Medicine Research Centre, Belgaum was envisioned to conduct research on herbal medicine as a major thrust area. The Centre's mandate is to bridge the gap between traditional herbal medicine and modern medicine through scientific research and validation; to conduct research on locally prevalent disease, and to develop local technical manpower. This centre has been envisioned as a National Centre for Research in Herbal Medicines in the near future and as a resource centre in terms of expertise, infrastructure and technologies available for medical research in the region.

Achievements

a) Preparation of a database on ethno medicinal plant of Western Ghats.; b) establishment of a museum for ethno medicinal plants of Western Ghats; c) development of a herbal garden for medicinal plants of the Western Ghats region with more than 200 medicinal plants in its campus; d) preparation of a directory of the local traditional practitioners (non-codified) from Belgaum district; e) identification of infectious diseases of local health importance, and f) providing of services to neighboring research institutes and NGOs in respect of plant indentification and authentication of medicinal plants/drugs, information on collection, cultivation and utility of medicinal plants, preliminary screening of phytoconstituents and screening of biological activities and consultation for experimental design and statistical analyses.

EXTRAMURAL RESEARCH

The Council supports and co-ordinates extramural research in basic biomedical sciences *viz*. Allergy, Anatomy, Anthoropology, Biochemistry, Cell & Molecular Biology, Haematology, Human Genetics, Immunology, Organ Transplantation, Pharmacology, Physiology, stem cell resion Toxicology, Traditional Medicine Research and Bioethics. During the year studies continued in various disciplines through Centres for Advanced Research (Cancer Genetics and Genomics, Molecular Cyto-genetics, Tumor tissue Pharmacogenomics, Reverse Pharmacology, Yoga, Evidence based medicine, Genetic disease registry, DNA finger printing of medicinal plants of North-East region, Stem Cell Research and Therapy) Task Forces (Genomics and molecular medicine, Stem Cell Research and Therapy, Inborn Metabolic Disorders and Basic Research in Aging).

Biochemistry

ICMR has set up a task force on Indian Normatives for clinical Laboratory Parameters (INCLAP) in order to set up standards of Clinical Laboratory Parameters for Indian population.

Human Genetics

Phase II of the study on inborn metabolic disorders in newborns continued at 5 newborn screening centres including Delhi, Mumbai, Kolkata, Chennai and Hyderabad along with 3 high risk screening centres at Delhi, Hyderabad and Bangalore.

Pharmacology

The Centre for Clinical Pharmacodynamics at Nizam's Institute of Medical Sciences, Hyderabad has been set up as a specialized facility for carrying out simple and non-invasive pharmacodynamics screening methods, to investigate the effect of drugs on cardiovascular and central nervous system functions and to conduct annual training programme in clinical pharmacodynamics methodologies.

Toxicology

Reproductive Toxicology Unit at NIRRH, Mumbai has been set up with the objectives to conduct reproductive and genetic toxicity evaluation of drugs, chemicals, and other agents including vaccines and biotechnological products and to undertake research at cellular and molecular level. Developmental and preclinical safety evaluation of Nisin (spermicide) a microbicide using rat and rabbit model has been successfully carried out.

Traditional Medicine

Department of AYUSH- CCRAS, CSIR and ICMR are working together under Golden Triangle Partnership (GTP) Scheme for validation of traditional Ayurveda, Siddha, Unani and Homoeopathy drugs and development of new drugs.

ICMR Advanced Centre of Reverse Pharmacology in Traditional Medicine was established at Medical Research Centre, Kasturba Health Society, Mumbai. The studies conducted include the first experimental study of antimalarial activity and clinical safety of the traditionally used paste formulation of leaves of *Nyctanthes arbor-tristis*. Trials on Sudarshan Ghanavati (SG, a complex multi-ingredient formulation) were initiated at KEM hospital, with a major component being Swertia chirata.

Review Monographs on Indian Medicinal Plants

During the year ninth volume (with botanical names Da-Dy) covering monographs on about 430 medicinal plants species carrying multidisciplinary information as part of series on Reviews on Indian Medicinal Plants have been published. The eighth volume (with botanical names Cr-Cy) covering monographs on about 270 medicinal plant species is in press). The programme aims at consolidation of Indian research contributions (published information) at the various National laboratories/institutions across the country in the area of medicinal plants and present the compiled information in series on "Reviews on Indian Medicinal Plants".Earlier, seven volumes of Reviews on Indian Medicinal Plants (with botanical names starting with A, B and Ca-Co) covering multidisciplinary research data on about 1,700 plants, were published. Each monograph includes regional names of the medicinal plant, its Sanskrit synonyms as well as the Ayurvedic description (wherever available), ethnobotanical studies, apart from the habitat and the parts used, properties and uses on one hand, and the details of botanical, pharmacognostical, chemical, pharmacological and clinical data on the other, backed by compete references and bibliography on each aspect of the information cited, besides the colour photographs of important medicinal plants.

Quality Standards of Indian Medicinal Plants

During the year the seventh and eighth volume on quality standards on 69 medicinal plants were developed, monographs prepared, technically reviewed and published as part of series on "Quality Standards on Indian Medicinal Plants". The programme aims at development of Quality Standard of important Indian medicinal plants and preparation of monographs thereof.The program is in progress at various national laboratories/ Institutions in the country. The monographs are on the pattern of WHO guidelines and focus on the diagnostic features and phytochemical studies, including markers besides having information on pharmacological, clinical, toxicological aspects along with dosage, adulterants/substitutes etc. Earlier six volumes have been brought out containing quality standards of a total of 205 plants. Monographs on another 35 plants are being finalized for eighth volume.

Medicinal Plants Monographs on Diseases of Public Health Importance

The activity aims at integration of leads/scientific information on diseases (including etiopathogenesis) and plant drugs as given in the ancient texts (ISM) and Allopathic system of medicine on one hand and the multidisciplinary research data generated on these plant remedies with focus on pharmacological, toxicological, clinical, phytochemical, pharmacognostic, on the other. The draft monographs of filariasis and diabetes mellitus are in different stages of review.

The Council jointly with DBT developed Guidelines of stem cell research and therapy in 2007. These guidelines incorporates the technical aspects of stem cell research and therapy, which would give a uniform guidance to the scientists and clinicians engaged in research in this area

Stem Cell Research & Therapy (SCRT)

The council jointly with DBT developed Guidelines for stem cell research and therapy in 2007. These guidelines incorporate the technical aspects of stem cell research and therapy, which would give a uniform guidance to the scientists and clinicians engaged in research in this area.

SOCIAL AND BEHAVIOURAL RESEARCH

During 2009-10 following studies were completed and the data was analyzed.

Study of Reproductive and Sexual Health Education of Adolescents

In view of the importance of adolescents' reproductive health and sexuality and the fact that they lack in information on many important issues, a study was carried out among school going urban and rural adolescents, in the age range of 13 to 17 yr (9th and 11th standard students) of both sexes in Delhi, U.P., Maharashtra, Tamil Nadu, Kerala and West Bengal. In each state three schools in urban areas and one school in rural area were taken for the study An IEC package was developed and used to impart class based education on different aspects of reproductive and sexual health by outside experts with the involvement of teachers. The IEC was provided twice over a period of one year. The impact assessment showed increased awareness about different issues among adolescents and intentions for safe practices.

Study of Health Consequences of Domestic Violence with Special Reference to Reproductive Health

In order to understand the socio-psychological and cultural dynamics of domestic violence against women and its impact on their health in general and reproductive health in particular, this study was conducted in 18 states covering about 15000 women and 15000 men. The study results showed an overall 39% women facing one or the other kind of domestic violence i.e. psychological, physical and sexual. 37% women faced psychological violence, 14% physical violence and sexual violence each in their families. The violence was found to be directly related with the educational level of the women.

About 14% women reported facing violence during the last pregnancy. Antenatal care was found much higher among the women who did not face domestic violence compared to those who faced it. The prevalence of sexual violence was more among women who suffered from RTI/STDs than those who did not have these problems. Similarly, use of contraception was low among women who faced domestic violence.

Study of Roles and Capacities of Panchayati Raj Institutions to Manage the Grass Root Health Care System

In order to understand the roles and capacities of Panchayati Raj Institutions and perspectives of the community and health care providers, a study was carried out in five States (Assam, Haryana, Kerala, Madhya Pradesh and West Bengal). These five states represent different geographical regions as well as different political spectrum. A total of 1127 PRI members at different levels, 684 health care providers and 4500 community members from general population from all the states were interviewed.

A large majority of PRI members in Haryana and Madhya Pradesh did not know that PRIs have the powers in relation to health matters. Regarding health committee, overall 34 % of the participants,

98 % in Haryana, 44%in MP, opined that there was no health committee working in their Panchayat. The situation was better in Assam, West Bengal and Kerala. 62 % of the participants told that there was no provision of health care in the budget of their Panchayat. Lack of funds (90%), lack of technical knowledge (81%) and lack of co-operation with the health staff (60%) were reported the major problems of the Panchayats to carry out their responsibilities.

Among the participants from general population, 65 % (ranging from 84% in West Bengal, 78% in Haryana, 72 % in Madhya Pradesh, 52% in Assam and 43% in Kerala) did not participate in *Gramasabha* meetings. Among those attending the *Gramasabha* meeting, only 47 % told that issues related to health were discussed. Only 26 % of the participants from general population felt that Panchayats have role in addressing health problems. At the same time, 64 % of the health providers told that Panchayats do not have necessary expertise to manage the local health system.

HEALTH SYSTEMS RESEARCH

Strengthening of health system research at country level was started at ICMR Hq. in June, 2009. To start with following activities have been initiated to meet the health needs of the people in the complex geographical, socio-economic, cultural, political, demographic and epidemiological environment in India – delivery of RCH services – public, public – private and NGO model, health insurance for the population living in rural areas and urban slums, strengthening research capacity and effective knowledge utilization. reduction of gap in the health system manpower and service delivery, reducing gender discrimination and improving adolescent health.

INTERNATIONAL HEALTH

ICMR co-ordinates international collaboration in biomedical research India and other countries and with national & international agencies such as Ministry of Science & Technology and WHO etc. There are few specific agreements signed by the Ministry of Health and family welfare with other countries as well as those signed directly by ICMR with international organizations/ institutions. Such as France, Germany, USA, Canada, Australia, *etc*.

The purpose of these agreements & Memorandum of Understanding (MoU) has been for exchange of scientific information; exchange of scientists/technicians; joint execution of scientific projects including support in the procurement of scientific equipments and organization of joint scientific meetings, seminars, workshops and symposia in identified areas of cooperation.

Joint working groups or joint Steering committees with various international institutes/ organizations are organized to review, develop and finalize joint collaborative programmers, decide future plans of action and identify priorities for bilateral cooperation. Progress under MOUs of ICMR with CIHR (Canada), University of Sydney (Australia), INSERM(France), BMBF & HGF (France), BMBF & HGF (Germany) and Boston University (USA) to work together n health issues f mutual importance has been made.

Joint working group meetings of indo-us agreements on HIV/AIDS &Maternal & Child Health in USA and CIHR (Canada) by telecom were held. S & T committees meeting of India –Spain was also held.

ICMR has also signed MOUs with Karolinska Institute, Sweden; London School of Hygiene & Tropical Medicine, UK and Medical Research Council, U.K.

The Council (IHD) also facilities the organization of international workshops, ICMR-INSERM workshops on pharmacogenomics of cancer at JIPMER, Puducherry ;ICMR-university of Minnesota on Cancer & Diabetes at Minnesota, USA; Indo-German workshops on predictive assays and innovative technology in radiotherapy at Manipal, India-Australia Workshop on adolescent obesity and diabetes at Hyderabad; ICMR-EU workshop on collaborative areas of cancer and neurosciences, at ICMR Hqrs. New Delhi were organized.

The Council supports and coordinates the international travel of Indian scientist s engaged in approved bilateral research projects under various memoranda of understanding or joint statements with other countries. A Total of 53 exchange visits of scientists to and from India were arranged under various international collaborative projects/programmes.

Applications for research projects involving foreign assistance and /or collaboration in biomedical/health research are submitted by the Indian investigators to ICMR for approval of Govt. of India through Health Ministry's Screening Committee(HSMC). The projects are peer reviewed. During the year 2009-2010 three meetings of Health Ministry's Screening committee (HSMC) were organized wherein approx.63 projects for international collaboration/assistance with

USA, Germany, France, Canada, Australia, WHO and several other foundations were approved by the Committee.

ICMR International Fellowships Programmes for Indian biomedical scientists aims to augment capacity strengthening of institutions involved in basic, applied, epidemiological and clinical sciences through exposure of Indian researchers to the latest international advancements in knowledge, to understand the disease and find strategies for their prevention and cure. During the year 2009-10. Fellowships were awarded to six senior and twelve young Indian scientists. A scientist from Nigeria (under the ICMR international fellowships from developing countries) visited NARI, Pune for training for 6 months.

The mission of the Indo-German Science Centre for infectious Diseases (IGSCID), established at ICMR is to co- ordinate joint research in identified areas of infectious diseases and to initiate proactive scientific cooperation with equal participation of Indian and German scientists. The council has taken up a project entitled, "Managing the Indo-German (ICMR-HGF) Science Centre for Infectious Diseases" which is in operation. Under this programme four collaborative projects have been approved and funded.

To provide detailed information about this new initiative to our scientific community and share the details of various collaborative ventures planned under this Indo-German Programme, the IGSCID website was launched at ICMR on 26th November, 2009 by Dr. V.M. Katoch, Secretary, DHR, Ministry of Health & Family Welfare, Govt. of India and DG, ICMR.

MANPOWER DEVELOPMENT

Junior Research Fellowship

During the period under report the Council conducted ninth National Level Examination for selecting JRFs to augment biomedical research in the country. Every year 150 *JRFs* (i.e. 120 for life sciences and 30 for social sciences including biostatistics) are selected for doing Ph. D. in biomedical sciences in different institutions. Number of candidates who appeared in the year 2001 was appox. 2000. This number increased to more than 12,000 in 2009-10. The examination was conducted at *7 centre*s (Chandigarh, Chennai, Delhi, Guwahati, Kolkata, Mumbai and Hyderabad). So far *694 JRFs* have joined these fellowship programmes in various national level institutions. The value of fellowships is at present Rs.12,000/- p.m.. The annual contingency grant is up to Rs.20,000/- p.a. + HRA *Top 5 most active institutions were AIIMS, New Delhi, JNU, New Delhi, PGIMER, Chandigarh, University of Delhi (North Campus), NCCS, Pune, TRC, Chennai and Aligarh Muslim University, Aligarh.

**The top areas selected by JRF's were molecular biology (8.4%), immunological studies (6.6%), gene expression (3.7%), genomics (2.7%), and metabolic disorders (2.5%).*

Financial assistance to MD/MS/DM/MCH Students in Priority Areas of Biomedical Research. (50/year)

Financial assistance of Rs.25,000/- is provided to MD/MS/DM/MCH students who are in the 2nd year of MD/MS course. The Steering Committee recommended financial assistance to a total of 226 thesis out of 563 proposals received during 2003-2009.

MD/ Ph. D. Programme (25 slots/ year)

Programme was revived to identify young medical graduates with brilliant academic record for pursuing post graduation & later to absorb them in its research cadre. The candidates who pass all MBBS examinations in first attempt with 60% or more aggregate marks are eligible for the examination. The candidates are selected through national level examination. Under this programme selected medical graduates are provided financial assistance for 4 to 5 years. The programme is ongoing at three centres *i.e.* King George University, Lucknow, NIMHANS, Bangalore & Sri Ramachandra Medical College, Chennai. So far 27 candidates have joined.

Short Term Visiting Fellowship (50 per year)

The objective of the award of the Short Term Visiting Fellowship programme is to provide opportunity to a scientist employed in a medical college, research institute, university etc. and actually engaged in research in the field of biomedical sciences to learn advanced research techniques/ methods in use in other institutes in India. The tenure is three months.

Other Training/Skill Development Programmes: Training courses were attended by 15 scientists.

Financial Support for participating in International Conferencs/Training Programmes/ Workshops for Non ICMR Scientists

One of the major mandates of the Council is capacity building of biomedical scientists of the country by providing them financial assistance for participating in International Conferencs/training programmes/ Workshops *etc*. Out of total 73 applications received 16 applicants were awarded during 2009-2010.

PUBLICATION, INFORMATION AND COMMUNICATION

PUBLICATIONS

Indian Journal of Medical Research

The Indian Journal of Medical Research (IJMR) continued to publish quality original research and review articles in the area of biomedical research as well as Editorials, Commentaries and Letters to the Editor (Correspondence). The Journal is brought out in 2 volumes 12 issues every year.

The IJMR is available full-text free on the internet (www.icmr.nic.in) from 2004 with a searchable menu. The IJMR is also available in the medIND, the online full-text database of Indian biomedical Journals developed by the ICMR-NIC Centre for Biomedical Information. Readability of IJMR is increased across the globe as evident from the increasing number of international submissions (about 50% each year) and articles published received from various countries other than India, and from increasing number of hits and downloads from the website each year. Efforts were continued to expand the reviewers' database by including more number of reviewers from abroad based on internet searching. .

The IJMR gained new height and highest ever impact factor among Indian biomedical journals. The Editorial Board of the Journal was revamped with international representation. The visibility and popularity among readers was increased worldwide as was evident from increasing number of submissions and reviewers. The journal was continued to be published in 2 volumes 12 issues per year and was indexed and abstracted in all major global indexing and abstracting services.

A special issue on "Human Papillomavirus" was brought out in September 2009. A special Section on " Maternal & Child Nutrition" was published in November 2009.

The digitization of all issues and volumes of the IJMR since 1913 was started in September 2008 in collaboration with C-DAC, NOIDA. Over 1 lakh pages have been scanned and after cropping and cleaning pdf of articles are made. The work is likely to be completed by the end of 2009.

The Impact factor of the IJMR increased from 1.670 in 2008 to 1.880 in 2009.

ICMR Bulletin

Publication of the ICMR Bulletin was continued and articles on Surveillance Strategy and Research Priorities of DF/DHF in India – A Review; Epidemiology of Drug Resistant Falciparum Malaria with Special Reference to Orissa; Integrating Mass Drug Administration with Vector Control for the Elimination of Bancroftian Filariasis in India, *etc.* were published.

Hindi Publications

ICMR Patrika

Publication of in-house popular Hindi periodical *i.e*. *ICMR Patrika* was continued. The electronic version of the articles in pdf format was also made available at ICMR website for wider circulation.

Biennium ICMR Puraskar for Popular Medical Books in Hindi (2006-07)

The book entitled '*Dama Evan Allergy : Kaise Chhutkara Payien'* by Dr Rajendra Mehta of Indore got the 1st Prize of Rs. 50,000. The second prize of Rs. 30,000 was given to Dr Panna Lal of MAMC, Delhi for his book '*Sukhi Balika*' and the 3rd prize of Rs. 20,000 was shared by Dr Diwakar Dalela and Dr Prateek Sinet of KGMC, Lucknow for their book '*Mutranali ka Katheter aur Apka Swasthya'*. Shri Satyavrat Chaturvedi, Hon'ble Member of Parliament, Rajya Sabha gave away the prizes, certificates, mementos to the winners during an award distribution ceremony held on 5th May, 2009.

Debate

The Unit organized a scientific debate in Hindi on the topic '*Bharat mein Chikitsiya Parikshano mein Neetivishyak Pehluon ka Anupalan'* (Ethical Compliance in Clinical Trials in India) on 26th September, 2008 at ICMR Hqrs.

ICMR *Patrika*

Publication of this popular periodical was continued and an article on 'Arsenic Toxicity and Human Health' was published in April-May 2009 issue of the Patrika.

INFORMATION

Modernization of ICMR Library & Information Networking initiative has been reviewed by a team by visiting majority of ICMR libraries for on the spot assessment of progress made since modernization initiated. Based on this it was felt that the usage of e-resources is satisfactory among ICMR institutes and the subscription to ProQuest Health Medical & Complete full text database has been renewed located at seven ICMR institutes. The usage of the JCCC@ICMR among the ICMR institutes has been reviewed and has been renewed for one more year. ICMR continued as member of ERMED consortia sponsored by NML under DGHS of MOHFW. The subscription for consortia of Five e-journals is reviewed and renewed for one more year.

Dissemination of Biomedical Information

Poster exhibits were prepared for the IPR Unit of the Division which participated in an exhibition organized by the FICCI during 2nd week of August, 2008 at New Delhi.

Poster exhibits were developed and prepared for the IPR Unit of the Division which participated in an exhibition organized as part of Bangalore Bio. during June 18-20, 2009.

Scientometric Studies

The annual document '2008 Research Output of ICMR Institutes' with analysis of publications from all the institutes including Regional Medical Research Centres is being compiled as also mapping of papers from medical colleges of India from the PubMed database for the calendar year 2008 is being finalized. A new project on 'Preparation of Web Based Directory of Indian Science & Technology (including Medical) Journals' awarded from DST has been initiated.

Human Resource Development in Biomedical Communication and IPR

In the area of human resource development in biomedical communication, information and IPR, workshops will be organized for both ICMR and non-ICMR scientists.

Bioinformatics Centre

Eight Biomedical Informatics Centres and a Coordinating Unit were established with the objectives to provide services and training to use modern biology tools in medical research. The Centres have initiated/completed 22 projects involving molecular modeling and 17 projects involving analysis of protein or DNA sequences, and published/communicated 26 research papers in peer-review journals and presented work in several National/International conferences. The Centres conducted 28 workshops and training programs on modern biology tools and techniques for the benefit of researchers and medical professionals. The Centres also developed 20 databases of Clinical and Bio-molecular data. Details are available at the Centre's website http://bmi.icmr.org.in/bic/. A decision has been taken to shift administrative control of the Centres from BMS Division to P&I Division from July 1, 2009.

An interactive web based system has been developed which takes part of the information from IRIS databases. A few other details relating to Project Review Committee, detailed budget etc. are entered by the staff of ECD. User friendly screens are developed for data entry. The system is helpful in monitoring the extramural research files within the Division. When fully implemented and populated, the system will automate major work of the Division including providing information of the committed budget. Various reports categorizing information in different ways are produced.

The IPR unit has text information downloaded from International databases on Patent. The programme developed by BIC facilitates searching the text, categorizing in different fields and patent uploading with different diseases.The database can be searched by fields like Inventor, Assignee, Publication Date, Title, Abstract, Countries, *etc.* Subject wise and other reports in form of tables can be generated using the programme.

Facility management and Annual Maintenance for networking of all ICMR institutes have been renewed for three years. Video conferencing facility has been created in eight major ICMR institutes and in ICMR Headquarters.

ICMR website provides current static and dynamic information of research activities of ICMR. As per Web statistics software hosted by NIC, the site had an average 13 lakhs and 17 lakhs hits per month during 2007 and 2008 respectively. This included 62% viewers from abroad. The most popular pages are IJMR issues, Publications, Ethical Guidelines, Employment Opportunities, Grant Schemes (Short term Research studentship, Junior Research Fellowships) etc. There were more than 32 lakhs downloads from the site during 2008.

It is proposed to create a Central data repository of all data generated by ICMR institutes for easy deposition and access of research data with adequate authentication. ICMR institutes are undertaking Clinical Trials where clinical data are generated. Some of the institutes have hospital facility where other types of clinical data are generated. The DHR therefore needs to adopt a uniform clinical data management system of International standard. A brainstorming session under the chairmanship of the secretary, DHR, involving Directors of all ICMR Institues/Centres was organized in May, 2009.

Expert Committee meeting of Biomedical Informatics Centres of ICMR took place in June, 2009. Decision has been taken to continue the project for two more years. The Council has taken decision to implement from July 1, 2009, Office Procedure Automation (OPA) software developed by NIC for tracking movements of Files. The BIC customized the software for ICMR and provided training.

A Grievances Redressal Cell is being setup in the Council. The BIC has developed a Information System for monitoring Grievance Cell.

INTELLECTUAL PROPERTY RIGHTS UNIT

Patents

A total of 3 Indian patents generated from intramural research have been filed by the Unit (details enclosed).These are i) New bacterial culture media for the production of mosquito pathogenic Bacilli using industrial wastes, VCRC, Puducherry; ii) Immunodiagnostic reagent as an antibody probe from detection of *Plasmodium vivax* antigen, NIMR, New Delhi; iii) Development of Dot Blot assay for prognosis of sequelae to *Chlamydia trachomatis* infection in women using chlamydial heat shock protein 60, IOP, New Delhi; iv) Sputum processing method for Mycobacteria, TRC, Chennai; v) Active principles in *Cl. Collinus* extract are proton transport inhibitors; and vi) Potent mosquito larvicidal extracts from the plant *Linostoma decandrum*, RMRC, Dibrugarh

Publications

The publication of Newsletter supported to WITT was continued and a total of 8 issues were brought out (4 on vaccines and 4 on diagnostics).

- Exhibited ICMR's technologies at Bangalore Bio 2009 to disseminate the technologies for commercialization.
- Updated document "Technologies for Commercialization"
- Prepared brochure of IPR Unit.
- Technology transfer efforts were made with NRDC, New Delhi and BCIL, New Delhi.

ANNEXURE

SUMMARY OF IMPORTANT AUDIT OBSERVATIONS PERTAINING TO THE DEPARTMENT OF HEALTH RESEARCH

Report of the Comptroller and Auditor General of India for the year ended March 2008, Union Government (Compliance Audit) No. CA 16 of 2008-09. Tabled in the Parliament on 10th July 2009

Indian Council of Medical Research

Works management in Indian Council of Medical Research

Audit test checked 20 capital works costing Rs.160.48 crore executed in Indian Council of Medical Research (ICMR) during the period 2002-08. Audit observed that ICMR irregularly transferred 9714 sq m land to a private Housing Society at a significantly lower rate, leading to conflict of interest besides grant of undue benefit of Rs.22.82 crore to the members of the Housing Society. Delay in approval and release of funds by ICMR resulted in non-commencement of works for upto 13 years and cost overrun of Rs.30.94 crore besides non-achievement of objectives. Blockade and wasteful expenditure of Rs.21.82 crore was observed in nine works as a result of delayed decisions in commencement of works and payment of penalty. ICMR did not have adequate budgetary and financial control mechanisms in place for exercising periodical review of expenditure by its Institutes. ICMR also did not have a mechanism to watch progress of works and adjustment of advances to its Institutes and ensure, thereby, timely completion of works within the scheduled cost.

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Contents