

Introduction

The President notified the creation of the Department of Health Research (DHR) 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:

1. 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.
2. Promote and provide guidance on research governance issues, including ethical issues in medical and health research.
3. Inter-sectoral coordination and promotion of public – private – partnership in medical, biomedical and health research related areas.
4. Advanced training in research areas concerning medicine and health, including grant of fellowships for such training in India and abroad.
5. International co-operation in medical and health research, including work related to international conferences in related areas in India and abroad.
6. Technical support for dealing with epidemics and natural calamities.
7. Investigation of outbreaks due to new and exotic agents and development of tools for prevention.
8. Matters relating to scientific societies and associations, charitable and religious endowments in medicine and health research areas.
9. 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.
10. Administering and monitoring of Indian Council of Medical Research.

Besides Indian Council of Medical Research (ICMR), other nine functions are new to the Department. These nine new functions pertain to strengthening of infrastructure and human

resource for health research; research governance; prevention and management of epidemics/ outbreaks and intersectoral coordination for translational and implementation research. ICMR concentrates on knowledge generation and affordable technology development, and serves as the fulcrum of the department. During the year, the five new schemes developed for the XIIth plan period focusing on infrastructure development in medical colleges and States; development of network of laboratories for management of epidemics/outbreaks due to viruses; human resource development and grant-in-aid to support research projects involving intersectoral coordination and translational/implementation research were approved and rolled out for implementation. The Department has taken up these new schemes in view of major gap in programmes and infrastructure that exists today with respect to health research.

During the year under report, the Indian Council of Medical Research continued to serve as the fulcrum of the Department of Health Research and further intensified its research programmes and development of newer technologies for the benefit of the Indian public. It is pertinent to mention that, the proposed seamless integration between the ICMR (generation of new knowledge) and the DHR (Putting this new knowledge to public good) which began in recent past, has been progressing well in the right direction. Some of recent important achievements during 2013-14 are: development of indigenous affordable technologies for patient care and public health, strengthening the network for viral diagnosis and research, joint programmes on vector borne diseases and diseases affecting tribal and other marginalized communities.

Some of these areas, where there has been tangible progress include the setting up of data repositories on medical and health research for wide public access as part of the national knowledge policy. Other areas like Mapping of Health Research Institutions, Knowledge Management Policy, Health Research Policy, and Accreditation of Health Research Institutes are in various stages of implementation.

Since the creation of the Department, after wide scale consultations, five new schemes have been initiated in order to finalize and firm up the interventions and policies required in order to establish and facilitate a vibrant, well functioning and relevant Health Research System in the country.

Organisation and Financial Performance

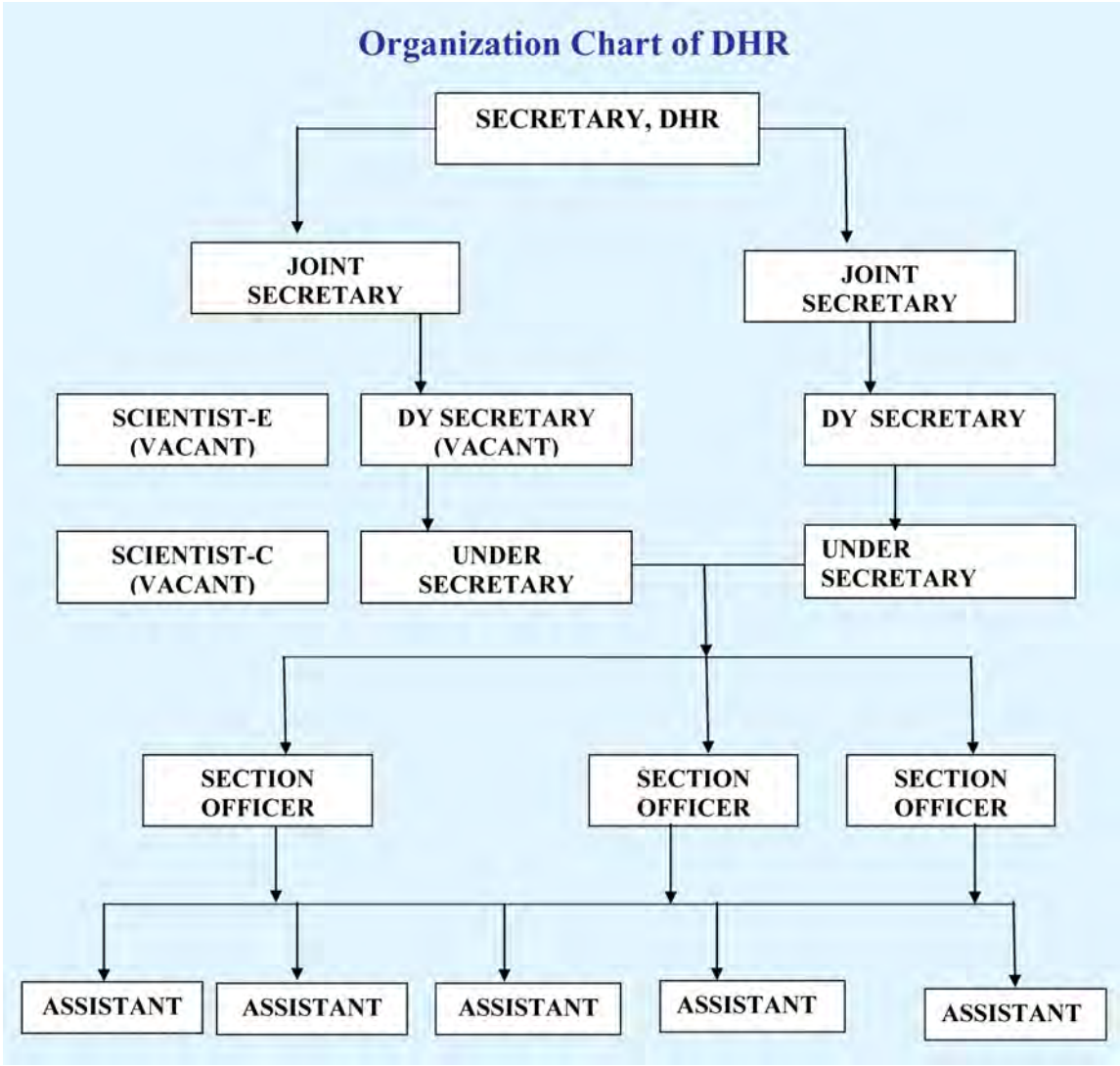
After the creation of Department of Health Research as a separate Department in 2007-08, the Department is functioning with a very small complement of staff. Six posts were transferred from the Department of Health & Family Welfare and 16 additional posts in different grades were created with the approval of Department of Expenditure. The latest status regarding sanctioned strength of the Department and the number of posts filled are as under:

S.No.	Name of post	No. of posts transferred from MoH&FW	No. of additional posts created	Total sanctioned strength	No. of posts filled
1.	Joint Secretary	1	1	2	2
2.	Director/DS	1	1	2	1
3.	Scientist 'E'	-	1	1	-
4.	Under Secretary	1	1	2	2
5.	Scientist 'C'	-	2	2	-
6.	Section Officer	1	2	3	3
7.	Assistant	1	4	5	2
8.	Private Secretary	-	2	2	1
9.	Stenographer	-	2	2	1
10.	LDC	1	-	1	1
	Total	6	16	22	13

The position of filling up of posts is as follows:

- 1. Scientists:** For the post of Scientist 'C' and Scientist 'E', the posts can be filled only after the Recruitment Rules are approved by the DoPT and Union Public Service Commission. The proposal in this regard has been referred to the DoPT.
- 2. Secretariat Posts:** While the Central Secretariat posts have been encadred by DoPT in July, 2012, postings against some posts are yet to be made. Moreover, the cadre controlling authority for the Department is the D/oH&FW and, therefore, actual posting of officers /staff is first made by DoPT to that Department and, thereafter, further postings are made by that Department to DHR. Meanwhile, consultants have been engaged from ICMR side to take up work related to DHR particularly requiring interphase with ICMR. They include one retired Director, a retired Deputy Secretary, a retired Under Secretary and a legal consultant. Steps have also been taken to establish the Project Management & Implementation Units (PMIUs) for effective implementation of all the five schemes rolled out during the year 2013-14.

3. **Additional Posts:** Steps have been initiated by the Department for augmentation of its existing strength by way of creation of additional posts.



Financial Performance:

The approved outlay for the 12th Plan for the Department is Rs.10029 Crores. Out of the approved allocation of Rs.10029 Crores, an allocation of Rs.5259 Crores has been earmarked for the schemes/programmes of Department of Health Research and Rs.4770 Crores for the various activities/programmes of ICMR. The scheme-wise allocations are as follows:

(Rs. in crores)			
S.No.	Schemes	Allocation (2012-17)	Approved Project Cost as per EFC/CCEA
1.	HRD scheme of DHR	812.00	597.00
2.	MRU in State Medical Colleges	1118.00	503.83
3.	MRHRU in the States	246.00	67.66
4.	Establishment of a Network of Laboratories for Managing Epidemics and Natural Calamities	1084.00	646.00
5.	Grant-in-Aid scheme of DHR	1953.00	1242.00
6.	Grant-in-Aid to ICMR	4770.00	4770.00
7.	Governance and departmental expenses	46.00	46.00
	Total	10029.00	7872.49

Expenditure

(Rs. in crores)						
Particulars	2012-13			2013-14		
	BE	RE	Actual	BE	RE	Actual (upto 31 st March, 2014)
DHR	142.00	24.00	0.17	195.00	95.00	89.42
ICMR	518.00	440.00	460.14 (including supplementary grant of Rs.20.14 crores)	531.00	480.00	480.20
Total	660.00	464.00	460.31	726.00	575.00	569.62

A statement indicating the BE/ RE (2013-14) and actual expenditure upto 31.03.2014 under Plan and Non-Plan and BE (2014-15) under Plan and Non-Plan is given at Annexure-I

Audit Observations

A statement indicating the audit observations pertaining to ICMR (Department of Health Research) is given at Annexure-II.

Activities in the North-Eastern States

A statement indicating Activities in the North East & Grievances Redressal at DHR is given as Annexure-III.

Establishment of Multi-Disciplinary Research Units (MRUs) in State Government Medical Colleges

Globally, health research is predominantly carried out in the Medical Colleges/Institutions providing education in allied subjects and other research institutions. Medical Colleges are the back bone of both teaching and providing specialized services to patients in India. They are also expected to set the trends in the thinking process and innovations to improve our understanding of the diseases and their management. However, over the years it has been noticed that majority of medical colleges have confined themselves to routine patient care and teaching based on conventional methods. Presently, quality Medical Research is largely confined to a handful of institutions and medical colleges in the country that too in few States only. The standard of papers published/ research projects undertaken by the students of post-graduate courses/PhD in most of the Medical Colleges are not inspiring. This can be attributed both to the lack of appropriate facilities for conducting research and a lack of motivation and knowledge on the part of faculty and students in Medical Colleges for conducting research.

Consequently, the Medical Colleges are not pursuing newer methods of investigation for understanding the pathological diagnosis, treatment and management practices. Newer health research has not been perceived as a priority area for States and even for many Central Institutes. This also affects the quality of clinical services being provided as well as teaching standards.

An urgent need was, therefore, felt to promote and encourage quality medical research in the country and provide assistance to the Medical Colleges to set up appropriate research facilities.

The scheme, which has been approved and rolled out during the year 2013-14, aims to provide infrastructural support to various State Govt. Medical Colleges across the country, in terms of civil works, equipment and recurring expenditure, to carry out focused research on non-communicable diseases.

The scheme entails setting up of 80 MRUs (35 in 2013-14 and 45 in 2014-15) in the Government Medical Colleges/ Institutions during the 12th Plan period. The faculty of the Medical College will be encouraged to carry out research projects on national and regional priorities. Total estimated cost of the project is Rs.503 crores.

Funding Norms

Rs.5.25 crore per MRU are provided under the scheme to the approved medical college towards equipment & civil works. In addition, recurring expenditure of Rs.34 lakhs towards staffing on contractual basis and consumables, etc. are given from second year onwards for five years.

Requirements from the State Governments

- To provide requisite space (minimum 300 sqmtr), free of cost, at the concerned Medical College.
- Signing of MoA with the Department of Health Research for taking over the liability of running the centres after five years. This would be about Rs.37 lakhs per year per Medical College.

Status of Implementation

- 29 MRUs have been already sanctioned and funds amounting to Rs.36.25 crores released during 2013-14
- Another 7 MRUs have been sanctioned and funds will be released during 2014-15 as soon as the requisite formalities like signing of MoA and commitment for providing space etc are completed by the State Governments/Medical Colleges.
- List of medical colleges covered for establishment of MRUs during the year 2013-14 is given below:

TABLE List of medical colleges approved for establishment of Multi-disciplinary Research Units (MRUs) during the year 2013-14	
I. Approved and funds already released:	
1.	Andhra Pradesh: Siddhartha Medical College, Vijaywada
2.	Andhra Pradesh: Osmania Medical College, Hyderabad
3.	Andhra Pradesh: SV Medical College, Tirupati
4.	Assam: Silcher Medical College and Hospital, Silcher
5.	Chandigarh: Government Medical College
6.	Chhattisgarh: Pt. JNM Medical College, Raipur
7.	Haryana: Pt. B.D. Sharma PGIMES, Rohtak
8.	Himachal Pradesh: Indira Gandhi Medical College, Shimla
9.	Jharkhand: MGM Medical College, Jamshedpur
10.	Karnataka: Mysore Medical College and Research Institute, Mysore
11.	Karnataka: Shimoga Instt. Of Medical Sciences, Shimoga
12.	Kerala: Medical College Thiruvananthapuram
13.	Calicut Medical College, Calicut, Kerala
14.	Punjab: Government Medical College, Amritsar
15.	Rajasthan: Dr. S.N. Medical College, Jodhpur
16.	Rajasthan: Sardar Patel Medical College and Associated Group of PBM Hospitals, Bikaner.
17.	Tamil Nadu: Madras Medical College, Chennai
18.	Tamil Nadu: Tirunelveli Medical College, Tirunelveli.
19.	Gujarat: M.P.Shah Medical College, Jamnagar
20.	Delhi: University College of Medical Sciences, Delhi
21.	Delhi: VallabhBhai Patel Chest Institute, Delhi
22.	J&K: Govt. Medical College, Jammu,
23.	J&K: Govt. Medical College, Srinagar
24.	West Bengal: R.G. Kar Medical College, Kolkata
25.	Manipur: Regional Institute of Medical Sciences, Imphal
26.	Tamil Nadu: Coimbatore Medical College, Coimbatore
27.	Tripura: Agartala Govt. Medical College, Agartala
28.	Uttarakhand Govt. Medical College, Haldwani (Nainital)
29.	Tamil Nadu: Dr. ALM Post Graduate Institute of Basic Medical Sciences, Taramani
II. Approved but funds will be released on completion of requisite formalities including clearance of pending UCs:	
	Maharashtra: Dr. Vaishampayan Memorial Government Medical College, Sholapur
	Maharashtra: Seth G.S. Medical College and K.E.M Hospital, Mumbai
	UP: G.S.V.M Medical College, Kanpur
	Madhya Pradesh: GR Medical College, Gwalior,
	Orissa: VSS Medical College, Burla, Sambalpur,
	Goa: Government Medical College, Panaji, Goa
	J&K: Sher-e-Kashmir Institute of Medical Sciences, Srinagar

Establishment of Model Rural Health Research Units (MRHRUs) in the States

Public health system in India has a wide network of primary health centers at the periphery, referral, secondary and tertiary level hospitals at district, State and other levels respectively. Over the last more than 60 years, preventive, diagnostic and therapeutic services have been provided through this network managed by States. It has been observed that a big gap exists between PHC/CHC and tertiary care hospitals with state-of-art- facilities created by Centre and also by some of the State governments. The professionals and policy makers are of the view that modern methods of diagnosis and management cannot be practiced at peripheral level. There is a mental block in a large number of professionals and policy makers who think that modern methods of diagnosis and disease management cannot be practiced at rural settings.

Medical doctors working in the State public health system do not get opportunity to get orientation on modern advances in a regular fashion in their settings and therefore, are unable to utilize advances in medical science in their work. Because of this, the transfer of technology to the end users becomes very difficult.

Further, wide variations exist in the pattern of diseases prevalent in different geographical areas, the local conditions which require development of state/area specific, disease specific strategy, transfer of research finding/technology at the rural level has been found to be major lacuna in the provision of quality medical services to rural population. To provide better health care facilities to the people living at the peripheral regions, the Department through MRHRU envisages to ensure that the modern technology is available to the general public.

To bridge the gap, Department of Health Research (DHR) has developed a scheme for the 12th Plan period to 'Establish Model Rural Health Research Units(MRHRUs) in the States, under the initiative of infrastructure development for health research in the country. The scheme is based on the experience of establishing such a Unit at Ghatampur under National JALMA Institute for Leprosy and Other Mycobacterial Diseases (ICMR), Agra, where the methods of diagnosis and treatment as well as epidemiology using a partnership approach among state services, medical colleges & ICMR institutes are shown to be workable. These Units will function as an interface between the new technologies developers (Researchers in the medical/other institutions; State or Centre), health systems operators (Centre/state health services) and the beneficiaries (community).

The Model Rural Health Research Units would undertake the following functions:

- Develop state/area specific models depending upon the disease profile, morbidity patterns and local conditions for transfer of the technology for providing better health care services to the rural masses.

- Training the health professionals of State health system for the use of modern field adaptable methods and the model developed.
- To undertake various research projects in close coordination with the State Government institutions and others that are relevant and beneficial to the rural population.
- The Units will develop State specific models depending on the disease profile, topography and the local conditions as per the priorities & location identified by the State Govt. in close coordination with State health authorities.

The MRHRU will be an interface between patient, health providers and health research to provide latest / sophisticated technology for diagnosis and management of diseases in rural areas. The activity will be entirely supported by DHR for its sustenance. In total, 15 MRHRUs will be established during the XII Plan period. Each MRHRU will be linked to the nearest ICMR institute to mentor and guide the research activities of MRHRU relevant to local needs. These research activities would be monitored/ guided by the Committee, consisting of eminent Scientists of National repute with representation from State Government, medical colleges and state health services providers, constituted with the approval of Secretary, DHR. Total estimated cost of the project is Rs.67.66 crores.

Funding Norms

Under the scheme Rs.3.00 crores are provided per MRHRU for civil works/Equipment. Besides, recurring expenditure of Rs.50 lakhs towards staffing, consumables, etc. is given.

Requirements from the States

To provide requisite land sufficient to construct covered space of about 620 sq. meters, in close proximity to the PHC/CHC, free of cost.

Signing of MoA with the DHR for implementation of the programme.

Status of Implementation

- 8 MRHRUs have already been sanctioned in the following States and first installment to each MRHRU aggregating to total amount of Rs.12.00 crores has been released during 2013-14.
- List of approved MRHRUs in the various States is given in the table below:

S. No.	State	Location of MRHRU	ICMR mentor Institute/Centre	Linked Medical College
1	Assam	PHC, Chabua	RMRC, Dibrugarh	Assam Medical College & Hospital, Dibrugarh
2.	Himachal Pradesh	CHC, Haroli	NJIL&OMD, Agra	Dr RPG Medical College, Tanda
3.	Rajasthan	Bhanpur Kala, Government Health Clinic, Jaipur	DMRC, Jodhpur	SMS Medical College, Jaipur
4.	Tamil Nadu	State Rural Health Centre, Tirunelveli	NIE, Chennai	Tirunelveli Medical College, Tirunelveli
5.	Tripura	Kherengbar Hospital, Khumulwung	RMRC, Dibrugarh	Agartala Government Medical College, Agartala
6.	Karnataka	PHC, Sirwar, Manvi Taluk, Raichur	RMRC, Belgaum	Raichur Institute of Medical Sciences, Raichur
7.	Punjab	CHC, Bhinga (Hoshiarpur)	NIOP, New Delhi	Govt. Medical College, Amritsar
8.	Maharashtra	Sub District hospital (SDH), Dahanu (Thane)	NIRRH, Mumbai	Grants Medical College and JJ Group of Hospitals, Mumbai

Network of Research Laboratories for Managing Epidemics and Natural Calamities

It is well known that diagnosis of viral diseases is a major problem in most parts of country and outbreaks of new viral agents is a common phenomena. The inadequacy of specialized laboratories in the country especially of secondary and tertiary level has been noticed in the past as well as during the recent H1N1 crises that gripped the nation. In the context of biological agents being used as weapons for man-made disaster and also outbreaks of new viral agents, it is considered necessary to establish a net work of laboratories for viral diagnosis. Such a network and active research programme will be important to generate evidence for interventions for various viral infections which are endemic to the country. For this purpose it is considered essential to establish network of laboratories across the country, with NCDC and NIV, acting as the apex laboratories for surveillance and research respectively. These labs will supplement the activities of the Integrated Disease Surveillance Project (IDSP) coordinated by NCDC, Delhi with special focus on viruses and will also be expected to deal with all common viruses like:

1. Viruses transmitted by respiratory route: Measles, Rubella, Mumps, Influenza viruses (A, B and C), Parainfluenza virus, Adenoviruses, Respiratory Syncytial Virus, Rhinoviruses, Polio, Coronaviruses.
2. Viruses transmitted by intestinal route: Hepatitis A, E. Rotavirus, Astroviruses, Caliciviruses, Norwalk viruses, Enteroviruses.
3. Vector Borne Disease Viruses: Dengue, Chikungunya, Japanese encephalitis, West Nile, Kyasanur Forest Disease, Chandipura.
4. Zoonotic viruses: Rabies, Nipah virus, Hanta Virus
5. Viruses transmitted by body fluids: HIV, Hepatitis B and C.

Priority will be given to develop infrastructure and expertise for diagnosis of viruses with a potential to cause outbreaks and/or which are responsible for significant disease burden like Measles, Influenza viruses (A, B and C), Respiratory Syncytial Virus, Polio, Hepatitis A, E, Rotavirus, Enteroviruses, Dengue, Chikungunya, JE etc. These laboratories will be expected to develop expertise for diagnosis of specific viruses circulating in their geographic area.

To cope with emergent situation & urgent need for Virology Diagnostic facility in the wake of outbreaks & endemic viral infections, ICMR had in the meantime started a Virology Diagnostic Laboratory (VDL) Network Programme in the extramural adhoc mode. The VDL Network programme involves identification of candidate institutions/ research centres/laboratories, which are in need of the facility and accept the offer to open/establish/upgrade the viral diagnostic laboratory. ICMR invites the Research proposals from the selected laboratories / institutions in the format of Ad Hoc Extramural Research Project and funds are facilitated by

ICMR Initial support with regard to-infrastructure development and running of the VDL for a period of five years; after which the state government/ health authorities are required to take over the facility (including its trained manpower) and maintain it at their end.

Ongoing laboratories under the ICMR System

- From 2009-12 a total of fifteen Virus Diagnostic Laboratories (VDLs) have been established in fourteen states of the country. Details are as follows:
- Nine Grade I laboratories have been established at King George Medical University, Lucknow, (Uttar Pradesh), Kasturba Medical College, Manipal (Karnataka) and Regional Medical Research Centres at Portblair (Andaman & Nicobar Islands), Bhubaneswar (Orissa) and Dibrugarh (Assam), SMS Medical College, Jaipur (Rajasthan), NIV Field Unit at Allapuzha, (Kerala), Rajiv Gandhi Centre for Biotechnology. (Kerala) and King's Institute of Preventive Medicine, Chennai, (Tamil Nadu),
- Five Grade II Labs have been established at Regional Medical Research Centre at Jabalpur, (Madhya Pradesh) Rajendra Memorial Research Institute of Medical Sciences, Patna, (Bihar), Andhra Medical College, Visakhapatnam, (Andhra Pradesh) and Rajendra Institute of Medical Sciences, Ranchi, (Jharkhand) and Government Medical College, Agartala, (Tripura).
- One Grade III lab has been established at Pt. Jawahar Lal Nehru Memorial Medical College, Raipur (Chhattisgarh).
- ICMR is providing equipment, manpower and consumables to different grades of laboratories for a total period of five years. Thereafter, as per the MoA signed between ICMR and VDL, the activity is expected to be taken up by the Institution itself. All labs are currently ongoing and need to be continued during the 12th plan period.

Establishment of a new network under DHR

Concurrent establishment of new VDL labs as well as Review of the progress of established labs at completion of two & four years is being undertaken by senior experts of ICMR on a regular basis.

Most of functional VDLs are now well established with basic diagnostic techniques for viruses and are generating data from their respective centres. DHR/ICMR envisage involving all VDLs in well-planned epidemiological studies related to viruses of national relevance to enable us to bring out data representative of the entire nation. Uniform Protocols/SOP's/Trainings/ Quality Assurance/Quality Control methods will be followed by all the Laboratories.

Network initiated by ICMR during 2010-2013			
S. No.	Name of the Centre	Grade	Date of Start
1.	King George Medical University, Lucknow	I	March 2010
2.	ICMR's Regional Medical Research Centre, Bhubaneswar	I	March 2010
3	ICMR's Regional Medical Research Centre, Portblair	I	March 2010
4	Kasturba Medical College, Jaipur	I	March 2010
5	ICMR's National Institute of Virology Field Unit, Allapuzha, Kerala	I	March 2011
6	SMS Medical College, Jaipur	I	March 2011
7	Rajiv Gandhi Centre for Biotechnology, Thiruvanthapuram, Kerala	I	March 2011
8	Pt. JLM Medical College, Raipur, Chattishgarh	III	March 2011
9	King's Institute of Preventive Medicine, Chennai	I	Dec. 2011
10	Rajendra Memorial Research Institute of Medical Sciences, Patna	II	Dec.2011
11	Regional Medical Research Centre, Jabalpur	II	Dec.2011
12	Rajendra Institute of Medical Sciences, Ranchi	II	Dec.2011
13	Andhra Medical College, Visakhapatnam	II	Dec.2011
14	Regional Medical Research Centre, Dibrugarh	I	Mar. 2013
15	Government Medical College, Agartala, Tripura	II	Mar. 2013

While ICMR initiated the programme in a research project mode and its 15 centers have contributed immensely, DHR has developed a new scheme to cover the entire country. The scheme envisages establishment of 10 Regional Labs, 30 State level Labs and 120 Labs in the State Government Medical Colleges for timely diagnosis and management of viral epidemics and new viral infection. The scheme has been approved during the year 2013-14 at an estimated cost of Rs. 646.83 crores. The geographic spread of the labs will be taken care of while establishing the labs to cover the entire country and the States not having any medical college will be linked to the labs in the nearby State/area.

Objectives:

Create infrastructures for timely identification of viruses and other agents causing morbidity significant at public health level and specific agents causing epidemics and/ or potential agents for bioterrorism.

Develop capacity for identification of novel and unknown viruses and other organisms & emerging-reemerging viral strains and develop diagnostic kits

Provide training to health professionals.

Undertake research for identification of emerging and newer genetically active/ modified agents.

In the network of research laboratories under this scheme, a three tier laboratory structure has been planned with varying degree of laboratory infra-structure *i.e.* Regional labs (10 in nos.), State level labs (30 in nos.) and Medical College labs (120 in nos.) to be established during the 12th Plan period at a total approved cost of Rs.646.83 crores.

The expenditure on the establishment of labs at the State level and at the Medical Colleges would be shared between the Central Government and State Governments in the ratio of 75:25 (90:10 in respect of North-Eastern, Hilly States, including Sikkim and J&K). Expenditure on the Regional Labs would, however, be fully borne by the Central Government.

Funding Norms

Regional Labs: The Non-recurring cost of a Regional Level Lab is about Rs. 15.00 crores for the development of infrastructure, which include civil works (Rs.4.20 cr), furnishing & furniture (Rs.50 lakh) and equipment (Rs.10.25 cr.).The recurring cost of Regional Lab per annum is Rs 81 lakhs, towards staffing (Rs.46 lakh), Consumables & Contingencies and Training (Rs.35 lakhs).

State Level Lab: About Rs.6.58 crores, comprising upto Rs.50 lakhs under civil works mainly for renovation/modification of the buildings and Rs.6.08 cr. for equipments. In addition, recurring expenditure of about Rs.50 lakh per Lab for engaging trained technical man power on contractual basis and expenses on training, consumables and contingencies.

Medical College Level Lab: About Rs. 1.44 crore for equipment and civil works /renovation of building. In addition, recurring expenditure of Rs.30 lakhs per annum, comprising expenses on staffing, consumables & contingencies and training.

Requirement from the States

- Allocating a building on the premises of a medical college/ institution for the establishment of the Viral Diagnostic Lab (VDL) or to provide space of mutually agreed dimensions (approx. 250-300 sq. meters for State Level Lab and approx.200-300 sq. meters for Medical College Level Lab) , free of cost, in existing premises for the establishment of the VDL.
- To sign MoA with the DHR.
- Deputing a mutually agreed number of its personnel to work in the VDL.
- Deputing personnel (including those belonging to the State Health Service) to undergo training/attend workshops at the VDL.
- Sharing of expenditure on the establishment of labs at the State level and at the Medical Colleges between the Central Government and State Governments in the ratio of 75:25 (90:10 in respect of North-Eastern, Hilly States, including Sikkim and J&K).

Status of Implementation

- Establishment of 2 Regional Labs; 4 State Level Labs and 8 Medical College level labs have been sanctioned during 2013-14.
- Proposals for 1 state level labs and 4 medical college level labs were approved in the meeting held on 20.2.2014 but funds will be released in 2014-15

VRDL Laboratories approved during 2013-14**Regional Labs:**

1. PGI, Chandigarh(UT)
2. Regional Medical Research Centre (RMRC), ICMR, Dibrugarh, (Assam)

State level Labs:

1. Indira Gandhi Medical College, Shimla, (Himachal Pradesh)
2. Sher-i-Kashmir Institute of Medical Sciences, Srinagar, (J & K)
3. B.J. Medical College, Ahmedabad, (Gujarat)
4. NEIGRIHMS, Shillong, (Meghalaya)

Medical College Level Labs:

1. Govt. Medical College, Jammu, (J & K)
2. Osmania Medical College, Hyderabad (Andhra Pradesh)
3. PGI, Rohtak, (Haryana)
4. Govt. Medical College, Amritsar, (Punjab)
5. Dr. S.N. Medical College, Jodhpur, (Rajasthan)
6. Indira Gandhi Medical College, Nagpur, (Maharashtra)
7. Patna Medical College, Patna, (Bihar)
8. M.P. Shah Medical College, Jamnagar, (Gujarat)

Proposals for 1 state level labs and 4 medical college level labs were also approved but funds will be released after completion of requisite codal formalities

State Level Labs (1) :

1. Gauhati Medical College, Guwahati (Assam)

Medical College Level Labs (4) :

1. Sarojini Naidu Medical College & Hospital, Agra, (UP)
2. G.S.V.M. Medical College, Kanpur (UP)
3. Uttar Pradesh Rural Institute of Medical Sciences & Research, Saifai, Etawah,(UP)
4. Govt. Medical College, Trivandrum (Kerala)

Grant-in-Aid Scheme for Inter-Sectoral Convergence & Coordination for Promotion and Guidance on Health Research

Presently about 12 Science Departments are significantly contributing to innovations related to different aspects of biomedical research. The scheme aims at providing support in the form of grant-in-aid to for carrying out research studies to identify the existing knowledge gap and to translate the existing health leads into deliverable products. There will be special focus on encouraging innovation, their translation and implementation by collaboration and cooperation with other agencies by laying special stress on implementation research so that there is a better utilization of available knowledge. The Scheme has been approved by CCEA on 6th February, 2014 at a total estimated cost of Rs.1242 crores.

The Scheme has the following components for funding:

(1) Research studies with emphasis on public health

The objective of this component is to support research studies on disease burden, risk factors, diagnosis & treatment, etc of major diseases. The studies will be limited to Non-communicable diseases. In this category a total number of 287 studies, with the maximum duration of 3 years and cost range between Rs.50 lakh - Rs.3 crores each, can be funded at a total estimated cost of Rs. 289.00 crores.

(2) Translational Research Projects

The objective of this component is to translate the already identified leads into products and processes in the area of human healthcare, through coordination among the agencies involved in basic, clinical and operational research for use in the public health system. It is proposed to take up 75 leads already available with ICMR, 25 leads from Extramural projects funded by ICMR and 15 leads from other Science & Technology Departments/Organisations. Total No. of 115 projects with a duration of 1-4 years and cost range of Rs.3-10 crores can be funded with a total estimated cost of Rs. 510 crores during the 12th Plan period.

(3) Inter-sectoral Co-ordination Including Funding of Joint Projects

The Objective of this component is to promote joint/collaborative research projects with other agencies involved in bio-medical/health research in the country for optimum use of resources and transfer of knowledge. Total number of 181 projects with a cost range of Rs. 50 lakh-10 crore and duration of 2-3 years per project can be funded under this component, at a total estimated cost of Rs.298 crores

(4) Cost effectiveness analysis of health technologies through a health technology assessment system

The aim of the studies would be to come up with appropriate recommendations and guidelines on cost effective but viable technology/process/diagnostics for managing various diseases, to facilitate public choice and controlling health care costs, while maximizing health outcomes. 171 projects with a cost range of Rs.50 lakh to Rs.2 crores and duration of 1-3 years can be funded under this component at a total estimated cost of Rs.136 crores

(5) Support to ICMR and non-ICMR scientists for participation in conferences abroad in identified priority areas of the Department and conduct of national & international seminars & conferences.

The component is intended to provide financial support for taking part in international conferences/seminars/symposia etc. The activity of organizing international conferences/seminars/symposia to share experiences on health research issues is also proposed under this component. Non-ICMR scientists would mainly cover the faculty and students of the medical colleges. Non-ICMR scientists would mainly cover the faculty of the medical colleges. Total estimated cost of this component is Rs.6.00 crores.

The scheme was approved by the CCEA on 6.2.2014 i.e. at the fag end of the financial year 2013-14. The administrative approval was issued on 25.2.2014 and the guidelines were issued in March, 2014. Since the scheme did not have the approval of the competent authority at the RE Stage, the allocation of Rs.40 crores in BE was reduced to Rs.5.35 crores at RE stage due to which only limited number of proposals could be sanctioned. The first year cost amounting to Rs.4.95 crores for a total number of 40 projects has been released under the scheme during 2013-14.

Scheme for Human Resources Development for Health Research

A major constraint in the health research sector is the lack of adequate and properly trained human resources for the health research. The objective of the scheme is to create a pool of talented health research personnel in the country by upgrading skills of faculty of medical colleges, etc by specialized training in priority areas of health research in leading national and international institutions and supporting the trainees to develop research projects for addressing critical national and local health problems and assistance to institutions for up-gradation of infrastructure to enable such institutions to provide training with state of the art technologies. The scheme has a separate component specifically for training of women scientists who have had break in their career and to encourage the Non-resident Indians (NRIs), Persons of Indian Origin (PIO), Overseas Citizen of India (OCI) serving abroad in health research activities, to come back to India for undertaking research in identified areas.

Total approved cost of the scheme is Rs.597.00 crores for the 12th Plan period, involving award of 2585 fellowships and development of 1694 research projects by the trainees.

The various scheme components are as follows:

(1) Support to Institutions

Support to 50 selected domestic institutions for providing training to candidates selected by the Department under this scheme in specially designed programmes/ identified priority areas.

(2) Short Term Fellowships

- i. Short term training (1-3 months) in Indian institutions to the researchers employed as regular faculty (not above the age of 55 years) at an approximate expenditure of Rs. 1.8 lakh per Fellow.
- ii. Short Term Fellowships for training abroad in identified areas (1-3 months) to persons employed as regular faculty (not above the age of 55 years) at expenditure of about Rs. 7.5 lakh per Fellow.
- iii. Short term specialized training (1-3 months) to mid-career or senior Level faculty of medical colleges working/involved with three other approved schemes of DHR. The approximate expenditure is Rs. 1.8 lakh per Fellow.

(3) Long Term Fellowships

- i. Long term training fellowships at Indian Institutions to persons employed as regular faculty, not above the age of 45 years, at an approximate expenditure of about Rs. 5.5 lakh per Fellow.

- ii. Long Term Fellowships for training abroad in identified priority areas (6 to 12 months) to persons employed as regular faculty, not above the age of 45 years, at an approximate expenditure of about Rs. 25 lakh per Fellow.
- iii. Long term training (6-12 months) to the faculties of medical colleges in Indian institutes (at least 2 persons per medical college per year) working/involved with three other approved schemes of DHR.

(4) Programme specifically for Women

Short /Long term training in Indian institutes followed by fellowship to women candidates who have had a break in their career but having demonstrable aptitude towards health research in front line and emerging areas.

(5) Scholarships /fellowships programme to young scientists in newer areas for three years

These fellowships aim to fulfill the objectives of creation of inclination / attitude of research among the young bright students from the medical colleges / universities.

(6) Start-up Grant for projects

The Start- up grant, with a maximum limit of Rs.30 lakhs, will be considered for each fellow /trainee, who has developed a research project.

(7) Strengthening of research through the establishment of online courses and web portal on health research for students, faculty and other researchers

The activity will be carried out in close coordination/association with Medical Council of India, Department of Information Technology, National Knowledge Network and other stakeholders. This programme will help prospective institutions and individuals to access resources- both financial and technical on research and promote research across the country.

(8) Support to Scientific/Professionals/Association/Bodies

Support will be provided to Scientific /Professionals/ Association/Bodies engaged in the fields of Medicine, Surgery, Microbiology, Pathology etc. for undertaking various activities/ events with a view to promote higher standards in medical/health research and for devising guidelines for policy making and prevention and management of different diseases.

(9) To encourage health research personnel [Non-resident Indian (NRI), Persons of Indian Origin (PIO), Overseas Citizen of India (OCI)] serving abroad, to come back to India for undertaking research in identified areas

This initiative aims to bring back and attract Indian scientists working abroad to pursue medical/health research in India. There will be provision to support brilliant medical doctors/ scientists of Indian origin from all over the world who wish to return to India, to take up research positions in the ICMR or other medical college/institute of their choice to pursue the objective. The norms/amount of stipend and other financial assistance for granting fellowships under this category would be similar to the existing schemes of Department of Science & Technology and Department of Biotechnology.

Due to cut in the Plan allocation of DHR at RE Stage and since the scheme could be approved in March, 2014 i.e. at the fag end of the financial year 2013-14, only 10 fellowships and

support to 3 institutes could be sanctioned at an estimated cost of Rs.1.51 crores, as per details given the table below:

Support to Institutes

S. No.	Name of the Institute	Area	Non-recurring (equipment etc)	Recurring @ Rs.10.00 lakhs per year	Total first year cost (Rs.in lakhs)
1.	J. N. Medical College, Belgaum	GLP	Nil	10.00	10.00
2.	JSS College of Pharmacy, Mysore	Drug Chemistry	19.0	10.00	29.00
3.	Manipal College of Nursing, Manipal	Geriatrics	8.10	10.00	18.10
Total					57.10

Fellowships

S. No.	Type of Fellowship	No.of fellows	Estimated cost (Rs. in lakhs)
1.	Long Term in Foreign Institutes	4	69.5
2.	Long Term in Indian Institutions	3	16.5
3	Short Term in Indian Institutions	3	4.6
Total		10	90.60

Knowledge Management Policy

Department of Health Research has developed a Knowledge Management (KM) policy which envisages capturing, creating, sharing and managing knowledge. KM comprises of three components (i) people who create, share and use knowledge as part of their daily work and help shape a knowledge sharing organizational culture (ii) Processes which include methods to acquire, create, organize, share and transfer knowledge to fit different situations and (iii) The technology including the mechanisms to store and provide access to data, information, and knowledge that must be integrated with the way people work, and address their real needs.

The implementation of any KM policy in Health sector will have essential ingredients and processes for improving the health of people by imparting benefits of various health programs to the targeted communities and improving the quality of education and research which will lead to evidence based policy. However, KM in health sector faces three major challenges:

(1) Unsatisfactory Quality of Data

With good quality data better policies can be framed, better decisions can be made thus improving the implementation of Health care programs and quality of medical research.

(2) Non-availability of Data for Knowledge Generation

Most of the data being captured may not be available in a suitable form for creating databases. Availability of digitized data in unified format helps in improving data quality and developing standards for knowledge generation.

(3) Inadequate Dissemination of Knowledge

There is a serious unavailability of information and knowledge to end-users which include health professionals, researchers, patients and students. Dissemination of quality information and knowledge through agencies like DAVP and appropriate media such as Internet, Information Kiosks etc. can provide relevant information to the end-users.

Health professional should take advantage of the data, experience, and expertise available in their own and other organizations to create and share their own knowledge with others.

The policy would catalyze creation of knowledge and translation of that knowledge from research setting to real world application in order to improve the health of common man specially marginalized sector of our society.

The focus of this policy would be creating an environment for connecting knowledge related activities in health into a coherent action plan.

Mission

To develop an efficient Health Knowledge Management System for collection, dissemination and utilization of knowledge for improving the quality of Health Services, Education and Research.

Policies

I. Service delivery

In order to create harmony among various health service providers and to impart their knowledge and services to the public at all times, the following essential components are proposed:

Empowering end user for better access to Health Service by:

1. Making available updated information about the service infrastructure such as manpower, equipment, medicines *etc.* available at different levels e.g. sub-centre, Primary Health Centre, Community Health Centre, District Hospital, Zonal Hospital, medical college and other tertiary care hospital *etc.*
2. Providing online information about functional status of the infrastructure *i.e.* availability of doctors, medical supplies including devices, vacant beds, surgical/ medical/ diagnostics facilities *etc.* at a given time.
3. Providing information about geographical locations and other logistics of various health service providers.
4. Promoting overall user awareness about available information sources by training of end users.
5. Promoting access to financial resources including insurance.
6. Ensuring access to all sections of society.

II. Enriching health professionals with knowledge about available resources around them by standardizing and linking functional, infrastructural and logistic information available with different healthcare service providers in Government and private sectors.

III. Increasing accountability of healthcare professionals and services towards human life by

1. Developing a well defined referral system for efficient utilization of resources between Central, state and other public/private healthcare providing institutes.
2. Creating a mandatory forward and back referral pathway over a period of 5-10 years. Responsibilities of every individual in the pathway to be enforced to ensure perfect accountability involving human life.

IV. Connecting remote areas and difficult terrains by effective use of telemedicine

Expert opinions of specialists need to be ensured on a structured fixed time interval basis as well as on emergency basis. The existing satellite connections and the optical-fibre-based National Knowledge Network (NKN) would be valuable in this context.

V. Efficiently handling health aspects of disasters by using Data Mining and Business intelligence tools on available data for finding information quickly about available resources around disaster site and mobilizing these resources.

VI. Establishing a user friendly but informative electronic medical record system.

This record system should be in a standardized, internationally compatible format.

VII. Education

In order to improve the quality of medical education uniformly across the country with help of knowledge network, following policy guidelines are proposed:

(i) Sharing knowledge by

1. Establishing an efficient physical network, connecting all medical/dental / nursing/other health related professional colleges
2. Creating tele-education portal to house resources which can be accessed online.
3. Creating and networking digital/ resources libraries for educational materials such as lectures, slides, video clippings etc. which can be accessed online as well as offline.
4. Organizing prescheduled interactive lectures and practical sessions by prominent teachers through tele-education through national and international networks.
5. Developing unified high quality standards in health education across the country
6. Updating knowledge of health professionals by conducting online continued medical education/ special training programmes.
7. Evaluating quality of in-service health personnel by conducting online examinations.
8. Training in-service health personnel by organizing localized interactive training courses.
9. Enforcing regulations for tele-education applications by following existing guidelines of regulatory bodies like Medical Council of India, Medical Universities, Dental Council of India, Nursing Council, Pharmacy Council, various councils for alternate medical systems, other relevant bodies for physiotherapy and other disciplines.

(ii) Research

Knowledge is both a key input for and output of health research. For increasing use of knowledge in medical research, both clinical research and basic research, following measures are proposed:

- **Creating information culture** by adopting recent advances in information and Communication Technologies. Improving interaction between National and international researcher and stakeholders working in different subject areas by developing collaborative networks and alliances
- **Creating an information system** and a policy framework to facilitate Indian medical researcher abroad to return and join Indian medical research institutions.
- Enhancing research to policy through **collaborations and exchange of information** between researchers and health professional ; between researchers and other stakeholders involved in policy making (political leadership, planners and civil servants etc)
- Enhancing **public-private partnership (ppp)** in health. Preparing national information system of research funding by different funding agencies.
- **Developing database of research resources** such as manpower, equipment etc available with different laboratories/ medical/ dental colleges/ universities etc.

- **Developing disease database** including clinical, epidemiological, genetic, biological and social parameters.

VIII. Achieving high impact of research by effectively communicating research outcomes:

1. Balancing between responsibility to share information for betterment of health of people and protecting intellectual property generated through research.
2. Empowering health research institutions to use tools of Knowledge Management for improving quality research as per the guidelines of Medical Council/ Dental Council of India.
3. Providing access to research data to other scientists and students for secondary analysis by taking care of ethical, copyright and IPR issues. Managing research priorities based on periodical in-depth analysis of existing research data.
4. Creating a National Health Knowledge Repository for free access to all researchers.
5. Encouraging the use of knowledge management for creation of different application groups and development of various disciplines like biomedical engineering.

IX. Strategy for implementing Knowledge Management Policy

Broad strategy for implementing knowledge management policy for health is given below:

1. There will be three important components/ tiers: policy framing, strategy planning and monitoring.
2. An expert advisory group should be constituted under the chairmanship of the Secretary, Department of Health Research with following mandate:
 - (a) To examine the policy document and modify it if necessary
 - (b) To decide the priority areas
 - (c) To classify the priority areas into short term, midterm and long term goals for implementation
3. To constitute three technical sub committees in the areas Service Delivery, Education and Research to manage knowledge network for help with following mandate:
 - (a) To carry out feasibility study/ studies, pilot study/ studies, model projects and preparing proposal
 - (b) To define parameters to be included in feasibility study
 - (c) To create liaison between the study group and other stakeholders of the proposed
 - (d) Knowledge network to facilitate preparation of feasibility report
 - (e) To examine the feasibility study report and present it to the Secretary, Department of Health Research
 - (f) To devise a strategy for implementation along with other stake holders
 - (g) To monitor implementation of work

X. Funding of the different components of knowledge Management Network

- i. The Responsibility of different stakeholders in providing infrastructure, manpower and other resources needs to be defined by consultative process among centre, state, other public and private stakeholders.

- ii. While the network connectivity may be provided by Central Systems, department of information technology, UGC *etc*, the local supplementary support could be provided by State systems.
- iii. A dedicated system will be required for keeping it functional all the times. For this IT connectivity will have to be ensured along with funds allocated for this purpose.
- iv. A strategic plan for providing financial support for development of modules, appropriate software, professionals for data analysis on specific areas, mechanisms of review will have to be drawn for estimating the financial inputs.

XI. Establishment of an Appropriate Authority

For developing and implementing a comprehensive plan for utilization of knowledge network for health service delivery, medical education and research, an Appropriate Authority under the Department of Health Research in the Ministry of Health and Family Welfare, Govt. of India may be desirable. Such an authority with committed resources will be responsible for strategic planning, for implementation and review of the progress from time to time. This Authority / Cell may establish units in the states for action at the local level.

Achievements

Action has been initiated for setting up of necessary infrastructure for its implementation. First workshop to develop a pathway to implement KMP was held at Dr. RP Medical College, Tanda (HP) on 28th Dec 2013. Besides creating a framework, a number of concept proposals to undertake model projects to implement KMP were discussed and several were selected for developing full proposals.

National Health Research Policy

The establishment of a Department of Health Research (DHR) in the Ministry of Health is recognition by the GOI of the key role that health research should play in the nation. The fact that the almost 300 medical colleges in the country are not contributing to their best to health research is highlighted by the fact that in 2007, 96% of the research publications in India emanated from 9 medical colleges. Much of this published research is not on priority health concerns and the translation of key research findings into policy, which could improve the health of the people, is very limited and needs to be enhanced. Epidemiological know-how, surveillance technology and diagnostic services which are essential for determining health priorities are very poorly developed. There is also a compelling need to build multidisciplinary research blending physical, medical and social sciences. Besides, there is also an equal urgency to establish regulations, strict ethical norms and transparency, standardize methodology and international standards of research. Such capacity is necessary for undertaking operational research as also large-scale evaluation of diagnostics and trials of drugs, devices of both modern and traditional systems of medicine. It is in this context that the DHR has formulated a draft National Health Research Policy.

Vision of National Health Research Policy

To maximize the returns on investments in health research through creation of a health research system to prioritize, coordinate, facilitate conduct of effective and ethical health research and its translation into products, policies and programmes aimed at improving health especially of the vulnerable populations.

Objectives of the National Health Research Policy

The broad objectives of the National Health Research Policy are:

- i. Identify priorities for effective and ethical health research to enable the achievement of the objectives of National Health Policy (NHP 2002), NRHM, Bharat Nirman and National Food security Act as well as global commitments such as Millennium Development Goals (MDG) and International Health Regulations (IHR), ensuring that the results of health research are translated into action.
- ii. Foster inter-sectoral coordination in health research including all departments within the Government, Private Sector and the Academia to promote innovation and ensure effective translation to encourage/ accelerate indigenous production of diagnostics, vaccines, therapeutics, medical devices etc.
- iii. Focus on the marginalized, the vulnerable and the disadvantaged sections of society.
- iv. Strengthen national networks between research institutes, academia and service institutes, and encourage PPP.

- v. Put in place strategies and mechanisms for assessing the cost-effectiveness and cost benefits of interventions for health.
- vi. Develop and manage human resources and infrastructure for health research and ensure that international collaborative research contributes to national health.

Prescription of the NHRP

1. Create a National Health Research System
2. Establish a National Health Research Management Forum
3. Operationalize a 10-point action programme

National Health Research System (NHRS)

In order to achieve inter-sectoral coordination and to make national priorities for health research, a new architecture of national health research system is envisaged. Health research system is a concept that integrates and coordinates the objectives, structures, stakeholders, processes, cultures and outcomes of health research towards development of equity in health and in national health system. It is a system for planning, coordinating, monitoring and managing health research resources and activities, and for promoting research for effective and equitable National Health Development. Health Research in the country would be developed into a National Health Research System (NHRS) wherein all research agencies, cutting across Ministries and sectors, identify priority areas of research and coordinate with each other to avoid duplication, fragmentation, redundancy and gaps in knowledge, in order to enable the results of research to transform health as a major driving force for development.

Goals of the NHRS

1. To generate and communicate knowledge that helps to form the National Health Plan and guide its implementation, and thus contribute, directly or indirectly, to equitable health development in the country;
2. To adapt and apply knowledge generated elsewhere to national health development; and
3. To contribute to the global knowledge based on issues relevant to the Country.

Functions of NHRS

The National Health Research System would be responsible for:

1. Developing National Health Research Plan

The DHR is responsible for the National Health Research Plan aligned with the Five Year Plans of GOI and its implementation and monitoring.

2. Set priorities

A Priority Research Agenda will be developed in tune with the National Programmes, and relevant to national and local needs.

3. Engage with Private Sector

The private sector, pharmaceutical industry, biotechnology and biomedical technology oriented Industries, private educational institutions, hospitals and nursing homes, research foundations and institutions, private practitioners, NGO's and CBO's working on a not-

for-profit basis etc are now major stake holders in Health care research and delivery. The National Health Research System would recognize their important role in health research and shall foster their participation in the system as partners. These engagements have to be concurrent and intense rather than linear and loose.

4. Strengthen International Linkages

In the current global scenario International collaborative efforts are recognized as one of the factors in successful research because of the complementarity of technology transfer, capacity building and access to diseased populations. There are a large number of potential partners and in the choice of partners the priorities of the National Health Research Plan and national interest shall be paramount. Linkages with International Developmental partners and WHO and other UN Agencies shall be further developed and strengthened to ensure that India plays a legitimate role as an emerging economy.

5. Ensure Ethical Research

The Bill on Research on Human Subjects and establishment of the National Biomedical Research Authority therein along with the guidelines developed by other agencies shall regulate all research. The Health Research System shall review these Guidelines from time to time, and harmonize them with International Guidelines. Facilitation of training in ethical research shall be the responsibility of the DHR. A major achievement has been the establishment of a National Clinical Trial Registry and all clinical trials are mandated to be registered by the DCGI.

6. Ensure Targeted Financing

The National Health Research System shall be responsible for ensuring equity in resource mobilization and allocation of public funds. It shall endeavor to ensure that the allocation/ expenditure on health research is at least 2% of the allocation / expenditure on health. International funds will also be mobilized in keeping with the priorities. The NHRS would track the resources available and spent on research in the country and monitor its impact on health. Though a minimum of 2% of health expenditure has been achieved, this may be too small a figure considering that the allocation for health itself is meager in relation to the population and health concerns of the country.

7. Monitor and Evaluate impact of health research

To ensure that resources are used efficiently and in line with agreed priorities, there is a need for continuous monitoring and evaluation. The health research system will develop explicit policies and procedures for reviewing proposals, and for monitoring and evaluating the output and impact of those that are funded. Indicators will be developed to monitor the development and effectiveness of the health research system. Indicators would also be defined for assessing health status, health system effectiveness, efficiency and affordability, in order to capture the contribution of research in reducing inequities. Direct indicators of National Development, would serve as indirect indicators of the efficacy of Health System Research as a vehicle of development. Set mechanisms to ensure that best practices are encouraged, and practices are evidence based.

8. Partnership with State Health System.

Encourage health research within States. Help set state level health research system by strengthening partnership between central and state systems.

Assess Health Research System

The health research system would need to be assessed periodically to provide evidence that it is functioning optimally.

The NHRS shall be managed by a National Health Research Management Forum (NHRMF).

The National Health Research Management Forum (NHRMF)

The National Health Research Policy envisages a System wherein all present and prospective players have their own space. However, an overarching National Health Research Management Forum is proposed, having representation of all key stakeholders, the DHR as its Secretariat, and the following functions / terms of reference:

- i) To advise on and evolve national health research policies and priorities and to evolve mechanisms and action plans for their implementation;
- ii) To develop a 5 year projection of the plans for health research and to prepare an annual National health research plan;
- iii) To do a mid-Plan appraisal for course correction, as needed
- iv) To promote the development of health research activities in the country;
- v) To review biomedical & health research management, and suggest strategies to overcome problems in implementation of policies;
- vi) To suggest mechanisms to nurture a scientific environment to attract talent and develop human resources for biomedical and health research; and
- vii) To facilitate utilization and dissemination of research results and advocacy for health research.

Structure of NHRMF

The NHRMF will be Chaired by the Minister of Health & Family Welfare and co-chaired by Minister of Science & Technology. The Minister(s) of State for Health would be the Vice-chairperson(s). The Secretariat shall be in the DHR and its Secretary shall be the Member-Secretary. All Secretaries of various departments in S&T would be the members, DGHS and 8-10 eminent scientists/ public health experts (numbers flexible) as well as selected representatives from State Governments would be the other members. These experts would also be the Chairmen of the various working groups which would be constituted to address the following areas:

1. Development and Evaluation of interventions for promotion, restoration, maintenance and protection of health.
2. Human resource management and infrastructure development
3. Knowledge management
4. Encouragement to translational research and originality in basic science research, and innovations
5. Optimizing intra- and inter-sectoral networks, coordination and collaboration especially with private sector and industry.

6. Track current resource flow and future requirements to address priority areas of health research.
7. Establishment of priorities for health research.
8. Implementation of health research policy, planning, monitoring and evaluation.

Responsibilities of NHRMF

Stewardship

This would encompass a range of activities for the national health system intended to ensure quality leadership, productivity, strategic direction and coherent action. Sub-functions would include Strategic Vision, Policy Formulation, Priority Setting, Performance and Impact Assessment, Promotion and Advocacy, and the setting of norms, standards and frameworks for the sound practice of research. The aim is to provide best practices for research management.

Financing

The essential functions of the System as regards finances would be to address issues related to resource generation, targeted allocation and judicious utilisation. On the basis of recommendations of the National Health Research Management Forum, funds would be allocated in ways that are consistent with national priorities. External Partners would be apprised of these priorities, while a national capability to monitor where and how research funds are being spent, and the quantities involved, would be created and put in place. Ensure that funds are spent where the burden of disease is. Efforts would be made to invest at least 2% of national health expenditure in research and research capacity strengthening.

Knowledge Generation

The research system would generate knowledge relevant to the Indian health situation, appraise the measures available for dealing with health problems, and suggest the actions likely to produce the greatest improvement in health.

Utilization and Management of Knowledge

The Research System fully endorses the principle that the research process does not end with Knowledge Generation, but includes the translation of results into policy or action, or absorption into the existing knowledge / technology base. For this to happen, links will be strengthened between researchers, policy makers, health and development workers, non-governmental organizations, communities, and media. Vertical and horizontal connectedness will be improved upon. More specifically, for better utilization and management of knowledge, an information culture would be fostered, supported by enhanced use of information technologies currently and likely to be available. A synergy with Knowledge Management Policy would be made.

Capacity Development

A long-term approach to the development and maintenance of research capacity will be adopted. Efforts will be focused on both the quantity and quality of skills available / needed, including research techniques, research priority setting, research management, use of research ('demand' side), policy and systems analysis, communications, development of partnerships including medical colleges and rural health research centres. A situation

analysis done periodically would ensure a phased and realistic plan for constructive and sustained capacity development. Thus, both the 'Supply' and 'Demand' sides of the research system needs will be addressed. It will encourage policy research.

The 10-point Action Programme

1. Harmonize optimally National policies in a variety of areas (education, social sciences, population, agriculture, nutrition, science, *etc*) to facilitate inter-sectoral collaboration and partnership, so that maximum developmental returns can occur from health research.
2. Ensure true inter-sectorality of health research and harness the resources in areas such as social sciences, economics and traditional systems of medicine.
3. Facilitate priority setting to guide the direction of health research and prepare Five-year Plan and strategy documents
4. Encourage the development of fundamental and basic research in areas relevant to health to ensure that a national critical mass of scientists who can contribute towards the benefits of modern technology to health research is created.
5. Foster translational research to ensure that the products of basic research can be appropriately utilized in health systems and services.
6. Establish linkages between health research and national health programmes to identify key operational issues and facilitate the operationalization of evidence based programmes and to obtain feedback for the optimization of health research
7. Build and integrate capacity for research in National Health Programs, research institutions and in the private sector (profit and non-profit organizations) both in rural and urban research settings utilizing as far as possible areas of excellence already available in the country.
8. Ensure that the global knowledge base is available for national programmes, and that research is channeled in relevant directions without unnecessary duplication by the optimal use of information, communication and networking technology.
9. Manage global resources and transnational collaborations optimally to ensure that collaborative health research primarily facilitates the development of national health systems and services.
10. Generate the evidence-base for health systems and services, to be significant promoters of equity and contribute to national development so that health research becomes a poverty reduction tool.

Achievement

The Policy is under the consideration of the Government for approval. Action has been initiated for setting up of necessary infrastructure for implementation.

Mapping of Health Research Institutes

During the year under report, The Directory of Health Research Institutions, supported by the WHO is being updated. This is data base of more than 800 Health Research Institution from India. The institutions belong to ICMR, CSIR, DST, DRDO, DSIR, Department of Biotechnology, Ministry of Health & Family Welfare, Department of AYUSH, Department of Pharmaceuticals, Ministry of Social Justice & Empowerment, and Medical Colleges with active research activity, NGOs and Private Organizations. A CD with “user friendly software” is available for users. The database can be searched on the DHR web site (<http://202.141.106.123/httpdocs/DHRI/DHRIDefault.aspx>).

Updation and analysis of the Database of Research Papers published by ICMR institutes in Scholarly Journals with Value addition has been completed for all the institutes/RMRC till 2010 and as part of ICMR centenary celebrations a “Compendium of ICMR Research Papers (1919-2010)- A consolidation” have been published. Along with this two more publications namely “ICMR’s Most Cited Research Papers: A Chronicle (1950-2010)” and “Citation Classics of ICMR’s research Papers (1950-2010) –Five Most Cited Papers in Priority Area of the Council”. The PDFs of the documents can be accessed on ICMR website <http://icmr.nic.in/Publications/centenarybooks/compendium/index.htm>, http://icmr.nic.in/Publications/centenary_books/Most%20Cited%20Rearch%20Papers/index.htm, “http://icmr.nic.in/Publications/centenary_books/citations_classic/index.htm” respectively.

Accreditation of Health Research Institutes

The DHR has been given the mandate of developing guidelines for accreditation of Health Research Institutes. The institutions engaged in research activities related to basic, applied, epidemiological and translational research may get recognition under this scheme.

Achievement

Guidelines for application and its processing as well as criteria for accreditation / recognition as Health Research Institute have been finalized. Approval of the competent authority has been accorded and process initiated for actual implementation for accreditation/ recognition of Health Research Institutions.

INDIAN COUNCIL OF MEDICAL RESEARCH

Indian Council of Medical Research

Introduction

The Indian Council of Medical Research is the apex body in India for the formulation, coordination and promotion of biomedical research. In the year 1911, when the idea of establishing the Indian Research Fund Association was taking shape, it had become clear that the mandate would be of sponsoring and coordinating medical research in the country. It is now recognized as one of the oldest medical research bodies in the world, even preceding the birth of the Medical Research Council of Britain. As the work relating to medical research in India gained momentum after independence and the scope and functions of IRFA expanded considerably, it was re-designated as the Indian Council of Medical Research in the year 1949. It was registered as a Society under Govt. of India Societies Registration Act, 1860 and it is fully funded by the Union Ministry of Health and Family Welfare.

The Indian Council of Medical Research (ICMR) completed hundred years in 2011. The Centenary Year was launched by Hon'ble Union Minister of Health & Family Welfare Shri Ghulam Nabi Azad at a function held at New Delhi on 15 November 2010 and the concluding ceremony was held on 15th November 2011. A series of events were organized on this occasion by the ICMR Headquarters and its Institutes/Centres. In 1911, officers of the then Indian Medical Services had the vision and foresight to create Indian Research Fund Association. Soon after Independence, it was rechristened as Indian Council of Medical Research.

Over 100 years of its existence, ICMR blossomed into a vibrant network of 32 permanent Institute/ Centres and nearly 70 field stations, employing over 5000 personnel including 750 scientists.

The ICMR has evolved over the year in line with changing health research needs, effectively addressing the new challenges that have emerged as a result of the economic, demographic, nutritional and epidemiological transition of the country. With the changing health challenges, the demands on the ICMR are also increasing. The Mission of ICMR continues to be the promotion of better health through research.

ICMR has accepted a twin track approach to meet its objectives – intramural (through its Institutes) and extramural research (through grants-in-aid) to project in non-ICMR institutions.

The permanent Institutes of ICMR are mission oriented discipline/disease specific laboratories strategically located in different parts of the country. Extramural research is promoted basically to strengthen the biomedical expertise and infrastructure especially in medical colleges and the university system, aimed at developing and fostering a culture of research in academia. Currently, the ICMR spends over 40% of its budget on the extramural research programme.

The research priorities of the Council coincide with health policy and priorities of the country. The Council works very closely with the national programmes, which have well designed targets for control, elimination and eradication of diseases. The ICMR is actively engaged in various aspects of research for control of communicable diseases (HIV/AIDS, tuberculosis, malaria and others); infectious diseases targeted for elimination (kala-azar, lymphatic filariasis, leprosy) and those targeted for eradication (yaws, poliomyelitis); non-communicable diseases (cardio vascular diseases, neurological disorders, metabolic diseases, cancers, injuries, etc.); and improving maternal and child health including nutrition. The

Council also carries out basic, applied, operational, social and behavioural, and health systems research *etc.*

The majority of the research activities of the ICMR are directed towards diseases that have significant links with poverty. The Council has a special focus on health of marginalized and under privileged sections of society and is responsive to issue of equity, gender, ethnicity, race and caste.

The ICMR has provided critical research support whenever the health needs of the country demanded rapid responses. With globalization, international collaborative research has also increased. The Council has played an important role in defining the limits of collaborative research and ensuring that such research is conducted in an ethically acceptable manner.

Historical Background

The history of ICMR, in many ways, is the history of public health research in India. In view of the fact that variety and vastness of interests in the history of ICMR are sought to be wrapped, the first part covers the genesis and administrative history whereas in the second, scientific contributions are presented, as appeared on the scene in a time-frame.

Indian Research Fund Association (IRFA) was established in 1911 by the Government of India in order to address the research needs of the medical and health problems (tropical) relevant to India, which had seen no sustained and organized research efforts by our own scientists and those of the Western World.

During the last hundred years, ICMR and its predecessor IRFA have been in the forefront for conducting, coordinating and promoting scientific and biomedical research. The insights gained through the sustained research endeavor saved numerous lives and led to several historically significant innovations that are being utilized across the world. The year 2011 was a centurian landmark in the evolution of the Indian Council of Medical Research (ICMR), the apex organisation for medical research in India. ICMR was established on the corpus of the Indian Research Fund Association (IRFA), one of the oldest medical research organizations in the world in modern era. Needless to say, this is the right occasion to record the events and dedication that led to the establishment of the Indian Research Fund Association and its subsequent growth. Many scientists associated with IRFA and ICMR have also been able administrators in contributing to issues most relevant to understanding and improving Public Health in the country.

The New Age

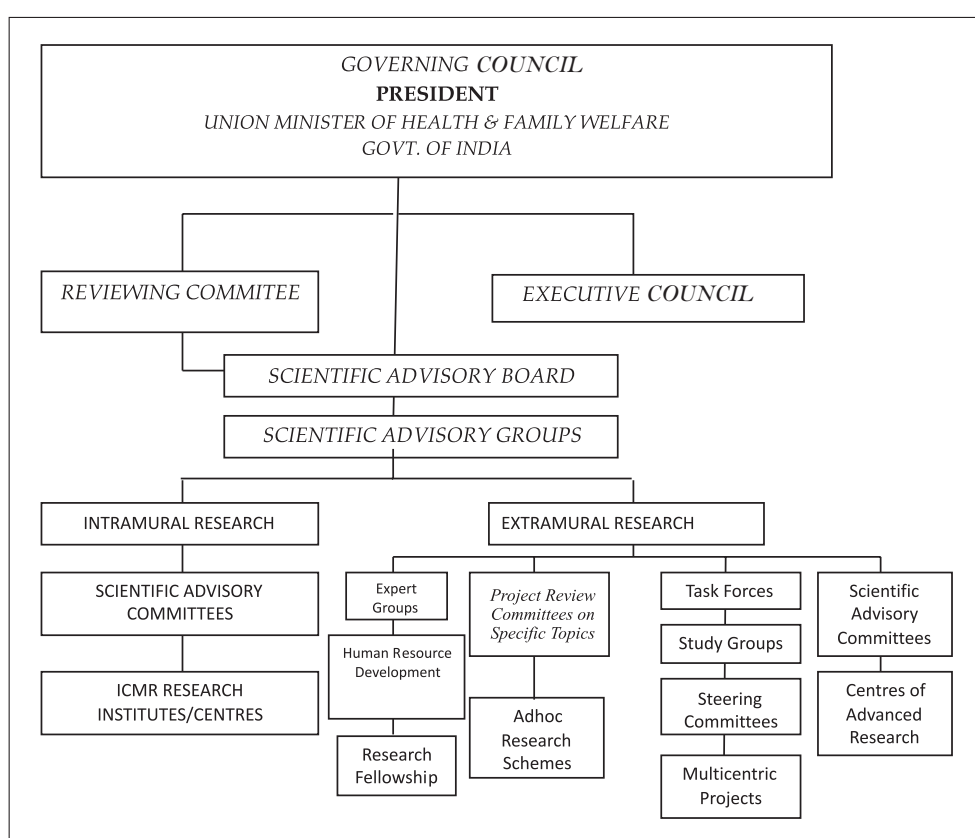
The broad areas of priority in which the Indian Council of Medical Research conducts, coordinates and funds bio-medical research in basic as well as clinical sciences may be indicated in the following manner:-

1. Control and management of infectious diseases/vector-borne diseases
2. Reproductive biology and fertility control, maternal and child health
3. Human nutrition and nutritional disorders
4. Developing alternative strategies for health care delivery and health systems research
5. Environmental and occupational health problems
6. Non-communicable diseases such as cancer, cardiovascular disorders, blindness, diabetes and other metabolic and hematological disorders

7. Mental health research
8. Drug research and monitoring of clinical trials (including traditional remedies)
9. Modern biology including genomics, proteomics, bio-informatics, nano-medicine, stem cell research
10. Translational research

Considering the vastness and complexity of research work that ICMR undertakes both as intra mural as well as by supporting open-ended or extra mural research through the medical colleges, institutions and universities in the country, one needs to deeply look into historical perspective to gain insight into its evolution and, in due course of time, setting up of a network of research Institutions.

The following flow-chart might help in gauging the Council's hierarchy and functional web:



The President of the Governing Council of ICMR is the Union Minister for Health & Family Welfare, Govt. of India; the Health Secretary being the Vice-President. The Governing Council comprises eminent scientists/public health experts as also elected members of the Parliament of India.

The Scientific Advisory Board is the highest scientific body of the Indian Council of Medical Research. It reviews the scientific work of the Council and suitably advises it from time to time on short- as well as long-term policies and strategies for research, particularly those that need to be taken up on priority in accordance with the national policies. Besides Finance and Administrative Divisions/Units, there are many technical divisions/Units in the Headquarters office of the Council that ensure smooth functioning and coordination of research work viz.:

- Epidemiology & Communicable diseases
- Non-communicable diseases
- Reproductive & Child Health
- Nutrition
- Basic Medical Sciences
- Publications & Information
- International Health
- Health Systems Research
- Social and Behavioural Research
- Human Resource Development
- Medicinal Plants

Technical Divisions of ICMR	Institutes/Centres under the Division
Epidemiology & Communicable diseases (ECD)	CRME, EVRC, MCC, NARI, NICED, NIE, NIMR, NIMS, NIRT, NIV, NJIL&OMD, RMRIMS, VCRC, Virus Unit of ICMR, RMRC, Bhubaneswar, RMRC, Port Blair, RMRCT, Jabalpur
Non-Communicable Diseases (NCD)	BMHRC, NCDIR, ICPO, NIREH, RMRC, Dibrugarh, DMRC, Jodhpur, NIOH
Reproductive & Child Health (RCH)	NIRRH, GRC
Nutrition	NIN, NCLAS, FDTRC
Basic Medical Sciences (BMS)	NIIH, NIOP, RMRC, Belgaum

The scientific activities of the Divisions are synchronized by respective Scientific Advisory Group (SAG) for each, comprising of experts drawn from the relevant fields, which annually meet for reviewing the activities of the concerned divisions.

The role of the Indian Council of Medical Research is to conduct as well as to promote biomedical research in the country. It fulfills this function through intramural as well as extramural research. Intramural Research is carried out by the Council's permanent Institutes/Centres/Units. As of today, ICMR has 32 Institutes and Centres that work in specific and highly specialized areas of bio-medical research and have acquired reputation in their respective fields. The permanent Institutes are:

- ♦ **26 Mission Oriented Permanent National Institutes:** These Institutes are located in various parts of the Country, addressing to research on specific areas such as Tuberculosis, Leprosy, Cholera and Diarrhoea, viral diseases including AIDS, Malaria, Kala-Azar, Vector Control, Nutrition, Reproduction, Environmental and Occupational Health, Immuno-haematology, Oncology, Medical Statistics, food and drug toxicology, viral diseases, handling micro-organisms of highly infectious nature, prenatal diagnosis for neonatal retardation etc. and supply of various animal models and feeds for experimental purposes etc.
- ♦ **6 Regional Medical Research Centers:** The Centers were established to address regional health problems and strengthen or generate research capabilities in various geographical areas of the country.

Each of the ICMR Institutes has a Scientific Advisory Committee (SAC), comprising of experts in specific areas of research. The reports of the SACs of Institutes and SAGs of Technical Divisions of ICMR Headquarters are placed before the Scientific Advisory Board (SAB) for its consideration, whereas the report & recommendations of the SAB are placed before the Governing Council.

In 2010, ICMR established The National Institute for Research on Environmental Health (NIREH) at Bhopal. Lately, a new Institute, National Centre for Disease Informatics and Research, was established at Bengaluru to sustain and develop a national research database on cancer, diabetes, cardio-vascular diseases and stroke through technological advances in IT with a national collaborative network so as to undertake and conduct aetiological, epidemiological and clinical research in these areas.

Apart from intra mural research, ICMR also promotes and supports independent extramural research, through setting up of centres for Advanced Research, Task Force studies and ad-hoc, open-ended research schemes.

Centres for Advanced Research are set up in specified research areas around existing expertise and infrastructure in selected departments of Medical Colleges, Universities and other non-ICMR Research Institutes. This scheme was formulated to encourage in-depth research on an identified research problem with the aim of generating new knowledge and having a better understanding of a disease or a health condition.

Task Force studies are national projects, centrally planned and coordinated and usually implemented on a multi-centric basis. These projects are time-bound, with a goal-oriented approach and clearly defined targets, specific time frames and conducted by standardized and uniform methodologies.

Open-ended Research

The Indian Council of Medical Research provides financial assistance to scientists to promote biomedical and health research in the Universities, medical colleges, postgraduate institutions, recognized research and development laboratories and NGOs. Proposals in fundamental/strategic research; development and evaluation of a tool, clinical and operational research are considered for ICMR support.

In addition, the Council offers the position of Emeritus Scientist for retired medical scientists and teachers, to enable them to continue or take up research on specific biomedical topics. The Council also awards prizes to Indian scientists in recognition of significant contributions to biomedical research. At present, the Council offers 37 awards of which 10 are meant exclusively for the young scientists (below 40 years).

Chronicles of Indian Medical Research from Ancient to Modern Times

The Ancient Medical Systems and Early Research Endeavours in India

India has had a glorious history of science and medicine since ancient times. *Ayurveda* comes from the Sanskrit words 'Ayus' and 'Veda' which mean duration of life and unimpeachable knowledge respectively. The earliest instances of the healing science are found in the *Rig Veda* and the *Atharva Veda* both created in the second millennium BC.

The science of *Ayurveda* is seen to develop and gain greater structure and rigour with time. As a science it witnessed research endeavors and generation of new knowledge and thereby creating a rich heritage of medical research in India.

A large number of students used to come to Indian universities, particularly Taksh Shila and Nalanda, and many Ayurvedic schools spread throughout the country to learn the Indian system of medicine and surgery. Learned men of yore from China, Tibet, Greece, Rome, Egypt, Afghanistan, Persia and a few south Asian countries used to travel to India to learn and carry the wisdom in medicine back to their own countries.

With the introduction of Galenic tradition, there gradually appeared a hybrid of Muslim-Hindu system known as the Tibb. They differed in theory, but in practice both traditions seem to have interacted and borrowed from each other. From the Islamic side the concept of arka entered Ayurveda. Several Sanskrit medical texts were translated into Arabic and Persian, but instances of Islamic works being translated into Sanskrit are rare. The concept of individual case studies and hospitals (bimaristans) also came from the Unani practitioners. Later interaction with the European travelers and medical men grew in the eighteenth century. Yet while the European medical men were gradually moving, thanks to the works of Vesalius and Harvey, from a humoral to a chemical or mechanical view of the body, Indians remained faithful to their texts. Asia kept doing what it had been doing for centuries; Europe changed fundamentally.

Rebirth of Medical Science and Research in Modern India

The British colonizers swiftly moved to establish their own system of medicine, first for themselves and later for the natives as the Indian system was summarily rejected as paga rituals.

The Portugese, British, French and the Dutch had entered India during the medieval era when Islamic rule was at its zenith. The geographical diversity and natural bounty of the Indian sub continent evoked great interest in the minds of the aliens. Thus, as the Europeans (the British to be precise) grew in power and influence in the subcontinent, growth in scientific enquiries in the basic fields of knowledge witnessed transformation.

The history of modern scientific research in India, in a way, made a beginning in 1784, when the first scientific society – *The Asiatic Society of Bengal*, for the promotion of science was formed and modeled after the Royal Society in England that was founded in 1660 (30 years ahead of the establishment of Fort Sir Williams in Calcutta in Bengal by the British). It was possibly the oldest and the most sought after body of scientific research in the world at the time. Despite the fact that its activities encompassed all important fields such as Zoology, Botany, Anthropology, Chemistry, Physics, Mathematics, Geology, Meteorology whereas the field of medicine was largely unexplored.

In 1763, the Bengal Medical Service was established, which in 1775 had been expanded to all the Presidencies in the British governed territories of India. However, its primary aim was to provide services to the military camps and it was discouraged from participating in any activity relating to innovation and research. The first important pointer toward health research was the appointment of a Royal Commission in the year 1859 to enquire into the heavy mortality in the military and civilian population of India. The need for scientific research in medical sciences in India was truly recognized with the identification of many tropical diseases, peculiar to India that was normally not encountered in the West. The subsequent research was driven by the realistic considerations for understanding the problems encountered in public health and finding practical solutions to solve them by the application of scientific knowledge developed in the West.

By early nineteenth century a more sophisticated conception about various tropical illnesses and their causes emerged, which ascribed pathogenic qualities to a range of environmental, economic and social factors.

The physicality of India turned into a serious threat as Europe lost more men to colonial diseases during the eighteenth and nineteenth century than armed conflicts and wars. In the woods of Odisha, malaria was the main enemy as many British soldiers had died at the hands of the disease instead of the 'enemy' they were battling with. More than anything else, it was the need for the safety and health of the British men and their families that necessitated an interest and start of regular medical research.

The Commencement of Medical Research

In the second half of the 19th century many major developments took place in the way the scientific research could be organized and viewed. It also set the groundwork for development in scientific research in India as elsewhere. From 1850 to 1874, Edward Hare had successfully introduced the practice of administering quinine in cases of fever. Vandyke Carter investigated the origin and development of famine fever, elephantiasis, mycetoma and, perhaps, leprosy. Leprosy, one of the world's most misunderstood diseases, said to have originated in India, had afflicted people around the world for ages. Its disfiguring nature, search for an effective therapy that was hitherto most inconsistent, its association with sin and the fear of contagion caused the Indian society, from ancient to modern times, to socially marginalize those that suffered from this disease. The combination of these factors endowed leprosy with a unique stigma that persists even today and evident from the fact that the diseased were treated with scorn and seclusion for therapeutic intervention.

However, over a period of next 30 years, three events occurred that strengthened the argument for isolation of leprosy patients and reviving the research for development of a cure for leprosy. In 1872, the first Leprosy Census was carried out that indicated that out of every 10,000 individuals, 54 suffered from it -a very high prevalence level. In 1873, Dr. Gerhard Henrik Armauer Hansen first detected 'rod-shaped bodies' on leprous nodules, which came to be known as *Mycobacterium leprae*. These he postulated to be the transmitting agents of the disease. Dr. Hansen's discovery of the *M. leprae* was historic, leading to leprosy being called 'Hansen's disease'. Father Damien, a Belgian missionary priest who went to Hawaii to take care of the leprosy patients on the island had contracted the disease and died, which proved the contagious nature of the disease.

Another important contribution in the understanding of tropical diseases also took place around this period in Secunderabad where Surgeon-Major Ronald Ross discovered that it was the female mosquito that was responsible for the transmission of malaria.

Sir Ronald Ross, who in exposing the role of the female mosquito in the transmission of malaria, had laid the foundation of malaria research and its control in 1897. For the discovery he won the Nobel Prize. There had been some previous developments in the field brought about by Dempster in 1845 with the introduction of spleen rate as a measure of malarial endemicity and by Laveran in 1880 by the discovery of the malaria parasite in human blood. It was discovered in 1887 that bark yield from Cinchona plant was a reliable source for manufacturing pure quinine sulphate that could cure malaria.

In 1897, Dr. Waldemar Mordecai Haffkine developed the prophylactic vaccine for plague.

On the 10th of August 1899, a mansion, which was at one time the residence of the Governor of Bombay, was formally handed over to Haffkine by Lord Sandhurst, the Governor of the

province. It was designated as the 'Plague Research Laboratory' with Haffkine as its Director in Chief. In 1906 the Institute was renamed as 'Bombay Bacteriology Laboratory'. Lastly, in 1925, due to the efforts of Lt. Col. F.P. Mackie, the Institute was aptly named 'Haffkine Institute' that became one of the first institutes and important cornerstone of medical research in the country.

The momentum of research was carried forward into the 20th century, among others by Charles Donovan who in 1903 traced the cause of Kala-azar to a parasite (known as *Leishmania Donovanii*) in the spleen of the affected cases, and in 1904, Leonard Rogers showed by culture that this parasite was a flagellate. One of the earliest descriptions of fever with splenic enlargement caused by Kala-azar was made by William Twining, a surgeon in Calcutta from 1824 until his death in 1835. In an article in the 'Transactions of the Medical & Physical Society of Bengal', he noted that splenic disease 'prevails in Bengal (in those days the greater Bengal also comprised large areas of modern Bihar and Odisha) to a very great extent and indeed is frequent through all the low districts of Hindoostan'.

The first outbreak of Kala-azar was traced by Dr. J. Elliot, back in the year 1824, to a village called Mahomedpore, near Jessore in Lower Bengal (now Bangladesh). It reached Burdwan in 1860, where it caused an epidemic that came to be known as the 'Burdwan fever', considered at that time to be an unknown form of malaria. Dr. John G. French, the Civil Surgeon of Burdwan at the time noted that the disease incidence varied with the time of the year.

The discovery of the parasite responsible for transmission of the disease of Kala-azar was credited to Lt. General Sir William Boog Leishman and Colonel Charles Donovan, who worked independently and made the discovery at around the same time. In 1903, Leishman reported the case of a British soldier at Netley who was suffering from a resistant form of malaria, and died of emaciation and enlargement of spleen, having contracted the disease when he was stationed at Dum-Dum near Calcutta (Dum-Dum fever). Leishman discovered unknown parasites from the spleen taken post mortem, which he found to be similar to degenerated forms of trypanosomes – this he published in an article titled, 'On the possibility of the occurrence of *Trypanosomiasis* in India' in the British Medical Journal (1903). By June 1904, Leonard Rogers had cultivated *Leishmania donovani* in vitro, and demonstrated that the parasite was a flagellate.

Epidemics of tropical diseases aggravated by frequency of famines due to failure of summer rains had thus become a periodic occurrence from 1780 to 1943 AD, in India. Tropical diseases such as Plague, Cholera, Malaria, and Kala-azar were particularly rampant throughout the 18th & 19th centuries. The British East India Company and later the Government under the Crown had to devise ways and means to deal with the fatality of these diseases recognizing them as a major public health issue. Other diseases like Lymphatic Filariasis though not very well known were endemic in many parts of the country. Lymphatic filariasis (LF) is even nowadays an important public health problem in India in which about a third of the global population lives at risk of this disease. In India, description of a disease that resembles filariasis was found in '*Susruta Samhita*' as early as 600 B.C. *Madhavakara* in his treatise '*Madhava Nidhana*' (700 A.D.) has described the signs and symptoms of this disease and has referred to the elephantoid legs in Cochin as 'Malabar Legs'.

The period between 1891 and 1901 saw a large number of severe droughts caused by frequent failure of both the summer and winter rains across the entire Indian sub-continent caused widespread shortage of food grains and fodder that resulted in unexpected misery and

wastage of large number of people and cattle. The famines not only ravaged the countryside but also forced the Govt. to prepare plans to combat undesirable consequences. Ration was introduced through the public distribution system, energy stocks of food grains were created in years of abundance supply, irrigation channels dug across fertile lands and more waste lands brought under regular cultivation to increase food grains production. Obviously, availability of nutritious foods was the first casualty during any famine. The recurrence of famines had also brought changes in the feeding patterns and habits of the people as was later discovered that it manifest also into some genetic traits of overeating and several metabolic disorders such as diabetes.

The initiation of a medical research organization in India dates back only to 1867, when Dr. Lewis and Dr. Cunningham were appointed as Special Assistants to the Sanitary Commissioner with the Government of India. They initiated researches on diseases such as Malaria, Beriberi, Kala-azar etc. which have been discussed in brief earlier. Another important area of research that was given attention in these early years was the dreaded disease Cholera.

The world has seen eight cholera pandemics in the 19th and 20th century, starting from 1817, the year in which cholera ceased to be endemic only in Lower Bengal and spread outwards, through South Asia, Central Asia, the Middle-east and from there reaching Russia in 1823. According to John Harrison, "the dangers of the tropical environment became increasingly evident in India after 1817, in which year cholera spread outwards, for the first time from its home in lower Bengal to decimate Northern and Eastern India and ultimately much of Eurasia". The high morbidity and mortality associated with cholera made it one of the most dreaded diseases of the 19th Century.

In 1830, Robert Hermann, a German Chemist proposed the idea of injecting fluids into the veins of a cholera patient as treatment as the second pandemic of cholera hit the world. In 1883, Robert Koch, a German scientist, who came to Kolkata after investigating the cholera pandemic in Alexandria, Egypt, successfully identified and isolated the comma shaped cholera bacillus (*Vibrio cholerae*, later known as *Vibrio cholerae* Pacini) as the causative agent of the disease. In 1854, another significant discovery was made, when a British physician John Snow, investigating an outbreak of cholera in London, discovered the role of water in the transmission of the disease. Eastern India, particularly the Gangatic delta had been considered as the 'homeland' of cholera and a focal point of many of the epidemics and most of the pandemics, for a long time.

The first attempt at organized medical research in India was made in 1894 when the Indian Medical Congress submitted a resolution to the Government of India for the establishment & endowment of a research Institute. Facilities for systematic investigation of problems of tropical and other diseases were provided in the early years of the 20th century with the establishment of laboratories in different parts of India - the intention was to provide a central laboratory and encouraging formation of laboratories in the major provinces wherever they could be suitably situated.

The establishment of Pasteur treatment, a treatment for infection by the rabies virus in which a series of increasingly strong inoculations with attenuated virus was given to stimulate antibody production during the incubation period of the disease, in India necessitated the provision of laboratories. Further impetus to medical research was given by the occurrence of epidemics, particularly the plague epidemics which necessitated the creation of laboratory facilities to investigate it. 'Plague' according to Sir Pardy Lukis, the then Director-General

of the Indian Medical Service (IMS), '*did for medical research in India, what cholera did for sanitation in England!*' Consequently, this led to the establishment of central and provincial laboratories and institutes, namely, the Bacteriological laboratories at Agra, The Bombay Bacteriological Laboratory which later became the Haffkine Institute, Pasteur Institute at Kasauli (1900), King's Institute at Guindy (1903) and Pasteur Institute at Coonoor (1907). A Central Research Institute was set up at Kasauli in 1906.

Birth of Indian Research Fund Association (IRFA)

The Bacteriological Department of the Government of India, originally with 13 officers mostly from IMS was constituted as a cadre of scientific research workers, to staff these institutes. It however, soon became evident that these officers were being increasingly charged with administrative duties and, instead of being freely available for research work, were fixed up as Directors and Assistant Directors in the Institutes.

Besides, the department was caught up in complex recruitments which, among other things, required a prior sanction of the Secretary of State for India, in London. To obviate these aberrations the government flagged off the Indian Research Fund Association in 1911 for the prosecution and assistance of research, propagation of knowledge and experimental measures usually in connection with the causation, mode of spread and prevention of communicable diseases.

During the British Era (1911-1947)

The first meeting of the governing body of IRFA was held at the Plague Laboratory, Parel, Bombay on 15th November, 1911 with Sir Harcourt Butler as the Chairperson. At this meeting the very first Scientific Advisory Board, which consisted of four members was appointed. Surgeon General Sir Pardy Lukis was appointed the chairman of the board. The first meeting of the Scientific Advisory Board also subsequently took place on the same day with the agenda of appointment of a number of committees to plan and promote research on medical problems of tropical interest.

At this stage priority was given to the study of malaria, kala azar, plague, cholera etc. Therefore special committees were appointed to individually deal with each of these destructive diseases. It was also proposed to initiate or co ordinate research in other important fields like medical entomology, vital statistics, practical sanitation and schemes of model towns and other measures by which the importance of sanitation could be demonstrated to the public. Sanitation was in fact one of the major areas identified as priority not just by the Fund but by the Government given its (already identified) impact on communicable diseases. The main issue in the agenda for the meeting was '*causes for decrease in population in India!*' It must be remembered that incessant famines and widespread epidemics had led to an exceedingly high death rate at the time.

During the decade 1911-20 the death rate among the census population of 228 millions was in four years within a fraction of 30 per thousand; in four other years it was considerably higher; in one year the rate, owing to influenza prevalence, rose to 62.4 per thousand; the lowest rate recorded in any year was 28.72. These statements were based on a statistical abstract issued as a parliamentary paper. It was pointed out also that the mean expectation of life of the Indian male at birth, which was 24.59 in 1891, had decreased to 23.63 in 1901, and to 22.59 in 1911. In England the expectation of life of the male infant, which was 40.17 in 1841, had risen to 51.50 by 1910-12. The death rate of England and Wales during the time was 12.9. There would seem, therefore, to be a good deal for the skilled consultant and

technical adviser in public health to do in India. And indeed these were the major concerns that IRFA had to tackle during the very first decade of its existence.

The 2nd meeting of the Governing Body, led to another historic decision of starting a journal for Indian medical research. IRFA had realized that dissemination of scientific knowledge, both among the known and the layman, was as important as its creation. It decided to bring out the journal -Indian Journal of Medical Research (IJMR), basically for the propagation of knowledge and intended to absorb the publications of similar nature already brought out under the name 'Paludism' in addition to a vast majority of the monographs known as the *Scientific Memoirs*. The Journal became the first official publication of the Association and regularly published since July, 1913. In 1914, the Government of India also extended its scientific Cadre under the new name 'Medical Research Department', increasing the strength to 30, of which the pay and allowances of 8 officers were met by the IRFA.

'Quinine and Malaria Enquiry' under Major Sinton at Kasauli, the 'Kala-azar Ancillary Enquiry', with Major Knowles and Dr. Napier and research on Indigenous Drugs under Colonel R.N. Chopra at the School of Tropical Medicine, Calcutta were a few among the notable enquiries started by the Association after the ending of the First World War. Perhaps the most important achievement among all these came on the close of the First World War (1918), when Sir Robert McCarrison commenced the work in Coonoor on 'Beri-beri Enquiry' under the auspices of the Fund. This step was of great significance in medical research it could ultimately evolve into an important national laboratory entirely devoted to nutritional research.

In the early 1920's, the idea of establishing a Central Research Institute had gradually started gaining ground. Professor E.H. Starling was consulted on vital issues like the location, the scope of work of the institute, and its relation with the existing research set up in the country. He submitted a report strongly recommending the formation of a central institute and felt that it should be located in Delhi. The Secretary of State for India sanctioned the establishment of the Central Research Institute. It was decided to credit Rs 2.5 lakhs each year to a fund specially earmarked to establish the proposed Research Institute at Delhi. It was also decided to appoint a Director of Medical Research for the task of co ordination of medical research in India. Realizing that the scope of work was mainly limited to Communicable Diseases, IRFA decided to extend the scope of research and its assistance to many other important fields. It also extended its financial support in the form of 25 per cent of its maintenance cost to the recently established School of Tropical Medicine in Calcutta.

Inchcape Committee & All-India Conference of Medical Research Workers

Science thrives on social demands, channelized by political priorities and applied through economic rationale. The post-war economic crisis did curtail the pace of medical research for a short time in India. Burdened with huge financial deficit, the government constituted the Indian Retrenchment Committee presided over by Lord Inchcape. Also known as the Inchcape Committee, it was appointed to study the state of the economy because of the financial crunch imposed by the conditions and constraints in the post-war period. The Committee presented its findings and recommendations in the year 1923, which led to far reaching changes in several aspects of public spending.

The First All-India Conference of Medical Research Workers was organized in the autumn of 1923.

At the conference most of the members were in favour of continuing the research programmes at the cost of the capital. This policy outlook was therefore considered as recommendation by the Scientific Advisory Board, which was accepted by the Governing body of IRFA. Another important recommendation of the Worker's Conference, which could be accepted by the government, was that henceforth research would only concentrate on issues of priority. For this a special sub-committee was appointed to judge the priority of each of the research areas and rank them accordingly, so that only the high priority researches could be supported.

Revitalizing IRFA

Financial constraints did not last forever. In less than two year's time, the government was able to restore financial grants to IRFA, partially in the later months of the year 1925 and fully in the successive year. As a result, the activities of IRFA had picked up and significant contributions were made during this period. The Organization was renamed as the Malaria Survey of India in 1927. As part of this project which was fully financed by the Fund, an experimental malaria station at Karnal town (now in Haryana) named after Ronald Ross was established.

The Malaria Survey of India with the assistance of parallel provincial organizations had carried out some noteworthy work in addition to the Kala-azar Ancillary Enquiry, financed by IRFA, recommending the appointment of the Kala-azar Commission by the Government of India, in 1924. Before its suspension in 1930 due to the decline of the disease this Commission had made considerable progress. Two other important issues related to medical research were also being considered by the Indian Government at this juncture. Firstly, it was the establishment of a Central Medical Research Institute at Dehra Dun and secondly, a Public Health Institute at Calcutta.

Fletcher Committee

The Government appointed a Special Committee with Sir Walter Fletcher as its Chairperson to look into Prof Starling's report and also to advise the government on the role of the proposed Central Institute in the face of the ongoing research activities being carried out under the auspices of IRFA. The Fletcher Committee submitted its report in 1928.

In 1928 the Rockefeller Foundation made a donation of \$ 648000 to the Fund for the establishment of the Public Health Centre, which finally set the wheels in motion.

In 1934, the government decided that IRFA, which was a Governmental Body, would be made a local body independent of the direct administrative control of the government. This decision primarily gave IRFA greater freedom in utilizing the funds at its disposal. The Memorandum of the Association with its rules and regulations was prepared in consultation with other departments of the Government and on 22nd March, 1938 the Fund was registered as an independent local body as Society under the Government of India Act No. XXI of 1860.

Formation of Advisory Committees

In 1938 the Malaria Survey was renamed as the Malaria Institute of India (MII), primarily to expand its scope of activities. As more and more information of practical utility came to be collected, recommendations were made by the Research Workers Conferences and the Scientific Advisory Board of the Association to use this knowledge in the Public Health Programmes of the Country. Consequently, it was decided by the Government in 1940

to take over the Public Health and Advisory Sections of the research activities. With the outbreak of the Second World War the activities of the Institute were attuned to meet the new situation as temporary barracks and tents were erected to accommodate the troops that entailed frequent movement through the Indian territory. As troops required to be protected from malaria and other mosquito borne diseases, several suitable chemical formulae were evolved for development of insecticides and mosquito repellants, which were tested and later adopted for use. Appropriate sprayers were designed for the use by Defense Forces. The Institute was also involved in staffing and training the first two military Anti Malaria Units which were the forerunners of several such institutes as MII.

IRFA continued to pursue research work almost unabated and immensely facilitated the war-affected government by regulating its activities in accordance to the military requirements. These included the development of anti-malarial operations, extraction and manufacture of important nutrients such as Vitamin C for inclusion in rations for the troops. However, investigations of emergency nature such as the Bengal Famine continued to receive aid.

An important achievement in the midst of the turmoil was the discovery of the transmission cycle of the parasite of Kala azar. In spite of the almost debilitating restrictions imposed by the War it must have been heartening to see that the investigations supported by IRFA were successfully accomplished having contributed to improving the public health situation in the country.

Bhore Committee

The support offered by IRFA during the War encouraged the government to reorient its structure and research plans. Accordingly, in the year 1943, the government constituted the Health Survey & Development Committee -popularly known as Bhore Committee, with Sir Joseph Bhore as its Chairperson. After analyzing the situation, the Committee submitted its review report in the year 1946. The Committee had appreciated IRFA's contribution in promoting medical research despite constraints. The Committee had made a few imperative recommendations for improving the health conditions in India. The integration of preventive and curative services at all administrative levels could be seen as most desirable. Besides recommending the establishment of primary health centres complete absence of organized research activities in the medical colleges in the country was also highlighted in addition to pointing out lack of training facilities, which were important for the young scientists in developing a scientific approach towards medical matters. The Committee, therefore, recommended that research activities should be encouraged in medical colleges saying further that the important branches of medicine included under the purview of IRFA. The Committee observed that a full-time Secretary should be appointed for the efficient management of the diverse functions and activities of IRFA. The Committee had also recommended the formation of a central organization for undertaking, promoting and coordinating medical research in India on similar pattern as pursued and accomplished in UK, USA, France, Germany and Canada. The credit for the implementation finally went to the first National Government headed by Pandit Jawaharlal Nehru.

After the attainment of Independence, many important changes were brought about after a patient wait in re-structuring the Indian Research Fund Association and its activities. Three years later the consolidation of work and expanding the activities of the Association to other branches of medicine and health were accomplished. Subsequently, the important recommendations of the Bhore Committee were taken up for implementation; one of which was the appointment of a full-time Secretary at IRFA. Dr. C.G. Pandit became the first

full-time Secretary of the Indian Research Fund Association, in 1948. Structural changes, viewed as more prominent than others, rolled on steadily. Acting on the recommendations of the Bhore Committee, the Government of India re-designated the Indian Research Fund Association as the Indian Council of Medical Research in the year 1949. Dr. Pandit assumed charge as the first Director of the Indian Council of Medical Research. The role of ICMR was considerably broadened with enlarged scope of functions and responsibilities. The dream of a central research institute had finally come true culminating in the start of a new era in medical research in India.

Another aspect that was gradually assuming importance was the transformation in the public health purview with regard to industrial health, environmental and sanitation, psychiatric medicine, maternal and child welfare, study of blood disorders, study of cardiovascular diseases -particularly ischemic and coronary heart diseases, and dental diseases apart from research into infectious diseases. The Bhore Committee had also highlighted the absence of research work in Medical Schools and universities as one of the foremost concerns for public health and medical research in India. However, as early as 1945, IRFA had already appointed a Clinical Research Advisory Committee for paying greater attention to clinical research and its expansion in medical colleges and universities. Annual meetings of the Advisory Committees and the Scientific Advisory Board were purposefully held in various medical colleges, by rotation. The Council started a programme for training junior members of the staff of medical colleges in methods of research. It also set up several units such as the Drug Research Units, Polio Research Unit, Cardio-vascular Diseases Research Units, *etc.* in several medical colleges. The Council also continued to support ad-hoc projects, united to a more specific nature of inquiry, from eminent members.

INTRAMURAL RESEARCH

ICMR carries out intramural research through its institutes/centres. Of 32 institutes/centres 17, deal with communicable diseases and coordinated by Division of Communicable Diseases; 7, with non communicable diseases (NCDs) and are coordinated by Division of NCD; 2, deal with diseases related to reproductive and child health and are coordinated by Division of RCH; 3, deal with diseases related to nutrition and are coordinated by Division of Nutrition and 3, deal with diseases related to basic medical sciences and are coordinated by Division of BMS.

Centre for Research in Medical Entomology (CRME), Madurai

Vector-Borne Diseases

Lymphatic Filariasis

To assess the operational feasibility of integrated vector control (IVC) at community level, in augmenting the effectiveness of MDA for the suppression of LF on a large scale and to determine the cost effectiveness of the intervention strategies, a study in 36 endemic villages was carried out. Vector control was implemented in 24 villages segregated into two arms.

Reductions of Mf prevalence were ranged from 61 to 76% in the three arms' based on the pre intervention (Table). The significant difference was observed between the pre and post intervention – II ($P < 0.0005$). Antigenaemia survey was carried out in children of age 2-10 years by immune-chromatographic (ICT) test kit. Entomological evaluation revealed the overall per man hour density of female *Cx. quinquefasciatus* as 11.61, 5.99 and 4.38 in MDA alone, MDA+EPS and MDA+EPS+PIC arm villages, respectively. Overall PMH declined by 13%, 54% and 75% in three strategy arms respectively. Significant difference was recorded in pre and post intervention – III of both VC arms. The range of infection rate was 0.19 to 0.45 in the three strategy arms. The infectivity rate was 0.03% in MDA alone arm whereas it was found to be nil in MDA+EPS and MDA+EPS+PIC arm villages, respectively (Fig.).

Table: Microfilaraemia prevalence in the 36 selected villages (All age groups)								
Intervention strategy	Base line (February 2009)		Pre Vector Control (February 2010)		Post Vector Control - I (February 2011)		Post Vector Control - II (February 2012)	
	No. Screened	Mf rate (%)	No. Screened	Mf rate (%)	No. Screened	Mf rate (%)	No. Screened	Mf rate (%)
MDA alone	2853	2.70 ^{a,x} (2.15-3.34)	3249	3.76 ^{b,x} (3.14 - 4.45)	3093	2.00 ^{a,d,x} (1.55 - 2.54)	2924	1.47 ^{c,d,x} (1.09 - 1.97)
MDA+EPS	2181	2.48 ^{a,x} (1.88-3.19)	2187	3.66 ^{b,x} (2.93 - 4.45)	2146	1.91 ^{a,c,x,z} (1.39 - 2.55)	2279	1.36 ^{c,x} (0.96 - 1.92)
MDA+EPS+PIC	2063	2.18 ^{a,x} (1.61-2.88)	2232	2.82 ^{a,x} (2.19 - 3.57)	2202	1.18 ^{b,c,y,z} (0.79 - 1.70)	2468	0.69 ^{c,y} (0.43 - 1.1)
^{a b c d} Comparison between year, the values followed by the same letter do not differ significantly from each other ($P > 0.05$)								
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Centre for Research in Medical Entomology (CRME), Madurai

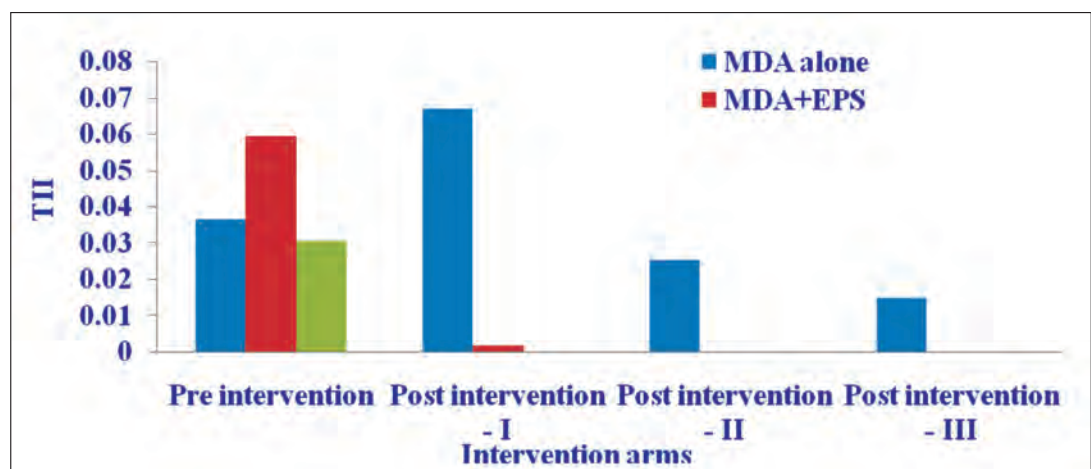
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Impact of vector control on Transmission intensity index in three strategy arms

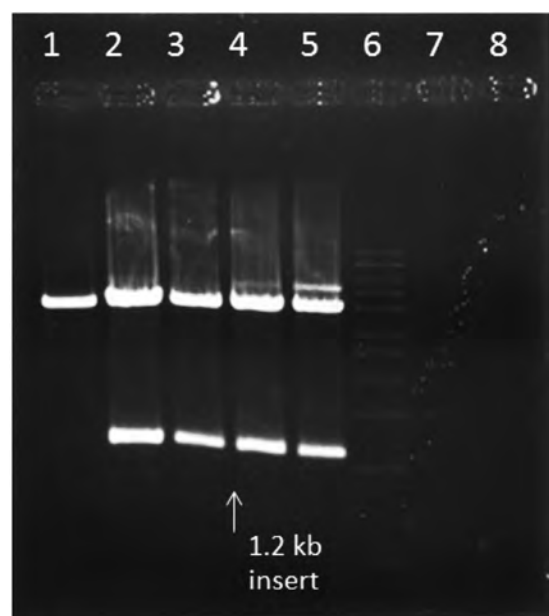
National network for genotyping of human filarial parasite, *Wuchereria bancrofti* from different endemic areas was carried out following standard procedures. Genomic DNA was isolated from a pool of 100 microfilariae picked up from the stained slides. The Internally Transcribed Spacer- Full Length (ITS-FL) gene and Abundant Larval Transcript-2 (ALT-2) gene were amplified using gene specific primers. The PCR products were ligated into TOPO sequencing vector and cloned into *E. coli* cells. Plasmids were extracted from the positive clones and the presence of inserts was confirmed by restriction digestion with EcoRI enzyme (Fig.). These plasmids will be sequenced further to study polymorphisms.

Japanese Encephalitis

JE virus activity in Cuddalore district was continuously monitored and species succession of vector mosquitoes recorded in the study villages of Cuddalore district. *Culex tritaeniorhynchus* (29.29%) the primary vector of JEV, was taken over by *Cx. gelidus* (61.88%) which is vital in disease transmission spectrum.

The ground information such as vector density, meteorological data, physico-chemical parameters of the breeding area were collected and submitted for developing RS-GIS based model to forecast JE vector Abundance and Transmission risk in Cuddalore district. The physico chemical parameters such as salinity, pH, Temperature, TDH, conductivity, alkalinity, hardness, fluoride, nitrate, nitrites, dissolved oxygen etc. were analyzed.

A study was undertaken on the JE virus transmission dynamics in Tirunelveli endemic zone, Tamil Nadu and its implication for the occurrence of impending JE outbreaks in future. A total of 6193 adult mosquitoes were collected, belonging to 23 species of mosquitoes from four villages namely Magiladi, Senthimangalam, Kuthalaperi and Ariyanayagipuram



Confirmation of ITS-Full length inserts in TOPO vector restriction digestion with Eco R1

in Tirunelveli district. *Culex tritaeniorhynchus* was the predominant species in all the study villages (4442 numbers). *Cx. gelidus* (689) and *An. subpictus* (477) were the next predominant species. The other JE vector species namely *Cx. vishnui* was very few in number (80). There was no *Cx. pseudovishnui* collected from the study villages.

CRME team visited Tirunelveli district from 23rd May 2012 to 26th May 2012 and carried out Entomo-sero-virological survey in the affected area. *Ae. aegypti* was the predominant species among collected.

In addition to that *Ae. albopictus* and *Ae. vittatus* were also collected. Mosquito samples collected from West Bengal and screened for viral infection by ELISA. The results revealed 3 pools of *Cx. tritaeniorhynchus* 1 pool of *Cx. vishnui* 1 pool of *Cx. pseudo vishnui* 3 pools of *Cx. gelidus* 1 pool of *Cx. fuscocephala* 2 pools of *Ma. uniformis* 1 pool of *Ma. annulifera* and 1 pool of *Cx. quinquefasciatus* were found positive for JEV. 21 pools of vector mosquitoes collected from Gorakhpur district, UP were screened and found negative for JEV.

Entomological survey conducted during the pre monsoon (July'2012 and August) and post monsoon (December and January 2013) periods in the index villages of Thanjavur district showed a total of 3961 mosquitoes belongs 15 species, which comes under 6 genera had been collected during dusk hours. *Cx. tritaeniorhynchus* was the dominant mosquito with the PMH 85.83 and in its composition was 78.01% followed by the average PMH 8.78 of *Cx. gelidus* (7.98%) For Anophelines, the PMH was 13.00 with species composition of 11.81%, along with *An. subpictus* PMH was 11.19 with species composition of 10.17% others were PMH was 1.81 with species composition of 1.64%. Only one pool of *Cx. tritaeniorhynchus* which was collected during July 2012 was found positive for JEV.

Dengue

The burden and economic cost of dengue in India: a study at major teaching hospitals and nearby ambulatory institutions

A multi-centric national level study was conducted to understand the true burden of dengue infection and to analyse its impact in terms of economic cost of dengue illness in India. Country was alienated based on geography and socio-cultural diversity into five regions *i.e.*, North, South, East, West and Central India. There are two major teaching hospitals from each region, a total of ten hospitals were selected. This study is one of the large scale study which will help the policy makers in future to understand the disease burden and formulate effective public health policy towards dengue prevention and management.

Monitoring susceptibility status of vectors of various arthropod-borne viral diseases against different insecticides was carried out. *Aedes aegypti* exposed for 30 minutes to 5% malathion was 100% susceptible; 48% to 0.04% dieldrin. *Culex tritaeniorhynchus* exposed for 30 minutes to 5% malathion, 1% fenitrothion, 0.4% dieldrin was 100%, 10% and 49.33% susceptible respectively.

Mosquito Taxonomy and Biodiversity

CRME established a unique mosquito museum, which contains a total of 233 species from >71000 specimens belonging to 33 genera and 30 subgenera. The salient findings include four new species and nine underscribed stages of mosquito species. The CRME has recently described a new species, *Toxorhynchites tyagii* and has brought on record 105 species. Of these, six species *Armigeres* (*Armigeres*) *theobaldi* Barraud, 1934, *Lutzia* (*Matalutzia*) *vorax* Edwards, 1921, *Orthopodomyia flavicosta* Barraud, 1927 *Stegomyia flavopictus* Yamada

1921, *Toxorhynchites (Toxorhynchites) albipes* Edwards 1992 are additional records to the CRME museum; with one new area record, i.e., *Toxorhynchites (Toxorhynchites) albipes* and redescription of *Heizmannia (Heizmannia) chandi* n.sp. It was recorded in Gudalur forest area in Western Ghat *Toxorhynchites (Toxorhynchites)* region) as well as northern west Bangal districts.

Mosquito fauna survey was carried out in five hill ranges viz., Nagercoil, Tirunelveli, KMTR, Srivilliputtur & Palani hills of Western Ghats. A total of 107 mosquito species (20 genera & 20 subgenera) were recorded in different hill ranges. Studies on mosquito taxonomy and systematic emphasis on revision of FBI Monographs on Indian mosquito fauna at present inventory in India enlisted a total of 403 species under 50 genera & 43 subgenera.

Outbreak Investigations in Tamil Nadu

An outbreak of suspected virus aetiology was investigated in certain rural areas of Melur Taluk in Madurai district, and Ramnad district Tamil Nadu, during the last week of November 2012. In addition to the arboviral infections, 5% of the sera (4/75) were reactive to *Orientia tsutsugamushi* by IgM ELISA test. Dengue virus aetiology was confirmed by nucleotide sequencing. The results were communicated to the Tamil Nadu health department for implementing appropriate vector control strategies.

Enterovirus Research Centre (ERC), Mumbai

Poliomyelitis Surveillance

Wild poliovirus transmission in India and neighbouring countries like Bangladesh, Sri Lanka and Myanmar is detected by testing stool samples from Acute Flaccid Paralysis (AFP) cases at Enterovirus Research Centre, Mumbai. In 2013, a total of 8102 stool specimens were collected from 4038 AFP cases reported in Maharashtra, MP, Goa and Chhattisgarh and tested until the end of November 2013, where as in 2012 we received stool samples from 2897 AFP cases from Maharashtra only. The samples were tested for the presence of wild and vaccine derived polioviruses. Polioviruses isolated in India, Bangladesh, Sri Lanka and Myanmar were also received at our Centre for maintaining poliovirus bank, reconfirmation of the results and further characterization. A total of 4572 poliovirus isolates were received until November 2013. Wild poliovirus has not been isolated in India in 2013 till date. India has remained free from wild poliovirus since January 2011. Finally India is declared Polio free in February 2014.

Year	Total AFP cases tested	Polioviruses positive cases	NPEV cases
2012	2897	90 (3.1%)	783 (27.02%)
2013	4038	95 (2.47%)	1313 (32.50%)

Detection of Vaccine derived polioviruses (VDPV)

India has been successful in maintaining wild poliovirus free status since January 2011, a major challenge faced by the polio surveillance programme is vaccine-derived poliovirus (VDPV). VDPVs are viruses from the oral polio vaccine (OPV) which regain wild-type transmissibility and pathogenicity resulting in large outbreaks. A total of 162 discordant isolates were molecular characterized by complete VP1 sequencing. Type 2 VDPVs were isolated from 5 AFP cases during the period of January to November 2013, out of which 2

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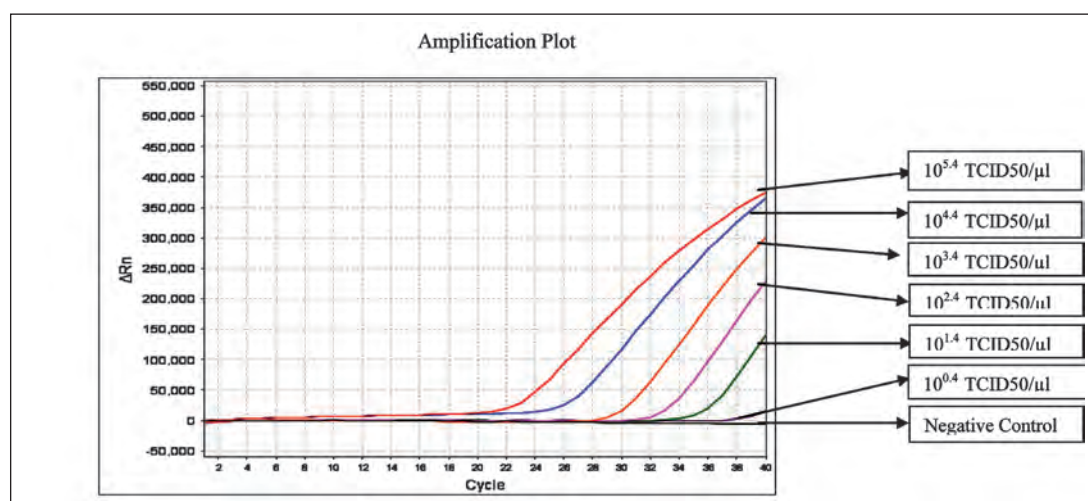
cases were from Maharashtra and 1 each from Bihar, Orissa and Delhi. Two of these cases (1 each from Maharashtra and Delhi) were identified as iVDPVs (immunodeficient VDPV).

Supplementary Surveillance for Detection of Wild Poliovirus

Supplementary surveillance was established at the centre in the year 2001 for detecting presence of wild poliovirus in Mumbai. The surveillance was later expanded to Delhi, Kolkata and Patna in the year 2010 and 2011. In 2013, surveillance was further expanded in two additional states - Punjab and Ahmedabad. No wild poliovirus could be detected from 132 sewage samples collected from the three high risk blocks in Mumbai and 82 samples from Patna. Two poliovirus type 2 VDPVs were detected in sewage samples, one each in Mumbai and Patna. In addition, one poliovirus type 3 VDPV was detected in Patna. The results indicate absence of wild poliovirus circulation in India.

Real Time Reverse Transcription PCR Assay for detection of wild type 1 poliovirus

The real time RT-PCR assay used for intratypic differentiation of polioviruses identifies Sabin strains. A negative reaction with primers specific for Sabin vaccine strains is used as an indicator for the presence of wild poliovirus. Thus wild polioviruses remain undetected in samples containing homotypic mixtures. An assay was required which should be wild poliovirus specific. Real time RT-PCR assay for detection of wild poliovirus type 3 has already been developed at our centre. We have also developed an assay specific for wild poliovirus type 1 (WPV1) using wild polioviruses isolated in India. The assay detected WPV1 in the presence of large excess of Sabin 1, 2 and 3 and non-polio Enteroviruses (Fig.).



Titre of undiluted WPV1 stock : $10^{5.4}$ /μl
Sensitivity of WPV1 specific rRTPCR assay.

Enterovirus Surveillance in Healthy Children in Eastern UP, Gorakhpur

The prevalence of HEV infections was studied in healthy children in JE/AES infested areas of Gorakhpur, UP during September and October, 2013. The most commonly detected serotypes included CVA4, EV99, CVB1, E1, E24, E33, CVA13, CVA17 and CVA20. Newly identified HEV serotypes (EV76, EV89, EV90, EV91, EV99, EV101, EV102, EV107) were also detected.

Virological Investigations of Hand Foot and Mouth Disease (HFMD) and Herpangina (HA)

Hand foot-mouth disease (HFMD) and Herpangina (HA) are closely related but clinically distinct childhood infections caused by Human enteroviruses (HEV). HA is caused by multiple serotypes of Coxsackie viruses including CVA2, CVA4-6, CVA8-10, CVA24, and EV71 where as HFMD is mainly caused by EV71 and CVA16. However in recent years CVA6 has also been reported to cause HFMD outbreaks worldwide.

HFMD and HA outbreaks occur simultaneously between May to November every year in Thane, Maharashtra. The outbreaks have been clinically, epidemiologically and virologically studied by virus culture and molecular diagnostic methods to identify the etiological agents. Multiple HEV serotypes were isolated from clinical samples of HA cases. CVA4 and CVA10 were the most predominant serotypes isolated during HA outbreaks in 2011 and 2013 where as CVA2 and CVA5 were the main serotypes causing HA in 2012. HFMD was mainly caused by CVA16 in 2010 and 2013 where as CVA6 caused HFMD outbreaks in 2009, 2011 and 2012 in Thane. The study suggested cyclic pattern of HA and HFMD outbreaks caused by different EV serotypes.

Table 1: Enterovirus etiologies of HA cases in Thane (2011-2013)

EV serotypes	2011	2012	2013
Most Predominant	CVA10 (43.3%) CVA4 (28.3%)	CVA2 (51%) CVA5 (26.4%)	CVA10 (46.4%) CVA4 (35.7%)
Less Predominant	CVA2, CVA6, CVA8, E12, CVB4, CVA21 (28%)	CVA10, CVA6, CVA4, CVA8, CVB3, CVB4 (22.6%)	CVA8, CVA16, E6 (17.8%)

Table 2: Enterovirus etiologies of HFMD cases in Thane (2009-2013)

EV serotypes	2009	2010	2011	2012	2013
Most Predominant	CVA6 (61%)	CVA16 (64.3%)	CVA6 (41%)	CVA6 (40%)	CVA16 (96%)
Less Predominant	CVA16 (3%)	CVA6, CVA8 (2.8%)	EV71 (4.5%)	CVA2, EV71 (6%)	E6 (4%)

Outbreak of Acute Gastroenteritis due to Norovirus in South Mumbai

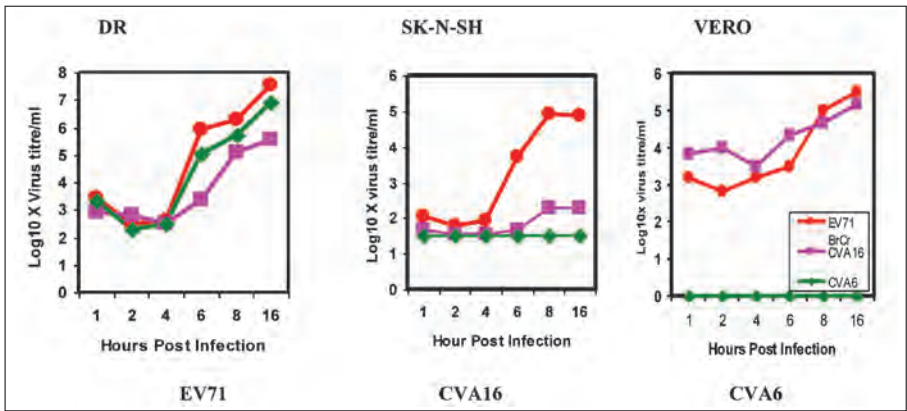
During June-July, 2013 an outbreak of acute gastroenteritis was observed in children from high socio economic families (1-2 years of age or younger, median age = 18 months) in a paediatric clinic in south Mumbai. There were no hospitalizations and the outbreak subsided by August. The study highlighted that NoV genogroup GI and GII were responsible for causing outbreak in the young children from high socio economic families.

Host virus interaction and significance of apoptosis in infections by viruses causing Hand-Foot and Mouth Disease (HFMD)

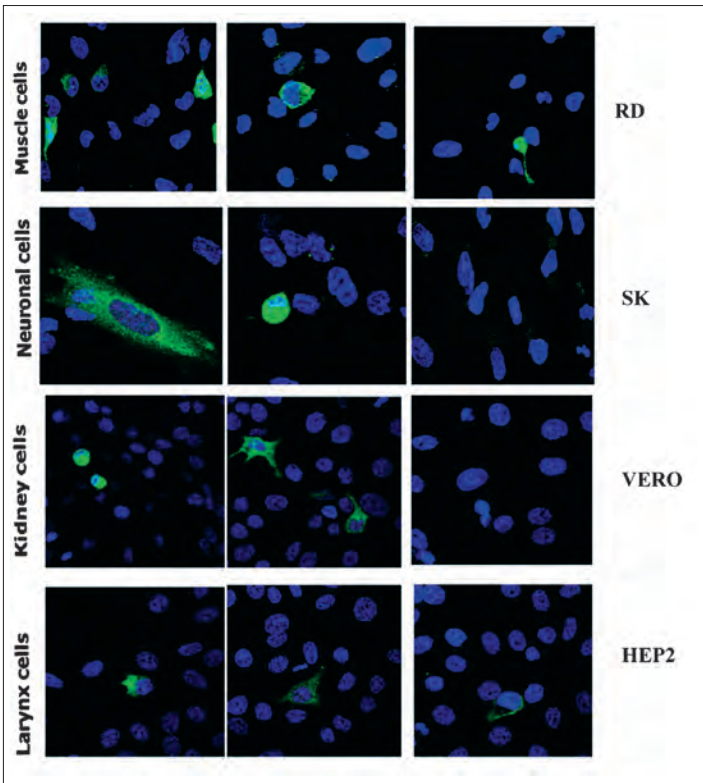
Coxsackievirus A16 (CVA16) and Enterovirus 71 (EV71) are the major etiological agents of HFMD. CVA16 and CVA6 are the major pathogens of HFMD in India. Although genetically close to each other EV71 leads to severe fatal neurological complications but not CVA16 and CVA6. Mostly these viruses cause asymptomatic infection with blisters on hand, foot and mouth and do not cause AFP.

We studied the host pathogen interaction of CVA16 and CVA6 isolated at ERC and compared that with EV71 prototype strain (EV71 BrCr).

EV71 replicates well in all the three cell lines, CVA16 replicates in RD and vero cell lines but shows delayed growth in neuronal cells which is detectable after first cycle of replication. CVA6 replicates only in RD cell line and failed to grow in Vero and SK-N-SH cell lines. None of the viruses grew in HEp2 cells. Confocal microscopy study to detect the viral antigen corroborated the data where in EV71, CVA16 and CVA6 viral antigens could be seen in RD cells at 8 hpi (Fig.). EV71 and CVA16 antigens were observed in SK-N-SH and Vero cells also at the same time point but not CVA6, corroborating the single step growth curve data. Although none of the viruses grew in HEp2 cells, slight patches of antigen could be seen for all three viruses at 8 hpi. Quantification of viral RNA by real time PCR showed presence of EV71 and CVA16 viral RNA in all the four cell lines at 8 hpi. CVA6 RNA could not be detected in SK-N-SH, Vero and HEp2 cell lines confirming that CVA6 viruses do not grow in SK-N-SH, HEp2 and Vero cells. The findings will provide insight into the nature of virulence and pathogenesis of CVA16 and CVA6 infection as compared to EV71.



Single step growth curve of EV71 BrCr (red lines), CVA16 (pink lines) and CVA6 (greens lines) in human Muscle, Neuronal and Kidney epithelial cell lines



Confocal microscopy of human cell lines infected with HFMD causing viruses at 8 hours post infection (8 hpi).

Genetic Research Center (GRC), Mumbai

Genetic Research Center runs an outpatient clinic for clinical diagnosis, counseling, and testing for patients with genetic disorders. A total of number of 512 new patients were registered and a total of 1536 patient follow up visits were recorded during the period Jan 2013 till date . The spectrum of diseases could be classified into single gene disorders (30 %), recurrent reproductive losses (32%), chromosomal disorders (10 %), and non- genetic conditions mimicking genetic disorders (28%).

Prenatal Diagnosis Component

Prenatal counseling and diagnosis was offered in 27 cases till date. Indications include Tay Sachs disease (n=5), Sandhoff disease (n=5), Hunter disease (n=1) genetic skin disorders (n=3), skeletal dysplasia (n=6), Rett syndrome (n=3), spinal muscular atrophy (n=2), lipoid adrenal hyperplasia (n=1), Duchenne muscular dystrophy (n=1). Seven fetuses were found to be affected and parents chose discontinuation of pregnancy thereby reducing the burden of genetic disease.

Studies on Inborn Errors of Metabolism

The inborn errors of metabolism include lysosomal storage diseases (LSD) (n=72), organic acidemias (55) and Wilson disease (22). LSDs included Tay Sachs disease (28), Sandhoff disease (12), Pompe disease (5), metachromatic leukodystrophy (8), GM1 gangliosidosis (5), Morquio disease (4), Maroteaux Lamy syndrome (2) and Hunter disease (2). Founder mutation p.E462V was identified in HEXA gene in patients with Tay Sachs disease from the Gujarat State. Majority of mutations were point mutations whereas in Sandhoff disease majority of mutations were in form of private mutations (large indels). Most mutations were nonrecurrent. Molecular study of organic acidemias included patients with glutaric aciduria (n=21), maple syrup urine disease (n=17), propionic academia (n=10), HMG-CoA lyase deficiency (n=5) and tyrosinemia (n=5). Out 21 families with glutaric aciduria, 16 families screened positive for *GCDH* gene mutation. R402W, the most common mutation in Caucasians, in whom it shows an allele frequency of approximately 40%, was found only in one Indian patient. Complete sequencing analysis revealed sixteen different mutations in twenty one families and one common mutation viz. p.L179R found in two different families. We identified known pathogenic mutations c.536T>G (p.L179R), c.1015A>G (p.M339V), c.1298C>T (p.A433V), c.1205G>A (p.R402Q).

We also identified ten novel mutations. Molecular study of *ATP7B* gene in patients with Wilson disease (n=22) identified mutations in all patients. The mean liver copper value of the patients under study was calculated to be 119.27 ug/g and mean 24hrs urinary copper was calculated to be 216 ug. The only recurrent mutations was p.T977M in two unrelated patients with neurological phenotype. Other mutations include p.P1352L, c.3146delC, p.D1215H, IVS6+1delG, p.L1209P, c.365_366delAG and p.G1149R.

Studies on Genodermatoses

The spectrum of genodermatoses (genetic skin diseases) observed were ichthyosis (n=16), xeroderma pigmentosum (n=9 families), Griscelli syndrome (n=10 families), epidermolysis bullosa (n=15), ectodermal dysplasia (n=10), dyskeratosis congenita (n=5). Mutations were observed in *TGM1*, *XPA*, *XPC*, *RAB27A*, *COL7A1*, *DKC1* genes. Notably, a founder mutation was identified in *XPA* gene in patients with neurological type of xeroderma pigmentosum from Maharashtra. The panethnic mutation p.R184X was also identified in Griscelli patients.

Studies on X-linked Mental Retardation

Males with autism were screened for Fragile X using a Polymerase Chain Reaction (PCR) based assay. Three unrelated males were found to be positive out of a total of 125 screened. They showed the typical facial features, hyperactivity and autistic features.

Rett syndrome is the commonest cause for X-linked mental retardation in females. Mutation analysis was done in 90 patients with Rett syndrome. The most frequent pathogenic changes were: missense p.T158M (11%), p.R133C (7.4%), and p.R306C (7.4%) and nonsense p.R168X (11%), p.R255X (7.4%) mutations. Two novel mutations namely p.385-388delPLPP present in atypical patients and p.Glu290AlafsX38 were present in a classical patient of Rett syndrome. Sequence homology for p.385-388delPLPP mutation revealed that these 4 amino acids were conserved across mammalian species. This indicated the importance of these 4 amino acids in structure and function of the protein.

Institute for Cytology and Preventive Oncology, (ICPO), Noida

The Institute has mandate of cancer prevention as its main goal. This is being achieved by following different action lines keeping in mind the multistep process of cancer development. Main strategy to prevent cancer is to find out cancer causative factors like environmental, behavioral, genetic and their interaction, and managing such factors to prevent cancers. Another strategy is to detect cancer early by way of finding molecular genetic markers of cancer that has obvious role in cancer prevention by way of minimal treatment and management. The activities are directed towards: -

1. Epidemiological studies and early cancer detection activities
2. Genetic susceptibility studies
3. Genetic markers

Screening for Cervical Cancer

ICPO developed a magnifying device named "Magnivisualizer. A non disclosure agreement and an agreement on technology transfer were signed between ICMR and M/S Swart Scientifics.

To get the feedback from the users about AV Magnivisualizer in relation to Suitability and user friendliness of AV Magnivisualizer instrument in the hands of Gynaecologist, Dentist and Para-medicals (nurses).

A study was carried out in Obs and Gynae Department of Lok Nayak Hospital , New Delhi, BARASAT Cancer Centre, Kolkata, LRM Medical College, Meerut, Mahatma Gandhi Institute of Medical Sciences, Jaipur, Tripura Medical College, Agartala, Tripura Institute of Paramedical Sciences, Agartala , Institute of Obstet. & Gynaecology, Govt. Maternity Hospital, Egmore, Chennai and Dental department of GTB Hospital, Delhi, Mahatma Gandhi Institute of Medical sciences, Jaipur and Sai Center, Noida.

The utility survey for both cervical and oral cavity examination clearly revealed that 95 to 100% of the examiners were comfortable with the instrument and were satisfied with different parameters of the examination. The comparative performance of Magnivisualizer vs. tungsten light for the examination of the cervix (20.5% vs. 12.7%) and oral cavity (24.8% vs. 16.5%) revealed that Magnivisualizer detected 1.5 to 1.6 times more lesions compared to tungsten light. Ninety percent of the cervical lesions detected by Magnivisualizer were

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also detected positive by cytology (LSIL +). Ninety three percent of oral lesions detected by Magnivisualizer were also detected by cytology (Benign, dysplastic, or cancerous lesions). Magnivisualizer could differentiate oral lesions most efficiently (95%) vs. Tungsten light (44.3%).

Magnivisualizer has been found to be a good option for examination of cervix and oral cavity for early detection of pre-cancers and cancerous lesions.

A field based study at Dadri CHC, completed earlier, for studying the comparative performance of the three modalities for screening cervical cancer using VIA, VILI and cytology involving about 5000 women of age group 30-60 years Based upon this experience, it is planned to have permanent centers at different places in UP around NOIDA. Detection of HPV will be made part of screening using various methods like PCR, HCII and other available approved commercial kits utilizing the experience of our earlier concluded field based study for evaluation of new test kit (Care HPV) for detection of HR- HPV (High Risk 14 HPV types).

Molecular Screening for Cervical Cancer

The major activities and achievements in the field of molecular screening of cervical cancer are as given below:-

- I. ICPO has been recognized as a National Referral Centre for HPV & Cervical Cancer Screening.
- II. ICPO has developed Multiplex PCR to detect various HPV types in one PCR reaction saving biological material, cost and time.
- III. Detection of variant HPV types in Indian population for the purpose of developing HPV vaccines.

Basic Molecular Understanding of Cervical Carcinogenesis

Development of Naturally Occurring Plant-based Anti-cancer Compound-Activity-Target (NPACT). NPACT has information on 1574 experimentally validated plant derived natural compounds exhibiting anti-cancerous activity, to facilitate drug discovery in the area of cancer by providing researchers a resource for screening as well as making available scaffolds for design of novel drugs. It provides information on their structure, *in vitro* and *in vivo* data, inhibitory values, various properties (physical, elemental and topological), cancer types, cell lines, protein targets, commercial suppliers and drug likeness of compounds.

Targeting of EGFR by curcumin: Epidermal growth factor receptor is a well established target for cancer therapy. A molecular docking investigation of curcumin analogues was carried to discover potent EGFR inhibitors. Molecular dynamics simulation showed that a condensate of curcumin can be used as starting blocks for developing effective leads capable of inhibiting EGFR.

Identification and Characterization of Stem Cells in Precancer and Cancer of the Uterine Cervix: Contribution of HPV in the Development and Progression of the Disease: Recent studies have suggested that only a small subpopulation of cells within solid tumors are capable of self-renewal and of generating tumors, which has led to a new model of tumorigenesis called the Cancer Stem Cell (CSC) concept. Our initial investigation addressing a phenotypic and functional characterization of such cells in cervical cancer cell lines have revealed presence of cervical cancer-specific cancer stem cell in HPV positive cell lines only. We studied Notch signaling pathway which is mechanistically associated with molecular

characterization of stem cell by regulating their self-renewal behavior. Results provide leads demonstrating essential role of HPV in cancer stem cell signals to promote disease progression via its interaction with Notch signaling.

Investigations on Crosstalk between Stem Cell Signaling and HPV Genes/Oncogenes in Cervical Carcinogenesis: The present study is designed to investigate the role of GLI activation and its expression related to the HPV genes/oncogenes expressions and its functional contribution in the development of cervical cancer as GLI is thought to play an important role in maintaining cancer stem cells. The expression and DNA binding activity of GLI is found to increase in HPV positive cell lines as compared to HPV negative cell lines. Moreover, the inhibition of GLI using its specific inhibitor, cyclopamine, or by specific siRNA is shown to reduce the expression of HPV.

Transcriptional targeting of Human Papillomavirus Gene Expression by Herbal Derivatives: In an effort to discover potent anti-HPV activities, we examined an anti-cancer and anti-HPV activity in the leaves of *Bryophyllum pinnata* (*B. pinnata*) of Indian origin which is a common medicinal plant used in traditional medicine of India and of other countries. Investigations of anti-viral activity of the extract and its fraction revealed a specific anti-HPV activity on cervical cancer cells through dose-dependent inhibition of constitutively active AP1 and expression of AP1-family proteins specifically c-Jun and c-Fos which are the components of canonical functional forms of AP1.

Detection of Human Papillomavirus Infection in Cervical Scrapes in Tribal Population of Andaman and Nicobar Islands: The present study has been designed to determine the prevalence of HPV infection in the tribal population of A&N and to find out the most dominant HPV types present in this population. Results shows an overall 6% prevalence of HPV in A&N population and HPV16 was found to be the leading HR-HPV types. Though the data is based on a very small sample size which is being improved further, it is the maiden report indicating a moderate HPV prevalence and a similar HPV type distribution in this geographically and culturally distinct population as in main land of India.

Lung Cancer

Therapeutic Strategy for Lung Cancer

Epidermal Growth Factor Receptor (EGFR) is shown to be implicated in the development and progression of Lung cancer due to mutations in the tyrosine kinase domain (TKD). We predicted deleterious non-synonymous Single Nucleotide Polymorphism (G719A, P733L, V742A, S768I and H773R) of EGFR gene that disrupts the wild conformation of EGFR-TKD and causes cancer. Binding interaction studies of EGFR inhibitors suggested that gefitinib, the clinically used Lung cancer drug can be administered for combating cancer in tumors harboring these mutations.

Breast Cancer

BRCA1 Expression Status in Relation to DNA Methylation of BRCA1 Promoter Region in breast cancer: The present study to understand the biological role of BRCA1 in sporadic breast cancers, the relationship between DNA methylation of the *BRCA1* promoter region and BRCA1 expression was studied using molecular biological and immunohistochemical methods. These findings indicate that *BRCA1* methylation might greatly influence its expression and BRCA1 expression might play an important role in sporadic breast cancers.

Expression of Breast Cancer susceptibility Genes BRCA1 and BRCA2 Proteins and their Correlation with Clinical Staging in Breast Cancer: The aim of the study was to evaluate expression level of BRCA1 and BRCA2 proteins in sporadic breast cancer cases to determine the functional role of these genes. The present study shows down-regulation of BRCA1 protein during breast carcinogenesis and in a subset of cases, decline in BRCA1 expression may be associated with potentially compensatory increase in BRCA2 protein, which may depend on grade of tumor as well as menopausal status of the patients.

Oral Cancer

This study evaluates the influence of genetic polymorphism of GSTM1 and GSTT1 gene loci on esophageal cancer risk in Assam and Delhi from India. DNA from blood samples of esophageal cancer cases (203,112) and controls (286,150) from Assam and Delhi, respectively, were extracted. GSTM1 and GSTT1 polymorphisms were analyzed by multiplex PCR procedure. Cancer development is not only due to exogenous or endogenous carcinogens but depends on their interaction with genes that are involved in the detoxification of these carcinogens.

ICMR Biobank

Designing a Biobank for Biological Samples Collected from a Mega Study on Acute Coronary Events in Indians

The aim of this study is to improve strategies for early diagnosis, prevention and treatment of coronary artery disease through development of novel biomarkers specific for the Indian population. Till date, samples from 7400 subjects have been received at ICPO, Noida and processed by using a set of standard operating protocols (SOPs) in the laboratory.

DNA vaccines against HPV

Human papillomavirus (HPV) is a causative factor in the etiology of cervical cancer and HPV type 16 is the most prevalent genotype. Currently, virus- like particle (VLP) based prophylactic HPV vaccines, 'Gardasil' by Merck and 'Cervarix' by GSK have been developed and marketed. Despite showing great promise, the wide scale use of these vaccines is of particular concern in India, mainly due to its high cost and lack of therapeutic utility. Therefore, there is a need to develop indigenous low cost alternative Second Generation Vaccine for HPV, preferably DNA vaccine. Instead of prototype, Indian specific HPV-16 DNA based variant constructs will be suitable for the generation of specific immune response in Indian population. Vaccine is being developed and its immunogenicity is being tested in animal model.

National Aids Research Institute (NARI), Pune

Development of a Culturally Tailored Scale to Measure Domestic Violence (DV) among married women in Pune, India

This study aims to develop a culturally-tailored scale to measure domestic violence (DV) and control among married women in India. The study is being conducted in two phases: Phase I (qualitative/formative) and Phase II (quantitative). Phase I of the study was completed and key themes identified through key informant interviews and focus group discussions which include different DV perpetrators; control, sexual and physical domains. Phase II study is ongoing to define DV with in Indian context, redesigning and validating Indian Family Violence and Control Scale (IFVCS). Instrument was pretested and the 63-items pilot

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scale consisting of 14 control items and 49 violence items was used to interview 630 women in this ongoing study. The scale shows high reliability score of 0.88. This scale can be used to evaluate interventions for domestic violence.

Expanded Safety and Adherence Study of a Nonmedicated Intravaginal Ring: Study of the Microbicide Trials Network (MTN 005)

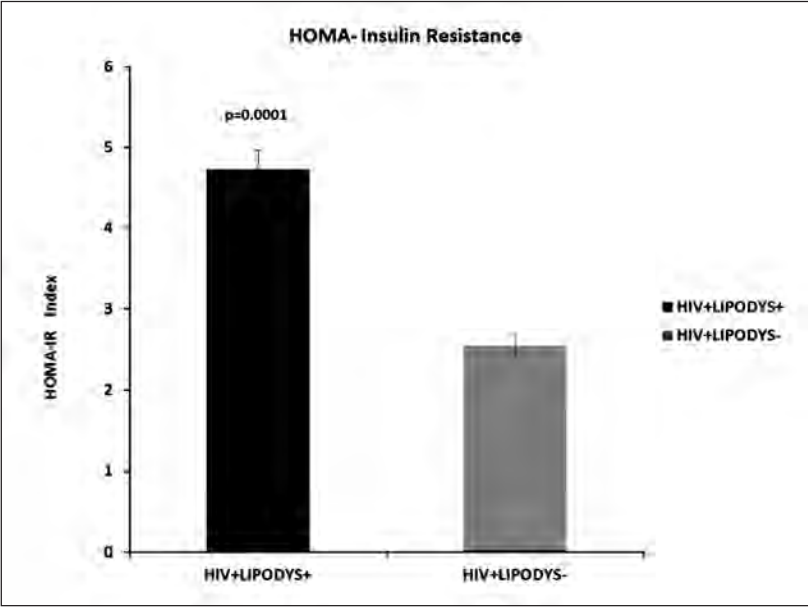
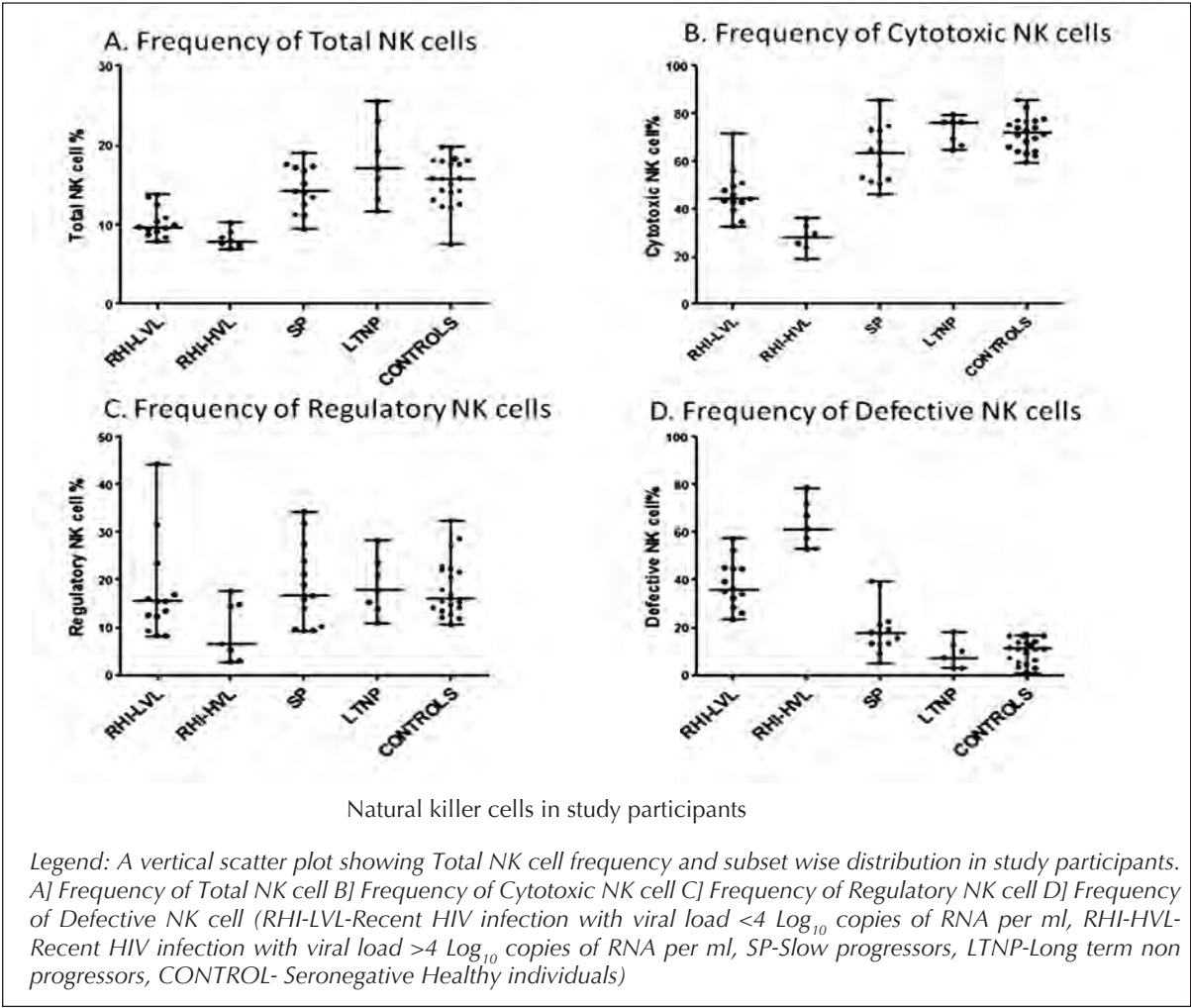
A Multi-site, open-label, two-arm, clinical trial entitled "Safety and adherence study of a non-medicated Intra Vaginal Ring (IVR)" has been completed at National AIDS Research Institute. The safety of the research participants was protected by due vigilance and scientific integrity of the investigators in identifying defects in the study product and by taking appropriate and timely action. All necessary steps were taken to inform the Indian regulatory bodies of the new finding. The NARI site was given an 'Appreciation Award' at the MTN annual meeting at Washington D.C in February 2013 for the role played by the site in protecting participants' safety.

Role of Natural Killer Cells in Recent HIV1 Infection

Changes occurring in the NK cell compartment during early HIV-1 infection and correlation of these changes with HIV disease progression were studied. The patients with Recent HIV infection (RHI) showed lower percentages of NK cells as compared to Long Term Non Progressors ($p < 0.0001$), Slow Progressors ($p < 0.001$), and healthy HIV uninfected controls ($p < 0.0001$). The cytotoxic and regulatory NK cell percentages were significantly lower in RHI as compared with the other study groups whereas the defective NK cells showed significant expansion. The findings indicate that the NK cells may play important role in the early control of HIV multiplication and also in maintaining the disease free status of the HIV infected individuals.

A Pilot Study to Explore the Association between HIV1 Lipodystrophy/ Dyslipidemia and Gene Polymorphisms in the TNF α gene in an HIV1 Patient Cohort in Pune

This case-control study was undertaken to find the association of TNF- α gene in the development of HIV-1 lipodystrophy among HIV infected individuals who have been receiving antiretroviral treatment (ART). The study revealed that expression of TNF- α gene was twofold higher in patients with lipodystrophy as compared to those who did not have lipodystrophy. Insulin resistance was also significantly higher in cases as compared to controls. Carotid intima thickening was observed in the left carotid artery among those who had lipodystrophy. Though Stavudine, one of the most commonly administered antiretrovirals is being phased out in India, those receiving a protease inhibitor based second line ART (excepting Atazanvir based regimen) are more likely to show lipodystrophy and dyslipidemia. The high proportion of patients showing insulin resistance observed in the study can pose challenges in the management of chronic morbidities associated with HIV infection. It may enhance the risk of development of metabolic syndrome.



Insulin Resistance among HIV infected individuals on ART having lipodystrophy/dyslipidemia

Prevalence of Anal HPV Infections and Associated Abnormalities in HIV Infected Women: A Feasibility Study

Rates of cervical and anal HPV infection and abnormal cytology as well as anal cancer are much higher in HIV-infected women. As HIV-infected women live longer with HAART, they continue to be at risk for HPV associated diseases including dysplasia and cancer of the cervix, vulva and anus. An exploratory cross-sectional study was conducted among HIV infected women to assess the prevalence of type-specific anal HPV infection and anal cytologic abnormalities. The recently completed study found that about 10% women were positive for high risk subtypes of anal HPV (which can cause cancer), while overall 15% women showed any anal HPV virus.

NARI - AIDS Rural Research Initiative in Maharashtra (N-ARRIM)

This is a rural initiative by National AIDS Research Institute in collaboration with Krishna Institute of Medical Sciences, Karad and International AIDS Vaccine Initiative (IAVI) at Karad in Satara district of Maharashtra. The centre was inaugurated on 1st December 2012. During 2012-13, various activities were conducted like Poster exhibition; World AIDS Vaccine Day; Week long community awareness and stakeholder sensitization programmes. A Community Advisory Board (CAB) was set-up which has already met twice and has provided valuable inputs. For broader outreach and sensitization on HIV prevention, street plays by professional group were organized in Karad Taluka on 18th May 2013 at different strategic locations. 'Situational Analysis of Satara District' was done to build an in-depth understanding of HIV and broader public health scenario at the project intervention site, which, in turn will provide critical inputs to understand and identify gaps of the major indicators pertaining to Health, Social infrastructure, Economy, Geography and Millennium Development Goals for HIV, TB and Malaria. An 'Awareness Campaign' was organized with the help of poster exhibition, stall installation, information education communication (IEC) distribution, interactive discussion, filling feedback forms.

Attitudes and Practices of Indian HIV physicians with respect to management of HIV sero-discordant couples and the use of 'Early ART' as a prevention method: results from a web based survey of HIV physicians

The WHO guidelines released in June 2013 recommend 'Early ART' to HIV infected individuals if the spouse is uninfected and raised the cut-off for ART initiation to 500 cells/mm³. An online web-based survey among HIV physicians in India was conducted between August–October 2013 to understand attitudes and practices with regards to management of sero-discordant couples in India and awareness of new WHO guidelines for ART. The respondents from eleven states in different parts of India showed a very high awareness of WHO guidelines and evidence related to 'Early ART' and 57% respondents reported that they changed their practices as a result. ART was initiated at CD4 cell counts > 350 cells/mm³ by around 34% respondents and this proportion was much higher if the person had an HIV negative partner. The study showed that there is moderate to high level of experience in management of HIV discordant couples. While the level of appropriate attitudes and practices towards their management were fairly high (around 70%), there is still room for education in this area. A high proportion of HIV physicians felt that providing 'Early ART' to HIV discordant couples would be beneficial to the community. On the other hand a large proportion did not think that Pre-Exposure Prophylaxis (PrEP) was a good public health approach.

Validation of In-house HIV Drug Resistance genotyping assay using Plasma and Dried Blood Spots

Access to antiretroviral therapy in low and middle income countries increased with almost 47% coverage of people eligible for treatment, resulting in substantial decline in deaths related to AIDS during the past decade. To ensure continued efficacy of these drug regimens, WHO recommends monitoring of human immunodeficiency virus (HIV) drug resistance (HIVDR) in HIV-infected patients. *In-house* method using plasma and DBS could genotype HIV-1 group M subtypes.

International workshops conducted at NARI in 2013: Indo US joint workshop on 'HIV Database and Cancer Registry Match'[February 11-13, 2013]

The workshop was organized at National AIDS Research Institute, Pune under the aegis of the Indo-US Joint Working Group by ICMR-India and Office of AIDS Research, USA on 12th and 13th February 2013. Thirty three participants included seven international experts from USA and Italy and experts AIIMS, Tata Memorial Hospital, ART centers of excellence, cancer registries from across India including North East.



Neuro-AIDS workshop (September 24-25, 2013)

This workshop was organised for providing a platform for updating, discussing and exploring the areas for possible collaborations between scientists from India and USA on neuro-AIDS. This was funded by Indo US Science and Technology Forum (IUSSTF). The translational aspect of the study findings to the National programme was the focus of discussions. Speakers of the workshop provided overview of neuroAIDS, shared their own data and also discussed about the future directions in this important researchable area. The presentations, panel discussions, and formal and informal interactions were useful for producing key recommendations regarding priorities for Indo-US research.

The priority recommendations were developing a small screening battery that can be used as a screening tool in the busy clinic settings, developing a battery for illiterate population, conduct studies on cerebrospinal fluid and neurocognitive impairment in rural population.



NeuroAIDS workshop

NARI - AIDS Rural Research Initiative in Maharashtra (N-ARRIM) activities
Poster Exhibition

National Centre for Disease Informatics and Research (NCDIR), Bangalore

Commencement & collaboration of new Population Based Cancer/Stroke/Diabetes Registries

The 28th Population Based Cancer Registry was commenced at Nizam's Institute of Medical Sciences, Hyderabad. A project on "Development of Stroke Registry in India" has been initiated. Fifty one centres across the country have so far registered under this project. A project on "Population Based Diabetes Registry" has also been initiated. A letter of invitation with registration form was sent to all Govt. Medical Colleges & Hospitals and all Private Medical Colleges & Hospitals and Nursing homes. 105 centres across the country have so far registered under this project.

Annual Reports /Publications

The report of 25 Population Based Cancer Registries (PBCR) includes the data of four new PBCRs (Meghalaya, Nagaland, Tripura and Wardha) that have commenced working and included under the NCRP network since the last report for the years 2006-2008 was prepared and printed. The 25 PBCRs that comprise the basis of this report cover 7.45% of the population of India, with partial or complete representation of 16 States and one Union Territory. Eleven of the PBCRs are in urban localities and 2 in wholly rural regions. The remaining 11 correspond to both urban and rural parts by virtue of being state or district registries. Among males, cancers of lung, mouth, oesophagus and stomach are the leading sites across all the registries. Lung cancer is the leading site in Bangalore, Chennai, Delhi, Kolkata, Tripura, Kollam and Thiruvananthapuram. All the PBCRs in Gujarat and Maharashtra states and Bhopal PBCR have mouth cancer as the leading site of cancer. Cancer of the oesophagus is the leading site in the registries in the states of Assam and Meghalaya. Stomach cancer is the leading site in Sikkim and Mizoram while cancer of the nasopharynx is the leading site in Nagaland. Among females, cancer of the breast and cervix are the leading sites of cancer in 18 of 25 PBCRs. Cancer of the gallbladder and cancer of the oesophagus followed cancer of breast as the leading site in Dibrugrah and Kamrup respectively. Lung was the leading site in Manipur and Mizoram. Cancer of the oesophagus led the list of cancers in Meghalaya. Cancer of the thyroid followed cancer of breast in the two PBCRs at Kollam and Thiruvananthapuram in Kerala state.

The report on "Trends in Incidence Rates of Cancer: 1982-2010" was brought out. Among males, cancers of the tongue, mouth, colon, rectum, liver, lung, prostate, brain, non-Hodgkin's lymphoma and lymphoid leukaemia have shown statistically significant increase in incidence rates. Some additional sites of cancer for males that have shown a rising trend and included in this report are gallbladder, pancreas, kidney and urinary bladder. In females, cancers of the gall bladder, lung, breast, corpus uteri, ovary, thyroid, brain, non-Hodgkin's lymphoma and myeloid leukaemia have shown a statistically significant increase in AARs.

Development of an Atlas of Cancer in Punjab State

The project on "Development of an Atlas of Cancer in Punjab State", has been a major activity. Punjab Cancer website has been added with a map of Punjab (with the title "Online and Dynamic E-monitoring of Data Capture - Coverage of Cases").

Software Development

Development of Software Applications Programme with specific modules is a primary mandate of the NCDIR and a major activity of the centre. This software will be applied for the following: i) Development of an Atlas of Cancer in India; ii) Patterns of Care and Survival Studies; iii) Population Based Cancer Registry Data Management (PBCRDM 2.1); iv) Hospital Based Cancer Registry Data Management (HBCRDM 1.0); v) Monograph; vi) Development of an Atlas of Cancer in Punjab State; vii) Pathology; and viii) Radiotherapy

State wise Collaborating Centres as of November 2013							
Sl. No.	State	PBCR	HBCR	POCSS	HBCRDM Registered & Transmitting	PCA - Registered & Transmitting	NE Atlas
1	Jammu & Kashmir			1	1		
2	Himachal Pradesh				1		
3	Punjab	1				52	
4	Chandigarh (UT)		1	1	1	2	
5	Uttarakhand				1		
6	Haryana				1	1	
7	Delhi (UT)	1		2	2	4	
8	Rajasthan				1	1	
9	Uttar Pradesh				1		
10	Bihar			1			
11	Sikkim	1					
12	Arunachal Pradesh	2					2
13	Nagaland	1					2
14	Manipur	1					1
15	Mizoram	1					
16	Tripura	1					2
17	Meghalaya	1					3
18	Assam	3	2	3	2		6
19	West Bengal	1			2		1
20	Jharkhand						
21	Orissa				1		
22	Chhattisgarh				1		
23	Madhya Pradesh	1	1		2		
24	Gujarat	2		1			
25	Daman & Diu (UT)						
26	Dadra & Nagar Haveli (UT)						
27	Maharashtra	6		2	2		
28	Andhra Pradesh	1			5		
29	Karnataka	1	1	4	6		
30	Goa						
31	Lakshadweep (UT)						
32	Kerala	2	1	2	7		
33	Tamil Nadu	1	1	1	3		
34	Puducherry (UT)				1		
35	Andaman & Nicobar Islands (UT)						
Total		28	7	18	41	60	17
<i>PBCR = Population Based Cancer Registries</i> <i>HBCR = Hospital Based Cancer Registries</i> <i>POCSS = Patterns of Care and Survival Studies</i> <i>HBCRDM = Hospital Based Cancer Registries Data Management Software</i> <i>PCA = Development of an Atlas of Cancer in Punjab State</i> <i>NE Atlas = Development of an Atlas of Cancer in North East Region</i>							

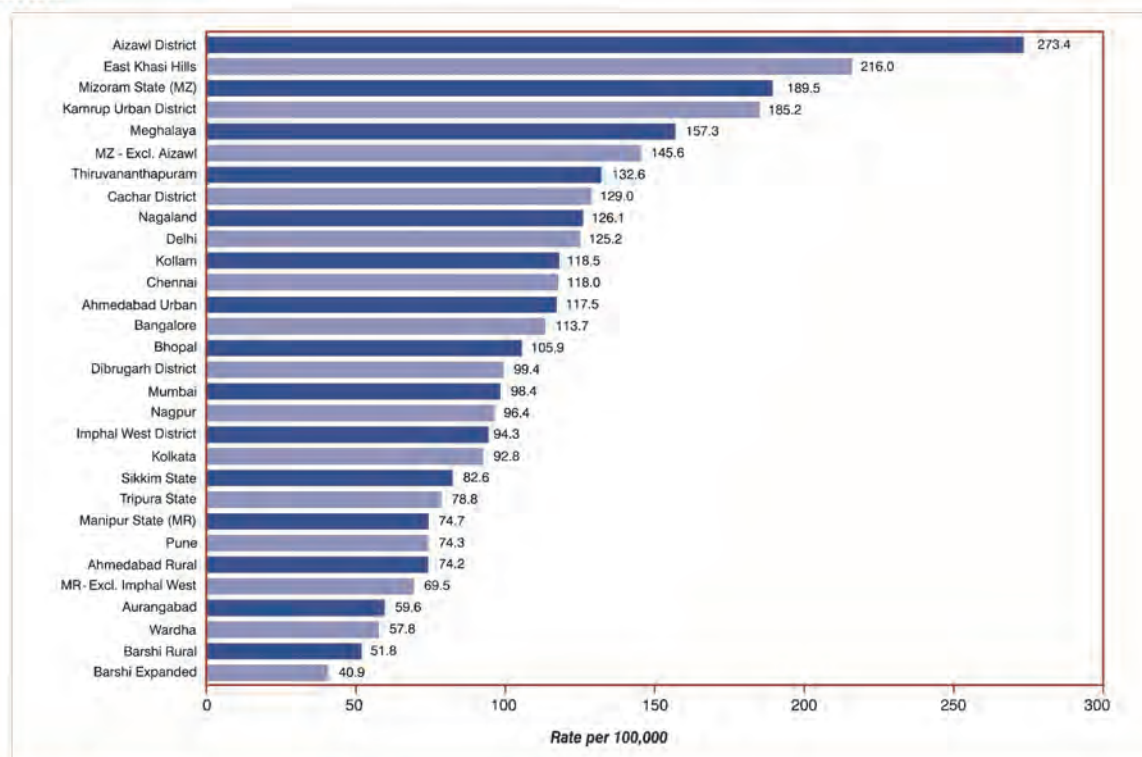
Apart from the above, 51 centres have been registered under the project on “Development of Stroke Registry in India” and 101 medical colleges have been registered under the project on “Development of Population Based Diabetes Registry”



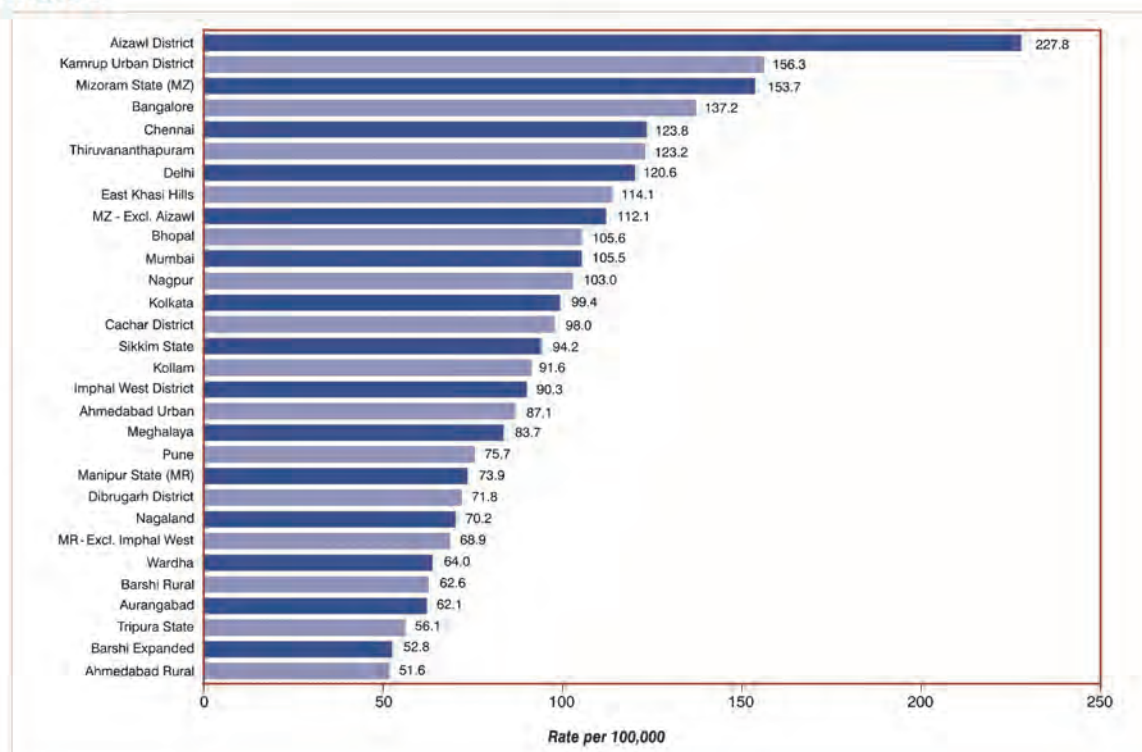
Map showing various registries and their location

Comparison of Age Adjusted Incidence Rates of PBCRs ALL SITES (ICD-10: C00-C97): 2009-2011

Males



Females



were received. All 603 strains were confirmed as *V. cholerae* O1 biotype El Tor. The typing patterns were T 27, T 26, T 23, T 14, T 6 T 3, respectively. All these strains have been included in phage typing study and reports have been sent to counterpart Institutions.

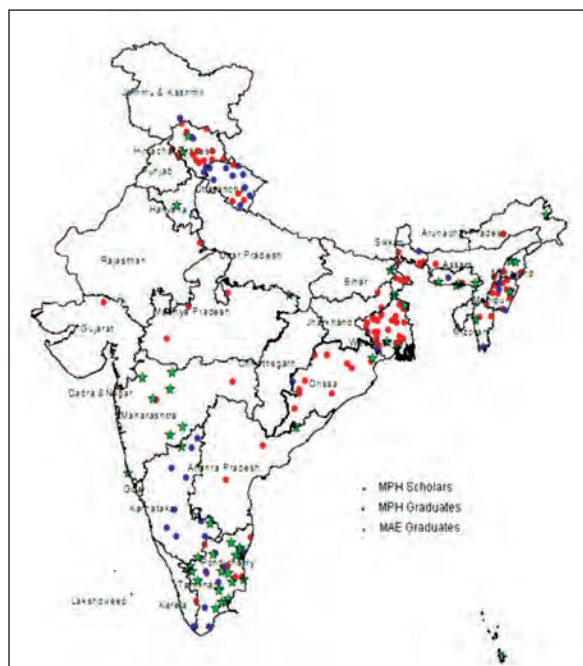
Considering the fact that huge numbers of gastrointestinal tract pathogens are being characterized routinely at this Institute, the Gastrointestinal Tract Pathogens Repository (GTPR) has been established as National Facility through special support from Indian Council of Medical Research (ICMR), New Delhi. Goals included for this facility are to archive, maintain and provide scope for retrospective analysis on medically important pathogens. A web based support and dissemination of information is available from www.gtp.org.in.

National HIV Reference Laboratory at NICED, Kolkata has been accredited in accordance with the Standard ISO-15189:2007, Medical Laboratories - Particular Requirements for Quality and Competence in the field of Medical Testing (Microbiology and Serology) for the duration from 08-09-2011 to 07-09-2013 with the scope of HIV Testing employing Rapid Immunoassay, ELISA and Western Blot.

National Institute of Epidemiology (NIE), Chennai

Public Health Training Programmes

As graduates of the Master of Applied Epidemiology and Master of Public Health courses of NIE, a workforce of 150 trained epidemiologists/public health specialist is now available from 23 Indian states/Union Territory. NIE also has initiated a one year Post- Graduate Diploma in HIV Epidemiology (PGDHIV) in 2012 and on-line post-graduate Diploma in Bioethics (PGDB) in 2011. Forty candidates from the PGDB and four candidates of PGDHIV completed the course.

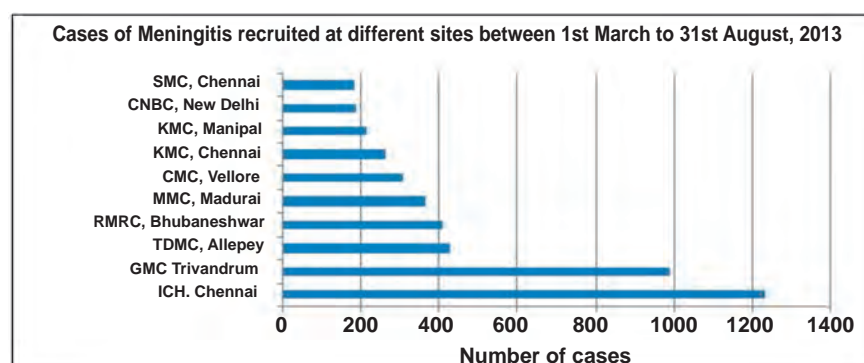


Disease surveillance

Hospital Based Sentinel Surveillance of Bacterial Meningitis in India

NIE has established surveillance for bacterial meningitis in 10 hospitals from 5 Indian states. More than 3500 suspected cases of meningitis cases were recruited from 10 sites during 1 Mar

2012- 31 Aug 2013. Of these, 11% were classified as probable bacterial meningitis (based on CSF microscopy/bio-chemistry). Nine percent of the suspected cases were laboratory confirmed.



National Hospital-based Rotavirus Surveillance Network

NIE is coordinating the expanded National Hospital Based Rotavirus Surveillance Network project in order to generate nationally representative data on rotavirus burden and circulating strains and to understand the potential health benefits of rotavirus vaccination in the country. The phase I of the surveillance was launched in 8 sites under CMC Vellore and one site under RMRC Port Blair. A total of 2459 children were enrolled in the study during September 2012 – October 2013. Stool specimens were collected from 2329 children and 32.3% were positive for rotavirus.

Leprosy

WHO/TDR multi-centric trial on Uniform MDT (U-MDT) regimen for all types of leprosy patients: At the end of first five years of follow up, lesions were inactive in 66% (I year), 80% (II year), 89% (III year), 90% (IV year) and 91% (V year) in PB patients. In the MB group, lesions were inactive in 41% (I year), 57% (II year), 74% (III year), 78% (IV year) and 79% (V year). These results indicate that (U-MDT) is promising in achieving remarkable suppression in activity of skin lesions of both PB and MB leprosy.

HIV/AIDS

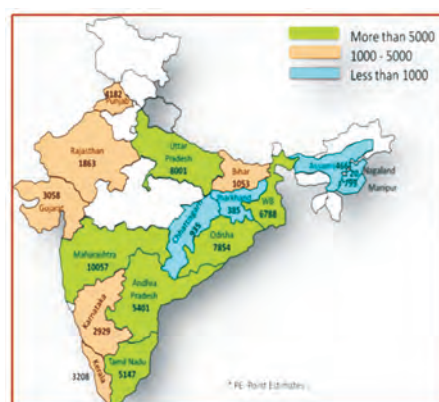
Mapping and size estimation of Eunuchs and other transgender populations in 17 states of India: The present study is aimed to map the Eunuchs/transgender (TG) populations across the 17 states of India. The overall purpose and the broad objective is to build an evidence base to prepare, implement and scale up targeted intervention of HIV prevention/care and social protection programs for the Eunuchs/TG population in the concerned 17 states.

Mapping and Size Estimation Methodology

Delphi consensus method was adopted for the size estimation of the Eunuchs/TG community. It involved identifying panels of local experts, which in this case were NGO/CBO staff and other (mainly) key informants. It involved independent and anonymous estimates by a minimum of 2 local informants; the estimates were revised till a consensus was reached. The methodology for mapping and size estimation was finalized in consultation with NACO, UNDP and NIE-ICMR. It was conducted in 17 States with 5821 sites and in 53280 LL, 74297 UL and 62137 PE.

Summary of findings

- Of all the 17 states, only Odisha reported to have more rural sites than urban. In the state, of the total of 696 sites that were mapped, 391 sites were located in the rural areas (around 56.2%) and the rest 305 sites were located in the urban areas (43.8%).
- Close to 45% of all sites across the study states were public sites. Among the rest around 1.4% sites were Brothel/hamams and close to 54% of the sites were other sites. The presence of brothels/ hamams was reported minimal in all the states except Karnataka (14.8% of all sites).
- The total TG population (point estimate) across the 17 states was reported to be 62137, with the lower level of the estimate at 53280 and the upper level of estimate at 74297. Around 21% of the overall TG population was mapped in the rural areas and the rest 79% in the urban areas.
- The top five states that reported the highest concentration of TG/Eunuchs were Maharashtra (10057), Uttar Pradesh (8001), Odisha (7854), West Bengal (6788) and Andhra Pradesh (5401). Together these five states comprise of a total of 38101 TGs/Eunuchs across the 17 states, which is around 61% of the total TG population.



Conclusion: Variations at the state level for the population of Eunuchs/TG population across the 17 states are evident. With states such as Uttar Pradesh, West Bengal, Odisha and Maharashtra share the majority of the population for the Eunuchs/TG population, the estimates in Assam, and other north eastern region states are low.

Across the 17 states covered in the current mapping and size estimation exercise, a total of 466 districts were covered. Of these 29 districts have a point estimate of at least 400, thus 29 potential districts/domains can be 'IBBS sites' for TGs. Close to 3/5th of the Eunuchs/TG population is involved in sex-work.

Diversity among clients of female sex workers in India: comparing risk profiles and intervention impact by site of solicitation - It seems generally accepted that targeted interventions in India have been successful in raising condom use between female sex workers (FSW) and their clients, with the new challenges being low condom use with intimate partners of sex workers and sex work becoming more hidden and potentially more risky. Data from clients of FSW have been under-utilised to analyse the risk environments of both partners.

The 2009 Integrated Biological and Behavioural Assessment (IBBA) survey sampled clients of FSWs at hotspots in Andhra Pradesh, Maharashtra and Tamil Nadu (n=5040). The risk profile of clients in terms of sexual networking and condom use are compared across usual pick-up place (public place/brothel/home/phone-based or via agents). We used propensity score matching (PSM) to estimate the impact of intervention messages on clients' consistent condom use with FSW.

Generally clients of the more hidden sex workers who solicit from home or via phone or agents had more extensive sexual networks reporting casual female partners as well as anal intercourse with male partners and FSW. Their reported condom use levels were 67% and 59% respectively. Clients of brothel-based sex workers, who were the least educated, reported the fewest number and categories of partners and the least anal sex, but they reported lowest condom use levels (41%). Consistent condom use with all sex workers varied widely by state: 65% in Andhra Pradesh 36% in Maharashtra and 29% in Tamil Nadu. Exposure to intervention

messages on sexually transmitted infections was lowest among men frequenting brothels, while 70% of men soliciting these less visible sex workers had been reached. Intervention exposure had significant impact on consistent condom use, including among clients of home-based sex workers in Andhra Pradesh (ATT 21%; $p=0.001$) and among men soliciting other more hidden FSW (ATT 21%; $p=0.001$). In Tamil Nadu no impact could be demonstrated.

Commercial sex happens between two partners and both need to be, and can be, reached by intervention messages. Commercial sex is still largely unprotected and as the sex industry gets more diffuse a greater focus on reaching clients of sex workers seems important given their extensive sexual networks

Health System Research

Concurrent evaluation of Non-Communicable Disease Program: Baseline survey for clinic based interventions in Tamil Nadu: Government of Tamil Nadu is currently implementing Non-Communicable disease program in all the 32 districts in Tamil Nadu. The Interventions include community-based awareness to self-help groups, involvement of media *etc.* and clinic based screening and treatment for hypertension, diabetes, cancer cervix and cancer breast. NIE is conducting the concurrent evaluation of the clinic based screening program.

Measles Case Fatality Ratio in Bihar

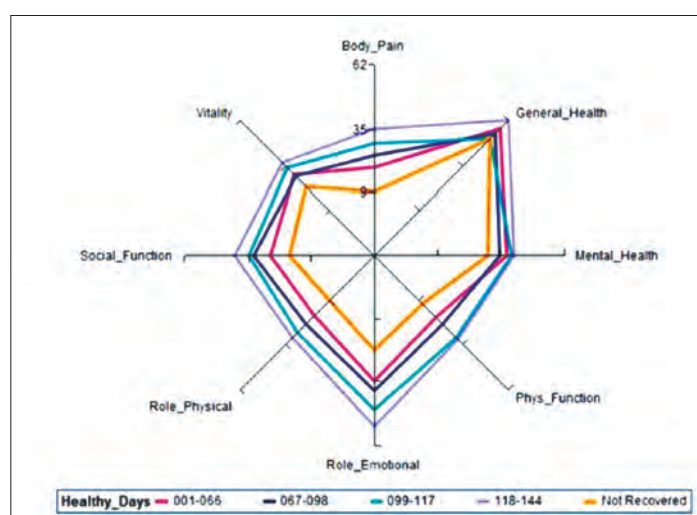
A community based study covering 18 measles outbreaks in 11 districts of Bihar revealed that the measles case fatality ratio (CFR) in the state was low at 0.74 (95% confidence interval: 0.33-1.16). CFR however was higher among children aged <5 years, belonging to scheduled caste/tribe and those who did not receive vitamin A during the illness. To further reduce case fatality, health authorities responding to measles outbreak need to focus the initial outbreak response activities including vitamin A administration in SC/ST communities and ensure regular visits by health-workers in affected villages to administer vitamin A to new cases.

Vector-borne Diseases

Impact of Chikungunya virus (CHIKV) infections on Health Related Quality of life in Chennai:

This study provided evidence for sharp reductions in the quality of life not only during active clinical Chikungunya virus infection but also for several months after clinical recovery compared to healthy normals. Younger age, male, absence of rashes, affliction of less than five types of joints and two weeks of joint swelling were significantly associated with recovery.

These study findings have implications for developing intervention programmes in countries with high risk of CHIKV outbreaks.



HRQoL scores of clinically recovered CHIKV patients according to duration of disease free days (healthy days) at five months of follow-up.

Persistent arthralgia and associated factors among CHIKV patients in Chennai

This cohort study among the Chikungunya patients revealed that approximately 40% of the patients suffered from joint pain for up to 1 month and 7% beyond 1 year. High-grade fever, involvement of four or more types of joints, and joint swelling were predictors of persistent arthralgia.

National Institute of Immunohaematology (NIIH), Mumbai

The NIIH continued to provide quality research in Basic Hematology and Clinical Hematology. The Institute has also taken active part in tribal research and in translational research which has two components:

1. Training people from various centres in India in various facets of hematology and immunohaematology
2. Devising research technology algorithms, protocols and product development.

Some major achievements of the year under review include:

- Normal HbA₂ β thalassemia is augmented by the demonstration that several of the normal HbA₂ β thalassemia individuals harbor the common IVS 1-5 G/C mutation. There is a necessity for integrating HPLC, the red cell indices, family history, as well as molecular data to say that the couple is not at risk of having a child with β thalassemia major.
- The quest for normal HbA₂ β thalassemia carrier has also shown delta globin gene mutations (which causes decreased HbA₂ levels) in around 25% of the cases. There is a pocket in Saurashtra in Gujarat where a particular delta globin gene CD 100 C/T mutation was found and this abnormal hemoglobin is appropriately named "Variant Hemoglobin Saurashtra".
- The demonstration of hydroxyurea as an iron chelator and its synergistic activity with other iron chelators in animal studies. This drug is also used for activation of fetal hemoglobin in Sickle Cell Anemia as well as β thalassemia intermedia patients. Hence additional iron chelating activity demonstrated by our study (patent application filed) is an important landmark in management of β thalassemia and sickle cell anemia patients.
- Our experience with the Government Medical College, Nagpur clearly shows that low dose hydroxyurea therapy is a feasible way of managing sickle cell anemia patients in that region and this treatment has averted many complications of sickle cell anemia.
- Delayed vitamin K deficiency in infants continues to occur even after primary prophylaxis at birth. Several molecular determinants were demonstrated in the VKORC1 and GGCX genes linking to this deficiency
- We have standardized the microparticle demonstration through flow cytometry to study recurrent fetal loss and various thrombophilic conditions in which standard thrombophilia markers are absent.
- In a study of inhibitor prevalence in Indian hemophilia patients, an overall prevalence of 6.72% in 4567 patients across the country is detected with regional variation; Chennai leading with a prevalence of 10-11%.
- Institute is offering prenatal diagnosis for hemoglobinopathies, red cell enzymopathies, primary immunodeficiencies, hemophilia, vWD, rare clotting defects and Fanconi anemia.

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- Molecular pathology of several hematological conditions have been described such as i.e vWD, hemophilia, Bernard Souliers syndrome
- A study showed mitochondrial mutations as important determinants in the progress of myelodysplastic syndrome.
- The technique for studying the UGTA1 gene promoter repeats as an important predictor for hyperbilirunemia in neonatal jaundice as well as well as other hemoglobinopathies has been established.

Translational Research Programmes

1. Workshops under the “Education of laboratory workers for the diagnosis of haemophilia and other bleeding disorders with a view to establish diagnosis in laboratories at selected centers in six states in Central and North East India” was carried out in the following centres:
 - a. An on spot training session was held in Rajendra Institute of Medical sciences, Ranchi from 27th to 29th December 2012. A total number of 50 Pathologists and Laboratory Technicians from different parts of Jharkhand participated in the proceedings. Hands on training was given to all the Technicians in screening coagulation assays, inhibitor screening and factor assays.
 - b. The workshop in Silchur, Assam was held from 18th to 20th February, 2013. Three Medical Colleges participated in this workshop i.e. Silchur Medical College, Assam Medical College and Guwahati Medical College.
2. Our team visited Government Medical College, Agartala -Tripura for giving training and initiation of the DBT project on “Newborn screening for red cell enzymopathies and hemoglobinopathies” from 4th – 6th April, 2013 under the Training Programme.

Hands – on-Training given at Government Medical College, Agartala – Tripura, from 4th – 6th April, 2013

Staff appointed at Govt. Medical College, Agartala, Tripura underwent training on HPLC and on the qualitative and quantitative estimation of G6PD and Pyruvate Kinase enzyme assay from 25th June to 2nd July, 2013 at NIIH, Mumbai

Workshop under “Establishment of basic red cell serology techniques in the blood banks of the North East Region of India” was carried out in the following centres:

Fifth training programme was conducted at Arunachal Hospital, Naharlagun, Arunachal Pradesh from 20th -22nd June, 2013. There were 15 participants (8 medical officers & 7 technicians) for the training programme. The trainees were from Blood banks in Naharlagun, Itanagar, Tawang, Ziro, Daporijo, Yingkoing, Pasighat, Changlang, Aalo, Tezu and Roing. Workshop comprised of lectures on blood group serology and hands – on-practicals on Basic Red Cell Serology Techniques and interactive session on problem solving in Blood Grouping and Crossmatching.



Follow – up of the Workshops “Screening and Molecular Diagnosis of Hemoglobinopathies” for Medical College

A pathologist from NEIGRIMHS, Shillong who had attended the workshop conducted by us at Kolkata came for further training to the Institute for one month to establish these technologies in Shillong.



Training in molecular techniques in Hemoglobinopathies given in the Dept of Hematogenetics from 3rd June to 28th June, 2013 to a pathologist from Shillong.

Service to the Nation

- Prenatal diagnosis was offered to 43 families with hemophilia and other bleeding disorders. 286 families with β thalassemia, 15 families with congenital immunodeficiency.
- In the current year 154 new cases of bleeding disease were diagnosed.
- A total of 3332 haemophilia patients from different states of India were screened for the presence of factor VIII/IX inhibitors. An overall prevalence of 6.72% was observed with regional variation in their prevalence, Pondicherry showing the highest i.e 11.12% followed by Chennai i.e 9%.
- Molecular evaluation including complementation analysis in Fanconi anemia.
- Around 28,000 patients were investigated for various hematological, autoimmune, transfusion medicine, transplantation, immunodeficiency related problems during the year under reporting. These patients were referred to us from medical colleges and hospitals from all over India.
- Christian Medical College, Ludhiana has now developed the capability to do prenatal diagnosis of β thalassemia under the mentorship of this Institute. They are now able to offer these services to families in Punjab, where the prevalence of β thalassemia is high.
- Our centre for Primary Immunodeficiencies (PID) provided prenatal diagnosis for 5 families. 580 Patients were investigated for PID, 85 for leukemia and 210 for paroxysmal nocturnal haemoglobinuria. Molecular characterization of cases of leukocyte adhesion deficiency (LAD-I), X-linked hyper IgM syndromes, Perforin deficiency and other rare primary immunodeficiency disorders was carried out.

Interaction with Other Medical Colleges and ICMR Institutes

- We continue to interact with GS Medical College and KEM Hospital, Bai Jerbai Wadia Children's Hospital, Navrosji Wadia Maternity Hospital and Sion hospital for different projects.
- Assam Medical College, Dibrugarh is twinned with NIIH for development of cytogenetics facility at the centre.
- Kolkata Medical College, Kolkata and Dinanath Mangeshkar Hospital, Pune are now regularly doing prenatal diagnosis of β thalassemia at their centres with confirmation of diagnosis by us in a few cases when required.
- Transfusion Medicine Department at NIIH has initiated a human resource development and transfusion training programme with NEIGRIHMS (North Eastern Indira Gandhi Regional Institute for Health and Medical Sciences) Shillong.
- Close association with Bai Jerbai Wadia Children's hospital for evaluation of primary immunodeficiency disorders.
- Under the Tribal Health Research Forum, neonatal screening for sickle cell disorders at two centres (Valsad in Gujarat and Jabalpur in MP) is initiated to raise a cohort of atleast 100 sickle homozygous babies at each centre and follow them up regularly to understand the natural history of sickle cell disease among tribal populations and to reduce the morbidity and mortality of the disease.

New Techniques

- Detection of NK cell function requires about 7-10 ml of blood for 51Cr release assay using K562 cell line. However it is often very difficult to get 7-10 ml blood from infant or newborn who suffer from primary HLH. Hence we standardized a micro method using > 1 ml whole blood for the NK cell assay using flow cytometric technique. This techniques has now been included in the regular investigative armament for diagnosis of HLH.
- Flowcytometry workshop on Primary Immunodeficiency Disorders from 4-6th Sept 2013 at National Institute of Immunohaematology, Parel, Mumbai.
- A workshop on PCR for prenatal diagnosis of sickle cell disorders and seminar on hemoglobinopathies was organized by Indira Gandhi Govt. Medical College, Nagpur from 19th to 21st September, 2013. The hands- on – training for prenatal diagnosis of sickle cell anemia included DNA isolation, gel electrophoresis, characterization of mutations by reverse dot blot hybridization and ARMS was given to the participants.

National Institute of Malaria Research (NIMR), Delhi

Epidemiological Studies

Evidence Based Assessment of Biophysical Determinants And Framework for Malaria Control in the North-Eastern States

This study is being carried out since 2009-10 in selected sites of Uttarakhand, Assam, Mizoram and Jharkhand for generating data on entomological, parasitological and climatic aspects. The changes in temperature were noticeable in study areas of Karbi Anglong and Almora districts up to ~ 2.5 °C. The indoor temperature was more than outdoor and water bodies, providing most conducive micro niche for mosquitoes inside the human dwelling in Assam while in Nainital area, it was fluctuating.

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Based on temperature, rainfall and observed density of *An culificaies*, it was predicted for Bhorsa (Nainital) applying Genetic Programming mathematical model. Correlation coefficient of 0.77 between observed and simulated density was observed. Similarly, model for other study area is in progress. Evidence of positivity of malaria vectors for sporozoites in the month of January, were also generated. In order to assess the capacity of health system and knowledge of communities in different study sites, interview schedules through structured questionnaires (>10% households from each villages) were filled up. Needs for capacity building of stakeholders in health system and IEC needs of communities have been identified.

Micro Stratification of Malaria in Problematic Districts of Rajasthan for Development of Strategic Plan for Control.

Village level ecological risk in selected Primary Health Centres of Barmer, Bikaner and Jaisalmer districts of Rajasthan is being determined using satellite remote sensing coupled with ground truth information. Using LISS IV satellite images with 5.8 metre resolution, distinction between mosquitogenic conditions in high and low malarious villages could be possible. In high malarious villages, in general, the proportion of water bodies, natural vegetation and agricultural land was more as compared to low malarious villages. In low malarious villages, the proportion of sandy/rocky area was more than high malarious villages. The analysis of Cartosat-II satellite data with 2.5 metre resolution revealed that breeding habitats like Tanka and smaller habitats close to human settlements could be detected.

Mapping of Malaria Risk in the Context of Climate Change in India

With the objective of generating risk map of malaria of India from the viewpoint of climatic determinants, malaria prevalence and anopheline vectors, monthly epidemiological data from 2010-2012 for all the districts of India were obtained from NVBDCP. Based on the data, monthly malaria incidence maps of *Plasmodium falciparum* were generated using ROLTA Geomatica software. Based on three years averaged Annual Parasite incidence (API), API map of India was generated. Published literature on distribution of malaria vectors in India was searched through internet search engine, and initiated the mapping of the distribution of major vector *An. culicifacies*.

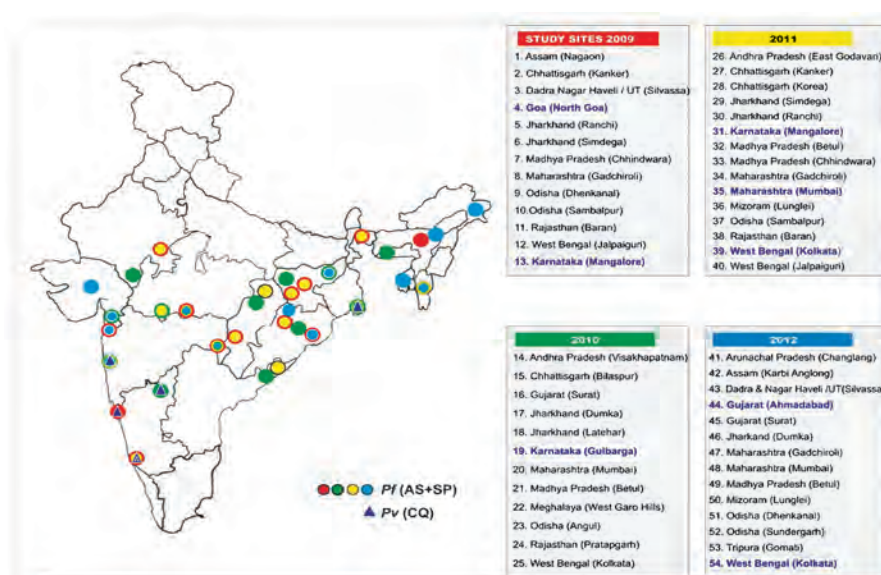
The maps reveal the gaps in vector distribution and intensity of *P falciparum* in eastern part of India. Results showed that malaria parasite *P. falciparum* was endemic in Orissa, The monthly malaria incidence of Pf was more during Nov- Jan and the peak was more in December. Overall API was highest in D & N Haveli (22.28), Orissa (7.16), and Meghalaya (6) states etc and least in Bihar (0.02). However, the highest API was found in district South Garo Hills (65) in Meghalaya followed by Raygada (53) in Orissa. Risk maps based on climatic determinants are being developed. Study is in progress

Monitoring the Therapeutic Efficacy of Antimalarial Medicines in India

Therapeutic efficacy studies of ACT (AS+ SP) in *P. falciparum* and CQ in *P. vivax* are being conducted at 15 sites in the country (13 for *P. falciparum* and 2 for *P. vivax*) in collaboration with NVBDCP and State Health Authorities using new protocols of World Health Organization. The studies have been continued in the fourth year (2012-13) in different malaria endemic regions of India where percentage of *P. falciparum* malaria is high. These studies (2012-13) have shown the efficacy of chloroquine for *P. vivax* as 100% at 2 sites. The PCR corrected cure rate of ACT (AS+SP) for *P. falciparum* ranged between 74.1 – 100% at 12 sites.

About 20% samples were analysed for molecular markers of partner drug-resistance. Majority of samples (53.7%) showed *dhfr* double mutation followed by single (20.1%), triple (15.4%)

and quadruple mutation (0.7%). Also, majority of the samples showed *dhps* wild pattern (40.5%) followed by triple (22.9%), double (20.9%), single (9.2%) and quadruple (6.5%) mutation. The K76T mutation in chloroquine transporter *Pfcr*t was observed in majority of samples (68.4%) followed by wild (12.3%) and mixed type response (9.0%). These results were shared with ICMR and NVBDCP which led to change of drug policy for malaria in North-eastern (NE) region by NVBDCP. Current ACT (artesunate + sulfadoxine pyrimethamine) has been replaced with co-formulated tablet of ARTEMETHER (20 mg) - LUMEFANTRINE (120 mg) for treatment of uncomplicated *P. falciparum* malaria in NE region.



A Multicentric, Randomized Trial to Detect *in vivo* Resistance of *Plasmodium falciparum* to Artesunate in Patients with Uncomplicated Malaria

Due to high proportion of treatment failures observed during therapeutic efficacy studies conducted at three sites in Northeastern region, artemisinin resistance studies were initiated at Gomati district, Tripura and Lunglei district, Mizoram using the same protocol of multicentric project "TRAC studies" with WHO supplied medicines and intramural funding. The above project has a primary objective to calculate the *P. falciparum* parasite clearance rate, at two different sites across international borders. Till date 68 cases have been enrolled at Tlabung Subdivisional hospital, Lunglei district in Mizoram and 44 cases at Sillachari PHC, Gomati district, in Tripura.

Effective and Safe Treatment for Malaria in Pregnancy in India: A Randomised Controlled Trial

In India, national policy for treatment of malaria in pregnancy in second and third trimesters is artesunate+sulfadoxine-pyrimethamine (AS-SP). However, data on safety and efficacy of Artemisinin based combination therapy in pregnancy are scarce. We assessed the safety and efficacy of AS-SP and artesunate+mefloquine (AS-MQ) for treatment of *falciparum* malaria in pregnancy in India.

This open-label, randomised clinical trial was initiated in October 2010 at three sites (Ranchi and Jamshedpur, Jharkhand state and Rourkela, Odisha state). Informed consent was obtained from women attending antenatal care (ANC) clinics with a gestational age between 12 and 36 weeks to screen for malaria at each ANC visit. Pregnant women having *P. falciparum* mono-infection of any parasite density with or without fever were randomised

to either AS-MQ or AS-SP arm of the trial. Blood slides and filter paper samples for PCR were collected on day 0,1,2,3,14,28,42 and 63 post treatment and followed up until day 42 postpartum.

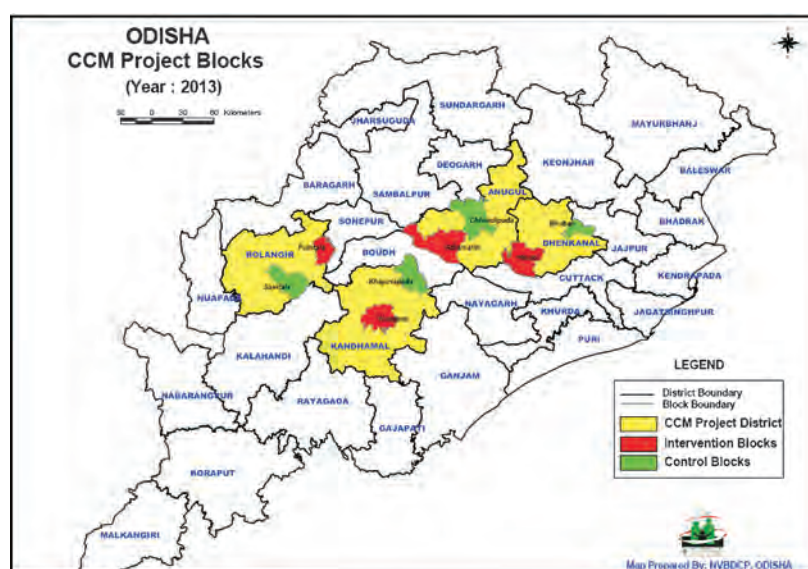
Between October 2010 and October 2013, 243 women were found to have *P. falciparum* mono-infection among 6975 pregnant women. They were randomised to receive either AS-MQ or AS-SP. There were no therapeutic failures on day 28, 42 or 63 in both arms of the study. There were twenty three serious adverse events during the study. None of the severe adverse events were related to the study drugs. Both artesunate+SP and artesunate+mefloquine are safe and effective for treatment of uncomplicated malaria in pregnancy in India.

Comprehensive Case Management Pilot Programme in Odisha, India

The project was initiated in April 2013 with the aim to assess the impact of a comprehensive case management system for uncomplicated malaria on the incidence of malaria in different transmission settings in the state of Odisha, India. The project is being carried out in four districts of Odisha: Dhenkanal (low endemic), Bolangir (mesoendemic), Angul (high endemic) and Kandhamal (hyperendemic). Of the two blocks selected for each district, one acts as a control while another is intervention block. The components of the comprehensive case management system have been implemented rigorously in the intervention areas, whereas in the control areas, the current routine case management system is continuing.

Microscopy has been introduced at all the PHCs of the intervention blocks. CCM implementation activities like project staff training and sector level training of all health staff are over. Sufficient RDTs and age wise ACT has been made available upto the ASHA level in the intervention Blocks. The buffer stock of RDTs and antimalarials has been made available at the CHC level and to avoid stock outs. The monthly data from the intervention Block are received in the reporting system developed for the BLM. Monthly review meetings of the BLM are taking place in the state headquarters.

According to the reports of July- October 2013 there has been an increase in the surveillance of malaria cases in the intervention Blocks of Bolangir, Dhenkanal as compared to the previous years of 2011 and 2012. The detection of Pv cases as compared to previous year has also increased in all intervention Blocks as Bivalent kits are available at the periphery level now.





De-weeding in canals under Narmada Nagar Unit

Control of Dengue and Chikungunya by Controlling *Aedes* Breeding in Key Containers in Pre-Monsoon Season Endemic Zone of Delhi

Four teams comprising of 2 NIMR field workers and 2 to 3 MCD field workers to identify *Aedes* breeding and for source reduction carried out surveys in 55 colonies of 25 localities in West Zone of Delhi. During non-transmission season (December – May) and during transmission season (June-November) fortnightly surveys were carried out for identification, detection and reduction of breeding in key and secondary containers respectively. Cross-Checking was done by NVBDCP officials. Intervention methods included community awareness, vector surveillance & source reduction, introduction of Temephos Granules and covering tanks broken lids with cloths (Fig.).

Since December 2012 to October 2013, 116702 containers from 64177 houses were checked, out of which 1078 containers from 976 houses were found positive. During pre-monsoon season (Dec'12- May'13), maximum CI was found in tanks (6.08%) followed by coolers (5.09%) and solid waste (3.65%). Whereas, during post-monsoon season (June'13 – October'13) maximum CI was found in solid waste (36.92%) followed by tanks (11.84%) and mud pots (1.47%).

As compared to 30% CI of Delhi, 28% CI was observed in West Zone and only 2% in selected localities. Statistically there is highly significant difference between CI of Delhi and selected localities ($P < 0.05$) and there is highly significant difference between CI of West Zone and Selected Localities ($P < 0.05$). Percentage of Dengue Case in West Zone also reduces from 13% (2011) to 5% (September 2013). It is noteworthy to mention that till date no dengue case has been recorded from surveyed localities.



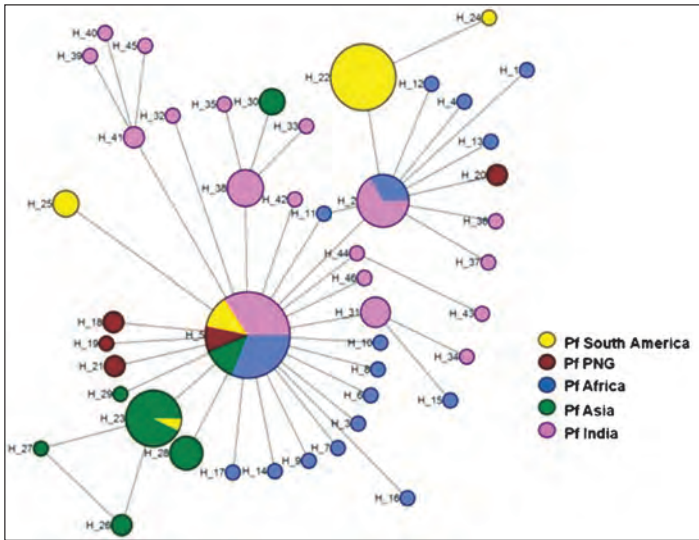
Source reduction in West Zone, Delhi

Parasite Biology

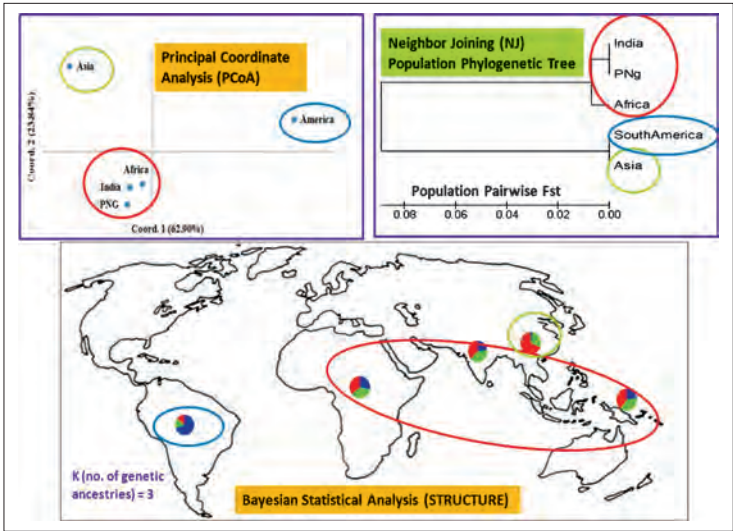
Mitochondrial Population Genomics of Indian *Plasmodium falciparum*

Indian *P. falciparum* isolates present the highest level of genetic diversity, maintain the highest effective population size and retain the most ancient TMRCA (Time to Most Recent Common Ancestor). The sequencing of the whole mitochondrial genomes of 44 Indian

field isolates and using the published global dataset of 96 genome sequences to present global genetic diversity and rewrite evolutionary history of this species. In the reconstructed haplotype network, a major proportion of the central (ancestral) haplotype was occupied by the Indian isolates and thus far the missing haplotypes were found in India. One (at the 725th nucleotide position) of the four Single Nucleotide Polymorphisms (SNPs) specific to malaria parasites of non-human primates which was never been detected in *P.falciparum* so far, was found to be segregating in five Indian isolates. These five Indian *P.falciparum* isolates also bear two other SNPs (one specific to *P. falciparum*-like isolates and the other to Indian *P. coatneyi* and *P. fragile*) in tight linkage with the 725th SNP, representing missing-link between the *P.falciparum*-like and *P.falciparum* malaria parasites (Figs.).



Inference of population history of global *P. falciparum* using whole mitochondria genome haplotype network. The global dataset includes 96 worldwide and 44 Indian mitochondria genomes (present study). Most of the Indian *P. falciparum* genomes contain the central (ancestral) haplotype and also haplotypes branching out to other *P. falciparum* isolates from other countries. Indian *P. falciparum* isolates thus could be considered ancestral, similar to African *P. falciparum*.



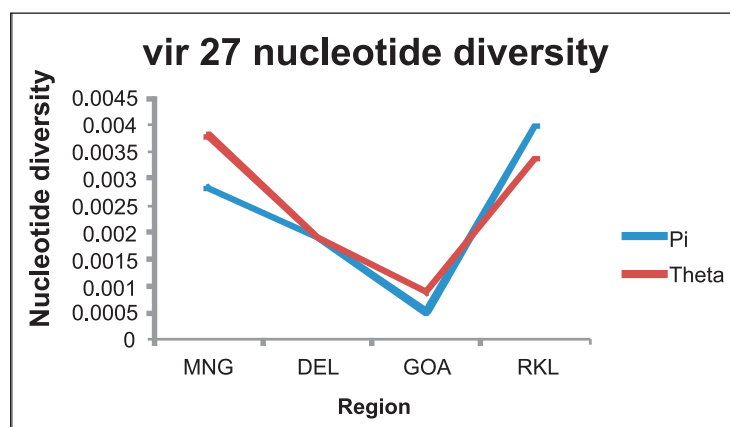
Inference of population genetic structure of global *P. falciparum*. All three different analyses involving different population genetic model and statistical algorithms (The Principal Coordinate, Neighbour-Joining Phylogenetic tree using pair-wise genetic differentiation matrix and with Baysain “STRUCTURE” analyses) indicate coherent patterns. While Africa, India and PNG are genetically close and ancestral, the Southeast Asian and South American *P. falciparum* isolates are genetically differentiated between themselves and also from the India-Africa-PNG ancestral clade.

Malaria Parasite Bank

Parasite Bank is supporting a large number of organizations working on various aspects of malaria. Biological materials including non-human and human *Plasmodia* preserved/maintained in Malaria Parasite Bank are supplied to various research organizations.

Existing Nucleotide Diversity of *vir* Genes in Indian *Plasmodium vivax*

The multigene family *vir* present in *P.vivax* is said to facilitate the parasite to escape the host immune system during infection. Sequence analysis of five *vir* genes *vir* 27, *vir* 4, *vir* 12, *vir* 21 and *vir* 1/9 belonging to subfamilies I, C, E and B and J showed the presence of high diversity in the genes both within the populations and between them. Five different populations of India were analyzed for the five *vir* genes to study their evolutionary history. Two different measures of nucleotide diversity π and θ_w were calculated for each gene in all five populations and for all *vir* genes in each population site by DnaSP v5.10 software. The average value of π was found to be higher than θ_w in *vir* 12, *vir* 21 and *vir* 1/9, lower in *vir* 27 and almost equal in *vir* 4 gene. The π and θ_w estimates were highest in *vir* 1/9 and lowest in *vir* 4. When the populations for *vir* 27 and *vir* 12 were compared, GOA has the lowest nucleotide diversity in comparison to the other populations (Fig.). The analysis of the sequences of *vir* genes across Indian populations allowed us to obtain a basic idea about the population genetic structure. A further attempt is being made to quantify the expression of the *vir* genes in severe and non-severe *P. vivax* malaria patients. More genetic studies are required to provide a better understanding of the *vir* genes as suitable vaccine targets in *P. vivax* (Fig.).

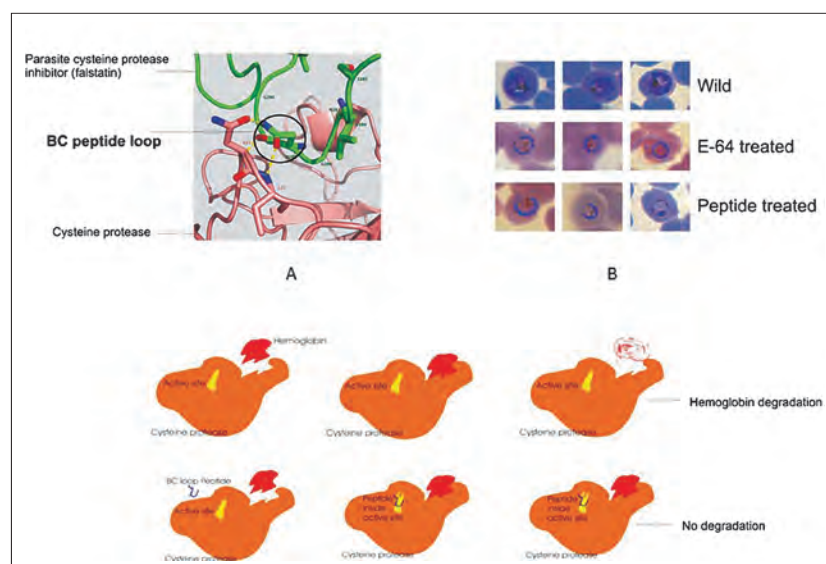


Graph showing region wise variation of *vir* 27 nucleotide diversity.

Proteases as Drug Targets for Malarial Parasite, and Structural-Functional Analysis of Falstatin, an Endogenous Inhibitor of Malarial Cysteine Proteases

The activities of cysteine proteases are regulated by a new class of endogenous inhibitors of cysteine proteases (ICPs). Structural studies of the ICPs of *Trypanosoma cruzi* (chagasin) and *P. berghei* (PbICP) indicated that three loops (termed BC, DE, and FG) are crucial for binding to target proteases. Falstatin, an ICP of *P.falciparum*, appears to play a crucial role in invasion of erythrocytes and hepatocytes. However, the mechanism of inhibition of cysteine proteases by falstatin has not been established. Our study suggests that falstatin is the first known ICP to function as a multimeric protein. Using site-directed mutagenesis, hemoglobin hydrolysis assays and peptide inhibition studies, we demonstrate that the BC loop, but not the DE or FG loops, inhibits cysteine proteases of *P.falciparum* and *P.vivax* via hydrogen bonds and hydrophobic interactions. These results suggest that the BC loop of falstatin acts as a hot-spot target for

inhibiting malarial cysteine proteases. This finding suggests new strategies for the development of anti-malarial agents based on protease-inhibitor interactions (Fig.).



Cross-Talk between Malarial Cysteine Proteases and Falstatin: the BC Loop as a Hot-Spot target to inhibit malarial cysteine proteases. A; A structural model is showing interactions between falstatin and cysteine protease of *P. falciparum* (falcipain-2). The BC loop of falstatin interacts with cysteine protease via hydrogen bond and hydrophobic interactions. B; Effect of a BC loop peptide on cultured *P. falciparum*, swollen food vacuole of trophozoite caused by inhibition of cysteine proteases. C; Model showing that a BC loop peptide binds to active site of cysteine protease and block hemoglobin hydrolysis.

Immunodiagnostic Reagent for the Detection of *Plasmodium vivax*

The culture supernatant of the 5 Hybridoma lines was collected and then was concentrated using a protein cut off filter of 30KDa (Amicon). *Plasmodium vivax* infected blood was collected from Chennai Field Station of NIMR. Fresh antigen was prepared from *P. vivax* infected blood and from cultured *P. falciparum* and fresh uninfected blood. We have tested two hybridoma lines (2.4B3UC and HYB 1+2+4) which showed reactivity with *P. vivax*. The antigens were run on SDS-PAGE and proteins were transferred to nitrocellulose membrane. The transferred protein was probed with two antibodies secreted by clones 2.4.B3UC and HYB 1+2+4. On western blot these antibodies identified proteins of ~52 KDa, ~42 KDa and ~34 KDa respectively. This showed the reactivity of the antibodies with patient's blood.

The call for proposals to develop the immunodiagnostic test was put on ICMR website.

Immuno-Modulatory Role of Mesenchymal Stem Cells in the Pathogenesis of Malaria Infection

In a rodent model, malaria manifests as a severe splenomegaly, with infiltration of cells and lymphoproliferation as major contributing factors of the immunopathology. We found that *P. berghei* infection of mice leads to massive recruitment of mesenchymal stem cells (MSCs) in secondary lymphoid organs. Infusion of these cells into naïve mice was able to confer host resistance against malaria. While MSCs exhibit immunosuppressive properties in most situations, in some experimental systems they have been shown to exert inflammatory properties. We sought to determine the functional properties of MSCs that accumulate in the spleen during malaria infection. We found that BM-derived MSCs were unable to provide host resistance against malaria infection. Thus, mice that received BM-derived MSCs exhibit similar infection kinetics as well as death rates as control mice. These observations suggest that MSCs recruited to the spleen during malaria infection are functionally distinct from

MSCs derived from the BM of uninfected mice. We tested NO production by MSCs recruited to the spleen during malaria infection as compared with MSCs derived from the BM of uninfected mice. We found that MSCs recruited to the spleen during malaria infection failed to produce NO, whereas BM derived MSCs from uninfected animals produced copious amounts of NO. Therefore, our observations indicate that MSCs recruited in response to malaria infection have inflammatory properties.

Center for the Study of Complex Malaria in India

Center for the Study of Complex Malaria in India (CSCMi), a collaborative project of National Institute of Malaria Research and New York University, is one of the ICEMR (International Centers of Excellence for Malaria Research) funded by the National Institutes of Health. The basic theme of the project is analysis of 'complex malaria', how complex malaria influences disease outcome, vector transmission, and drug resistance. The project has two major arms (i) Eco-Epidemiology and Transmission Project and (ii) Genomics and Drug Resistance Project: The project is being carried out at three field units of NIMR (Chennai, Rourkela, Nadiad) and at Delhi.

Delhi Laboratory has been equipped to undertake the genomics component of the project. A next generation sequencer (Ion Torrent PGM) have been imported in late 2013 and training of project staff is underway to carry out multiplex sequencing of polymorphic genes of *P. vivax* and *P. falciparum* for multiplicity of infection (MOI) and whole genome sequencing of *P. vivax* in order to construct genetic diversity map of parasite. Panel of microsatellite markers have been identified for population genetic analysis of malaria parasite *P. vivax* and *P. falciparum*.

Vector Biology and Control

Bionomics and Ecological Studies of Malaria Vectors

The preliminary studies in tribal district Latehar of Jharkhand state (API- 19 to 40 and *pf%* 7.5 to 22) have shown prevalence of 3 vector species *An. culicifacies*, *An. fluviatilis* and for the first time *An. minimus* in human dwellings. The species have shown indoor resting behavior and studies are in progress on sibling species composition and their role in transmission of malaria. Similarly, studies are in progress in districts of G.B. Nagar, U.P wherein, studies were continued in the last four years since 2009 but investigations have indicated that the appearance of *An. fluviatilis* was intermittent and was not affected by annual seasonal changes as in case of others but was interestingly associated with presence of water hyacinth on the surface of slow moving water in the drains.

Insecticide Resistance and Interventions

This year the Institute was designated as "WHO Collaborating Centre (CC) on testing and evaluation of public health pesticides" and was inaugurated by DG, ICMR and Secretary DHR on 11th April, 2013 and facilitated organization of "WHO Workshop on Capacity Strengthening for Pesticide Specifications" from 10th -12th April 2013.



DG, ICMR & Secretary, DHR Dr V.M. Katoch, inaugurating WHO CC Workshop

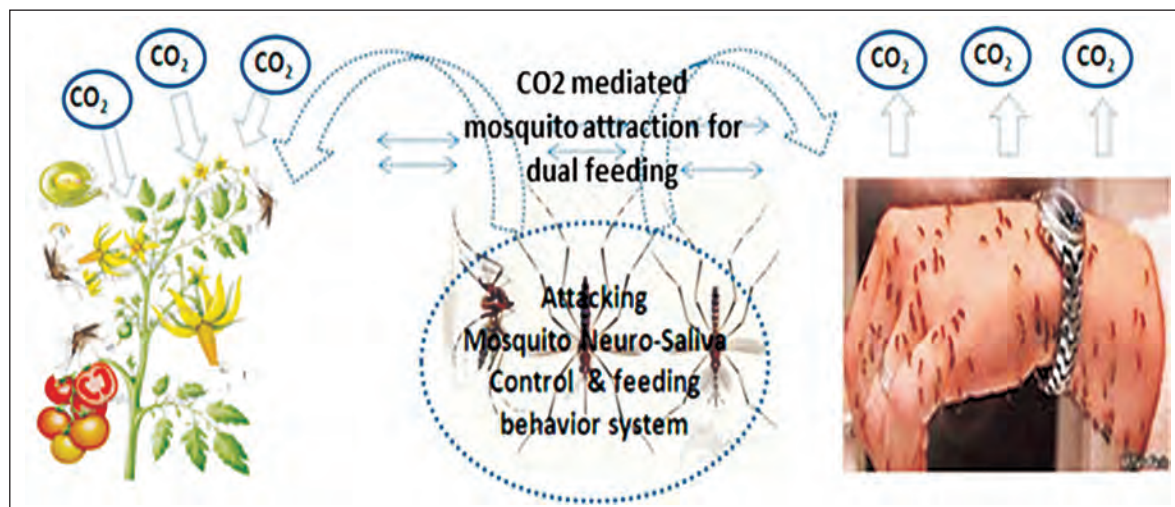
Differential Expression of Salivary Proteins between Susceptible and Insecticide-Resistant Mosquitoes of *Anopheles stephensi*

2D electrophoresis of salivary gland tissues of both *An. stephensi* sensitive and insecticide resistant strain were carried out. 17 protein annotations were found between resistant and susceptible strain when analysed by Protein PAGE software. Of the total of 17 spots, 9 spots were found to be up regulated and 8 spots were found to be down regulated in *An. stephensi* insecticide resistant strain. After analysis with Maldi-TOF with peptide mass fingerprinting and MASCOT search, total 42 proteins have been identified and among these 22 proteins are upregulated and 20 proteins are downregulated. We have found dehydrogenase/reductase role in xenobiotic metabolism as well as in redox sensor mechanism, Gluathione-S-transferase & Cytochrome-450 in insecticide resistance mechanisms. All enzymes were found to be upregulated in *An. stephensi* insecticide resistant strain. Their further details analysis in terms of transcription role is in process.

Designing New Molecular Weapons to Fight Vector Borne Diseases

Attacking Mosquito Neuro-control System

Adult female mosquito feeding behavior and food choice decision is a random process. Mosquito salivary glands are specialized organ which not only initiate first biochemical communication for sugar or blood meal acquisition, but also potentiate *Plasmodium* transmission. Molecular understanding of neuro-control of mosquito salivary gland may provide new molecular targets for feeding behavior alteration and minimization of mosquito-bite exposure risk to vertebrate host (Fig.).

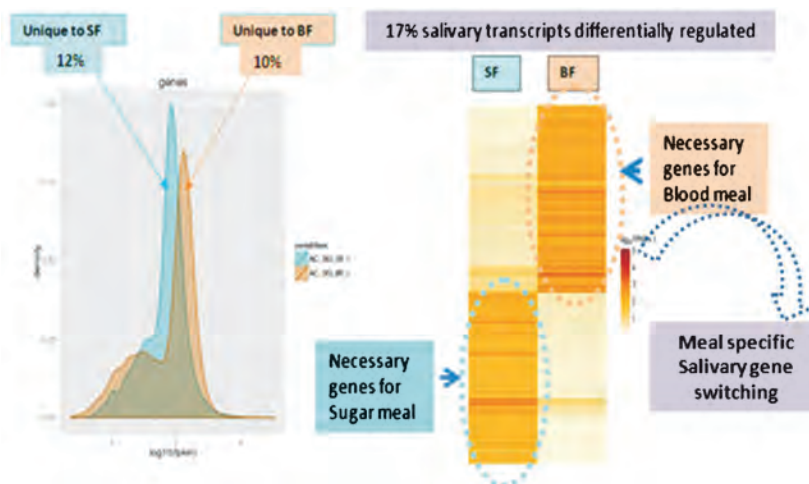


A working hypothesis to find out the molecular relationship of complex feeding behavior and adaptation towards dual feeding in adult female mosquitoes. CO₂ mediated vertebrate host seeking behavior is considerable importance, but for sugar meal seeking behavior is not investigated in detail.

Unraveling Molecular Strategies of Salivary Glands Towards Dual Feeding in *Anopheles Culicifacies*

To understand the global gene expression analysis of salivary glands in response to dual feeding by using Next Generation Sequencing (NGS) protocol, in the present study, we

examined and compared the sugar (SF) and Blood (BF) feeding associated salivary role in mosquito *Anopheles culicifacies*, an important rural malarial vector of ~65% malaria cases in India (Fig.).



Initial findings revealed meal specific restriction of 10-12% of salivary transcripts, while 17% transcripts undergo significant expression alteration through gene switching. Currently, we are trying to understand the regulation and control mechanism of switching, which could guide us to find suitable molecular target for functional validation and mosquito feeding alteration.

Changing Ecology of Anopheline Mosquitoes in Dadri CHC Area in Distt. G.B.Nagar, U.P.

An. culicifacies is the primary malaria vector species in Dadri CHC area in Distt. Gautam Budh Nagar in western U.P. The present study was continued to investigate the establishment of *Anopheles fluviatilis*, a potential malaria vector, in this area. During this study regular monitoring of the indoor resting mosquito density was made by hand catch method in six indicator villages of the Dadri CHC, from where *An fluviatilis* was also collected for the first time in Nov 2009.

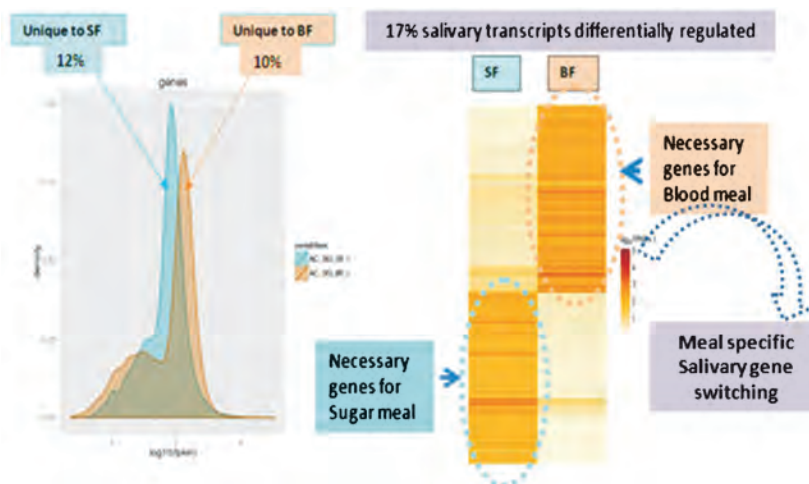
The study revealed that *An. culicifacies* continues to be the predominant malaria vector species in this area. The appearance of *An fluviatilis* in high densities in the Dadri CHC area was observed only during Nov.-Dec. 2009 till July 2010 and again in Jan 2012 till April 2012. *An. fluviatilis* has not reappeared in this area again after April 2012 till date. The prevalence of *An fluviatilis* in this area is not affected by annual seasonal changes, in contrast to other established anopheles species. An interesting observation was that the appearance of *An fluviatilis* was linked with the presence of thick vegetation of water hyacinth on the surface of slow moving water in the drain. These observations indicate that the appearance and disappearance of *An fluviatilis* in this area is probably due to the presence of thick vegetation on the surface of slow moving water in the drain. There is a declining trend in the overall density of *An culicifacies* and other anopheline spp., except *An subpictus*, in this area, probably due to land filling and increasing urbanization activities.

National Institute of Medical Statistics (NIMS), New Delhi

Extent of integration of Indian system of medicine & Homoeopathy (AYUSH) in National Rural Health Mission (NRHM)

This study aimed at measuring the extent of main streaming of Indian System of Medicine (AYUSH) under NRHM and to study the impact of NRHM programme in the utilization of AYUSH in the demographically weak districts of U.P.

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Findings showed that i) Doctors from AYUSH have been appointed on the Contractual basis in all the districts & participate in National Programs & prescribing only AYUSH Medicines which were available through State Govt. ii). There is increase in allocation of budget under AYUSH every year; and iii). Continuous supply of AYUSH medicines were the main suggestions for improving the AYUSH programmes.

Multi Level Modeling to Analyze RCH Services: Utilization and its Correlates

The study objectives were to assess the inequity in the access and utilization of maternal RCH services, ANC and PNC) and child health care (Immunization and treatment seeking behavior) and to investigate the degree to which the RCH utilization is influenced by the contexts within which the people live and other explanatory variables and to assess the superiority of Multi-level modeling approach over the Standard Logistic Regression for the current situation.

Data showed that comparing with the traditional regression model with same covariates, the intercept for the traditional model is -98.8528 as compared to -2.348727 for the multilevel model 3 in which district level and PSU level has been added to the model. The LR test for multilevel vs the traditional regression model results in a Chi-square statistics value 87.94 (33.01 for two level model) with $p\text{-value} < 0.001$, shows a stronger advocacy for the three level modeling.

The Institute carried out following activities

- A draft protocol was developed including the study design, methodology in collaboration with Centre of Dental Education and Research, AIIMS, New Delhi for discussion at ICMR.
- A final protocol has been developed by the Centre of Dental Education and Research, AIIMS, New Delhi for the conduct of the study.
- The NIMS is committed to provide further statistical support, monitoring and other data analysis services if needed from ICMR.

Ongoing activities/studies

1. The clinical Trials Registry – India (CTRI) www.ctri.nic.in
2. Acceptance level, knowledge, attitude and practice of Indian System of Medicine in NE.
3. A study on morbidity, mortality and maternal care in rural Delhi.
4. Development of Data Hub of Health Surveys and Use of Information for Modeling and Projection of Various Diseases.
5. Baseline Household Malaria Survey in World Bank Projects States, 2013.
6. Burden of disease due to cancer in India.
7. A Study on the potential gain in life expectancy after elimination of specified cause of death in selected states of India.
8. Knowledge Network Project on HIV/AIDS.

Statistical Consultancy

1. To faculty and PG students of different Medical Colleges in Delhi.

2. Review of articles from the following journals such as Indian Journal of Medical Research, Indian Journal of Cancer, Indian Pediatrics, AIDS, STI, AIDS & Behaviour etc.

Training/Workshops conducted/Lectures Delivered by NIMS Scientists

The Institute organized dissemination workshops of CTRI at CRME Madurai and another at Institute of Post Graduate Teaching and Research in Ayurveda, Jamnagar, Gujarat.

The Institute conducted summer training in Applied Statistics for the post graduate institute in statistics from university Delhi, IIT, Kanpur and Banaras Hindu University, Varanasi.

National Institute of Nutrition (NIN), Hyderabad

Community Studies

Assessment of Effects of Consumption of 'Carbonated water beverages' and Soft Drinks on Health of Adolescents and Young Adults

The above study was carried out to assess ill effects on consumption of carbonated beverages. A total 2,035 young adults (men: 48.6%) in the age group of 18-35 years were covered and similarly, a total 2,257 adolescents (boys: 56.5%) were covered for assessment. Adults, consuming CWBs ≥ 400 ml/week were defined as consumers and those who were not / occasionally consuming were defined as non-consumers. The mean consumption of CWBs per day was 65ml/day and 20ml/day among adult men and women respectively. The mean intake of CWBs was 47.3ml/day and 26.6ml/day among boys and girls respectively.

Nutrition Profile of Chenchu – A primitive tribe of Andhra Pradesh

The present study was carried out to assess their diet and nutrition status. There were no differentials observed in their food and nutrient intakes when compared to their tribal counterparts of the State. However, the prevalence of underweight, stunting and wasting was lower as compared to the general tribes of Andhra Pradesh. As observed in the verbal autopsy, the major cause of deaths among infants was premature delivery and low birth weight and among adults, it was cirrhosis of liver and accidents.

Assessment of Nutritional Status of below five year Rural Children and Performance of ICDS Functionaries in the Districts of Gujarat State

A survey and district-wise mapping of under-nutrition were carried out.. A total of 12,929 children (Boys: 52.3%) of <5 year age old were covered from the selected 10,424 households in 520 Anganwadi Centers for the purpose. Cluster analysis was carried out to identify three geographical areas/groups of districts in the state, with extent of underweight (high, medium and low) among children of <5 years as criterion. The overall prevalence of underweight was 59% in cluster 1, 46% in cluster 2 and 33% in cluster 3. It was observed that the proportion of children belonging to SC/ST population, joint families, illiterate parents, households having agricultural land and major occupation of parents being labour was significantly ($p < 0.01$) higher in cluster 1.

Microbiology and Immunology

Anticarcinogenic Property of Probiotic in Combination with *Allium sativum* and NSAIDs on DMH induced Colon Cancer and Colon Cancer Stem Cells in Rats

Treatment with *Allium sativum*, *Lactobacillus rhamnosus* GG and NSAIDs prevented DMH induced histopathological alterations and tumour formation in the colonic tissue; and inhibited Wnt and β -catenin expression. Microarray experiment demonstrated that PI3-kinase/Akt and Wnt/ β -catenin pathway mediates key signals for intestinal epithelial cell proliferation and inhibition of

2. Review of articles from the following journals such as Indian Journal of Medical Research, Indian Journal of Cancer, Indian Pediatrics, AIDS, STI, AIDS & Behaviour etc.

Training/Workshops conducted/Lectures Delivered by NIMS Scientists

The Institute organized dissemination workshops of CTRI at CRME Madurai and another at Institute of Post Graduate Teaching and Research in Ayurveda, Jamnagar, Gujarat.

The Institute conducted summer training in Applied Statistics for the post graduate institute in statistics from university Delhi, IIT, Kanpur and Banaras Hindu University, Varanasi.

National Institute of Nutrition (NIN), Hyderabad

Community Studies

Assessment of Effects of Consumption of 'Carbonated water beverages' and Soft Drinks on Health of Adolescents and Young Adults

The above study was carried out to assess ill effects on consumption of carbonated beverages. A total 2,035 young adults (men: 48.6%) in the age group of 18-35 years were covered and similarly, a total 2,257 adolescents (boys: 56.5%) were covered for assessment. Adults, consuming CWBs ≥ 400 ml/week were defined as consumers and those who were not / occasionally consuming were defined as non-consumers. The mean consumption of CWBs per day was 65ml/day and 20ml/day among adult men and women respectively. The mean intake of CWBs was 47.3ml/day and 26.6ml/day among boys and girls respectively.

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apoptosis in an experimental model of colon cancer. Inhibition of Wnt and β -catenin pathways and induction of GSK-3 β , which may eventually activate apoptosis and block key signals for intestinal epithelial cell proliferation appear to be the potential molecular pathway.

Metabolic Endotoxemia and Associated Metabolic Disorders in rats fed with Different Diets and their relation to Selective Gut Bacteria and changes in Intestinal Permeability – Phase 1 & Phase 2

Effect of various cooking oils

Effect of 10% groundnut oil, sun flower oil, palm oil, ghee and hydrogenated fats in an isocaloric diet fed to Sprague-Dawley rats for 5 months was studied. The study showed adverse effects on body composition, insulin sensitivity, bone mineral density and altered gut bacteria (lower bifidobacterial count and higher bacteroidites) in rats fed hydrogenated vegetable fat (oil) for 5 months. Nevertheless, endotoxin levels, ASMase and reactive oxygen species were normal.

Effects of feeding high carbohydrate diet

In the rats fed high carbohydrate diet (starch at 78%), there were changes in body composition like increased body fat%, decreased lean body mass, decreased fat free mass and decreased HDL/cholesterol ratio, increased plasma triglycerides. Rats, which received higher percentage of starch had higher Firmicutes bacteria.

Effects of feeding high fat diet

Palmolein at 30% induced systemic inflammation and altered the gut bacteria profile unfavorably. Supplementing flax seed oil significantly ameliorated many of the high fat diet induced adverse effects and increased the beneficial bifidobacteria and reduced the firmicutes level. While high fat diet is found to influence immunity, systemic inflammation and gut bacteria unfavorably, high carbohydrate diet was found to have atherogenic effects like adversely affecting body composition and lipid profile. Flax oil had a prophylactic role in reversing many of the high fat diet induced changes.

Basic Studies

Enhancing Dietary Iron and Zinc Bioavailability in Indian children

The iron and zinc absorption was assessed simultaneously from habitual rice-based meal diversified with 100 g of guava in 16 girls and 16 boys of 13-15 years using stable isotopes. The results demonstrated that dietary diversification with guava enhanced bioavailability of non-heme iron from 10% to 20% but not that of zinc. This can form simple inexpensive intervention strategy to combat iron deficiency anemia in India.

Stress, Allostatic Load and Micronutrient Status

Impact of dietary advice: The one year prospective institution- based study was carried out in 370 adolescent boys (15-19y) from 5 schools of Greater Hyderabad Municipal Corporation. One third of the participants had allostatic load and the AL index showed a positive association with controllable life events of adolescent life event stress scale. Psychological stress was associated with elevated concentrations of inflammatory marker CRP and hepcidin which did not contribute to hypoferraemia, which may be due to the influence of various factors including multiple micronutrient deficiencies. Among the micronutrients, vitamin B-12 was positively associated with adaptive coping which needed to be probed further. Even though there was an improvement in knowledge on micronutrients after intervention, only ascorbic acid and retinol status improved while vitamin B-12 and ferritin concentrations declined, but there was no reduction in allostatic load or stress. These results suggest that high psychological stress

leads to high allostatic load. Psychological stress was found to be pro-inflammatory leading to elevated hepcidin concentrations but not hypoferrremia and therefore the low-grade inflammation appeared to not interfere with iron absorption among adolescents.

Amino acid–Metal complexes as model for the Glucose Tolerance factor of yeast: Hypoglycaemic Activity and Therapeutic Potential in Diabetes; Synthesis, Structure and Mechanism of action in Yeast and Animals

To validate/ negate the hypothesis that Binary / ternary AA – Chromium complexes could be useful as insulin like / hypoglycemic agents in the treatment of Type 1/ 2 Diabetes, the effects of synthetic Phe-Cr, Lys-Cr and Cys-Cr complexes on OGTT in five month old male SD rats (control and STZ induced diabetic) were evaluated. The salient findings are: (i) Phe – Cr complex but not others showed a significant improvement in OGT (decreased AUC glucose) albeit in only diabetic rats but not age / sex matched controls; (ii) chronic oral supplementation with Cr:(Phe)₃ improved glucose tolerance in a high sucrose induced rat model of insulin resistance; (iii) Modulation of insulin signaling but not altered secretion of insulin during OGTT appears to underlie Chromium Phe complex mediated alleviation of diet-induced insulin resistance; (iv) That skeletal muscle from Cr (D-phe) 3-treated rats had enhanced Akt-phosphorylation and membrane translocation of GLUT4 compared to untreated diabetic controls appear to suggest that nutritional supplementation with chromium complexes may have potential therapeutic value in alleviating or preventing insulin resistance and the associated type 2 diabetes and metabolic syndrome.

IGF1 and BDNF signaling in the Brain of Wistar NIN Obese Mutant Rats during Ageing: Effect of Calorie and Micro-nutrient Restrictions

To validate / negate the hypothesis that modulation of brain IGF1/ BDNF signaling and/or greater oxidative stress underlie accelerated ageing in WNIN – Ob rats, studies were conducted in WNIN/ Ob and corresponding control rats. The salient findings of these studies are: (i) altered IGF1 and BDNF levels and signaling in brain and / or high oxidative stress could underlie accelerated ageing in the obese mutant rats of NIN; (ii) Significant changes were observed in plasma CRP levels in WNIN/Ob rats as compared to controls *albeit* at 12 months of age but not earlier; (iii) increased expression of glial fibrillary acidic protein (GFAP) in the hippocampus of 6 months old WNIN Ob rats compared to controls, whereas at 12 months of age GFAP expression was lower in WNIN/Ob than controls probably suggesting that it could underlie impaired synaptic plasticity and hence brain ageing in WNIN/Ob rats; (iv) At 12 months of age WNIN/Ob rats showed higher ($p < 0.001$) expression of ORX-A and ORX-A positive neurons in the brain than controls. Considering the importance of orexin in energy balance, feeding, wake–sleep cycle, stress response, aging, and reproduction, the increased ORX-A expression could be another factor underlying accelerated ageing reported earlier in WNIN/Ob rats.

Functional Assessment of Adult Human Pancreatic Islets following Autologous Transplantation

The present study used immuno-isolatory devices (Theracytes) to test the viability and functionality of monkey islets in these devices following auto- or allo-genic transplantation in monkeys. The results showed that the islets remain viable and functional for 12 months in pancreatectomized non-human primates in both autologous and allogenic islet transplantation; allo transplanted islets were viable and functional in the absence of an immunosuppression; poly tetra fluoro ethylene devices (TheraCyte) has engraftment potential to sustain islet with functional /insulin secreting responses; vascularization was more extensive in the neck region and explants obtained from interscapular region denoted it to be relatively a better site for implantation as compared to the thigh.

Establishment of Propagable cell lines from Pancreas and Adipose tissue of Embryo and Adult WNIN obese rats (WNIN/Ob & WNIN/GR-Ob)

WNIN Mutants rats (WNIN/GR-Ob and WNIN/Ob) were used as the model to study the adipose and pancreatic stress/inflammation as a phased gene expression studies, markers of stem cells, and their lineage commitment to form adipocytes or islets using primary cultures stromal stem cells/ductal epithelial cells. The data showed alterations in tissue milieu (to adapt to physiological shifts) happening in conditions of obesity and metabolic syndrome (MS) both during early and prolonged phase of obesity/insulin resistance (IR). The study showed the participation of several confounding factors that collectively co-precipitate for a state of profound inflammation in target tissues being appreciable in Mutants > lean > Controls and get worsened as the animals age. Studies both *in vitro* and *in vivo* amongst phenotypes advocate for the alteration in stem cell milieu during the state of metabolic lesions depicted in Mutants with Obesity/IR /IGT/ HI, associated with patho-physiological conditions (adipose tissue, pancreatic, BM-MSCs), portraying features of pre-diabetic/T2D as compared of human scenario.

Characterization of Active Principles and Mechanism of action of Dietary Aldose Reductase Inhibitors and Antiglycating agents: (v) Isolation and Characterization of β -glucogallin as a novel aldose reductase inhibitors from *Emblica officinalis*

Aldose reductase (ALR2) is a major target for the development of therapies to treat diabetic complications. The study described the bioassay-guided isolation and structure elucidation of 1-O-galloyl- β -D-glucose β -glucogallin, a major component from the fruit of the gooseberry that displays selective as well as relatively potent inhibition of ALR2 *in vitro*. Further, it has been shown that β -glucogallin effectively inhibits sorbitol accumulation under hyperglycemic conditions in an ex-vivo organ culture model of lenses excised from transgenic mice over-expressing human ALR2 in the lens. This study demonstrates that molecules from natural products such as β -glucogallin as therapeutic leads in the development of novel therapies to treat diabetic complications.

Impact of agents with Potential use in Functional Foods on Biomarkers for Induction of Age Related Diseases

Accumulation of intracellular sorbitol due to increased aldose reductase (ALR2) has been implicated in the development of diabetic complications. We have described the inhibition of ALR2 by ellagic acid (EA) a bioflavonoid present in many dietary sources. EA inhibited ALR2 with an IC_{50} of 46 nM in a non-competitive manner. Further EA is relatively more specific towards ALR2 over other member of aldo-keto reductase family. Molecular docking studies substantiate these findings. EA suppressed sorbitol accumulation in human erythrocytes, rat lens and rat retina under high glucose conditions. Finally, significance of EA was demonstrated in terms of prevention of loss of lens transparency under high glucose conditions in ex vivo conditions. Together, these observations suggest that EA holds a therapeutic promise to prevent or treat complications of diabetes.

Potential Role of Dietary Nutrients vitamin A and Polyunsaturated Fatty Acids (PUFA) on Regulation of Development and/or Control of obesity using a Genetic Obese Mutant Rat Model (WNIN/GR-Ob)–Nutrient-Gene Interaction

Chronic feeding of vitamin A-enriched diet (129mg per kg diet) to glucose-intolerant obese rats of WNIN/GR-Ob strain improved the hyperglycemia, glucose tolerance and muscle insulin sensitivity. qRT-PCR data suggest the transcriptional regulation of the various important lipogenic pathway and adipokine genes of visceral adipose tissue and it was well corroborated

with the increased adiposity and insulin sensitivity observed in these obese rats. Importantly, it appears that vitamin A-mediated improvement in muscle insulin sensitivity in obese rats is due to regulation of phosphorylation status of glycogen synthase, which in turn resulted in increased glucose uptake and glycogen synthesis.

Abdominal Obesity and its Relation to Plasma Homocysteine and other Biochemical CHD risk factors in Middle Aged Men

With 58% prevalence of hypertension in men with abdominal obesity measured by waist circumference (WC) ≥ 90 cm and with a significant ($p < 0.001$) positive correlation of four obesity measures (BMI, WC, WHR and % of BF) with systolic and diastolic blood pressures, regression analysis in the present study shows that WC alone predicts systolic and diastolic blood pressure. A graded increase in insulin resistance was observed from lower ($\geq 18.5 - < 23$), to medium ($\geq 23.5 - < 27.5$) and to higher range of BM (≥ 27.5) among men in the present study. Regression analysis shows that BMI predicts insulin resistance. The inflammatory marker, C-reactive protein levels were found to be positively associated to waist circumference and % of body fat. With a 28% prevalence of hyperhomocysteinemia ($\geq 15 \mu\text{moles/L}$) in the overall study population, vegetarian men had double the prevalence of hyperhomocysteinemia compared to non-vegetarian men. In relation to body composition, in a similar range of BMI, men with high WC had significantly ($p < 0.05$) higher plasma homocysteine concentrations than the men with normal WC (< 90 cm). In the present study, men with low HDL cholesterol levels were found to have significantly ($p < 0.05$) higher plasma homocysteine concentrations than men with normal HDL-cholesterol levels. A negative correlation was observed between plasma homocysteine and HDL cholesterol levels is an important finding.

Food and Drug Toxicology Research Centre (FDTRC)

Creation of Demand for Millet Foods through PCS Value Chain

A project was initiated to create demand for millet foods through PCS value chain with a view to commercialize several products of sorghum. The studies revealed that products prepared from sorghum were organoleptically on par with similar recipes prepared from wheat or rice. They were acceptable to children also. Consumption of sorghum resulted in better control of hyperglycemia. The glycemic index of some of the products were lower than recipes prepared from other cereals.

Value chain on Commercialization of Maize Products

National Agricultural Innovative project, a division of ICAR has initiated project to develop innovative products of maize for commercialization. Two varieties of maize were used to prepare selected food items and evaluated for acceptability and management of blood glucose in Type 2 diabetics. The studies indicated that QPM variety of maize had better quality of protein than Nityashree. Regular consumption of maize based foods had significantly lowering effect on levels of glycosylated hemoglobin although they were not low in glycemic index and load. The resulting beneficial effect could be due to the fibre content in the grain.

Micronutrient Profile of Population Residing in Fluoride Endemic Areas

A study was conducted to understand the role of micronutrients in fluorosis. The levels of magnesium, selenium and zinc were significantly higher in individuals from areas endemic for fluorosis. Thyroid function test showed that levels of T3 was significantly higher in people

with the increased adiposity and insulin sensitivity observed in these obese rats. Importantly, it appears that vitamin A-mediated improvement in muscle insulin sensitivity in obese rats is due to regulation of phosphorylation status of glycogen synthase, which in turn resulted in increased glucose uptake and glycogen synthesis.

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belonging to areas where fluorosis exists. There were no changes in hematological parameters. Overall the survey demonstrated that adverse effect due to exposure of high fluoride through water was less in the population studied due to their good nutritional status.

Assessment of Pesticide Exposure and Various Cancers among Agricultural Farming Community Guntur District

A project was taken up to understand the role of farming practices, exposure to pesticides and cancer incidence among the farming community of Guntur District of AP, where organophosphate and synthetic pyrethroid pesticides are used a lot. The results revealed that 89 subjects out of 670 cancer subjects showed presence of P, P'DDE and four of them had high levels. The survey also indicated that most of the farmers were not practicing proper spraying methods or adopting precautionary measures prior to/immediately after spraying.

Assessment of Dietary Intakes of select Chemical and Processing Induced Contaminants in various Socio-economic Groups in Hyderabad

In the present study information on foods consumed (conventional and processed) by high income, middle income and low income was collected. Foods were cooked as in culinary practice. The data showed that the intakes of conventional and processed foods differed between different socio-economic sections among the Hyderabad population. Intakes of trans fat through selected bakery items and other sources were less than 1% of energy. Dietary exposure to lead and cadmium were below the respective provisional tolerable weekly intakes (PTWIs). Estimated dietary exposure to pesticides were within the acceptable daily intakes.

Evaluation of Herbal and Nutraceutical Product for Anti-atherosclerotic activity

Our earlier research findings have demonstrated anti-atherosclerotic activity (*in silico*, *in vitro* & *in vivo*) of Poly Herbal Nutraceutical Formulation (PHN). The current studies suggest Prevention of Foam Cell Formation due to possible attenuation of CD36 cascading pathway, which promote entrapment of lipid laden foam cells due to ROS, inflammation and oxidized LDL (oxLDL) activation.

National Centre for Laboratory Animal Sciences (NCLAS)

Establishment of Baseline Values of Body Composition and Blood Pressure in Different Species of Laboratory Animals Maintained at NCLAS

A Study on mice strains: Progressive changes in the body composition of three commonly used mice strains in nutritional and toxicological research VIZ., Swiss albino, BALB/C and C₅₇BL₆J were analyzed by TOBEC initially and subsequently by DXA compared with chemical method and parameters like lean body mass (LBM), fat, fat %, fat free mass were determined. It was observed that the TOBEC analysis did not correlate with the carcass analysis for mice. DXA is superior, constant method and correlated with chemical method. Swiss albino mice had significantly higher body weights compared to BALB/C and C₅₇BL₆J. This was more pronounced in males than females. LBM is reduced, fat and total fat percentage was found to be more in Swiss albino than the other two strains. Similar pattern of results were obtained in terms of their food intake and clinical chemistry parameters. In conclusion our findings unequivocally show that for body composition analysis of lab animals like mice, hamsters, guinea pigs and rabbits, DXA is superior and constant as compared to all methods. For rats, TOBEC could match with carcass analysis.

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Preclinical Toxicology

Pre-clinical efficacy (IBD, Anti-inflammatory) and safety evaluation of Novel Peptide Genoep 4 (Issar 4)

Inflammatory bowel disease (IBD), a major health problem in the developed world which comprises i) ulcerative colitis (UC) and (ii) Crohn's disease (CD) a chronic relapsing and remitting inflammatory disorders of the gastrointestinal tract. Our Centre has evaluated a beneficial role through immune regulatory activity and anti inflammatory properties of IS-217 having similarities like interleukin10 (IL-10).

Pre-clinical Toxicology study of Recombinant Interferon beta-1b (IFN β 1b)

The Interferon beta – 1b using recombinant DNA technology developed by private organization to promote it for the treatment of multiple sclerosis. The Pre-clinical toxicity investigation (Acute and sub-chronic) has been conducted as per DBT/Schedule Y of DCGI guidelines and report submitted for clinical trials through RCGM and DCGI.

Pre clinical Toxicity Evaluation of Transgenic Cotton (Cry1ac Event-1& Cry1EC (event-24)

The Bt cotton with stack genes Cry1Ac (event-1) & Cry1EC (event-24) have been developed by one of the private companies for economical advantages has been evaluated for preclinical toxicology as a part of Bio-safety norms of DBT.

National Institute of Occupational Health (NIOH), Ahmedabad

Neuron Specific Enolase and the Relationship between Blood Lead Levels and Neurobehavioral Function in Lead-acid Battery Manufacturing Workers

The study was aimed to evaluate serum neuron specific enolase (NSE), biogenic amino-acids (dopamine & serotonin), neurobehavioral performance in 146 male workers exposed to Lead (Pb) from lead-acid storage battery plant. These parameters were compared with blood lead levels (BLL). BLL was assessed by using an atomic absorption spectrophotometer. Serum NSE and biogenic amino acids were estimated using ELISA kits. Neurobehavioral function tests were assessed by using CDC- recommended tests: simple reaction time (SRT), symbol digit substitution (SDST) and serial digit learning test. Multiple linear regression analysis was used to evaluate the association between neurobehavioral function tests and BLL with controlling of age, alcohol consumption, body mass index, experience, smoking, serum NSE, dopamine and serotonin. The levels of serum NSE and dopamine found increased with increase of BLL. The level of serum serotonin decreased with increase of BLL. The SRT and SDST tests showed positive and significant association with BLL. Study results illustrated the significant association of BLL with neurobehavioral domains of visual motor speed, attention and perception among lead exposed workers.



Lead acid battery workers

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Lead acid battery workers

Study of Levels of Cytokine in Sputum of Cotton Dust Exposed Workers

Inhalation of cotton dust may cause severe acute pulmonary and systemic inflammation, which may lead to different respiratory disorders such as byssinosis, respiratory tract irritation, which is marked by chest discomfort, cough, dyspnea, chronic obstructive pulmonary disease (COPD) etc. Inhalation of endotoxins induces the influx of neutrophils and production of pro-inflammatory cytokines and biomarkers, which may reflect in airway fluids. Current study assessed general health status and pro-inflammatory cytokines levels in sputum of cotton dust exposed workers. Total 375 workers aged 26.9 ± 9.5 years with working duration 5.8 ± 6.1 years from 23 cotton-ginning factories of Kadi, Gujarat participated in the study. Pro-inflammatory cytokine levels of IL-1 β , IL-4, IL-6, IL-8, IL-10, IL-12, IFN γ and TNF α were analyzed in sputum of subjects by protein array assay using Luminex xMAP based technology and pulmonary function test (PFT) was performed. The data showed, almost two thirds of workers reported of having cough (64.8%) with nearly one fourth of them with acute cough (25.76%). On PFT, normal profile was observed in 90.1% workers, whereas, restrictive, obstructive and combined ventilatory impairments were observed in 5.1%, 3.0%, and 0.6% workers, respectively. High values of IL-10, IL-12, IL-6 IL-1 β and TNF- α was observed among workers having pulmonary obstruction and byssinosis like symptoms.



Cotton dust exposed workers

Assessment of Airborne Toluene Diisocyanate (TDI) at Process Plants of Flexible Foam Industries

Industrial workers are exposed to toluene diisocyanate (TDI) at Flexible foam industries. Long-term exposure to TDI can produced significant health effects such as occupational asthma. A study had been carried out at flexible industries located in Gujarat and Silvassa-Dadra & Nagar Haveli area-UT to assess the airborne exposure to TDI and its effect on respiratory health during 2010 to 2013 period. Under environmental monitoring 129 air samples were collected at different process plants. About 17.83% of air samples had exceeded the American Conference of Industrial Hygienists (ACGIH) Threshold Limit Value - Time Weighted Average of 0.005 ppm for TDI. Under health monitoring 194 workers were covered. The health examination results indicated only 5.6% of subjects had respiratory complaints such as cough, sputum production and complaint of breathlessness. Spirometry revealed that 87.1% of the subjects were not having any pulmonary impairment while 19(9.8%) and 4(2.1%) had restrictive and obstructive type of pulmonary impairment respectively. As per Indian Factories Act 1948, India does not have permissible exposure limit for TDI. Based on our study results, we suggest to include

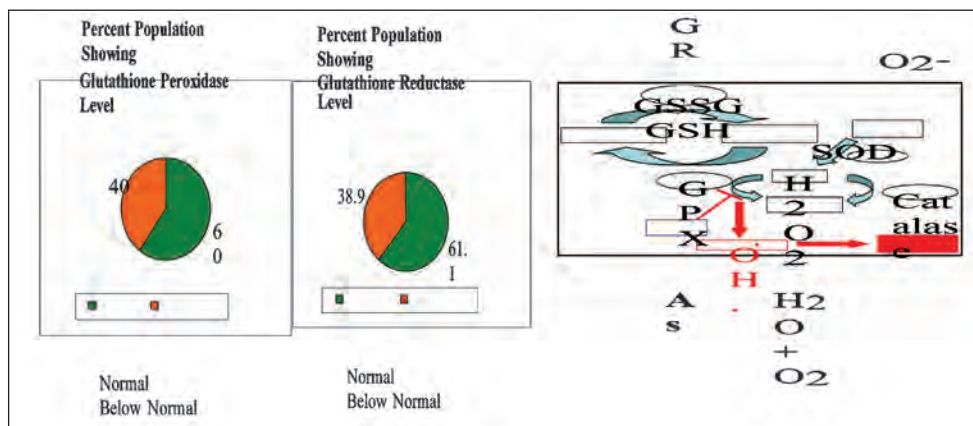


Flexible foam industry workers

permissible exposure limit of 0.005 ppm for TDI in order to protect and improve safety and health of the flexible foam industry workers.

Biomarker Study of Arsenic Toxicity in the Light of Oxidative Stress

The study was conducted to detect and characterize suitable biomarker for detection of early exposure. Elevation of serum uric acid, a metabolic product of pyrimidine nucleotide (constituent of DNA) derived from oxidative stress, indicated the possibility of considering total antioxidant status (TAS) and glutathione related enzymes as biomarker of arsenic exposure. The study indicated significant increase ($p < 0.001$) in serum uric acid in 58%, decline of TAS in 31.6% and reduced activity of glutathione peroxidase (GPX) among arsenic exposed population ($n=108$). These observations are probably be due to presence of less amount of glutathione (GSH) as substrate for GPX to take part in catalysis. This idea is also supported by lowering of glutathione reductase (GR), enzyme responsible for GSSG to GSH transformation, in exposed subjects in 38.9% cases. It is also noted that 6.4% of the exposed population showed keratosis and skin pigmentation indicating signs of arsenic exposure. Their serum uric acid were significantly higher (than normal range), which is further corroborated by lowering of TAS, GR, GPX than normal range. This study also showed reduced oxidative stress parameters in a significant number of cases without signs and symptoms of arsenic exposure. It may be concluded that cyto-oxidative phenomenon /oxidative stress takes place in both the categories among which high arsenic consuming group could not compensate leading to symptomatic disease.



Proposed model of arsenic induced oxidative stress

Assessment of Physiological and Metabolic Status and their Effects on the Morbidity Pattern of the Bus Drivers

Thirty two drivers were enrolled in this study. History of the past and present illness, general survey, clinical examination, anthropometric measurements and pulmonary function test (PFT) were carried out. They were interviewed to assess subjective workload and were asked to point out work related bodily musculoskeletal pain or discomfort. Metabolic status of drivers was determined by biochemical analysis of blood and spot urine samples. Parameters such as, plasma glucose (fasting), serum total protein, albumin, triglyceride, cholesterol, HDL, VLDL and LDL cholesterol, homocysteine, blood urea and serum creatinine, urinary protein creatinine ratio and liver enzymes levels like SGOT, SGPT and GGT were estimated. Working heart rate was recorded continuously using a heart rate monitor during work.

Mean value of body mass index indicated almost three fourth of bus drivers were of 'normal healthy' category; however, some were overweight (16%) and underweight (15%). Waist-Hip

ratio indicated that 91% subjects had abdominal obesity. The average working heart rate (AWHR) and peak working heart rate (PWHR) showed the workload category as moderate to heavy. Considering Energy Expenditure (kcal/min) of driving a bus, the workload was found to be as moderate. This may be due to work in sitting posture. On subjective assessment drivers reported, workload as very heavy (50%), heavy (28%) and moderate (22%). The feeling of 'very heavy' is due to long working hours. Nearly one-fourth (25%) of the bus drivers reported of musculo-skeletal pain and discomfort with most affected body part was being back (38%), followed by neck (25%) and shoulder (25%). Intensity of body pain varied from 'moderate' to 'severe'. The PFT showed within normal range of lung volumes and the flow rates. The result of biochemical analysis showed that the mean and median values of liver enzymes like SGOT and SGPT were higher than that of the reference value.



Study on Bus Drivers

Muscular Loading during Manual Handling Tasks

Study on (Manual Muscular Load Handling) MMH tasks in a simulated laboratory setup was carried out with the hypothesis that muscle activity may be influenced by the changes in methods of MMH tasks as well as increase in load of material. Results showed that MMH tasks when performed repeatedly or over long periods of time may lead to fatigue and injury. It is evident from the Root Mean Square (RMS) values of Electromyography (EMG) signal during load bearing activities that with higher range of load difference (from 4 kg to 12 kg) posed a significant influence on muscles of upper extremities (deltoid, upper trapazius and erector spine) ($p < 0.01$). However such influence was not observed in case of lower range of load difference (from 4 kg to 8 kg, as well as from 8 kg to 12 kg). Increase in level of handling of load from ground to knee to waist to chest for increasing grades of load (4 kg-8 kg-12 kg), the RMS values of deltoid, rectus femoris and semitendinosus hamstring muscle also increases. Further, increase in load holding time demonstrated in decreased median frequency (MDF) values of the muscles. The decreasing trend of MDF values was observed, starting earlier with higher magnitude load as compared to lower one indicating muscles became fatigued faster with higher grade of load. Overall the study indicates that any MMH activity involving holding of load for long duration may manifest in fatiguing nature of muscles.

Role of Heavy Metals in Human Male Reproduction

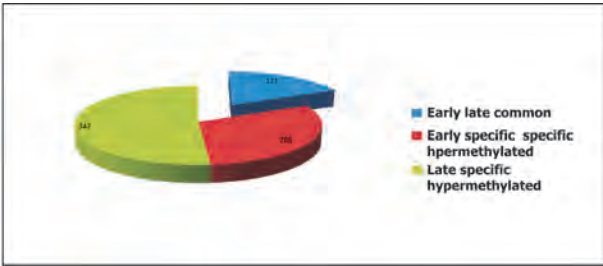
Exposure to different heavy metals may cause toxic insult to male reproductive system. The study was conducted among the men attending for infertility problem at OPD of Obstetrics and Gynecology, Ahmedabad. Based on history of exposure to heavy metals, subjects were divided into exposed and non-exposed group. The occurrence of azoospermia was significantly higher among the exposed subjects as compared to the non-exposed subjects. Mean lead and cadmium levels in blood were compared between the groups based on sperm count, motility and morphology. A negative relationship was found between sperm count, total progressive motility and normal morphology with both blood lead, as well as cadmium levels. The seminal plasma copper, serum copper, serum zinc and seminal zinc level was not differed significantly between exposed and non-exposed groups. The results indicated that the metals, lead and cadmium might have some role in deteriorating semen quality.

National Institute of Pathology (NIOP), Delhi

At National Institute of Pathology the thrust areas of research are tumor biology, infectious diseases including *leishmaniasis*, *tuberculosis*, *leprosy* and *chlamydia*, stem cell biology and environmental toxicology. The primary approach of research was to understand genetic mechanism associated with virulence and drug resistance and to identify biomarkers for risk, prognosis and new therapeutic targets in various cancers and infectious diseases with attempts to bridge basic studies to the clinic.

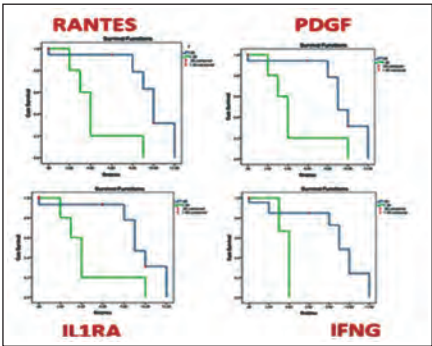
Tumor Biology

Study on Gene Expression and Hyper-methylation Profiles in Early Onset Breast Cancer had been aimed to identify methylated tumor suppressor genes associated with breast cancer that occurs at early age (<40 years) and late age (>40 years). Among them hypermethylation of 246 genes was unique to early onset cancers while 347 genes were found hypermethylated in late onset cancers only and 121 genes were found methylated in both late and early onset cancers. Experiments targeting the ALDH-positive BCSCs revealed that ellipticine can reduce the proliferation and self-renewal ability of ALDH1A1-positive BCSCs *in vitro* and can be used in combination with a cytotoxic drug like paclitaxel which helps in debulking the tumor mass. *In silico* data suggests that ellipticine reactive metabolites 13-OH ellipticine and 12-OH ellipticine could be good candidates for targeting breast tumors with high ALDH activity.



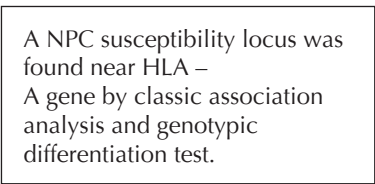
Genes differentially methylated in early and late onset breast cancer

Characterization of host immune factors associated with progression of Superficial TCC of bladder showed enhanced immune response in patients with NFκB and COX2 upregulation in tumour tissue, Systemic immune response showed increased serum IL1ra and VEGF in recurrent cases of bladder cancer and low concentrations were associated with better recurrence free survival. Increased urinary PDGF, IL-1ra and IFNγ were associated with recurrence and lower urinary concentration of PDGF, IL-1ra and IFNγ were associated significantly with better recurrence free survival of bladder cancer patients.



Lower concentrations of Urinary cytokines RANTES, PDGF, IL1RA and IFNG are associated with better recurrence free survival

To understand the etio-pathogenesis of nasopharyngeal cancer (NPC) in NE states of India 31 microsatellite markers spanning the HLA region were studied to investigate immunogenic



Genome-wide analysis of genetic alterations in patients with esophageal cancer from NE India using single nucleotide polymorphism arrays showed amplified COL11A1, FGF12, PAK1 and deleted regions DLC1, NPHP4. Functional analysis of these key genes in esophageal cancer cell lines is undergoing to understand their role in esophageal carcinogenesis. Epigenetic Studies in esophageal cancer in high risk region of Northeast India showed promoter hypermethylation of OPCML (Opioid binding protein/cell adhesion molecule-like), NEUROG1 (Neurogenin1), TERT (Telomerase reverse transcriptase), WT1 (Wilms tumor 1); Up regulated Histone methylases DOT1L (DOT1-like, histone H3 methyltransferase), PRMT1 (Protein arginine methyltransferase 1), and Up regulated Histone acetylases KAT7 (Lysine acetyltransferase 7), KAT8 (Lysine acetyltransferase 8), KAT2A (Lysine acetyltransferase 2A).

Study on dynamic regulation of lymphocyte signaling of acute leukemia showed that higher ROS level were found in CD3 positive cells in T-ALL samples as compared to AML samples. It was also found that expression of Co-stimulatory (CD28 and CD27) and co-inhibitory molecules (CTLA4 and PD1) in ROS +ve T-cells were dynamically changed in T –ALL and AML suggesting that they may be responsible for the dysfunction of T-cells in ALL and AML.

Drug resistance in Leishmaniasis

Widespread resistance against sodium antimony gluconate (SAG) has resulted in introduction of miltefosine (MIL) as the first line drug in parts of Bihar, however, long half-life treatment poses threat of development of resistance. Reports of relapses following MIL treatment have surfaced already. Hence, it is essential to monitor the treatment efficacy and understand the mechanism of resistance towards MIL for effective control of VL. We earlier reported that expression pattern of LdMT/LdRos3 genes therefore, does not appear to be suitable marker for monitoring drug susceptibility in clinical *Leishmania* isolates. We analysed SNPs in MIL resistant and sensitive parasite and evaluated mRNA expression level of selected genes in clinical isolates of *L. donovani*. Sequence analysis of LdMT and LdRos genes revealed the previously reported single nucleotide polymorphism, C1259→A resulting in substitution of

Thr 420→Asn in the MIL resistant cell lines. Additionally a novel SNP, T 527→ A resulting in substitution of Val 176→ Asp and in LdMT gene of resistant cell lines was observed. However, no point mutations were detected in case of LdRos.

Paromomycin (PMM) is a promising new antileishmanial agent registered for visceral leishmaniasis (VL) treatment in 2006, which is also effective in combination therapy. It is vital to understand the mechanism of PMM resistance to safeguard the drug. In the present study, we have utilized experimentally generated PMM resistant *L. donovani* to understand the mechanism of resistance and parasite biology. We found increased membrane fluidity accompanied with decreased intracellular drug accumulation in the PMM resistant parasite. There was a marked increase in gene expression of ABC transporters (MDR1 & MRPA) and protein phosphatase 2A that evince increased drug efflux. Further, evaluation of the parasite tolerance towards host leishmanicidal mechanisms revealed PMM resistant parasite as more tolerant to the nitrosative stress, at both promastigote and amastigote stage. The PMM resistant parasites also predicted a better survival capacity as indicated by resistance towards complement mediated lysis and increased stimulation of host IL-10. The susceptibility pattern of PMM resistant isolate towards other antileishmanial agents, sodium antimony gluconate and miltefosine, remained unchanged. Data implicated the role of altered membrane fluidity, decreased drug accumulation, increased expression of ABC transporters and higher tolerance capacity of parasite towards host defence mechanism in conferring PMM resistance in *Leishmania*.

Development of live attenuated vaccine candidates for leishmaniasis

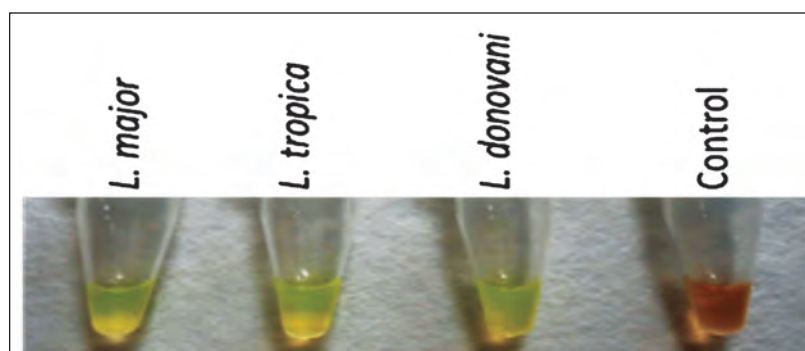
Currently, only treatment option available for leishmaniasis is chemotherapeutic which is costly, limited and associated with high relapse and resistance rates. Despite substantial effort there is no licensed vaccine against human leishmaniasis. Parasite persistence may be important for effective protective response and could be achieved by immunization with live attenuated parasite strain with known irreversible gene defect. Live attenuated *Leishmania* parasite, generated by deletion of Centrin 1 and p27 gene have been found to be safe and protective in mice, hamster and dog model. Evaluation of immune responses generated by Centrin knock out (KO) and p27 KO live attenuated *Leishmania* parasite in comparison to the wild type in human PBMCs was undertaken.

Th1 response was evaluated by estimating four cytokines (IL2, IL12, TNF- α and IFN- γ) that favor Th1 response. Results showed an increase in levels of IL-2, TNF- α and IFN- γ production by PBMCs after infection with wild type (LDS), Centrin KO and p27 KO parasite in comparison to control uninfected PBMCs. In case of IL-2; healthy, PKDL and HVL, all three groups showed significant stimulation in comparison to control uninfected cells after exposure with Centrin KO, p27 KO as well as for wild type. However, TNF- α and IFN- γ showed significant stimulation only in HVL and PKDL group. Further, stimulation of IFN- γ was much higher compared to IL-2 and TNF- α . Results showed no significant stimulation of IL-4 and IL-10 after infection with wild type, Centrin KO and p27 KO in any of the three groups. However, IL-6 showed significant stimulation after infection with wild type, centrin KO and p27 KO in all the three groups. IL-17 also showed stimulation after infection.

Development of Loop-mediated isothermal amplification (LAMP) assay for diagnosis of *Leishmania* infection

Previously we reported utility of *L. donovani* specific loop mediated isothermal amplification (LAMP) assay based on 4 primers as a diagnostic tool for VL and PKDL. We have now established a new LAMP assay which detects *L. donovani*, *L. infantum*, *L. tropica* and *L. major* with variable sensitivity and higher sensitivity towards *L. donovani* and *L. tropica*. The new assay is based on 6 primers which impart increased sensitivity and specificity to

the assay. Addition of two extra primers, known as loop-primers, accelerates the product formation, thereby shortening the required reaction time from 50 min (in published assay) to 30 min. We have evaluated the new assay with different *Leishmania* spp. parasite DNA. The assay was positive in *L. donovani*, *L. tropica* and *L. major* spp. using 10 ng DNA showing its specificity towards different species of *Leishmania* parasite (Fig.).



Specificity of LAMP assay for different *Leishmania* spp. parasite DNA (10 ng). The assay was positive for *L. major*, *L. tropica* and *L. donovani* species of parasite.

Chlamydia

The study aimed to find the prevalence of *Chlamydia trachomatis* infection in the synovial fluid of patients with reactive arthritis (ReA)/ undifferentiated spondyloarthropathy (uSpA) and to understand the cytokine pattern in the joints of infected patients. Both molecular and antigen based methods were used for establishing chlamydial infection: 14% ReA/ uSpA patients were positive for *C. trachomatis* in the synovial fluid using nested PCR (nPCR). The sensitivity and specificity of semi-nested PCR was 75% and 100%, with respect to nested PCR. Positive nPCR patients were compared with presence of *C. trachomatis*-specific IgA antibodies in the synovial fluid. Among nPCR *C. trachomatis*-positive ReA/ uSpA patients, 11.1% were IgA-positive. As the enigma of this disease is reflected in its ill-defined pathogenesis, hence, cytokine levels were also studied, wherein, it was found that serum IFN-gamma and IL-4 concentrations were significantly higher in *C. trachomatis*-infected ReA/ uSpA patients as compared to uninfected control osteoarthritis patients ($p < 0.05$, for IFN-gamma and $p < 0.02$, for IL-4). Work is in progress for understanding the underlying mechanism of ReA, whereby an imbalance between type 1 and type 2 immune responses seems to be critical in determining susceptibility to chlamydial disease.

Leprosy

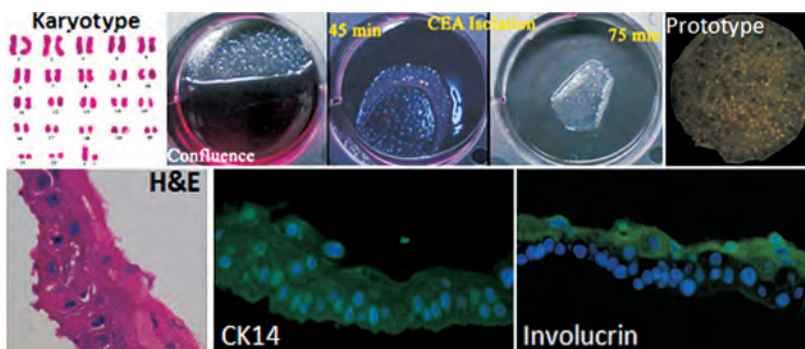
Leprosy reversal type 1 reaction is under diagnosed on histopathology compared to clinical diagnosis. A study on 120 cases showed increased expression of chemokine receptor CXCR3 mRNA in BT type 1 reaction as well as BB type 1 reaction. CXCL10/IP-10 mRNA shows statistically significant increase in BB type 1 reaction. Since BB Leprosy is the most unstable form in the leprosy spectrum, it is BB Hansens in type 1 reaction that shows the tendency to develop a type 1 reaction as shown by increased expression of CXCR3 both at m-RNA and protein levels. The increased expression of CXCL10 has been demonstrated in serum of patients from type 1 reaction by another author. However, these findings may prove to be useful laboratory aids in the diagnosis of type 1 reaction and it can be concluded that elevation of CXCR3 /CXCL10 axis is a better marker to diagnose a type 1 reaction than iNOS as previously believed.

Tuberculosis

Having established earlier that resistin level increases in patients with tuberculosis and decreases in patients as a function of treatment the role of resistin in pathogen signalling was investigated. Different pro and anti-inflammatory cytokines (IL-10, IL-6, and TNF- α) were scored using ELISA. Resistin treatment induces the secretion of IL-10, TNF- α and IL-6 as a function of concentration. This reveals a complex network of signalling events in response to resistin. Crosstalk between inflammation and ER stress induced unfolded protein response (UPR) influences pathogenesis/disease progression involving the immune cells such as macrophages. Normal functioning of these cells require trafficking of large amount of protein through ER. Human resistin, predominantly secreted from macrophages as a proinflammatory cytokine during infection is retained inside the ER in stressed cells where it functions like a chaperone. Resistin therefore have a role in modulating UPR during ER stress under physiological conditions in addition to its role as a regulator of inflammation. The role of hRes as a chaperone-like molecule is strongly indicative of this chemokine acting as a connecting link between stress response and inflammation which is central to disease pathogenesis.

Adult Stem Cell Biology

The objectives of study on a novel arithmetic approach for fool-proof production of growth arrest in 3T3 cells suitable for human epidermal culture to test a hypothesis that feeder effectiveness depends on calculated exposure availability of MMC and Swiss 3T3 cells are used as feeders aimed at producing human epidermis for application in burns, has almost been completed. The growth stimulatory influence of feeders produced by minimal, medial & maximal inhibitory concentrations and the respective dose per cell combinations of MMC were verified by growth patterns of epidermal keratinocytes at various passages and at varying feeder-keratinocyte ratios with γ -irradiated feeders as controls. It was demonstrated that feeders inhibited by the medial MMC concentrations produced significant growth stimulation than the minimal and highly toxic concentrations whose influence was comparable to γ -irradiation. BrdU incorporation studies and colony forming efficiencies revealed similar influence. The medial MMC concentrations further sub-divided into dose per cell yielded significantly varying keratinocyte growth stimulation which was inversely proportional to the feeder extinctions. The optimized technique was employed to produce well characterized prototype of cultured epidermis. The present approach identified a cost-effective and optimized growth of epidermal keratinocytes.



A prototype of cultured epidermis produced by using Swiss 3T3 feeder cells which were growth arrested and optimized by a cost-effective in house technique. The keratinocytes exhibited normal human male Karyotype with histological features of human epidermis.

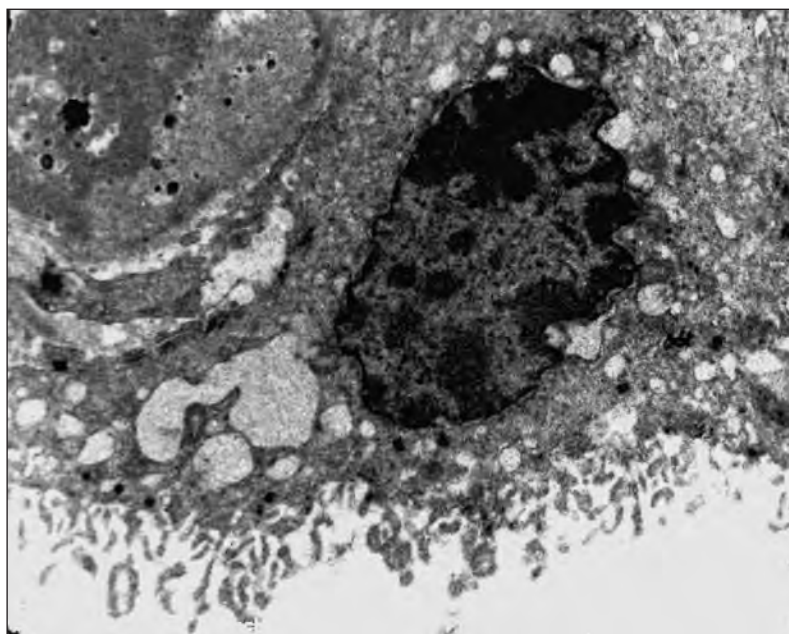
Another study on epithelial-mesenchymal interactions using human epidermal keratinocyte stem cells and innovatively growth-arrested fibroblast feeders in 3-D collagen model involved designing of experiments using *in vitro* 3-D skin model to assess qualitative and

quantitative differences in the morphogenesis of epidermis. The minimal, medial and maximal concentrations of MMC treatments resulted in significantly varied feeder cell extinctions in collagen synonymous to 2-D experiments. The basic technique of constructing whole skin model consisting of 3T3 fibroblasts in Type-I collagen gel as Dermal Equivalent and epithelialization by human epidermal keratinocytes followed by complete stratification of the epidermis at air-liquid interface were accomplished.

Environmental Toxicology

Ultrastructural study of placenta has revealed that the villi in placenta of tea garden workers exposed to pesticides are comparatively shorter and thinner and less vascularised as compared to non exposed group. Fibrinoid, a homogenous extra-cellular material similar to fibrin was frequently observed in villous stroma. The density of apical microvilli appeared considerably reduced and occasional microvilli-free areas were observed. The underlying trophoblastic basement membrane appeared significantly thicker than that of non-exposed workers. Occasionally fusion of cytotrophoblast and syncytiotrophoblast was also observed. Syncytial knots were numerous in exposed workers. In most of the cases of tea garden workers, trophoblasts (especially syncytial trophoblasts) showed dynamic changes in the nuclei such as increased heterochromatin content and nuclear aggregation. There was increased collagen in the villous stroma and shrunken endothelium in foetal capillaries.

It is plausible that deleterious effect of pesticides on placental barrier of tea garden workers could result in impairment of placental barrier, restrict nutrient supply from mother to foetus and thus could be the cause the Low birth Weight (LBW). Therefore, it can be concluded that exposure to pesticides during pregnancy is likely to be detrimental to the growth of foetus and the extent of damage (foetal outcome) is related to the level of pesticide exposure.



Pesticide exposed placenta

National Institute for Research in Environmental Health (NIREH), Bhopal

The genesis of ICMR's 31st permanent Institute on 11th October, 2010 as National Institute for Research in Environmental Health (NIREH), Bhopal is mainly to address Research on Environmental Health in general and in MIC particular. The Institute strives to achieve excellence through its transnational research activities on Environmental Health Issue. The NIREH will be complimentary to Bhopal Memorial Hospital and Research Centre (BMHRC) as one will concentrate research, other on treatment and medical education.

The epidemiological study of ICMR that began in 1985 on 80021 exposed & 15931 unexposed cohort populations is continued with objectives:

1. To register sample cohorts in the affected and unaffected (control) areas of Bhopal.
2. To collect base line data on socio-economic and demographic profiles and to study changes over a period of time in context of exposure to the toxic gas.
3. To observe mortality and morbidity in the registered cohorts of population and to establish relationship with the grades of exposure of the affected population.
4. To identify sub-cohorts for in-depth clinico-epidemiological studies to establish linkage between various studies and with the studies on the affected population outside the cohort.

Cohort

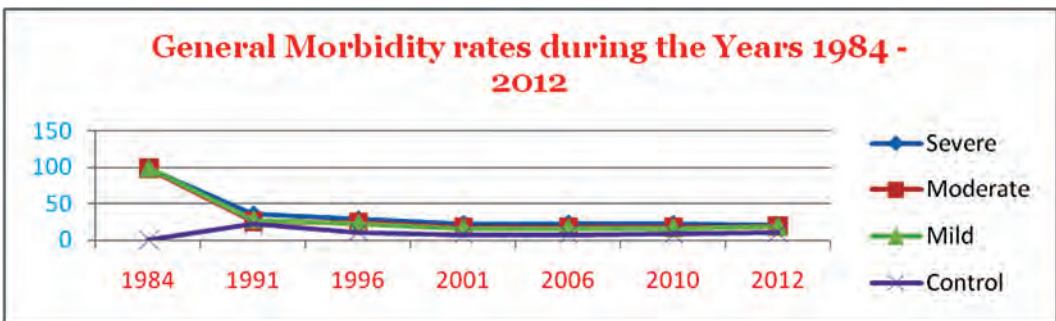
In 1985, when study was conceived, acute effect of toxic gas release were studied on a cohort of 80021(26382, 34964 and 18675 from severely, moderately and mildly affected localities) along with a control population of 15931. However, when study was actually started in 1986, a population of 19260, 28261 and 15185 from severely, moderately and mildly affected area respectively and 13526 from control area could be contacted for study. Of the actually available cohort of 62706 from affected area and 13526 from control area in 1986 in 2010 only 5658, 6533 and 4669 from severely, moderately and mildly affected area respectively (total-16860) and 5741 from control area was actually available for study.

Active steps are being taken for this loss of cohort by locating these individuals/family and study the reasons for the loss, during the 47th round that would be completed in December 2013.

General Morbidities

The table with graph regarding general morbidities is given below:-

General Morbidities (1984-2012)

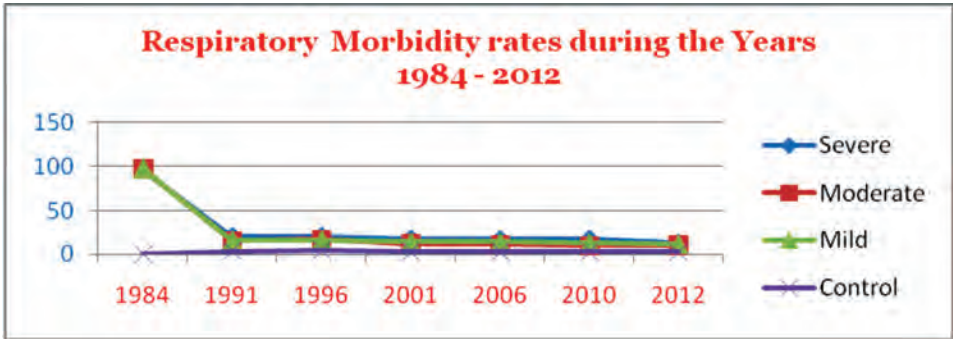


General morbidities (1984-2012)

Respiratory Morbidities

The table with graph regarding Respiratory morbidities is given below:-

Respiratory Morbidities (1984-2012)



Respiratory morbidities (1984-2012)

Ophthalmic Morbidities

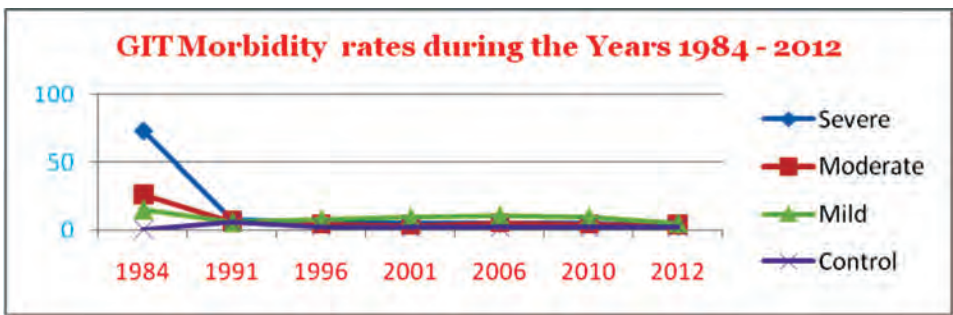
The table with graph regarding Ophthalmic morbidities is given below:-



Ophthalmic morbidities (1984-2012)

Gastrointestinal morbidities

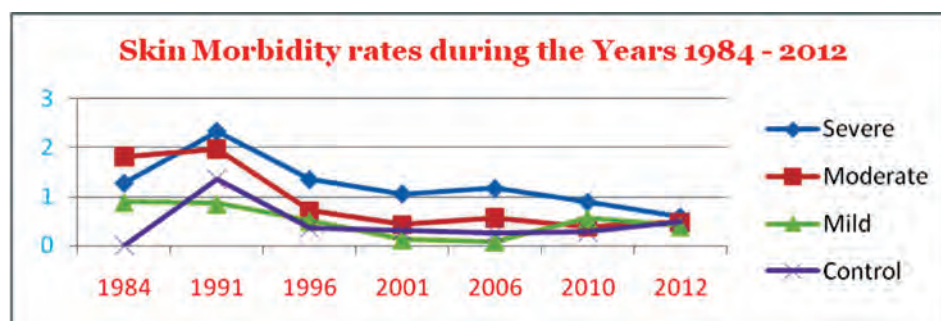
The table with graph regarding Gastro intestinal tract morbidities is given below:-



Gastrointestinal morbidities (1984-2012)

Skin morbidities

The table with graph regarding Gastro intestinal tract morbidities is given below:-



SKin morbidities (1984-2012)

The main reason for fluctuation of these morbidities is that this study has done only a symptom survey and symptoms could have seasonal or other variations at the time.

Mental Health Activities

To understand the magnitude of the prevalence of psychiatric disorder in the community, 600 families were screened in the year 2011 using the WHO screening tool, namely Self Reporting Questionnaire (SRO). A proportion of patients screened positive were examined by a Psychiatrist. The survey revealed that nearly 50% of screened population expressed emotional distress. Out of this 20% was attributable to diagnosable psychiatric disorder, while the rest of the group psychological distress was associated with chronic medical problem.

New Research Proposals

Development of Institutional Building at Bhauri, Bhopal

Madhya Pradesh Govt. has allotted 8.00 Hectare of land at "Bhauri", Bhopal for the construction and setting up of laboratory for 'National Institute for Research in Environmental Health (NIREH), Bhopal. The Government of Madhya Pradesh has allotted the above land free of cost. The Detailed Project Report (DPR) including layout plan of the institute to be constructed at Bhauri has been submitted for approval.

Technical Report: on Population Based Long Term Epidemiological Studies-II (1996-2010) on health Effects of the Toxic Gas Leak from the Union Carbide Methyl Isocyanate Plant in Bhopal was released by Dr.V.M.Katoch, Secretary DHR & Director General ICMR on 11th of October 2013.

Guidelines for Management of COPD: in MIC exposed subjects at Bhopal was released by Dr.V.M.Katoch, Secretary DHR & Director General ICMR on 30th June 2013. Training on this subject have been given to all the doctors of Gas Relief and Rehabilitation Department of hospital and mini units of BMHRC.

Other Activities

- **Treatment manual for Management of Mental Health problem**

Along the exposed population of Bhopal, has been prepared and under the process of publication. Six rounds of training for the doctors of Gas Relief & Rehabilitation Department & BMHRC have been given and will be continued as per requirement.

- **Special Respiratory Clinic**

This is being carried out at NIREH daily under the supervision and specialized services by Dr. V.K. Vijayan, Advisor to DG-ICMR. Here only severely ill COPD cases, identified at field level during epidemiological survey are being transported to NIREH. We are doing this special job with the help of Kamla Nehru Hospital and BMHRC. Till October 2013, 264 patients had benefitted by this programme.

- **Community based Health Services**

Severely ill patients who need emergency care/specialized care are being examined at doorstep and if needed transported to BMHRC for investigation and treatment on every Wednesday and Friday. Till October 2013, 204 patients had benefitted by this programme.

- **Respiratory Physiotherapy Centre**

Started at Mini Unit, BMHRC by the doctors of NIREH. One Physiotherapist has been providing services daily. It was suggested that the same system will be incorporated in Community Centre for Yoga under Gas Relief Department, Government of Madhya Pradesh. Till date 30 cases of COPD have been benefited.

Mental Health Training

Activity initiated during March 2013, two mental health-training programmes have been completed covering about 20 medical officers. These medical officers are from BMHRC and Sambhavana. The training programme is of 10 hours duration spread over four half working days for BMHRC and 2 days for Sambhavana. The training programme started with pre-training assessment of 10 clinical situations, and documenting the expectations of the participants from the training programme. The 10 case vignettes that represent the type of patients seen at the BMHRC, Sambhavana and their management. Analysis of the responses of the participants brought forth the following needs on psychiatric knowledge and skills: (i) the diagnostic terms used are limited and non-specific; (ii) there is limited diagnostic skills; (iii) knowledge of psychiatric medicines is limited; (iv) there is near absence of psychological interventional skills; (v) the knowledge of course and outcome of mental disorders and emotional problems associated with physical conditions is limited. The training was an interactive one, using videos of patients with various types of emotional problems from the survivors of gas disaster and standard videos on the specific syndromes prepared by the WHO, India office. Following each topic, detailed discussions were held to bring out the applicability of the approaches in the clinics.

National Institute for Research in Reproductive Health (NIRRH), Mumbai

The Institute continued to strive towards accomplishing its mandate *i.e.*, increasing contraceptive choices, preventing unsafe abortions, making pregnancy and child birth safer, understanding the causes of various reproductive disorders, and in assisting the Government of India in the formulation of policies for reproductive health for all.

Fertility Regulation

Potential of Synthetic Peptides of 80kDa HSA and hSPI for Development of Antifertility Vaccine

Active immunization with synthetic Peptide 1 of 80kDa Human Sperm Antigen (80kDa HSA) elicited gradual increase in antibody titer and induced infertility in male bonnet monkeys

- **Special Respiratory Clinic**

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Started at Mini Unit, BMHRC by the doctors of NIREH. One Physiotherapist has been providing services daily. It was suggested that the same system will be incorporated in Community Centre for Yoga under Gas Relief Department, Government of Madhya Pradesh. Till date 30 cases of COPD have been benefited.

Mental Health Training

Activity initiated during March 2013, two mental health-training programmes have been completed covering about 20 medical officers. These medical officers are from BMHRC and Sambhavana. The training programme is of 10 hours duration spread over four half working days for BMHRC and 2 days for Sambhavana. The training programme started with pre-training assessment of 10 clinical situations, and documenting the expectations of the participants from the training programme. The 10 case vignettes that represent the type of patients seen at the BMHRC, Sambhavana and their management. Analysis of the responses of the participants brought forth the following needs on psychiatric knowledge and skills: (i) the diagnostic terms used are limited and non-specific; (ii) there is limited diagnostic skills; (iii) knowledge of psychiatric medicines is limited; (iv) there is near absence of psychological interventional skills; (v) the knowledge of course and outcome of mental disorders and emotional problems associated with physical conditions is limited. The training was an interactive one, using videos of patients with various types of emotional problems from the survivors of gas disaster and standard videos on the specific syndromes prepared by the WHO, India office. Following each topic, detailed discussions were held to bring out the applicability of the approaches in the clinics.

National Institute for Research in Reproductive Health (NIRRH), Mumbai

The Institute continued to strive towards accomplishing its mandate *i.e.*, increasing contraceptive choices, preventing unsafe abortions, making pregnancy and child birth safer, understanding the causes of various reproductive disorders, and in assisting the Government of India in the formulation of policies for reproductive health for all.

Fertility Regulation

Potential of Synthetic Peptides of 80kDa HSA and hSPI for Development of Antifertility Vaccine

Active immunization with synthetic Peptide 1 of 80kDa Human Sperm Antigen (80kDa HSA) elicited gradual increase in antibody titer and induced infertility in male bonnet monkeys

(n=4). Two out of four animals regained fertility after decline in antibody titer and remaining two animals are being monitored for regain of fertility following decline in antibody titer. Acute toxicity studies in mice and rabbits with synthetic Peptide 1 was found to be safe and is being investigated for further safety studies.

Gender Equity-Focused, Male-Centered Family Planning for Rural India

Recruitment of key components of Counseling Husbands to Achieve Reproductive Health and Marital Equity (CHARM) was completed. A total of 1057 couples from control and experimental villages have been part of the study. This was followed by intervention with couples from experimental villages. Intervention program included three sessions, first two sessions for husband and third session for couple by local health care practitioners. First two sessions included counseling on issues like contraceptive methods, spacing between two children, family size, gender equity, marital communication and violence and third session is the summary of first two sessions. Of the total 454 intervention participants, 91.6% attended first session, 77.8% attended second session and 53.1% attended third session. Subsequently 9 month follow-up survey was initiated in all control and experimental villages along with participant satisfactory survey in experimental villages. Until now a total of 885 couples were interviewed for 9-month follow-up. Refresher training was conducted for health care practitioners from all villages. Process evaluation in-depth interview was conducted with 10% couples from experimental villages and all health care practitioners. In total, 46 couples and 22 health care practitioners were interviewed.

Study on Determinants of Vasectomy Acceptance in a Block of Thane district of Maharashtra

A study on determinants of high vasectomy acceptance in Jawahar block of Thane district of Maharashtra indicated early marriage, early completion of family and early adoption of permanent FP method which seems to be norm in the tribal community of Jawahar. The awareness and utilization of spacing methods is low; awareness on vasectomy among males is very good, major source being paramedical staff, friends and PHC doctors. There is a good agreement among couples on acceptance of vasectomy as 79% took joint decision; the major reason on acceptance by male is the concern for wife's health, wife also aware of health risks to her, male responsibility and knowledge of NSV as safe and simple procedure.

1. Infertility and Reproductive Disorders

A Genetic Study of Non-Classical Congenital Adrenal Hyperplasia as a cause of female infertility

Non- Classical CAH is a genetic disorder leading to infertility and is often indistinguishable from PCOS due to similarities in clinical features. A study was therefore undertaken with an objective to develop a panel of genetic markers that can distinguish Non Classical CAH from PCOS. A total of 200 hyperandrogenic women with anovulatory infertility were analysed along with 100 age matched controls. Mutations / polymorphisms in the 21- hydroxylase gene, along with the promoter region were screened in these women. A cluster of 11 variants was found in the promoter in 43% of study subjects as against 4% of controls. The variants were found to be in complete linkage disequilibrium suggesting their applicability for differential diagnosis of Non Classical CAH from PCOS.

Genetic Analysis of Polycystic Ovary Syndrome (PCOS) with Special Emphasis on Genes involved in Insulin Resistance

In order to comprehend the impact of gene polymorphisms on the development of PCOS, its associated phenotypes and long term consequences, several genes related to insulin action, obesity and inflammation have been selected for study via the candidate gene approach. The PON1 gene encodes for the paraoxonase enzyme which has an important role in maintaining healthy cardio-metabolic and antioxidant function. Its concentration and activity have been partially attributed to genetic polymorphisms. The coding region polymorphism, Q192R exhibits similar genotypic distribution between control and PCOS while L55M shows a significant association with PCOS in the study population thus far.

Quantitative Proteomics Analysis of Human Follicular Hormone in Women with PCOS

In an attempt to understand the molecular defect of follicle development in PCOS, the proteome profile of follicular fluid from women with PCOS with that of normal menstruating women undergoing in vitro fertilization was compared by isobaric tag for relative and absolute quantification followed by high-resolution mass spectrometry. Follicular fluid proteome from women with PCOS is distinct from normal women, where several vital proteins indispensable for follicle growth were found to be altered. These include proteins of extracellular matrix, immune function and several enzymes. This altered follicular fluid proteome may in part explain the aberrant folliculogenesis observed in these women.

Embryo loss due to Epigenetic Disturbances in the Male Germ Line – A study in Recurrent Spontaneous Abortions

Nearly 1% of all women in the reproductive age group experience Recurrent Spontaneous Abortion (RSA). A study to examine the epigenetic status in spermatozoa of male partners of women undergoing RSA of unknown etiology revealed significant hypomethylation at the *H19 ICR* in the RSA group as compared to that of control group. Methylation status of differentially methylated regions of other imprinted genes namely, *DLK1-GTL2*, *MEST (PEG1)*, and *ZAC (PLAGL1)* imprinted genes and global methylation levels revealed no significant difference in the methylation status at any of the loci mentioned, suggesting that these loci, unlike *H19 ICR*, may not be associated with RSA. The study indicates the possibility of paternal epigenetic disturbances being involved in idiopathic RSA. The observed difference in methylation may be researched further in a larger population so as to establish it as diagnostic marker to identify potential causes of recurrent spontaneous abortions.

Mutations in FSHR gene: Implications in Female Reproduction

Normal functioning of follicle stimulating hormone receptor (FSHR) is crucial for female reproduction. Two novel mutations in the FSHR gene identified in infertile women were characterized by *in-vitro* functional studies. FSHR activity was found to be completely abolished in a mutant (TMH-6) detected in women with primary amenorrhea. The second mutant (EL2) which was detected in normo-gonadotropic women not responding to FSH treatment demonstrated decrease in receptor activity. This study has helped in understanding the cause of infertility and also the significance of amino acid residues in receptor function.

Investigations on the Role of SP-A, SP-D and MBL in Fertility and Embryo Implantation

SP-D is expressed in the murine endometrium during estrus cycling in a hormone regulated manner and during early pregnancy. Studies were carried out to compare the fertility of SP-D

gene deficient (SP-D $-/-$) mice with that of the wild type mice. The number of implantation sites in the 15.5dpc SP-D $-/-$ mice (41 sites in 5 mice) was significantly lower than the wild type mice (SP-D $+/+$) (56 sites in 5 mice), suggesting that SP-D may be contributing to the process of embryo implantation. The estrus cycles of gene deficient mice ($n=5$) were altered as compared to wild type mice (SP-D $+/+$) ($n=5$) with prolonged metestrus and diestrus phases. Metestrus phase in the wild type mice was for 8-12h, while the SP-D gene deficient mice were in metestrus phase for 48-72h. Diestrus phase in the wild type mice was for 48-57h while in SP-D gene deficient mice the diestrus phase was for 96-144h. Importantly, there was an increased infiltration of leucocytes in the vagina of gene deficient mice as compared to the wild type mice in all phases of the estrus cycle.

Collectins and other Immune Related Proteins in Immuno-regulation during Pregnancy Maintenance

Studies were undertaken to delineate the role of elevated levels of placental SP-D during parturition. The SP-D and recombinant human SP-D treated placental tissues showed significantly increased production of pro-inflammatory cytokines IL-1 α , IL-1 β , TNF- α , IL-6, IL-8 and MCP-1 in comparison to the controls in a dose responsive manner. These pro-inflammatory cytokines have important roles in the process of parturition.

Investigating the Role of Immune Cells and Mesenchymal Stem Cells (MSC) in the Pathogenesis of Endometriosis

The mesenchymal stem cells (MSCs) isolated from endometriotic lesions showed significant down regulation of immune suppression of PBMCs and upregulation in expression of pattern recognition receptors (TLRs 1, 2, 4, 5, 7, 9 and 10, collections CLL1, CLP1, CLK1, and NOD like receptors NOD1 and NOD2) in comparison with the MSCs isolated from healthy endometrium. The data suggests that MSCs in the endometriotic lesions are pro-inflammatory and could be contributing to the chronic inflammation observed in association with endometriosis.

Autoimmune Markers for Early Diagnosis of Endometriosis

A non-invasive test for early diagnosis of endometriosis has been set up. A multicenter study has been initiated for validation of peptide ELISA based on epitopes of Tropomyosin 3 (TPM3), Stomatin like Protein 2 (SLP2) and Tropomodulin 3 (TMOD3) proteins for non-invasive diagnosis of endometriosis. Total study participants recruited so far in Mumbai, Kolkata, Goa and Nagpur centres were: Group I: Endometriosis ($n=244$); Group II: Disease Control ($n=91$) and Healthy Controls ($n=45$). From our observations, sera were reactive against all 11 individual peptides of TPM3, SLP2 and TMOD3. However, sera reactivity for endometriosis is higher than healthy controls. On the other hand for SLP2 and TMOD3 peptide cocktail ELISA, sera reactivity increased when compared to its performance against individual peptides.

Study of Endometrial Tuberculosis among Infertile Women by Detecting *M. tuberculosis* in Menstrual Blood

Molecular diagnostic tests are done on endometrial biopsy samples as well as on menstrual blood samples. However there is a need to compare the results of the molecular diagnostic test with that of culture since further treatment and counseling depends on the results.

Group 1: 80 participants in whom only menstrual blood at one visit was collected for the required tests GEN-PROBE AMPLIFIED Mycobacterium Tuberculosis Direct (MTD) TEST for tuberculosis (TMA) & VersaTREK culture.

Group 2: 40 participants in whom menstrual blood was collected at one visit and additionally, in next menstrual cycle, menstrual aspirate was collected with a probette on day one of menses for the required tests. (MTD & VersaTREK culture). *M. tuberculosis* was found positive by culture in only one menstrual blood sample. Out of the positive results, *Mycobacterium* other than Tuberculosis (MOTT) was found in 3 samples of menstrual blood on culture reports. One of the MOTT sample was identified to be *Mycobacterium intermedium*, possibly contaminant. In our study, we did not find molecular diagnostic test on menstrual blood sample as a good alternative for diagnosis of endometrial tuberculosis.

Inventory of Secreted Proteins and their Modified Forms in Uterine Fluid

Our proteomic based studies revealed less abundance of high mobility group box protein (HMG-B1) in the uterine fluid during the receptive phase, compared to that in the pre-receptive or non-receptive phase. This pattern was evident in rats as well as humans. *In vitro* studies provided a direct evidence of HMG-B1 secretion from endometrial epithelial cell lines. Further, not only the levels of secreted HMG-B1, but also of the cellular HMG-B1, were found to be less in the receptive phase, compared to the pre-receptive phase. An exogenous administration of recombinant HMG-B1 in the uterine cavity led to pregnancy failure in a rat model. Excess of HMGB1 in the uterine cavity caused alterations in the endometrial histology.

Development of a Non-human Primate Model for Endometrial Hyperplasia

Studies were undertaken to develop a nonhuman primate model for endometrial hyperplasia, with an aim to elucidate the mechanisms underlying endometrial hyperplasia and thereby identify the pathways, which can be targeted for therapeutics. We have shown that the unopposed exposure of estrogen in ovariectomized marmosets leads to excessive stromal and glandular epithelial cell proliferation, akin to endometrial hyperplasia. Immunohistochemical analysis demonstrated dysregulated expressions of PTEN, ER- α , COX-2, PCNA and pAKT, also implicated in the development of human endometrial hyperplasia.

Design of Constructs using Testis Specific Promoters and Generation of Transgenic Infertile Mice

The proliferation, differentiation and survival of spermatogonial cells (SGCs) are dependent on the signaling pathway guided by c-Kit gene. Our earlier studies demonstrated that though we could succeed partially in generating transgenic c-Kit mice, they were unable to survive due to high copy number integration and non-specific c-Kit expression by cells other than germ cells. Therefore, the objective of the study is to identify putative Cis-Regulatory Elements (CREs) within c-Kit promoter region and introduce selective mutations in CREs. For this, upstream mouse c-Kit promoter -1000bp region of transcription initiation site (TIS) was amplified and cloned into TOPO-TA vector. c-Kit promoter and +58 bp 5'-UTR (-942/+58 bp) was subcloned into pGL3-basic vector at XhoI & HindIII sites. To determine promoter activity of the c-Kit, we generated reporter plasmid (-1000/pGL3-basic) by introducing 5'-upstream region of c-Kit promoter (-942/+58 bp) followed by Luciferase reporter gene in pGL3-basic vector. To screen minimal Cis-acting elements, four 5'-deletion constructs carrying different lengths of 5'-flanking regions of c-Kit promoter were generated. Further studies are in progress.

Pathways and Molecular Mechanisms Regulating Sperm Motility

A differential proteomic analysis of the phosphoproteins in asthenozoosperm vis-à-vis normal sperm revealed that Carbohydrate and energy metabolism, cAMP mediated PKA

signaling, PI3K / AKT signaling and pathway regulating actin based motility by Rho were key to the regulation of sperm motility. Alpha tubulin isoforms TUBA 3C, 3E, 4A and 8 were amongst those differentially expressed in asthenozoospermatozoa. A deeper insight into the testis specific isoforms TUBA3C, 4A and 8 revealed that the protein as well as the transcripts for the same was differentially expressed in asthenozoosperm. We further deciphered the mechanism of the differential expression of the acetylatable isoforms 3C and 4A and how they might regulate sperm motility. Our studies investigating the alpha tubulin specific deacetylase, HDAC6 revealed that HDAC6 is present on the sperm flagella where it colocalizes with acetyl α tubulin and is catalytically active; pharmacological inhibition of HDAC6 increases α tubulin acetylation and abrogates sperm motility. We propose that HDAC6 and not tubulin acetylation is the key determinant of sperm axonemal microtubule stability.

Role of Homeobox Genes in Reproduction

Intersex disorders arise due to disorders of sex differentiation (DSD) during embryonic development. While relatively common and generally arise due to a genetic defect, the genetic defect in more than 70% of cases with DSD is hitherto unidentified. This is in part due to inadequate understanding of the process of gonad formation. Our work has shown that the homeobox gene Lhx2 is expressed by the mouse embryonic gonads in a sexually dimorphic pattern. Further it has been demonstrated that mice constitutively knocked out for Lhx2 have defects in gonad differentiation mainly vascularization suggesting an involvement of Lhx2 in regulation of gonadogenesis.

Deciphering the Roles of Collectins (SP-A, SP-D & MBL) in Testicular Immunoregulation

Alterations in the immune-privilege status of testes adversely affect male fertility. The study showed that levels of immunoregulatory proteins SP-A, SP-D and MBL are developmentally regulated in the murine testes and the highest levels are attained post-puberty. SP-D was localized in the interstitial spaces, Sertoli cells and developing germ cells of the seminiferous epithelium of postpubertal mice testis.

A Study on Cystic Fibrosis Transmembrane Conductance Regulator gene screening in Indian Infertile men having Congenital Bilateral Absence of Vas Deferens

Congenital bilateral absence of vas deferens (CBAVD) occurs in 2-6% of infertile but otherwise healthy men and is associated with mutations in cystic fibrosis transmembrane conductance regulator gene (CFTR). Studies have been carried out to identify the spectrum and frequency of CFTR gene mutations in Indian infertile males with CBAVD. Forty five CBAVD males and their female partners were recruited. Out of these 45 CBAVD patients, four patients were found to have renal anomalies. The sequencing analysis of all 27 exons, exon-intron boundaries and essential promoter of CFTR gene resulted in identification of novel as well as previously reported mutations and variants. The female carrier status was also evaluated.

2. Osteoporosis

Circulatory monocytes are precursors of bone resorbing cells osteoclast and their increased migration towards bone microenvironment results into increased formation of osteoclast and leads to increased bone resorption. Thus a proteomic approach was designed to study the differences in cellular proteome of monocytes from pre and post-menopausal women with varying bone density. The results of 4 plex iTRAQ coupled to 2D nano LC-MS/MS revealed the identification of 48 proteins of which vimentin; filamin A and integrin linked protein kinase were differentially expressed for early detection of osteoporosis.

3. Reproductive Tract Infections including STI/HIV

Association of Host Immunogenetic Factors with HIV infection

In HIV serodiscordant couples (DCs), one spouse is seropositive (HSP) while the other remains seronegative (HSN) even after repeated exposure. Hence, study on DCs offer more scope to highlight the possible “immunologic advantage” that characterizes HSN. Our study on human leukocyte antigen (HLA) with HIV transmission in DCs revealed significant association of HLA-B*35 (HSP vs HSN; $p < 0.02$) with HIV transmission. HLA-B*40, specifically *B40:06 (HSN vs HSP; $p < 0.01$) and HLA-B*18 (HSN vs HSP; $p < 0.02$) were significantly associated with HSN. HLA-B*39 was observed exclusively in HSP. Our observation in DCs confirmed the association of HLA-B*35 with susceptibility while HLA-B*40 (specifically *B40:06), -B*18 with protection. These identified alleles can be used as possible markers associated with HIV transmission. Further study on cytokine gene polymorphism in DCs revealed significantly ($p=0.01$) high frequency of TNF- α -238 AG and IL-4 -33 TT in HIV seropositives (HSP), while frequency of TNF- α -238 GG ($p=0.02$) was significantly high among the HSN. These variations at genetic level might help to explore new insights into treatment and HIV prevention strategies.

Differential Expression of Host Immunogenetic Factors in Development of Cervical Cancer in Indian Women with Human Papillomavirus (HPV) Infection

The immune response raised against HPV determines whether the virus will be cleared or whether it will persist and eventually result in cervical cancer. Patients with defects in cellular immune competence are more likely to remain chronically infected rather than clear the virus. Immune responses mediated by T cells especially cytotoxic T lymphocytes (CTL) are important in controlling both HPV infection and HPV associated cancers. Cytotoxic T lymphocyte associated molecule-4 (CTLA-4) appears to be the main negative regulator of T-cell mediated antitumor immune responses. Our study on polymorphisms in CTLA-4 gene (+49 A/G and -318 C/T) in HPV positive women with ($n=104$) or without cervical cancer ($n=57$) and in 105 healthy women without HPV infection revealed significant association of +49 A/A genotype with cervical cancer. No association was observed in polymorphism at CTLA-4-318C/T, however distribution of -318 C/T genotype was reported for the first time in Indian population. Presence of CTLA-4 +49 A/A SNP can be considered as a risk factor in management of cervical cancer.

Studies on the Modulation of Vaginal Immunity during Host-pathogen Interactions in Response to Microbicide

Mucosal epithelial cells represent the primary barrier encountered by pathogens and play a crucial role in initiating innate immune responses via pattern recognition receptors (PRRs). In human endocervical cells (End1/E6E7), induction of cytokines, IL-6 and IL-8 was abolished in response to TLR9 ligand (CpG-ODN) after initial stimulation with same ligand, thus mimicking “PRR tolerance”. However, stimulation with ligands of RIG-I/TLR3 [poly (I: C)-LL or poly (I: C) respectively] did not induce tolerance as cells secreted abundant levels of IL-6 and IL-8 upon re-stimulation with same ligands.

Characterization of AMPs isolated from Rabbit Vaginal Fluid and their Role in Vaginal Innate Immunity

In the present study, a panel of human hemoglobin alpha (Hb- α) peptides and their derivatives were designed *in-silico* and their anti-HIV-1 activity evaluated using different assays. Further, this peptide was not cytotoxic to TZM-bl, CEM-GFP and Vk2/E6E7 cells even at the

concentration as high as 285.60 μM . Further, this peptide inhibited CCR5-tropic, Ada-5, and CXCR4-tropic IIIB and NL4-3 strains of HIV-1. Surface Plasmon Resonance (SPR) and ELISA results revealed a direct interaction between HbAHP-25 and HIV-1 envelop protein, gp120. The peptide prevents binding of CD4 to gp120, thereby blocks subsequent steps leading to entry and/or fusion or both. In summary, the study demonstrated that HbAHP-25 inhibits early stage of HIV-1 infection by direct interaction with gp120. HbAHP-25 is thus a promising candidate for further development of anti-HIV drugs.

Approaches for Controlling Biofilm Formation by *Gardnerella vaginalis*

Despite being the drug of choice for the treatment of *bacterial vaginosis* (BV), metronidazole exhibits variability with respect to biofilm control in individuals suffering from BV. Studies carried out to investigate the effect on metronidazole on biofilm formation by *G.vaginalis*, the predominant anaerobe associated with BV, revealed strain specific differences. The efficacy of metronidazole for controlling *G. vaginalis* biofilms was of the order ATCC14019 > ATCC14018 > ATCC49145. These results suggest that inter-strain differences in biofilm control coupled to individual heterogeneity with respect to the presence of *G. vaginalis* strains may underlie the failure of metronidazole to prevent the frequent recurrence of BV.

Anti-HIV Activity of a Formulation Comprising Recombinant Human Surfactant Protein D

The recombinant human SP-D (rhSP-D) effectively inhibited HIV-1 replication in the two major target cells, viz. Jurkat T cell line or U937 monocytes. The rhSP-D significantly reduced levels of HIV-1 induced IL-2, IL-10, IFN- α and VEGF in Jurkat T cells and HIV-1 induced IL-2, IL-6, VEGF, IFN- α and MCP-1 in U937 monocytic cells. These experiments suggest that rhSP-D may be relevant in host defense against HIV-1 challenged T-cells and monocytes.

Enhancing Knowledge and Promoting Health Seeking Behaviour of Couples on STIs and Cervical Cancer in Urban Slums

Endline data were collected from 1025 couples from control area and 1013 couples from intervention area to study KAP about STIs & cervical cancer. To sustain the programme, Pap smear camps were continued every month during this period. Results of endline survey indicate significant increase in awareness on sexually transmitted infections (STIs), cervical cancer and Pap smear test among husbands and wives in the intervention area with respect to control area. It was observed that, inter personal communication by project and health post staff, group meetings and educational programme was contributing factors in increasing the awareness about Pap smear test among both husbands and wives during post intervention. Three Pap smear camps were organized and a total of 147 women had undergone screening and findings revealed that 64 percent smears were associated with inflammatory reactive changes and 36 percent were negative. About 48% smears were positive for infections. Human Paplioma Virus (HPV) infection was found to be common (38.8%), followed by Bacterial Vaginitis (29.9%), Fungal infection (19%) and Chlamydia trachomatis (12.9%). Multiple infections were detected in 29.3% women. Women with positive result of Pap smear test were referred to maternity home for treatment.

Strengthening Linkages between HIV (ICTC/PPTCT) and Family planning Services for Prevention of Unwanted Pregnancies among Women living with HIV/AIDS

A study was initiated to strengthen linkage between HIV services (ICTC/PPTCT) and Family Planning (FP) services to reduce unintended pregnancies among women living with HIV/

AIDS and also to improve correct and consistent use of condom along with other modern FP method. The study was conducted at two tertiary hospitals based in Mumbai using a prospective experimental control design model for a period of one year. Three hundred HIV positive married women aged between 18 to 40 years who were either using condom or were not using any modern FP method and had no desire for another child or for at least next one year were enrolled. Interventions were provided in the experimental group comprising of training service providers, availability of IEC material on dual contraceptives and provision of referral slips. Linkages were operationalized between ICTC and Family Planning center in the intervention area by providing counseling on contraceptives/dual method use, provision of linked referrals to the family planning centers from ICTC and maintaining MIS on the relevant indicators. Cases were followed at quarterly intervals for one year to assess contraceptive uptake, consistent use of condom and occurrence of pregnancy among enrolled participants.

Findings of the study indicate a three times increase in acceptance and continued use of modern contraceptive methods in experimental group than in control group. Regular use of condom among acceptors in the experimental group was significantly higher than the control group along with a significant increase in knowledge about contraception, safe sex and dual protection. The trained counselors are continuing to provide information on dual protection / dual method use and referral to the family planning centers after assessing their fertility desires and current contraceptive use. MIS on these issues is also being maintained. The study experience reveals that this linkage is feasible and effective in improving dual contraceptive use among PLHIV.

4. Stem Cell Biology

Studies were carried out to characterize the cord blood VSELs. Recently doubts were raised about the very existence of VSELs mainly because their isolation is challenging and difficult to reproduce in various laboratories. Flow cytometry analysis done on human cord blood shows that majority of small LIN-/CD45-/CD34+ VSELs are present in the red blood cells (RBC) pellet after Ficoll-Hypaque centrifugation. They are quiescent, diploid and show telomerase activity. They can be easily enriched from RBC pellet using CD133 and SSEA4 antibodies by immuno-magnetic method. Results show that VSELs express pluripotent (OCT4A, SSEA4, SOX2, and REX1) as well as primordial germ cell (STELLA and FRAGILIS) markers. Results will be useful for future application of VSELs in regenerative medicine.

Animal models have been successfully made for myocardial infarcts in rabbits and for diabetes in mice which are being utilized to study the regenerative potential of human embryonic stem cells derived cardiac and pancreatic progenitors.

Ovarian stem cell differentiation into oocytes is directly modulated by FSH through a novel receptor isoform FSH-R3. This transcript lacks the large exon 10, which has remained the main focus in the canonical FSH-R1 for detecting mutations resulting in POF and ovarian cancers. Results provide newer understanding of FSH action on the ovary and also highlight the need to detect mutations in Exon 11 in POF and ovarian cancer cases.

While culturing ovarian cortical tissue to understand the effect of FSH and bFGF on primordial follicle growth, a large number of stem cells were found to be shed onto the cell culture insert which also retain ability to spontaneously differentiate into oocyte-like structures. Thus despite a huge body of literature using cortical tissue as a source of

primordial follicles, it has been shown that cortical tissue pieces are also an excellent source of stem cells which may be used to differentiate into oocytes to restore fertility in cancer patients from ovarian cortical tissue pieces cryopreserved prior to therapy.

5. Reproductive Cancers

Hormonal Regulation of Telomerase and its Implications in the Pathogenesis of Prostate Cancer

Previous studies have demonstrated the role of androgen receptor (AR) in regulation of ZEB2 or SIP1 (smad interacting protein 1), a telomerase regulator, in androgen dependant prostate cancer cell lines. These studies implicated AR as a positive regulator of the ZEB2 expression in androgen dependant PCa cell lines (LNCaP). However, in androgen independent PCa cell lines such as PC3, enforced expression of AR led to down regulation of ZEB2 expression. A decline in the levels of ZEB2 further caused reduction in the invasiveness of PC3 cells. These studies demonstrated that ZEB2 or SIP1 is regulated by androgen receptor.

Membrane Bound Estrogen Binding Proteins in Prostate Cancer Cell Lines and their Functional Significance

Investigations are being pursued on the characterization and functional significance of cell surface localized estrogen binding protein(s) in prostate cancer cell lines. Activation of cell surface localized estrogen binding proteins was found to modulate the phosphoproteome of androgen dependant prostate cancer, LNCaP cell line. Some of the proteins which are differentially phosphorylated in response to the activation of cell surface estrogen binding proteins were identified using MALDI-TOF-TOF. β -actin and cytokeratin were found to be more phosphorylated in cells stimulated with cell impermeable estradiol conjugate. These results indicated the possible role of cell surface estrogen binding proteins in cytoskeletal protein rearrangement.

6. Maternal and Child Health

Socio-behavioural Aspects of Smokeless Tobacco with Implications on Reproductive Health of Low Income Married Women in Mumbai Slum Communities

The study explored the patterns, reasons, benefits and risks perception associated with use of smokeless tobacco (SLT) products such as *mishri*, *paan* with tobacco, *gutkha*, *gul* and tobacco with lime among 409 women of reproductive age group currently using any one smokeless tobacco product daily. Women use multiple types of SLT products and continue to use them throughout their pregnancy which is a serious concern to the health of infant. The pattern of use varies depending on the type of smokeless tobacco consumed. Mean consumption in grams per day of tobacco is more than 5 gms for majority of *mishri* and *gutkha* users. Women perceive more benefits than risks associated with SLT use though do identify significant risks associated with SLT use on infant health. Sixty-seven percent of women in the survey have expressed their intentions to stop use of any form of SLT. However there are no resources in the community to support their quit intentions. Banning *gutkha* may not decrease overall tobacco use, but it will eliminate initiation of SLT through *gutkha* use. Research findings were disseminated to the study community as well as experts in the field of smokeless tobacco and reproductive health.



Dissemination of research results to paan shop owners of the Mandala area

7. Intervention to Enhance Acceptance of Contraceptive Use among Couples by Reducing Domestic Violence from Husband

The objective of the study is to understand the role of an intervention program to improve contraceptive use among couples where the woman has reported of experiencing domestic violence. The two selected communities were Tunga Village and Kajupada areas covered under the Health post of the Municipal Corporation of Greater Mumbai (MCGM). A total of 1136 eligible women were selected using systematic random sampling procedure. The socio-demographic characteristic of women from baseline data show the mean age of the women was 26.5 (± 4.4) years. Twenty one percent of women ever experienced any type of violence viz: physical (16.8%), emotional (12.4 %), or sexual violence (4.8 %). Among women who have experienced any violence, more than three-fourth (79.7%) have experienced violence in the past 12 months preceding the survey. About three-fourth women had never used any contraceptive method. To enhance the acceptance of contraceptive methods, two specific groups, namely Group A (women reporting unmet need and violence from husband) and Group B (women reporting only unmet need) were formed. Group A received counselling sessions on both family planning and marital communication skills to reduce domestic violence and increase contraceptive use. Group B received information only on family planning to increase contraceptive use. The intervention sessions (Group A) include 3 individual sessions, 1 couple session and 1 group session with atleast two weeks' time gap between two sessions. Intervention is currently ongoing.



Family Planning Intervention being delivered to women as part of the project



Domestic violence intervention being delivered to couples as part of project

8. ICMR Biomedical Informatics Centre

The Center has developed an update to CAMP, which is a comprehensive database on sequences and structures of antimicrobial peptides. A prediction algorithm based on machine learning algorithms such as Artificial Neural Networks, Random Forests and Support Vector Machines has been developed to scan protein regions, with user-defined lengths for antimicrobial activity. The database and the prediction algorithm are available online for the benefit of researchers. The information available in the CAMP database is being mined to understand structure-activity relationship of antimicrobial peptides.

Peptidomimetics for human follicle stimulating hormone receptor were rationally designed based on structural studies on the gonadotropins and extracellular domain of their receptors. A combination of *in silico* methods such as virtual high throughput screening, docking and molecular dynamics simulations were used for design and validation of the molecules. The designed molecules are now being optimized based on results inferred from the computational experiments.

9. National Centre for Primate Breeding and Research (NCPBR)

The foundation stone for the acquired 25 acres of land for the National Center for Primate Breeding and Research (NCPBR) at Sasunavagar, taluka Vasai, Thane District, near Mumbai in 1976 was solemnized in the presence of the then Minister of Health and Family Welfare, Govt of India and officials from the Office of AIDS Research, National Institutes of Health, Bethesda, USA on 9th January 2005. The facility includes construction of a quarantine building, in-door and outdoor breeding (corals and corncribs), experimental animal and laboratory facility. The facility will also breed specific pathogen free animals (SPF) (Animals free of Simian Retroviruses 1-5 (SRV), Simian T Lymphotropic Virus (STLV) and Herpes B).

The Centre is a joint collaboration between ICMR, Dept of Science and Technology and the National Institutes of Health, USA.

Structural work and finishing works IPS flooring / plastering / fixing of windows, waterproofing etc. of the Quarantine Building are complete. Construction of outdoor breeding facilities, i.e. Corncribs and Corals is almost complete. The work of Stainless Steel fabrication of Corncrib structures is in progress in Corncrib area 1. The foundation work is completed in Corncrib area 2. The fabrication & installation work of Corncribs is likely to be completed

by end of October 2013. Other works *i.e.* construction underground water tanks; electrical sub-station, gas banks, road works *etc.* are in progress and will be completed by Dec 2013. Works of installation of remaining services (HVAC, BMS, CCTV, Fire, Gas Bank, Access Control, DG set, UPS, 22KV line *etc.*) will be taken up after availability of funds. Contractors for these internal services have been short-listed and tenders are ready. M/S HSCL has already initiated the process of tendering work of Fabrication of Coral work.

Proposal for acquiring additional 25 acres of land for NCPBR project is in the advanced stage at the office of Chief Conservator of Forest, Borivali, Mumbai.



Corncrib No 1- Installation work is in progress



Corncrib No 2- Foundation work is completed

10. National Centre for Preclinical Reproductive and Genetic Toxicology (NCPRGT)

Studies have been initiated to evaluate the effect of Bisphenol A (BPA), on spermatogenesis in Common Marmoset. A significant decrease in epididymis sperm count and motility was observed in BPA treated group as compared to control. Further, histology of testis demonstrated sloughing of germ cells in to the lumen of seminiferous tubules and thickening of interstitial septa in BPA treated animals. Further, a significant alteration in the expression pattern of testicular steroid receptors viz. ER-alpha , ER- beta and androgen receptor (AR) was observed. Preliminary data obtained is suggestive of human risk to BPA exposure.

Studies for safety and genotoxic evaluation of DH Lipomer were initiated as a collaborative study with Institute of Chemical Technology funded by Department of Biotechnology.

The safety evaluation of DH Lipomer (Doxycycline hydrochloride lipid polymer hybrid nanoparticle) was carried out as per tests and procedures mentioned in regulatory guideline. The acute and subacute toxicity test did not show any adverse effect at 1.0 mg/kg BW when compared with the control animals. The genotoxicity was evaluated using a battery of tests revealed low dose of DH Lipomer (0.5mg/kg BW) do not poses any genotoxic potential and that would be the safe dose for therapeutic purposes. As the Blank Lipomer revealed no genotoxicity, this novel biomaterial can be explored for the other biomedical applications.

Studies were undertaken to determine the effects of excess oxytocin exposure on the reproduction in adult male and female rats/mice. No significant changes were observed with respect to various fertility parameters in animals exposed to oxytocin. The study did not show any significant changes in biochemical parameters as compared to controls. Histopathology of the reproductive and vital organs did not show any significant change. No adverse effects of oxytocin at tested doses were observed on reproduction in adult male and female rat/ mice except the urinary calculi observed in male animals. Experiments are in progress to understand the mechanism of calculi formation.

National Institute for Research in Tuberculosis (NIRT), Chennai

The main focus of the National Institute for Research in Tuberculosis is to conduct research into the priority areas in order to improve TB control and reduce the burden of TB in the community. The institute conducts clinical research for better diagnostic and treatment options, socio-behavioural research to address the social determinants of disease and basic research to understand the host and microbial factors that impact development of TB infection and disease. Further, the influence of HIV and other co-infections and co-morbidities like parasitic infections and diabetes mellitus are also being investigated. A number of new operational research projects have also been initiated.

Randomized Clinical Trial to Study the Efficacy and Tolerability of 3- and 4-month Regimens Containing Moxifloxacin in the Treatment of Patients with Sputum Positive Pulmonary TB

The currently recommended 6-month regimen for the treatment of newly diagnosed pulmonary TB patients has been in use since the 1970s. Shortening the duration of TB treatment is recognized as a research priority. A randomized clinical trial is being conducted by the NIRT in Chennai and Madurai to study the efficacy of a standard 4-drug TB regimen supplemented with moxifloxacin (MFX), a fluoroquinolone with potent bactericidal and sterilising activities against *M. tuberculosis*

Interim findings of this study show that the proportion of patients who became sputum culture negative after the initial 2 months of treatment was significantly higher (94%) in the MFX arm (consolidated for all four test regimens) compared to the control arm (77%). Fig. 1 illustrates the proportion of patients with negative sputum cultures at 15, 30, 45 and 60 days of treatment. This is a significant finding as it shows that patients treated with the MFX regimens become less infectious earlier and to a greater degree compared to those treated with the control regimen.

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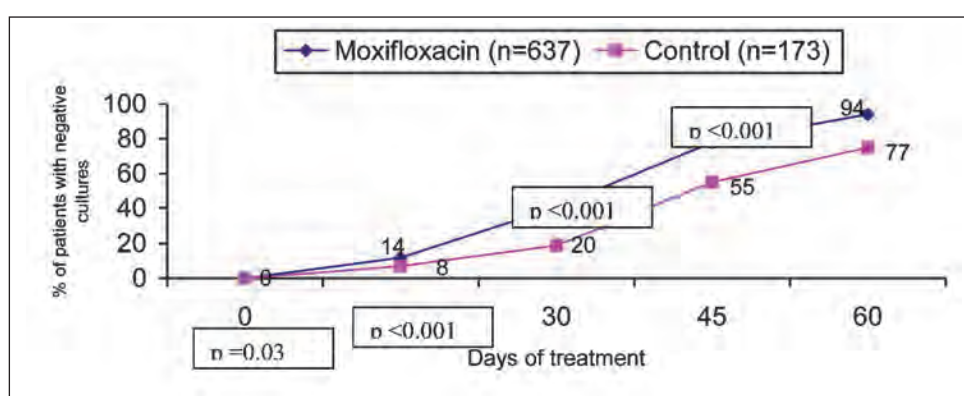
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Sputum culture conversion with treatment

Of patients treated with MFX regimens, 92 - 93% had negative sputum cultures at the end of treatment compared to 80% in the control regimen.

Randomized Controlled Clinical Trial Comparing Daily vs. Intermittent 6-month Short Course Chemotherapy in Reducing Failures & Emergence of Acquired Rifampicin Resistance in Patients with HIV and PTB

A randomized controlled clinical trial was initiated to compare various aspects of TB outcome such as bacteriologic response, immune reconstitution inflammatory syndrome (IRIS), emergence of acquired rifampicin (RMP) resistance (ARR), radiological improvement, pharmacokinetics of anti-TB drugs and toxicity profile between a daily and thrice-weekly anti-TB regimen. The regimens comprised of (i) RMP, isoniazid (INH), pyrazinamide (PZA) and ethambutol (EMB) daily for two months followed by RMP and INH daily for four months (ii) RMP, INH, PZA and EMB daily for two months followed by RMP and INH thrice weekly for four months (iii) RMP, INH, PZA and EMB thrice weekly for two months followed by RMP and INH thrice weekly for four months. Interim findings show that smear conversion was higher in the daily regimen than in the intermittent regimen, but did not achieve statistical significance. However, the culture conversion was significantly higher in the daily regimen compared to the thrice-weekly one. It remains to be seen if this has an influence over the final outcome of treatment after 6 months of ATT.

Anemia and Nutrition among Children with Perinatally Acquired HIV Infection in South India

The prevalence of anemia and micronutrient deficiencies (Fe, vitamins A, B12, and folic acid) were estimated among HIV-infected children in south India and also examined the nutritional and non-nutritional etiological factors contributing to anemia. The prevalence of anemia-iron deficiency and vitamin A deficiency was high in this cohort of 240 HIV-infected children recruited at three sites in south India, indicating that underlying micronutrient deficiencies were prominent. There was a high prevalence of malnutrition at baseline, with 47% being anemic. Independent risk factors for anemia were young age, presence of malnutrition, low CD4 counts and absence of anti-retroviral treatment (ART). Fe supplements and ART therapy appeared to provide the maximal benefit in Hb change, clinical and growth parameters. Despite supplementation, a substantial proportion of these children remained anemic after one year.

Predictors and Immunologic Characterization of TB-associated IRIS in HIV-TB Patients started on Antiretroviral therapy

Immune reconstitution inflammatory syndrome (IRIS) is the paradoxical worsening or unmasking of infection, tumor-associated pathology, or auto-immune disease in HIV-infected patients after starting ART. We evaluated early predictors and minimized the morbidity associated with IRIS. Data from 48 HIV positive patients with newly diagnosed culture confirmed PTB showed that low CD4, high viral load, opportunistic infection, miliary TB, presence of extra pulmonary focus, low hemoglobin and shorter ATT-ART interval were all associated with IRIS. Hemoglobin and time interval between ATT-ART remained significant in multivariate regression along with IL-6 and C-reactive protein.

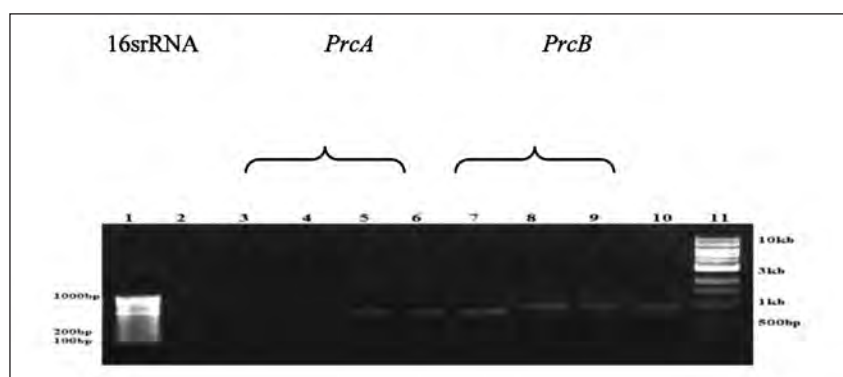
TB drug Resistance Surveillance in the State of Tamil Nadu, India

A population-based survey of anti-TB drug resistance was conducted in the state of Tamil Nadu to determine the proportion of drug resistance in new and in previously treated cases of pulmonary TB and to use the level of drug resistance as a performance indicator for the RNTCP.

A total of 1524 and 901 patients were enrolled respectively for new sputum smear positive (NSP) and retreated (RT) cases. The prevalence of MDR-TB among NSP and RT cases was 1.8% and 13.2% respectively. The prevalence of XDR-TB among RT cases was 0.6% and none of the isolates among NSP cases showed XDR-TB. The level of mono resistance to rifampicin was 2.6% and 15.1% among NSP and RT cases respectively. Drug resistance rates have remained stable in Tamil Nadu over 10 years.

Screening for Potent Proteasome Inhibitors of *M. tuberculosis*

Proteasome is important during the dormant phase of *M. tuberculosis*, making it an attractive target for compounds that may interfere with dormant bacilli. However, due to the inherent cytotoxicity of proteasome inhibitors, chemical compounds targeting the *M. tuberculosis* proteasome must exhibit high selectivity for *M. tuberculosis* over human proteasomes in order to be considered for development as chemotherapeutics for TB. We attempted to express the bacterial proteasome from different strains of *M. tuberculosis* and compare the levels of expression in them.



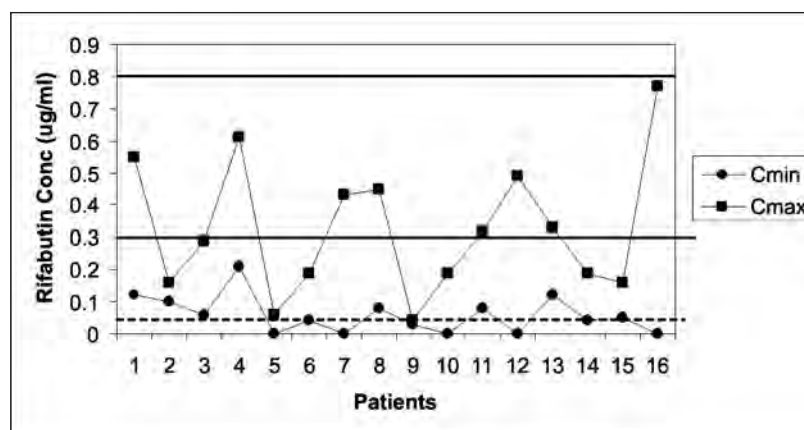
Antimicrobial susceptibility strains in dormant conditions

Proteasome genes (*PrcA* and *PrcB*) got expressed in both active and dormant strains of *M. tuberculosis* with various anti-microbial susceptibility (Fig.). 16srRNA was used as housekeeping gene to compare the expression of proteasome genes. With respect to active strains, *PrcB* gene showed more expression than *PrcA* and more or less equivalent expression with 16srRNA gene.

Pharmaco-kinetics of Rifabutin during Concomitant Atazanavir/Ritonavir Administration in HIV- infected TB patients in India

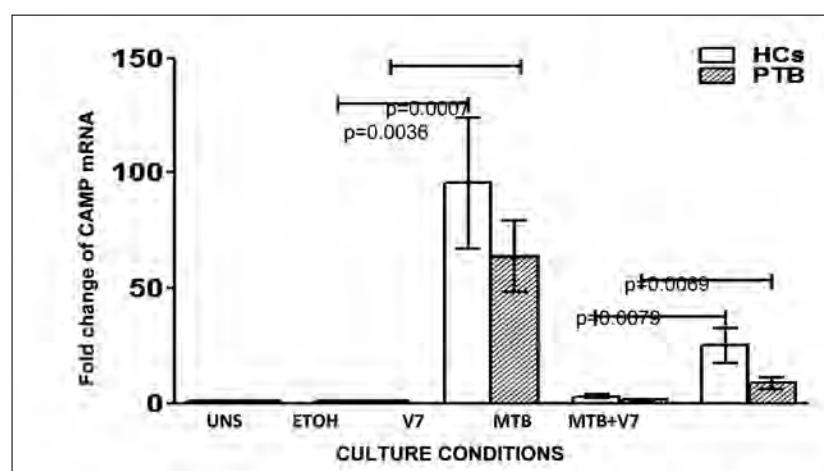
Rifabutin (RBT) is reported to be as effective against TB as RMP, and has little effect on serum concentrations of protease inhibitors. However, ritonavir (RTV), being a CYP3A4 inhibitor markedly increases serum concentrations and toxicity of RBT. The dose of RBT during RTV co-administration remains a matter of debate. We studied the pharmacokinetics of RBT at 150 mg thrice weekly dose during concomitant atazanavir/RTV administration in HIV-infected TB patients.

The peak concentration was below the therapeutic range ($0.3 - 0.08\mu\text{g/ml}$) in seven of 16 patients, while 10 patients had trough concentrations below the minimal inhibitory concentration of RBT against *M.tuberculosis* ($0.06\mu\text{g/ml}$), suggesting that RBT doses may have to be increased. The distribution of peak and trough concentrations of RBT is shown in Fig. A significant positive correlation between peak concentrations of RBT and RTV was observed ($r = 72\%$; $p = 0.002$). Unfavourable TB outcomes correlated with low RBT levels.



Distribution of peak and trough concentrations of RBT

Effect of vitamin D₃ on Cathelicidin, Defensin-1 α and Toll-like Receptor Gene Expression in the Neutrophils of PTB Patients



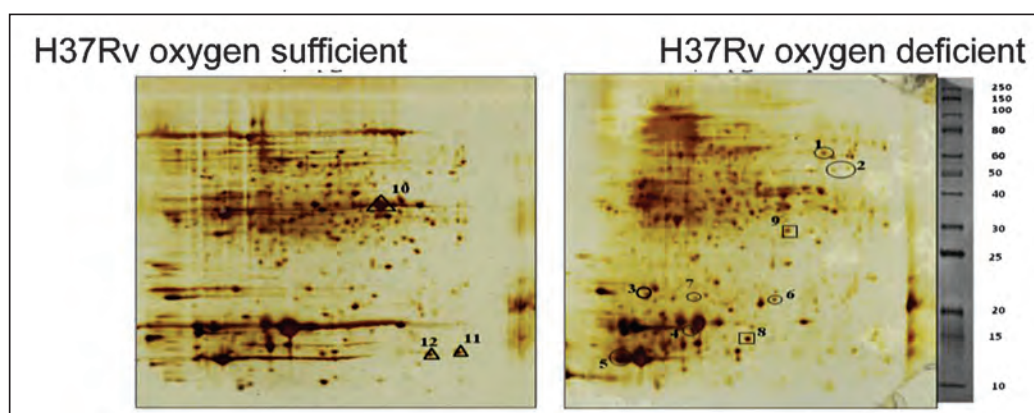
Effect of vitamin D₃ on the relative expression of CAMP mRNA

Uns: Unstimulated cells; ETOH: Ethanol control; V7: Vitamin D₃ 1×10^{-7} M concentration; Mtb: *M. tuberculosis*; HCs: Healthy controls; PTB: Pulmonary tuberculosis patients

Vitamin D₃, a potential immunomodulator, is known to influence innate and adaptive immunity. We studied the effect of vitamin D₃ on cathelicidin, defensin-1 α and Toll-like receptor (TLR) gene expression in the neutrophils of pulmonary TB patients. The study results suggested that vitamin D₃ may increase the TLR expression and lead to increased expression of antimicrobial peptides via TLR signalling and enhance the innate immunity against pulmonary TB (Fig.).

Dormancy Associated Antigens of *M. tuberculosis*

Analysis of the mycobacterial antigens associated with the slowly replicating, post-logarithmic phase growth of *M. tuberculosis*, the so-called “dormant” phase, is our interest. We used three strains of *M. tuberculosis*, laboratory strain H37Rv and two of the clinical strains, most prevalent in south India, S7 and S10 to identify and proteomically characterize dormancy associated antigens of *M. tuberculosis*.

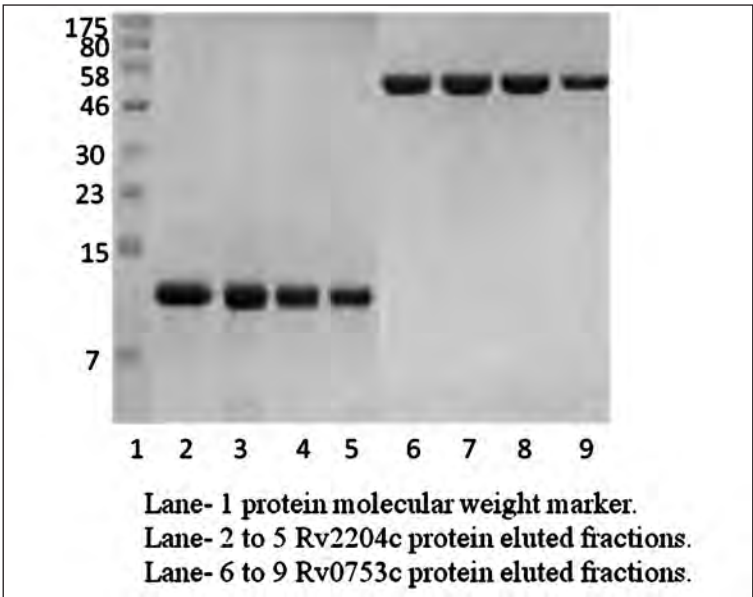


2-D electrophoresis of H37Rv

Rv2031c appeared in H37Rv and S7 and was over expressed in S10, during low oxygen tension. Mycobacterial chaperon protein GroEL 2 (Rv0440) was over expressed in both of clinical isolates used but not in H37Rv when oxygen is depleted from the culture media (Fig.). It is predicted that Guanosine Monophosphate Synthase is a key enzyme in the purine biosynthetic pathway.

Immunological Characterization of Novel T- cell Antigens of *M. tuberculosis*

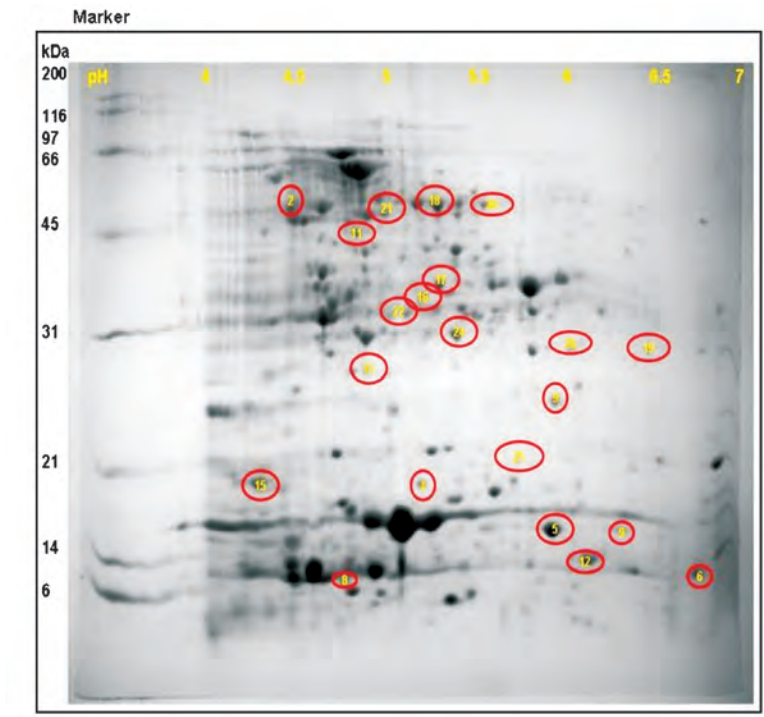
PpiA (Rv0009), Rv2204c (hypothetical protein) and mmsA (Rv0753c) were novel T-cell antigens, producing higher levels of IFN- γ in latently infected individuals (healthy household contacts) than active TB patients. We analysed the T-cell mediated *in vitro* cytokine response (particularly IFN- γ) to differentiate latent TB infection (LTBI) and active TB disease. All the three antigens induced significantly higher IFN- γ production in HHC compared to active TB subjects (Fig.). Preliminary findings have shown that these three antigens are good at differentiating LTBI from active TB disease in terms of IFN- γ induction.



Eluted protein fractions RV2204c & RV0753c in SDS Page gel

Global Proteomic Comparison of *M. tuberculosis* H37Rv and its Isogenic *pknE* Deletion Mutant

M. tuberculosis survives the hostile immune responses of the host by altering its physiology. These adaptations are governed in *M. tuberculosis* by serine / threonine protein kinases (STPK). We examined the proteomic differences between H37Rv and its isogenic *pknE* deletion mutant during growth in middlebrook 7H9. We observed that PknE has a role in regulating the metabolism of *M. tuberculosis* that could enable its survival in hostile environments (Fig.).



2D gel showing proteome profile of $\Delta pknE$

Genetic Characterization of HIV-type 1 Subtype C strains Circulating in South India

The HIV-1 subtypes display genetic variations that can potentially alter the functions of several proteins and thereby influence HIV-1 mediated pathogenesis. We attempted to clone and characterize the full genome of HIV-1 isolates circulating in the south Indian population, as this understanding would further our knowledge on the genomic heterogeneity and adaptive evolution of the circulating viral strains in the country.

Sequences of the six clones were analyzed for variability in each of the individual viral genes and proteins. Preliminary analysis revealed that the long terminal repeat (LTR) sequence of five of the six clones showed the presence of three nuclear factor- kappa B (NF- κ B) sites, while one had only two NF- κ B sites with a deletion of the III-Nf- κ B site. All Tat sequences had the cysteine – serine (CS) motif instead of the cysteine – cysteine (CC) motif which has been previously demonstrated to render the protein defective in its chemokine property. Rev genes of 4 clones code for a 107 amino acid protein while that of the other two clones code for a 100 amino acid protein. One of the clones had mutations conferring resistance to nevirapine in the reverse transcriptase (RT) gene, in spite of a recorded history of no previous exposure to antiretroviral drugs. Except for one clone, which revealed characteristics of CXCR4 usage/X4 tropism, all other clones had sequence motifs that predict CCR5 usage/R5 tropism.

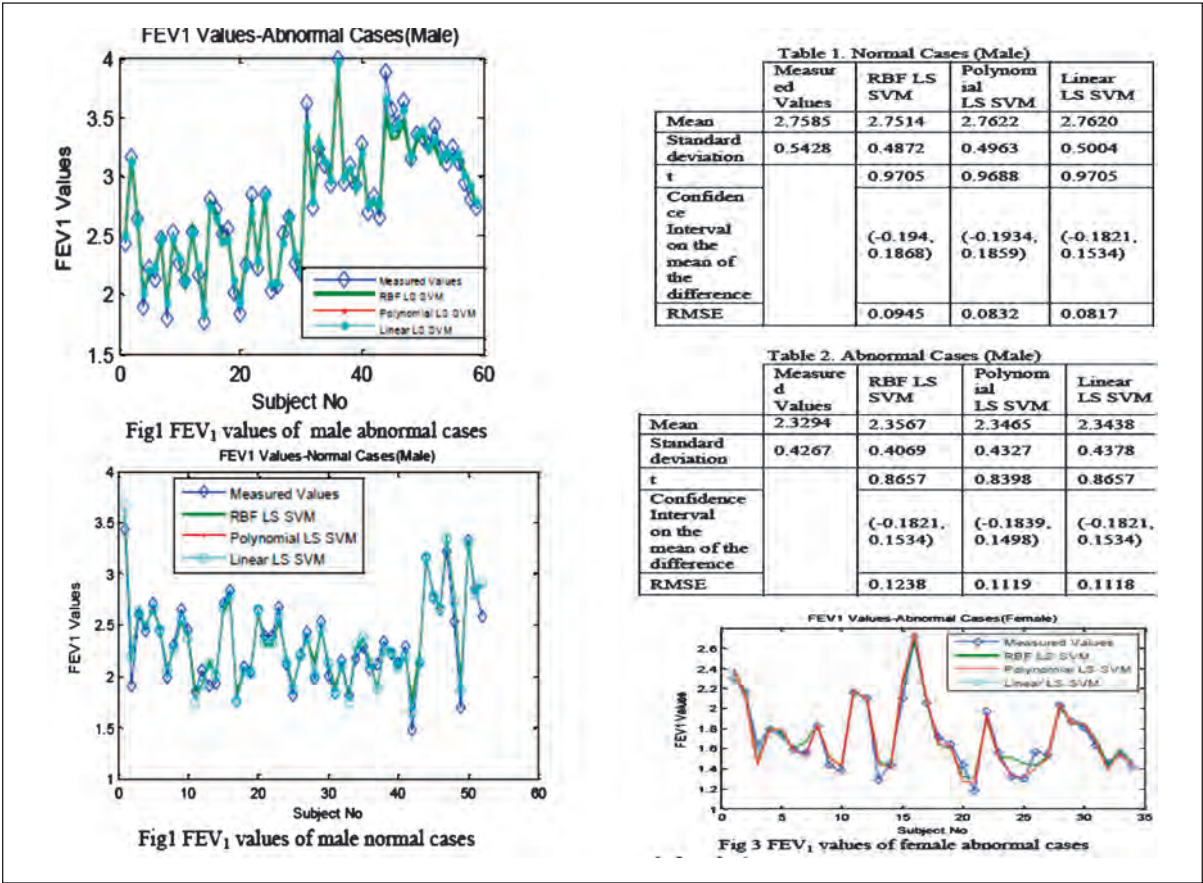
Health Seeking Behaviour and Awareness of TB Among Migrants – Brick Kiln Workers - A Study From Tiruvallur District, Tamil Nadu, India

Early detection and treatment of TB patients have been key principles of TB control. However this can be a challenge with some hard to reach populations and migrants are one such group. We undertook a study (i) to understand the knowledge, attitude and perceptions on TB among brick kiln migrant workers; (ii) to identify the prevalence of chest symptoms and health seeking behaviour among brick kiln workers; and (iii) to find out the perceptions of the health providers in providing treatment and management of TB care with special reference to brick kiln migrant workers

The study indicated that social determinants such as age, sex, alcohol, smoking and time spent within the chamber contributed to the development of chest symptoms. Furthermore, care seeking behaviour patterns were also strongly influenced by the duration of stay in one particular place, which is a big challenge to the RNTCP programme considering the mobility of this population.

Least Squares Support Vector Regression for spirometric Forced Expiratory Volume (FEV1) Values

SVMs are one of the recently developed machine learning algorithm under the supervised learning approach, from the statistical learning theory implementing the structural risk minimization (SRM) principle. It maps the data into high dimensional input space and constructs an optimal separating hyperplane in this space. A detailed analysis of prediction of FEV1 values for males and females showed the generalization capacity of LS SVM regression (Fig.), and computing FEV1 values through LS SVM regression would enhance the spirometric investigations. In case of incomplete spirometric tests, this method may give valuable suggestions and directions.

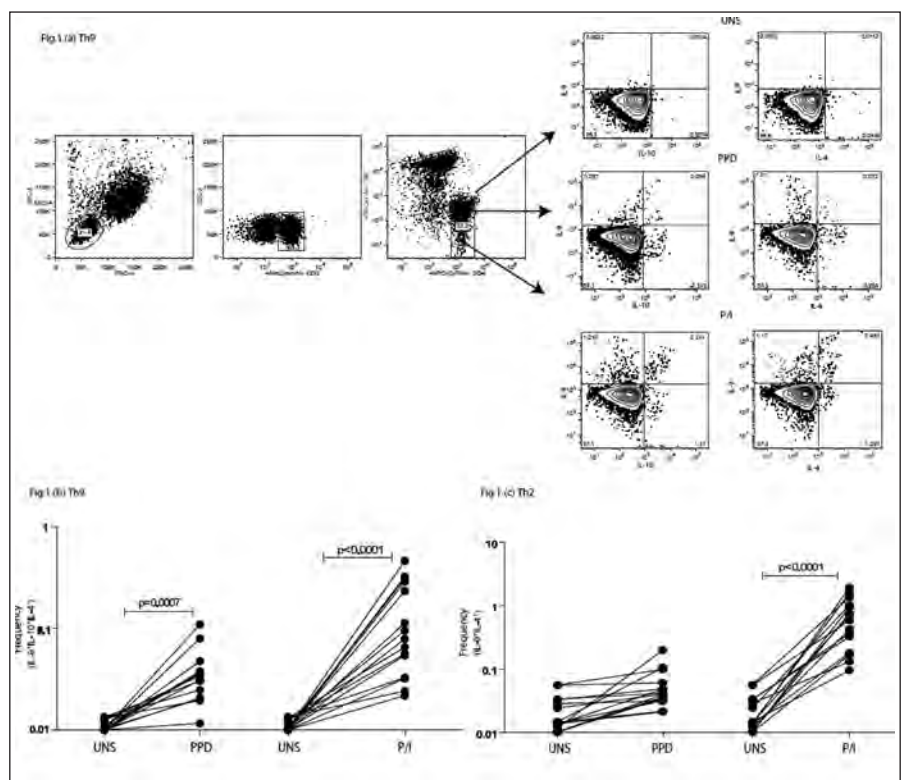


Predicted FEV1 values under different models

Filariasis-TB-Co-Infection

Parasite Antigen-specific, IL-4-, TGF-beta and IL-1- dependent Expansion of Th9 cells is Associated with Clinical Pathology in Human Lymphatic Filariasis

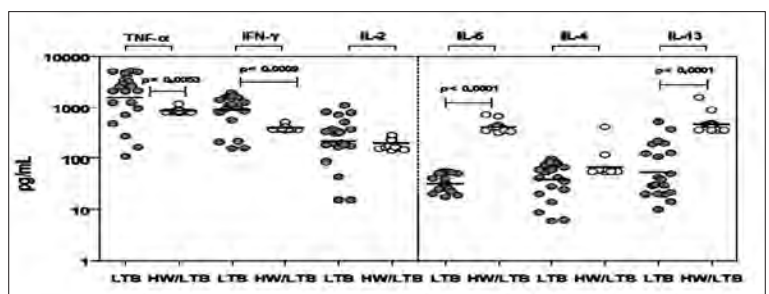
Th9 cells are a subset of CD4⁺ T-cells, shown to be important in allergy, autoimmunity and anti-tumor responses. However, their role in human infectious diseases has not been explored in detail. We studied the role of Th9 cells in filarial pathology. This study identified an important human CD4⁺ T-cell subpopulation co – expressing IL-9 and IL-10 but not IL-4, whose expansion is associated with disease in chronic lymphatic filariasis and could potentially play an important role in the pathogenesis of other inflammatory disorders (Fig.).



Identification of classical Th9 cells and their expansion in normal individuals

Modulation of Mycobacterial-Specific Th1 And Th17 Cells In Latent TB by Coincident Hookworm Infection

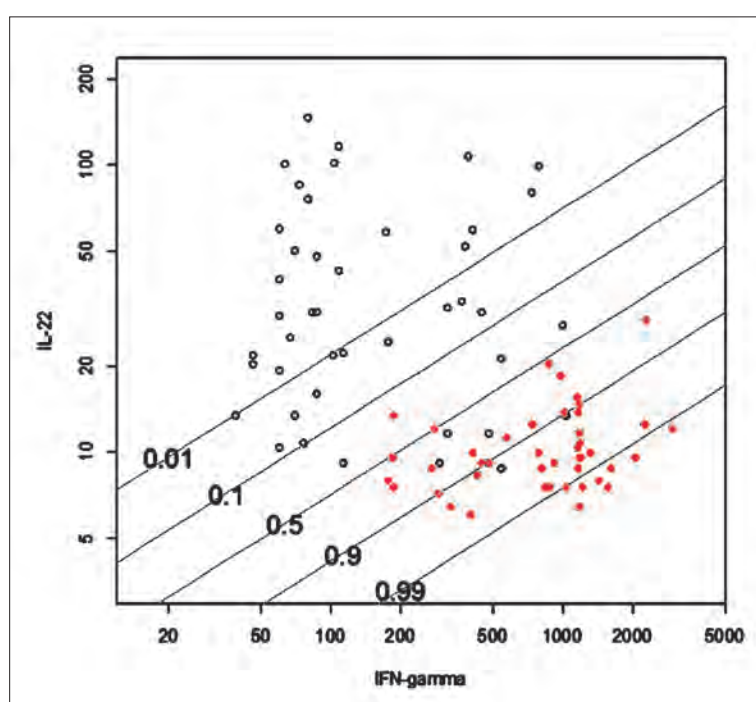
Hookworm infections and TB are co-endemic in many parts of the world. We studied the role of coincident hookworm infection on responses at steady state and on *M. tuberculosis* – specific immune responses in latent TB. Co-incident hookworm infection exerted a profound inhibitory effect on protective Th1 and Th17 responses in latent TB and may predispose toward the development of active TB in humans (Fig.).



Hookworm infection is associated with alterations in the plasma levels of Th1 and Th2 cytokines in latent TB

Type 2 Diabetes Mellitus Coincident with Pulmonary TB is Associated with Heightened Systemic Type 1, Type 17 and Other Pro – Inflammatory Cytokines

Type 2 diabetes mellitus is a major risk factor for the development of active TB, although the biological basis underlying this susceptibility remains poorly characterized. We aimed to identify the influence of coincident diabetes mellitus on cytokine levels in pulmonary TB patients.



Discriminatory value of cytokines in TB-Infected individuals

The study showed that TB with diabetes was characterized by heightened cytokine responsiveness, indicating that chronic inflammation underlying Type 2 diabetes potentially contributes to increased immune pathology and poor control in TB infection (Fig.).

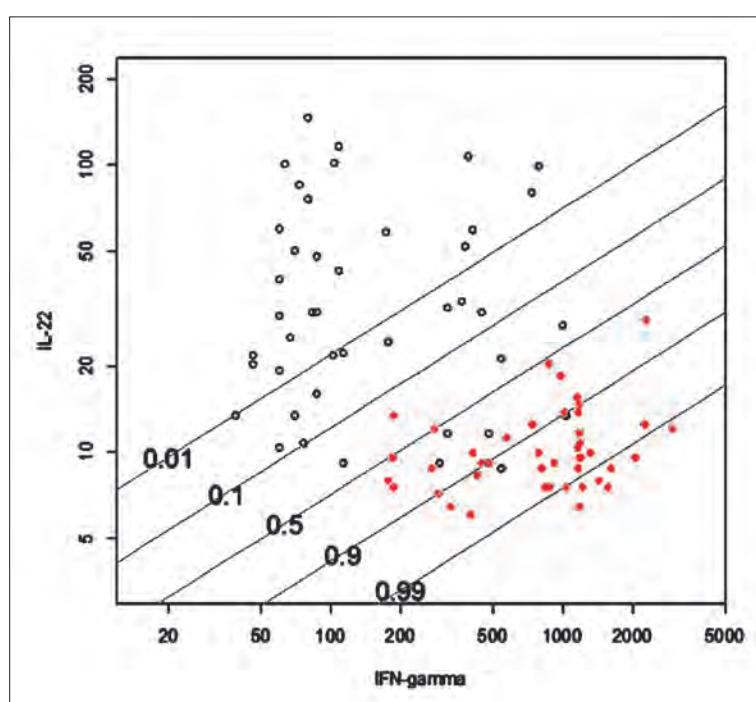
National Institute of Virology (NIV), Pune

The indigenously developed low cost vaccine against Japanese Encephalitis (JE) was launched on 04.10.2013 by the Union Minister for Health & Family Welfare, Govt. of India. It was developed under Public-Private Partnership of NIV with Bharat Biotech Ltd, Hyderabad.

- NIV also initiated diagnostic reagent development under highly infectious special pathogens program including Kysanur Forest Disease and Crimean-Congo-Hemorrhagic Fever (CCHF) viruses besides investigating CCHF outbreak in Gujarat.
- The institute continued research work on isolation, genetic characterization and drug susceptibility monitoring of pdmH1N1 isolates from India under national surveillance program, studies on influenza disease burden in rural areas, successful trials towards finalization of an indigenous JEV vaccine in collaboration with industry, immunogenetic profiling of dengue disease severity implicating OAS1-OAS2-OAS3 haplotypes and CD209 gene polymorphisms, development of an egg based oral formulation for treatment of rotaviral diarrhea and association of HLA-DRB1*11 allele and the emergence of DRB1*15/DQB1*06 & DRB1*10/DQB1*05 as susceptible haplotypes towards HEV infection is being reported for the first time.

Operationalization of the BSL4 Laboratory

Asia's first Maximum Containment Facility (Biosafety Level-4 Laboratory) at National Institute of Virology, Pune was inaugurated by Shri Ghulam Nabi Azad, Hon'ble Minister of Health & Family Welfare, Government of India on 28th December, 2012. The Secretary, Department of Health Research and Director General, Indian Council of Medical Research had setup



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the High Powered Committee to validate the BSL-4 facility at Maximum Containment complex, Pune. The Committee visited the facility and witnessed different operational procedures required for the best biosafety level work and finally declared that BSL-4 as well as the supporting BSL-3 and BSL-2 laboratories. They certified the laboratory as at par with international standards of the highest biosafety level practices.

Once again this year cases of CCHFV were recorded which was responsible for death of a medical professional in Gujarat state. Phylogenetic studies confirmed that the same viral strain is circulating in Gujarat State, India and responsible for causing deadly disease in these three years (2010-2012). This sends an alert to the public health department of the state for careful monitoring of suspected hemorrhagic fever cases for early detection of CCHF and ticks control in this area to deal with CCHF. It is required for medical professionals to take extreme care and bio-safety measures while treating patient suspected of hemorrhagic fever.

Two novel viruses were isolated from *Rousettus leschenaultii* species of bats collected from caves near Mahabaleshwar, Maharashtra State, India and both of the isolates were identified as a member of the family *Bunyaviridae*, genus *Phlebovirus*. A real-time RT-PCR assay was developed for Thottapalayam virus which is the only confirmed Hantaan virus isolated from *Suncus murinus*. The assay is sensitive enough to detect this virus from field specimen. Laboratory diagnostic services were provided nationwide.

Development of Serological and Molecular Diagnostic facility for Kyasanur Forest Disease Virus

KFD has its unique existence in five districts (Shimoga, Chikkamagalore, Uttara Kannada, Dakshina Kannada and Udupi) of Malnad region of Karnataka State and occurs as seasonal outbreaks during the months of January to May and affects annually 100-500 people. This year presence of KFD virus in monkeys, ticks and humans in Alegowdanakatte forest area and Chamarajanagara district showed the first outbreak of KFDV from this area. Affected villages were Molehole and Madhur colony near regional forest office, Bandipura Tiger Project, Gundulpet taluk, Chamarajanagara district.

In November 2012, death of twelve monkeys (*Macaca radiata* and *Presbytis entellus*) was reported from Bandipura National Park, Chamarajanagar district, Karnataka State. Typical KFD like clinical symptoms were also noticed from six human males of age group 20-55 years old, who were involved in handling and incineration of those sick monkeys. These handlers were admitted in taluka hospital Gundulpet. Later on few more suspected samples of human cases, monkey specimens and tick pools were received from Chamarajanagar area and adjoining border areas of Tamil Nadu for screening of KFDV. Monkey autopsy specimens (Brain, liver, lung, heart and kidney) and suspected human serum samples and tick pools were processed in BSL-3 laboratory. The nested RT-PCR and TaqMan based real-time RT-PCR assays confirmed suspected human samples positive for KFDV. Four-monkey samples were found positive for KFDV. Similarly, tick pools from this area were found positive. Monkey and human KFDV sequences showed 96% similarity with KFD prototype strain. There was no nucleotide diversity noticed in comparison with the earlier study. The very interesting finding was positivity of monkey specimen from Nilgiri area, which is border area of Tamil Nadu State and adjacent to Karnataka State.

Influenza Disease Burden In Rural Communities India

Patients with Severe Acute Respiratory Infections (SARI) cases and OPD cases were enrolled and respiratory specimens were collected at Vadu for identification of influenza and were

tested by real time PCR. During the reporting period 1243 samples were collected and subjected to real time RT PCR detection of influenza of which 150 (12%) –A(H1N1)pdm09, 31 (2.5%),-A(H3N2) and 107 (8.6 %) - influenza B samples were found to be positive. Representative real time positive samples were processed for influenza virus isolation in MDCK Cell line and 80 samples yielded influenza virus isolates: 51A(H1N1)pdm09 , 21 influenza type B with lineage subtype as Yamagata and 8 A(H3N2).Analysis was carried out to determine the burden of influenza associated hospitalizations and seasonality of influenza activity during and three years following the 2009 pandemic in a rural community. We calculated annual rates for influenza associated hospitalization adjusted for hospitalizations in non-participating hospital outside the study area. Overall annual influenza associated hospitalization rate (all ages) was 35.8 per 10,000 population with the highest burden at younger ages (43.7 and 41.7 for 5-14y and 15-29y age groups respectively). The influenza associated annual hospitalization rate (all ages) was 46.8 per 10,000 during the pandemic year and 40.5, 29.3 and 43.2 per 10,000 in the three years post-pandemic. Influenza B accounted for a substantial 38% of the total influenza hospitalization burden. Our study quantifies the high burden of influenza associated hospitalization in rural India. It highlights the need to strengthen virological surveillance with epidemiological information for high level of preparedness for early identification and control of influenza epidemics and pandemics.

Multisite Epidemiological and Virological Monitoring of Human Influenza, Surveillance Network in India, Phase II

NIV is both regional and referral centre for influenza. Regional center carries out surveillance in and around Pune and Referral center has the responsibility to reconfirm isolates received from regional labs, genetic analysis, drug susceptibility testing, & contribution of virus strains and contribute the data to global network. Referral center also conducts quality control of regional labs and strengthening of labs through training and technical support.

Activities of the Regional Centre

Surveillance in Pune

ILI surveillance was carried out among patients attending the various Pune Municipal Corporation (PMC) general outpatient (OPD) clinics. A total No. of 806 patients were identified and their respiratory samples were collected subjected to RT PCR for detection of influenza and 9.34% tested positive. Of these 35 (4.34%) were pandemic H1N1, 19 (2.4%) A/H3N2 and 21 (2.6 %) influenza B.

Influenza Virus Isolation

RT PCR positive samples (n=54) were processed for influenza virus isolation in MDCK Cell line and 27 samples yielded influenza virus isolates: 14A(H1N1)pdm09 , 13 influenza type B with lineage subtyping as 10 type B Victoria and 3 type B Yamagata.

Activities of Referral Centre

NIV as referral center carries out reconfirmation and genetic analysis for isolates received from other regional labs. Referral center also contributes strains to WHO collaborating center and surveillance data to GISN (Global Influenza Surveillance Network).

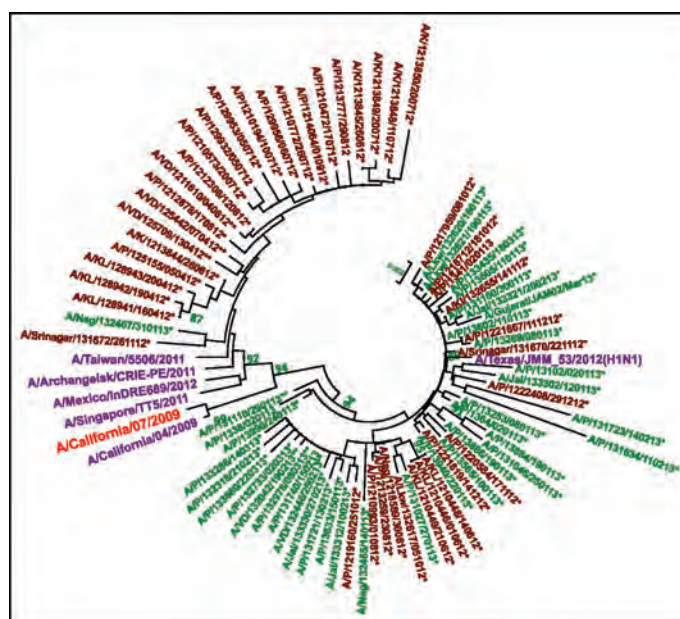
Reconfirmation of Isolates

NIV received isolates & clinical samples from all regional labs. Isolates were subjected to reconfirmation by real time PCR and representatives were re-isolated in MDCK cell line.

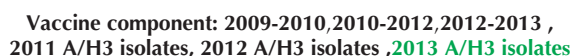
Reconfirmed isolates were further genetically characterized, HA1 gene was sequenced and phylogenetic relation with respect to recommended vaccine strains for the year 2009-2010 was determined for influenza A(H1N1), A(H3N2) and type B isolates. Amantadine susceptibility of H3N2 viruses were studied for molecular markers by M2 gene sequencing. For Neuraminidase drug susceptibility NA gene was sequenced.

A (H3N2): HA gene analysis of 18 isolates (6 of 2011, 7 of 2012 & 5 of 2013) (Pune- 6, Kerala-6 & Chennai-6) was done. 12 were similar to A/Victoria/361/2011 (2012-13 vaccine component) and 6 strains (2012) from Chennai were similar to NA/Perth/16/2009 (2010-2012 vaccine components (Fig.). All H3 strains were resistant to adamantane and sensitive to Oseltamivir.

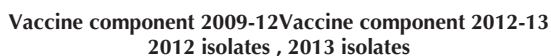
Type B: Fifty one type B isolates (49 of 2012, 2 of 2013) from Pune (32), Kolkata(5), Lucknow(4), Dibrugarh(3), Vellore(3), Kerala(2), Nagpur(1), Delhi(1) were analyzed for HA1 gene by sequencing. Phylogenetic analysis (Fig.) showed that 17 isolates 2012-15, 2013-2) clustered with vaccine component B/Wisconsin/01/2010(2012-13 type B vaccine components). The remaining isolates clustered with Brisbane/60/2008 (2009-2012 vaccine components). All type B strains were sensitive to Oseltamivir



Phylogenetic Analysis of HA gene of A(H1N1)pdm09



Phylogenetic Analysis of HA gene of A (H3)



* Referred samples, ** Vadu samples

Phylogenetic Analysis of HA gene of Type B

Quality Control for Regional Labs & Participation of Referral Lab in External QA/QC

For Regional Labs

For capacity building of regional centers, for diagnosis of pandemic A (H1N1) a panel of 5 coded samples (including seasonal strains as well as pandemic H1N1 strains) was sent to regional labs. All labs tested these samples by real time PCR as well as virus isolation.

For Referral Lab: Participation in WHO External Quality Assurance Panel (EQAP)

Referral Centre took part in the WHO External Quality Assurance Panel (EQAP) testing program. Panel contained 10 coded lyophilized RNA and deactivated influenza viruses which were reconstituted and subjected to conventional and real time RT-PCR assays. Panel 11 was also received; this consists of 10 vials of dried gamma-ray inactivated viruses. These samples were tested for influenza A (H3), Influenza A (H5), influenza A (H1N1) 2009 and influenza B. NIV results were concordant.

Immunogenetic Studies on Dengue Patients from Maharashtra

HLA-C typing was performed in 111 subjects who had a history of hospitalization for dengue (DEN) (82 DF cases and 29 DHF cases) and 106 healthy controls (HCs), who had no history of hospitalization for dengue using PCR based methods. The frequency of *HLA-Cw*07* allele was significantly higher in DEN cases as compared to HCs [$P = 0.0120$, $P_c = 0.168$, OR with 95% CI 2.00 (1.12-3.55)]. A trend towards lower frequency of *HLA-Cw*03* was observed in DEN cases as compared to HCs ($P > 0.05$). The frequency of other alleles was not different between DEN cases and HCs. When the DEN cases were categorized in to DF and DHF and compared with HCs, the frequency of *HLA-Cw*07* was significantly higher in both DF and DHF cases ($P < 0.05$). Though the frequency of *HLA-Cw*07* was higher in DHF cases compared to DF cases, it was not significant ($P > 0.05$). A trend towards higher frequency of *HLA-Cw*15* was observed in DHF cases as compared to DF cases, though the difference was not significant.

The results suggest that rs1799964 'C/C' genotype is associated with increased risk of symptomatic dengue and particularly DHF. The study also indicates an association of rs1800630 'T' allele and 'T/T' genotype with symptomatic dengue requiring hospitalization. The findings further indicate that *OAS1-OAS3-OAS2* haplotypes are associated with differential susceptibility to clinical outcomes of dengue infection. Importantly, the rs2287886 G/G genotype of *CD209* gene is associated with development of dengue requiring hospitalization while A/A genotype of rs735239 is associated with thrombocytopenia in dengue cases.

Development of a Diagnostic Kit for Group B Rotavirus

There is no commercially available diagnostic kit for rapid detection (antigen and antibody) of RVB infection. RVBs have not been adapted to cell culture. This has caused limitations in studying virological, serological and immunological features of RVB infections. Purified recombinant RVB VP6 protein that was expressed in baculovirus expression system was utilized for generation of hyperimmune sera in rabbits and guinea pigs from which capture antibody and specific immunoconjugates were prepared. An in-house ELISA protocol was standardized to detect anti-RVB IgM and IgG antibody in human serum samples. Serum samples collected from gastroenteritis patients whose stools were found positive for RVB RNA by RT-PCR were used as positive control and a panel of sera collected from healthy donors with the absence of RVB RNA in corresponding stools was used as negative control. The study is continued further to detect RVB antibodies in sporadic and outbreak settings and also in general population.

Development of an Egg based Formulation for Treatment of Rotaviral Diarrhea

Rotavirus A (RVA), a major etiological agent of diarrhea, is responsible for significant morbidity, mortality (6,10,000) and economic loss (>\$1 billion), worldwide. In India, rotavirus accounts for 122,000 to 153,000 deaths. The expenditure incurred in treatment of rotavirus diarrhea is ~Rs 2 to 3.4 billion. Efficacy and cost effectiveness of currently available rotavirus vaccines, Rotarix (monovalent) and Rota Teq (pentavalent) are yet to be resolved in developing countries. Passive immunization and therapeutic approaches remain alternative choice to reduce the disease burden. The objective of the study was to develop a hyperimmune egg antibody (IgY) formulation against rotavirus diarrhea for prophylactic and therapeutic use in children. MoU was signed between the authorities of NIV, Pune and Venky's (India) Ltd., Pune. To avoid cross contamination with avian pathogens, a separate facility for propagation of human rotaviruses was established in Venky's (India) Ltd, Pune. The required cell line certified to be mycoplasma free has been procured.

Association of HLA-DRB1*11 allele and the Emergence of DRB1*15/DQB1*06 & DRB1*10/DQB1*05 as Susceptible Haplotypes towards HEV Infection is being Reported for the First Time: Association of HLA-DRB1*11 allele and the emergence of DRB1*15/DQB1*06 & DRB1*10/DQB1*05 as susceptible haplotypes towards HEV infection is being reported for the first time. Association of HLA-DRB1*11 allele and the emergence of DRB1*15/DQB1*06 & DRB1*10/DQB1*05 as susceptible haplotypes towards HEV infection is being reported for the first time. Positive correlation of CD11c with HEV viral load suggested that increased frequencies of the same might be associated with HEV replication.

National JALMA Institute for Leprosy & Other Mycobacterial Diseases (NJILOMD), Agra

During year under report, the Institute has made significant progress in its research programmes on tuberculosis, leprosy and other mycobacterial diseases. Besides clinical and laboratory based research, the programmes of Model Rural Health Research Unit (MRHRU) at Ghatampur are important from public health point of view.

Studies on Leprosy

NJIL&OMD is the apex national institution on leprosy and undertakes research on clinical, therapeutic (medical and surgical) and epidemiology of leprosy.

Institute Approach: The studies carried out during the year using *in-situ* approach showed the expression of several genes associated with the immune response in the tissues. This information will help in understanding the host immunity in a better manner. The knowledge and training of *in-situ* PCR for early diagnosis of leprosy was disseminated to local medical college and ICMR's National Institute of Pathology, New Delhi as part of translational research.

Molecular studies: To understand the transmission of leprosy are a part of the multi-centric and multi-State ICMR project that were continued in selected areas of Uttar Pradesh (Ghatampur and nearby areas), Chhattisgarh and Tamil Nadu. Results showed the presence of DNA and RNA of *Mycobacterium leprae* in the water and the soil samples of the areas in which leprosy is prevalent. Such presence was noted in Ghatampur and Chattisgarh. This information will be used to trace the sources and determine transmission dynamics of the disease in high endemic pockets so that new strategies to prevent transmission of leprosy are developed.

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Immunological Studies in Leprosy: New data on mechanism of regulation of immune response in leprosy cases have provided new information about the type of regulatory cells and mediators associated with the immune regulation in leprosy. Studies on the effect of Notch and various transcription factors in the T cell regulation in leprosy showed an involvement of Notch in inducing T cell activation in BL/LL patients and regain of both Th1/Th2 type of response in these patients after 6 months of treatment was noted. Further, role of FoxP3+ regulatory T cells in polarized immunity among leprosy patients was evaluated. Higher proliferation of T regulatory cells were observed in BT/TT patients and healthy individuals in response to WCL and MLAM antigens whereas in BL/LL patients lower to WCL, MLAM and PGL-1 antigens. Longitudinal study of various T cell subsets and cytokines in TB patients revealed significantly higher percentage of TNF α expressing CD4+T cells in patients than IFN γ expressing CD4+ T cells at the time of enrollment and till 2 months of therapy which significantly decreased after 6 months of treatment.

Alternate Regimens for Leprosy: Follow up of the cases on uniform MDT (initially suggested by the Institute as a common regimen for leprosy) showed that it is a good alternate to the standard regimen and is user friendly.

Studies on Tuberculosis

Molecular Epidemiological Studies of Tuberculosis

Institute is engaged in studies based on molecular epidemiological markers for tuberculosis like Insertion Sequences (IS) 6110, spoligotyping, MIRU-VNTR and Ribotyping methods trace transmission especially in the slums, Tibetan population of Maklodganj area of Himachal Pradesh and tribal populations of Central India. Molecular profiling observed using these markers in these localities may establish a baseline to understand the transmission of diseases. However, there is no correlation observed of drug sensitivity profile with distribution of IS 6110 element. By doing spoligotyping, CAS-family was found dominant in these areas and the presence of Beijing family has not been observed so far in this study group.

Zoonosis: Tuberculosis and Other Mycobacterial Infections

Development of DNA Chip (Microarray based study)

This ICAR supported study provided original information about the distribution of *M. avium paratuberculosis* (MAP) strains present in specimens from HIV patients, animal and other human subjects. To study the difference in MAP isolates and expression profiling of native isolates a set of genes were selected for microarray based studies. The centre has come out with first indigenous partial DNA chip/microarray against the selected genes (ORF) of MAP. This chip could be useful in eliciting the strain variation in MAP isolates.

Proteomic Approaches

Proteomic approaches are being tried to understand the mechanism of resistance to aminoglycosides (drugs of choice especially for category II TB patients) and fluoroquinolones. The examination of kanamycin (KM) and amikacin (AK) resistant isolates of *Mycobacterium tuberculosis* using proteomic approach comprising of two dimensional gel electrophoresis, matrix assisted laser desorption ionization time-of-flight and bioinformatic tools has shown that twelve proteins were found to be consistently increased. The major finding implicates that the genes/proteins involved in iron metabolism (Rv1876) and the two hypothetical proteins (Rv3224 & Rv3867) might be playing some crucial role in contributing resistance to second line drugs. In-depth study of these proteins will give an insight into probable sites of drug action other than established primary sites and hence may help in search of novel

chemotherapeutic agents. A few proteins have been found to be over expressed in ofloxacin –monoresistant *M.tuberculosis* isolates and they are being investigated further.

National Reference Laboratory for Tuberculosis

As a National Reference Laboratory, the Institute is continuously involved in providing help/ guidance to four states (Uttar Pradesh, Himachal Pradesh, Uttarakhand and Assam) in their External Quality control Assay (EQA) and drug sensitivity testing for tuberculosis. As National Reference Laboratory for tuberculosis, NJIL&OMD has accredited 18 laboratories across the country for Line Probe Assay (LPA) so far and these laboratories are capable of taking the loads of patients in their respective areas in terms of early diagnosis of tuberculosis.

National Facilities: BSL-3 Facility and Mycobacterial Repository Center

This facility is running as a permanent facility of ICMR. This center has established linkages with a number of Institutes and centers. The number of participating centres currently is 40. Nearly 5000 isolates from different parts of country are being maintained in the Repository. This Repository continues to supply the reference material to different investigators all over the country and is the main resource for evaluation of the new compounds identified in the Open Source Drug Discovery Programme of CSIR. The Institute is also providing expertise/ help to other scientists who face difficulties in the characterization of mycobacterial isolates across the country. As a part of Repository formal / informal training in identification, handling of pathogens under Biosafety conditions, preservation of isolates, sensitivity screening and newer molecular DNA fingerprinting methods for characterization of mycobacteria is provided to scientists and technicians from different parts of the country. The Institute also continued to serve as a National Facility for Animal Experimentation in tuberculosis. This BSL-3 facility has been providing collaborative support to several Institutions for testing their drug and vaccine candidate against tuberculosis.

Human Resources Development

As a partner in NLEP and RNTCP, this Institute provides training to programme managers, doctors and laboratory staffs in different states. Further, the earlier programmes like research training in life sciences and project training for Postgraduate students for research training in life sciences and project training for M.D. thesis and Ph.D. thesis also continued as in previous years. The Institute has been running fortnight Summer Training Courses involving refresher course in biotechnology and allied subjects, biosafety procedures, updates on health problems like tuberculosis, leprosy and HIV infection, for students at Graduate and Postgraduate level.

Programmes of the Model Rural Health Research Unit (MRHRU), Ghatampur

The Institute is involved in epidemiological studies in Agra and Ghatampur districts of UP. However, major follow-up programmes are at MRHRU, Ghatampur. During the year, the MRHRU continued to assess the impact of various interventions (Standard and new methods developed by Institute) in leprosy and tuberculosis. These studies include the translational programmes for assessment of the long term impact of the cases treated with different regimens in leprosy and tuberculosis. The Unit is also undertaking studies on transmission dynamics of leprosy employing molecular epidemiological tools. The focus continued to be on strengthening the working linkages with state health systems. During the year, the Unit has taken the role of serving as the Mentor Unit/National Reference Centre for establishing other Model Rural Health Research Units in the country under a dedicated scheme funded by DHR, Ministry of Health & Family Welfare, GoI.

Rajendra Memorial Research Institute of Medical Sciences (RMRIMS), Patna

Epidemiology

Serological screening of 1104 kala-azar endemic population (male 522, female 582) with rK39 strip test revealed 46 asymptomatic cases, of which 6 converted to symptomatic VL during follow-up. IL10, Hb% and neutrophil count was observed as possible markers for conversion of asymptomatic to symptomatic.

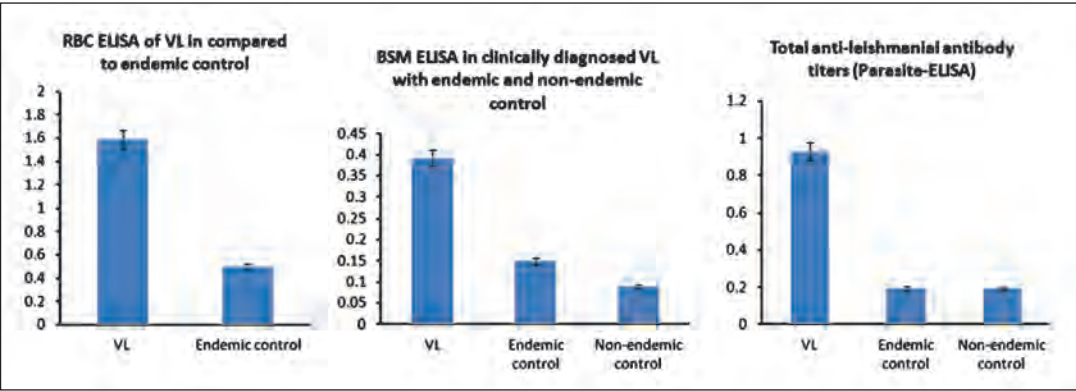
In continuation of the sentinel surveillance, altogether 2147 VL patients received treatment at the sentinel sites established in different districts (East Champaran 646, Muzaffarpur 612, Samastipur 366, Saran 523). Diagnosis with rk-39 (RDT) in about 99.81% confirms implementation of the national program guidelines. It was observed that about 57% VL patients were treated with miltefosine, followed by 27% with SAG, 10% with Combination therapy and about 6% were not treated at the site due to non availability of drugs and several other reasons thereof. Out of 948 women, 483 were in reproductive age group *i.e.* 16-45 years, and were treated with miltefosine as per the standard guidelines. During follow up of these females till six months for pregnancy and later on till child birth, no adverse event has been encountered as yet. About 98% of the total cases reported as new case is suggestive for either low relapse rate in these area or preference of private/higher level of treatment providers in case of relapse. Pharmacovigilance of miltefosine at peripheral level did not reveal any major side effects, other than known G.I. toxicity.

In order to assess drug association in progression of VL into PKDL development and time period of PKDL development after VL treatment, a study was initiated to follow-up all the VL cases (n=3647) treated at the Institute during the period 2007-2012. Till date, 54 patients of Muzaffarpur district were followed up, out of which 36 had been treated with Amphotericin B, 14 with Ambisome, 2 with Ampholyn, 1 with homeopathy medication and 1 with Amphotret. None of the followed up cases was neither clinically suspected for PKDL nor had past history of PKDL after end of treatment for VL.

Diagnostics

Sensitivity and specificity evaluation of RDT kits being used in programme and other commercially available kits revealed that Dia Med's IT-LEISH has maximum sensitivity of 96.66%, followed by InBios KA-Detect kit (95.55%), Span Diagnostic's Signal KA and CTK Biotech's Onsite Leishmania Ab (93.33%) and Span Diagnostic's Crystal KA (90%). All the RDTs were found highly specific (100%) and no significant variability observed in thermo stability test at different temperature in any kits. Though, KA_Detect kit (InBios) and IT-LEISH (Dia Med) performed almost equally, the InBios Kit may be preferred due to simplicity and early test reading.

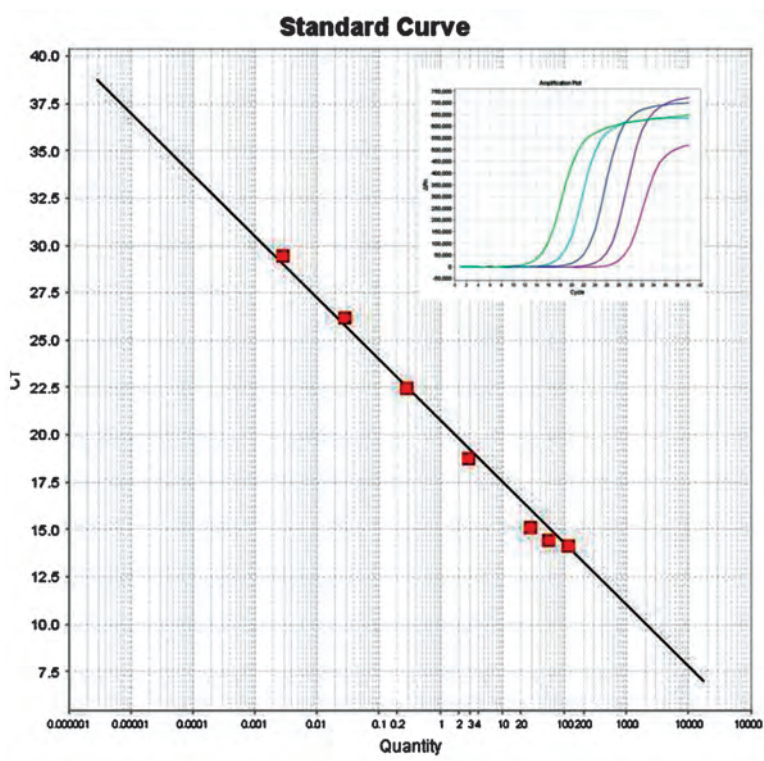
After confirming selective presence of 9-O-AcSA determinants on VL erythrocytes employing a 9-O-acetylated sialic acid binding lectin, Achatinin-H, the unique epitope has been identified on erythrocytes of VL patients, but absent in healthy individuals. A novel blood based antigen detection assay (RBC-ELISA), antibody based ELISA (BSM ELISA) and parasite ELISA for diagnosis and longitudinal follow up of VL patients have been standardized for screening a large population. Additionally, RBC-ELISA assay has prognostic potential that may be explored for early diagnosis of VL.



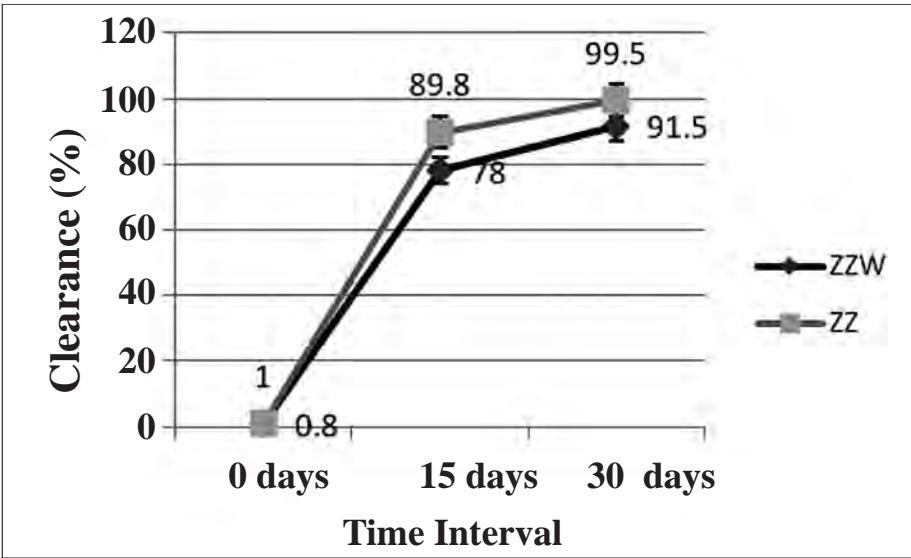
Standardization of RBC-ELISA, BSM-ELISA and Parasite-ELISA

Therapeutics

Zinc supplemented Amphotericin B therapy (test arm) in zinc-deficient kala-azar patients was observed to be better than Amphotericin B alone (control arm) as initial cure in test arm was 100% as compared to 91% in control arm. In test arm, level of IFN- γ was considerably increased and IL-10 level was quite high at Day 1st which dropped steadily with treatment. Interestingly, TNF- α level raised high at Day 14th but significantly dropped thereafter and almost reached to very low level at end of treatment. qPCR revealed earlier parasite clearance in Zn supplementation arm than Amphotericin B alone.



SYBR Green 1 based real time PCR by amplification of *Leishmania* K-DNA expressed as the number of parasites per reaction

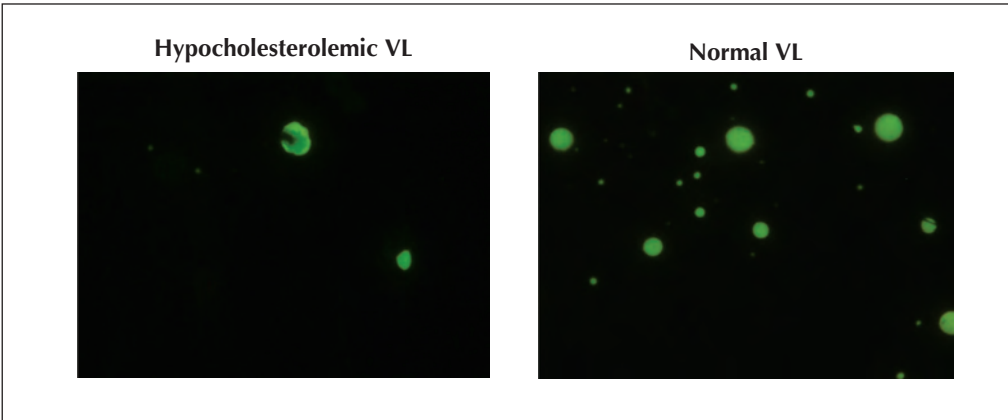


Comparative parasite clearance from the blood of patients of the ZZW and ZZ groups from day 0, i.e. baseline, to day 30.

Being one of the centres of a multicentric DNDi sponsored combination therapies of ambisome, miltefosine and paromomycin, out of 22 enrolled patients (Male 15, Female 7), 4 were administered single-dose AmBisome (5mg/kg BW) IV infusion followed by oral Miltefosine 2.5 mg/kg/day for 7 days, 2 were given oral Miltefosine 2.5mg/kg/day + Paromomycin sulphate 11mg/kg/day IM for 10 days and 16 were given single dose Ambisome 10 mg/kg. One patient withdrew his consent during treatment. All patients achieved initial clinical cure. Further recruitment and follow-up of treated cases in progress.

Basic Research

After establishing direct correlation of anemia and parasite index with hypocholesterolemia, IFN- γ was found down regulated during hypocholesterolemic conditions in VL infection. The membrane fluidity study using DPH probe revealed disturbed red cell membrane integrity, might be due to down regulated G6PDH. Further, the observed role of HDL in plasma fluid mechanics causing anemia in VL infection is suggestive for good cholesterol diet in improving anemic condition and protection against VL infection.

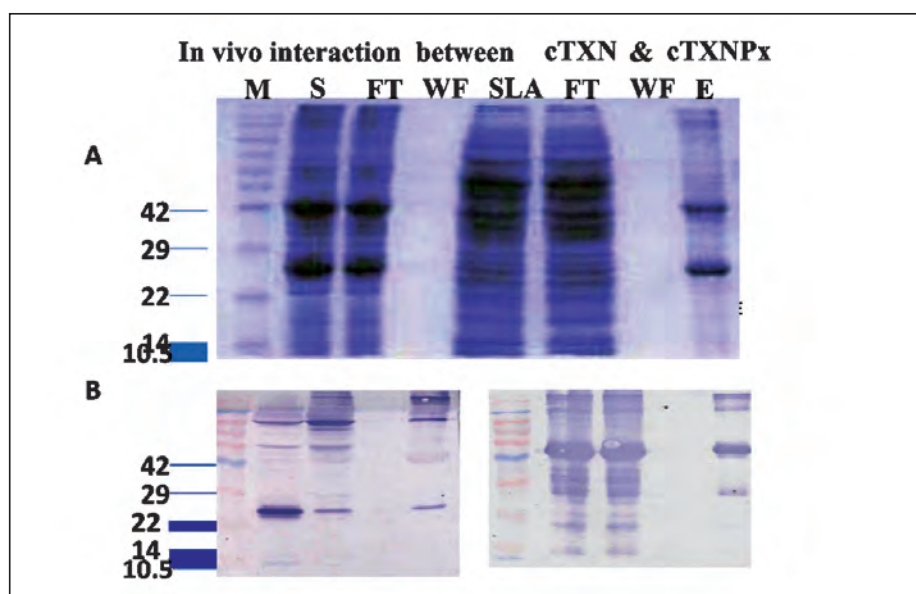


Increased microalbuminuria in PKDL cases may be an early marker of subtle renal damage and glomerulonephritis. Predominant MIP-1 α chemokine in all types of PKDL lesions with higher expression in macular lesions revealed its role in manifestation into different types of PKDL lesions.

The absolute number of circulating CD4⁺ T cell subpopulation and surface expression during active infection in PKDL cases was found markedly reduced in the dermal lesions as compared to healthy controls. The increased level of IL-10, IL-4 and TGF- β showed suppression of CMI. Activation and up-regulation of chemokine receptor particularly CCR3 and CCR4 was shown to be associated with PKDL. Further, it was observed that infiltration of CD4 cells more prominently decreases in macular lesions as compared to papular and nodular lesions. This pattern was also confirmed by *in-vitro* transmembrane experiment. The migration of CD4⁺ cells was also lower in response to the PKDL parasites. However, no significant difference was observed in the response induced by PKDL and VL derived *L. donovani* parasite.

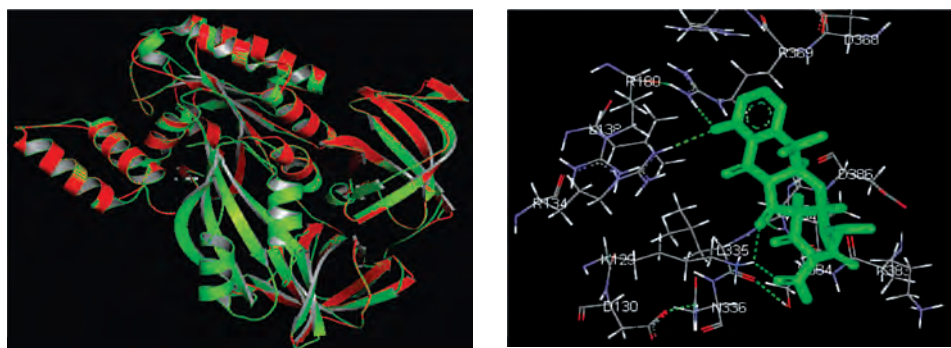
Bio-informatics

In-silico interaction between cytosolic TXN and TXNPx proteins was further confirmed *in vitro*. Further, mTXN interaction with mTXNPx was also observed through *in-silico* analysis. Up-regulated expression of cTXN in drug resistance *L. donovani* parasite in presence of 20 ng/ml of amphotericin B suggests its possible involvement in amphotericin B resistance.



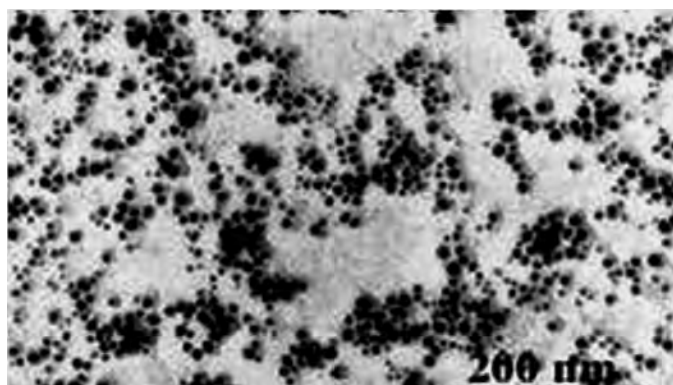
(A). 12% SDS-PAGE of cTXN and cTXNP in vivo interaction. (B). Immuneblotanalysis

The constructed Elongation Factor-1 alpha (EF1- α) protein was superimposed with target protein (fig. A). A hairpin of 12 amino acids, unique to the human EF1- α protein but missing in *Leishmania*, was modeled which may be explored to design novel, small molecule inhibitors that bind specifically to the region. Docking of EF1- α with various GTP analogues exhibited highest dock score (-10.8193) with Asp159. Protein-ligand interaction of EF1- α protein of *Ldv* with various tetracycline analogues showed the highest dock score 70.42 (Tetracycline n-hexylsulfamate) and involved amino acids are Arg 134, Arg180 and Arg369 (DS). Docking analysis with tetracycline analogues showed the highest dock score -27.9665 (Tetracycline n-hexylsulfamate) and involved residues are His15, Gly19, Ser21 and Asp91 (Fig.). Thus, the active site architecture and certain key residues responsible for inhibitor binding of EF1- α were identified for designing novel inhibitors of leishmaniasis.



Physical encapsulation of amphotericin B

Physical encapsulation of amphotericin B, an antileishmanial drug, has been done with PAMAM dendrimer accomplished by thermo mixing of the polymer and drug solutions where the hydrophobic drug associates with the non polar core through hydrophobic interactions. Characterization of nano-particle by transmission electron microscope (TEM) revealed its size of 15-25nm and is uniformly distributed that may further be explored for its application in drug delivery system.



Characterization of nano-particle by transmission electron microscope (TEM)

Operational Research

The host-preference analysis of *P. argentipes* revealed unequal preference for each host species during pre and post DDT spray ($p < 0.005$). During the post-DDT spray, bovine blood was found significantly preferred by vector in comparison to goat ($p < 0.003$) and mixed feeding ($p < 0.004$).

Out of 19 plants' extracts subjected to bio-assay test, 4 exhibited lethal effect to *P. argentipes*; 80% mortality in PK₄₈ leaves and roots (methanol extract), 87.5% in PK₈₁ leaves (methanol extract), 100% in PK₁ leaves (aqueous extract) and 80% in PK₉₀ root (hexane extract). Thin Layer Chromatography of Fraction 9 (methanol phase of PK₉₀ leaves, hexane extract) showed presence of a terpenoid, "Clerodin". HPLC analysis of 9th fraction of the extract of PK₉₀ showed presence of 9 compounds, of which 2 were identified as potentially active molecules for insecticidal effect.

In order to identify sustainable, cost effective and environmentally friendly alternative to DDT for vector control, three interventions viz. Indoor wall and floor plastered with lime (IWFPL), Durable wall lining (DWL) with deltamethrine (55 mg/m²) and KO TAB 123 Insecticide treated nets (ITN) were evaluated in altogether 1200 households of 4 highly endemic villages of kala-azar. DWL was found as the most efficient method for vector control in comparison

to ITN and IWFPL. However, ITN, which was better than IWFPL, was the most acceptable method by study population.

An autoregressive integrated moving average (ARIMA) (1,1,1) analysis of the weather data in the study area revealed that mean temperature, sea level pressure, relative humidity and mean wind velocity play significant role in sand fly abundance at a lag of one month. However, the overall log likelihood ratio (X^2) of the predictive model showed significant result ($X^2 = -160.42$ $p < 0.0000$). The value of AIC of the predictive model is 328.84.

Kala-azar transmission risk map was generated based on index model considering the demographic characteristics such as population density, family size, non-working/unemployed population, illiteracy rate, agricultural density and nutritional density derived through census data and remote sensing data of the study sites. A pair-wise comparison matrix was built via Saaty's Analytical Hierarchy Process (AHP) to differentiate sand fly abundance zone of the study district and the validated with the ground data to estimate its accuracy. The overall accuracy of the model in lean season was 63.33% while it was 68.63% in the peak season.

Others

59 cases of anophthalmia and or microphthalmia (including 35 reported cases) from different districts of Bihar viz. Bhojpur, Buxar, Rohtas and Patna were identified and 61 controls; from each district were studied. 95% of cases had 38-42 week gestational age (on term birth). Fever and night-blindness was found as highly significant ($p < 0.001$) risk factor for anophthalmia/ microphthalmia. The percentage of deficiency in vitamin B-12, Retinol, α -tocopherol, Copper, and Zinc was higher in cases than controls. Further, positivity % of T IgG, T IgM, R IgG, R IgM, CMV IgG, CMV IgM, HSV1 IgG, HSV1 IgM, HSV2 IgG and HSV2 IgM was higher in control than cases except IgM R (Rubella). All the mothers of cases and controls were aged < 40 years at the time of child's birth.

In ICTC centre, out of 2337 [Male 1391, Female 942 and transgender (TG) 4] individuals tested for HIV, 547 (23.4%) were found positive for HIV. 181 cases of HIV/TB co-infection was found. The number of patients put on ART reached to 499.

In MDR/XDR TB Lab, out of 773 sputum samples of pulmonary tuberculosis (PTB) patients referred from TBD Centres of all the 38 districts of Bihar (300), RMRI OPD (444) and RMRI ART centre (29), altogether 34% were found AFB positive. About 37% of the samples referred from TBD centres were also found positive for *M. tuberculosis* by solid culture in Lowenstein-Jensen Medium.

The virology laboratory provides diagnostic support for several viral diseases viz. diarrhoea, acute encephalitis syndrome (AES), influenza, enterovirus, swine flu, HZV, herpes simplex I and II. A total of 1098 blood, sera, throat swab and stool samples were collected from different districts of Bihar and analyzed for different viral diseases. In the year 2013, this laboratory provided diagnostic services during various disease outbreaks in Bihar such as Diarrhoea outbreak in Patna, AES in Muzaffarpur and Dengue in Rohtas.

Vector Control Research Centre (VCRC), Puducherry

Lymphatic Filariasis

- Towards developing an antibody assay for detecting the exposure to filarial antigen, BALB/c mice were immunized with *Wuchereria bancrofti* L3 stage parasites to get anti-L3 antibodies.

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Protein profiling of the L3 extract showed 14 proteins of which 43 kDa protein molecule reacted with L3 stage antibodies. Sequencing by LC-MS/MS analysis yielded 11 hits matching with *W. bancrofti* cDNA and out of six peptides with 20 or more of the amino acids synthesized, three showed high reactivity to antigen positive sera. Sensitivity was 100% and specificity was above 90%. These are potential candidates in developing marker to measure the exposure rate of an individual to filariasis in an endemic community.

- *W. bancrofti* specific epitope-WbL3PP2 was identified and the relevant peptide synthesized showed immuno-reactivity to *W. bancrofti* infection in humans and mosquito vectors. A concentration of 0.1 µg/well with the OD value of 0.276 was found optimum for testing the reactivity against human sera samples. Preliminary testing of 34 coded human sera samples showed 50% sensitivity and 59% specificity.
- RT-PCR based assay developed at the centre for the detection of infective (L₃) stage larvae of lymphatic filarial parasite, *W. bancrofti*, in vector mosquito *Cx. quinquefasciatus* from the four participating centres was validated through a multi-centric evaluation. This facility has been established in the four participating centres. Field evaluation showed that the assay has potential application in monitoring the transmission of LF.
- A prototype of an electrochemical detector of *W. bancrofti* developed at the centre was further refined to a miniaturized version to reduce the volume of the analyte and also to make the device user friendly and portable for the detection of vectors in peripheral areas. The probed experiment is showing appreciable results towards DNA hybridization and also it can provide a potential platform for the construction of DNA biosensor.
- A National Network for genotyping of *Wuchereria bancrofti* in different filariasis endemic areas was established and a workshop for the collaborating scientists was conducted for genotyping. The collaborating centres carried out surveys for mf carriers in their respective areas and morphometry have been completed. Isolation and purification of mf from archived blood smears, isolation of genomic DNA from microfilariae, amplification, cloning and sequencing of Alt-2 and ITS region and detection of albendazole resistance by real time PCR have been carried out by the participating centres.
- Vector sampling was standardized and PCR based methods of assessing vector infection have been developed to monitor vector infection to assess the impact MDA. This strategy was validated by conducting repeat surveys at two stages with a gap of two years. The results in stage 2 of the study suggest that as observed in stage 1, the proposed mosquito sampling strategy of collecting 7 pools of 25 gravid females each from each of 33 clusters (aggregating to a total of 231 pools of at least 5000 gravid females) would suffice to assess the vector infection rates by PCR assays even when the infection rates in human and vectors are below the transmission threshold level of 0.5%. The vector infection rates are independent of methods of extraction of DNA. The results also suggest that vector sampling is highly efficient when compared to human sampling for assessing Mf-prevalence, particularly when human infection prevalence is below 1%.
- A study carried out in four communities during post MDA period showed absence of recent transmission in two consecutive post-MDA surveys, indicating that 1% Mf prevalence was safe to discontinue MDA. Post-MDA Ag-prevalence between children and adult age class is not related, and therefore adult age class cannot be targeted for evaluation. There was no significant reduction in antigenemia prevalence in both children and adult age classes. Xenomonitoring after two years of stopping MDA did not show evidence for vector infection implying absence of potential mf carriers in the study community.

- Transmission Assessment Survey (TAS) was carried out in five evaluation units to assess the impact for stopping MDA. The results showed that the protocol require standardization to our operational settings. Migrant children and children from other implementation units should be excluded from sampling. Data from immunization records is recommended to calculate school enrolment of children. Inflated census data was observed in some areas. The results of TAS could serve as valuable input for developing national guidelines for TAS.

Malaria/Leishmaniasis

- The drug regimen ACT in treatment of uncomplicated falciparum malaria has good clinical response although the fever resolution is by crisis. Reduction of parasite density by 96% by day 3 suggests adequate response to artemisinin. However, there is late parasitological failure of about 27% of cases studied as observed both by microscopy and PCR suggesting failure of partner drugs: sulfadoxine and pyrimethamine. The adverse drug reactions were mild and abdominal pain was the predominant observation. About 28% ASHAs either do not know or take others' help for performing RDT. 60% of ASHAs give ACT for 3- days' dose on the 1st day of patients' visit and the remaining ASHAs distribute ACT on daily basis.
- A study is conducted in Kumbhari and Jogipaluru sub-centres (SCs) of Narayanpatana community health centre (CHC) of Koraput district of Odisha State to evaluate the impact of spraying DDT WDP 75% over DDT WDP 50% on abundance and survival of the vector, to determine the residual effect of the two DDT formulations on sprayed surfaces and to assess the quality of spraying, coverage and influence of wall smearing etc. on the effectiveness of residual spraying of both the formulations of DDT. Spray coverage ranged from 77.7% to 99.1% and mud plastering within two months of the spray was 28-42% in different villages. Density of the vectors (*An. fluviatilis* and *An. culicifacies* showed reduction after spray and one time mud plastered surfaces, the mortality was 98.9% with DDT 75% and there was a marked reduction in mortality to 49.1% with DDT 50%.
- A study on Cutaneous Leishmaniasis (CL) is conducted in 28 tribal settlements (Kani tribes) in Kerala. As many as 16 species of sand flies were recorded and *P. argentipes* and *P. colabaensis*, the implicated vectors constituted about 21%. The preliminary findings indicate that the climatic conditions such as copious rainfall, dampness due to relative humidity, abundant vegetation, canopy coverage with thick forest vegetation and moderate temperature prevailing in this area are the decisive factors, favouring sand fly abundance and distribution. Prevalence of sand flies and *L. donovani* carriers indicates the possibility of active CL transmission in the area.

Dengue/Chikungunya/JE

- IVM strategies designed and implemented for the prevention/control of *Aedes albopictus* in rubber plantations in Kerala and were monitored for its operational feasibility and impact. There was a significant reduction in vector density (PI: 97.4% & adult PMD: 62.79%). No incidence of any arbo-viral disease (Chikungunya or Dengue) was recorded in the IVM demonstration areas during the project period.
- Clinical data were obtained from 107 and 552 individuals who had the history of chikungunya infection from Alleppy and Kasaragod districts respectively to assess long-term morbidity. About 65% of the total 341 serum samples tested were CHIKV antibody positive in IgG immune-fluorescent reaction.

- The results of the study on the Development of RS-GIS based Model to Forecast JE Vector Abundance and Transmission Risk showed a significant correlation between crop height and vector densities (adult as well as larvae). The results of vector infection with JE showed that the trend in vector infection rates is qualitatively similar to that of MIR but differed quantitatively. In addition, the upper 95% confidence interval for the rates suggests that the rates are highly variable in some months yet the viral activity continues to occur throughout the study period. The Indian Satellite [RISAT-1 dual polarization (HH, HV) MRS and FRS data] data available for the last one year are used for identifying the different stages of paddy growth in the study villages. The values increase with stages of paddy growth suggesting that the backscatter coefficient could be used as a proxy for monitoring paddy growth and hence can be used to explore its possible relationship with JE vector density.

Scrub Typhus

- Scrub typhus continues to cause an acute febrile illness in Pondicherry region as evidenced both by the antibody detection and the detection of the DNA of the bacterium. ISS-11 is the most common genotype identified so far along with other genotypes like Inha Kp1186344, CMC Scrub E6, UT219 and CBNU-19.

Microbial/Chemical Agents for Vector Control

- The nanoparticle-based and EC formulations of temephos, pirimiphos-methyl and DPE-28 were evaluated in the laboratory for their larvicidal activity against *Cx. quinquefasciatus*. The LC₅₀ values of the nano formulations of temephos, pirimiphos-methyl and DPE-28 were 87 and 73 and 771 times more than that of their respective EC formulation. Field evaluation of nano formulation of the larvicides at 1 mg/l could produce >90% reduction in immature density of *Cx. quinquefasciatus* in breeding habitats only for 1 – 2 days. It is inferred that the use of nano-formulation for mosquito larvicides will have limited application in mosquito control.
- A study on the isolation and characterization of the mosquito larvicidal lead molecule from *Euphorbia lactea* crude extract by bioassay guided fractionation and spectral analysis showed that the molecule with chemical name 1H-Cycloprop[e]azulen-4-ol, decahydro-1,1,4,7-tetramethyl-, [1ar-(1aà,4á,4aá,7à,7aá,7bà)]- is one of the active principles responsible for the mosquito larvicidal activity. This is the first report of the mosquitocidal lead molecule from *E. lactea*.
- Characterization of *Bacillus cereus*, VCRC-B520 (NCBI: KC-119192) is a potent mosquitocidal agent isolated for the first time from marine soil. Bacterial growth, biomass, and toxin production is carried out. Larval bioassays were performed against mosquito species. The protein profiles of *B. cereus* were estimated by SDS-PAGE (10%).
- A method for *in vivo* screening of six promising 1-N-methyl-4-(substituted) benzoyl/phenyl acetyl piperazides for macrofilaricidal activity against *Brugia malayi* in animal models has been standardized.
- An optimized production medium and downstream process for obtaining the metabolite by the mosquitocidal bacterium *B. amyloliquefaciens* (VCRC B483) have been developed.

Translational Research

- Two macrofilaricidal combinations MCT-6 & MCT-7 have showed promising macrofilaricidal activity against adult *Setaria digitata* under in vitro conditions. Low

activity was observed with MCT-7 when given by oral route in animal models. This might be due to its poor aqueous solubility and bioavailability.

- An improved method of production and downstream processing of Thrombinase, a blood clot dissolving enzyme, from a *Bacillus sphaericus* (strain no. NRRL B 18949) resulted in decrease in the number of steps and time involved in purification of Thrombinase with a marginal increase in the yield. The peptide profile generated a total of 29 peptides ranging from 599 Da to 2716 Da and the M.W of thrombinase was determined to be 28.95 kDa. The enzyme activity was found to be optimal at neutral pH.
- A formulation of *Pseudomonas fluorescens* (VCRC B426) was developed and tested both in the laboratory and field conditions. Laboratory bioassay results showed that *An. stephensi* (LC50 0.92 and LC90 2.14 µl/100 ml) was more susceptible followed by *Ae. aegypti* (LC50 4.56 and LC90 6.92 µl/100 ml) and *Cx. quinquefasciatus* (LC50 6.48 and LC90 8.89 µl/100 ml). In a preliminary field evaluation against *Cx. quinquefasciatus*, the formulation was effective at a reduced dosage of 90 ml/m² resulting >90% pupal mortality up to 9 days post-treatment.
- Fermentation process for production of mosquitocidal lipopeptides of *B. subtilis* has been up scaled and optimized the downstream processing techniques. Seven different types of Aqueous formulations (I –VII) were prepared and evaluated against the pupal stages of *An. stephensi*. One formulation is found to be potential active mosquitoes.
- A trial with G30 formulation of Natular showed that it could be used for larval control against *Cx. quinquefasciatus* and *Cx. tritaeniorhynchus* at the dosage of 150 mg (a.i)/m² at three weeks interval in street drains and at 3-4 weeks interval in abandoned wells. Natural G30 formulation could be one of the options for larval control operations in Integrated Vector Control Programmes.

Human Resources Development

(a) M.Sc. Public Health Entomology

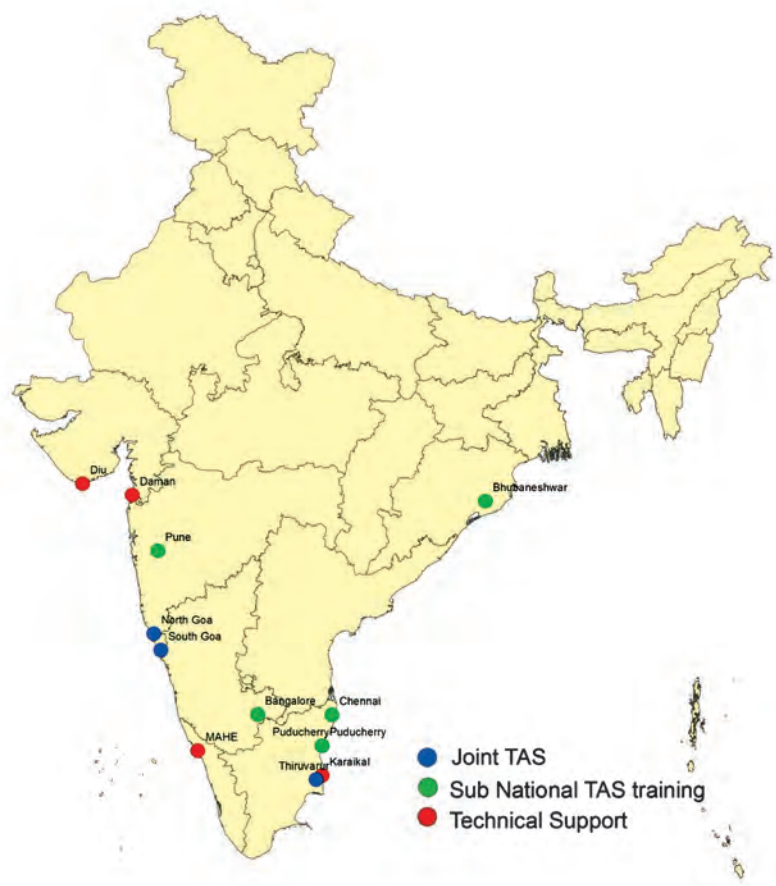
From the first batch of students who have successfully completed their course, award of internship has been given to two students with a stipend of Rs. 12,000/ per month, based on the inter-se merit list obtained from Pondicherry University.

(b) Ph.D. Programmes

Seventeen full time (Zoology –10; Microbiology – 5, Chemistry - 2) and two part time Internal (one each from Zoology and Microbiology) candidates continue to pursue their Ph.D. programme.

Training

Formal: Training course on Biologists/Senior Entomologists Jointly organized by VCRC, Puducherry & NVBDCP, New Delhi. 17 Biologists/Senior Entomologists (Gujarat, Haryana, Karnataka, Andhra Pradesh, Tamil Nadu & Puducherry).



Transmission Assessment Survey to evaluate LF elimination programme in India

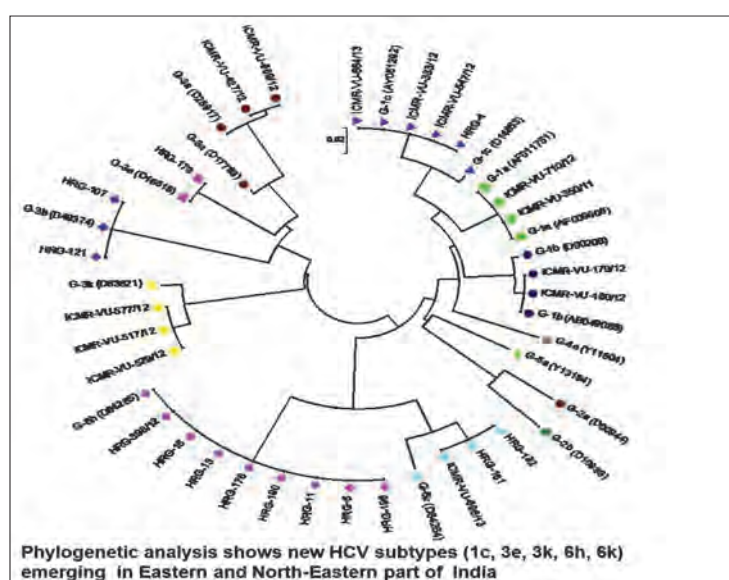


JE vector sampling in a JE prone village in Gorakhpur

Virus Unit (ICMR), Kolkata

Studies on Viral Hepatitis

The study designed to assess the hepatitis B virus (HBV) and hepatitis C virus (HCV) co-infection scenario among the human immunodeficiency virus (HIV) infected antiretroviral therapy (ART) naïve patients attending a tertiary healthcare unit in eastern India revealed that the prevalence of HIV/HBV co-infection was significantly higher among them. The prevalence of HBsAg was 11.3%, while anti-HCV prevalence was only 1.9%. Moreover, majority of the HBsAg positive HIV/HBV co-infected patients (87.7%) had HBV level significantly higher than that of HBsAg negative subjects. Multivariate analysis also showed that HBsAg-positive status was independently associated with higher HBV DNA level ($p=0.001$). Notably, 60.9% of the HBsAg negative co-infected subjects had HBV DNA $>2,000$ IU/ml of which 37.0% had HBV DNA $>20,000$ IU/ml, the cut off level recommended for initiation of therapy. HBsAg positivity could serve as an effective marker in order to prioritize the need for anti-HBV treatment under resource-poor settings lacking the HBV DNA quantification facility. Notably, majority of the HBsAg negative HIV/HBV co-infected patients also had considerably high HBV viremia and therefore required necessary anti-HBV treatment as well. Anti-HBV drug resistant mutations were detected in two (3.8%) of the ART-naïve patients, so pre-treatment screening for anti-HBV drug resistant mutations is not necessary before ART initiation. Genotype HBV/D (68.2%) was the predominant genotype followed by HBV/A (24.3%) and HBV/C (7.5%).



The sequencing results indicates that Gen-3 is the predominant circulating strain with 63.68% (3a=49.39%; 3b=49.79%; 3e=0.803%) followed by Gen-1 at 33.76% (1a= 57.57%; 1b= 41.67%; 1c= 0.756%) and new emerging cases of Gen-6 at 2.56% (6h= 70%; 6k= 30%). The data obtained from the population studied shows three major genotypes with eight subtypes including few rare subtypes like genotype 1c, 3e, 3k, 6h and 6k, the largest ever to be documented from any region of India.

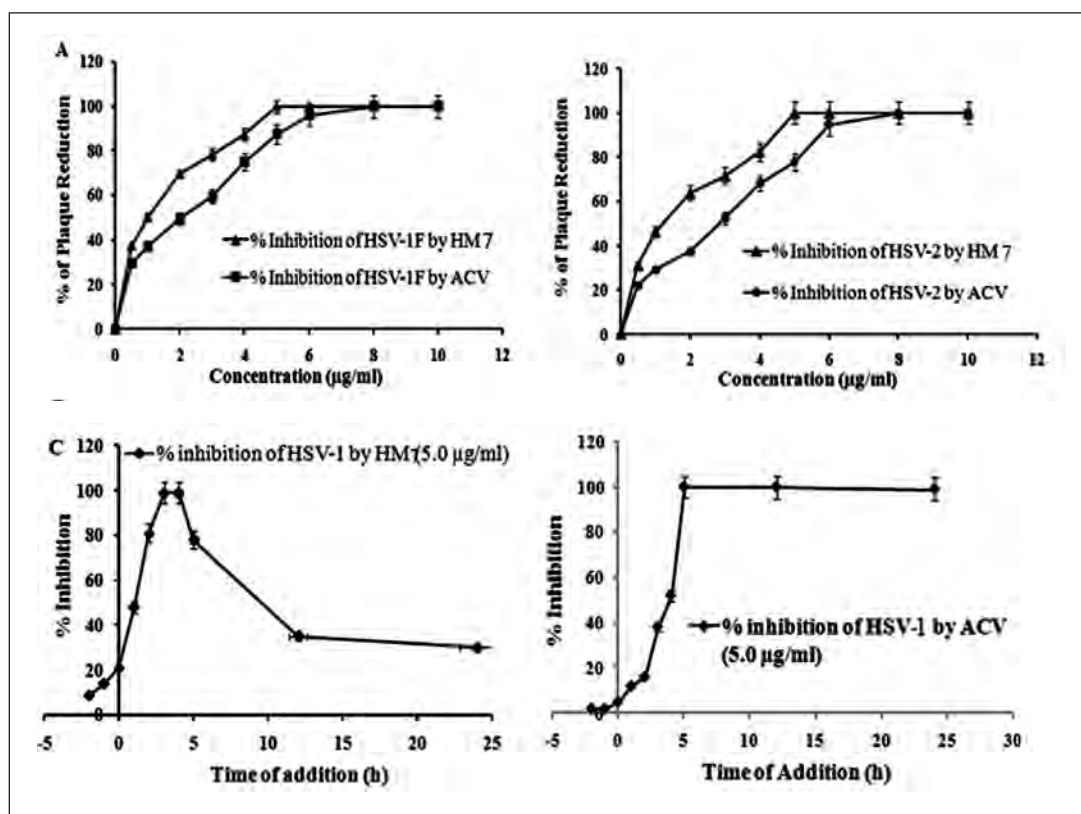
Studies on Arbovirus Infection

A total of 76 samples with a history of Acute Encephalitic Syndrome were referred for the detection of JEV infection. Of these 9 (11.8%) were tested positive for the presence of IgM

antibody by ELISA method. This year (2013) a total of 253 samples with a history of fever, head ache, body ache, joint pain were referred to this laboratory for the detection of DENV infection, if any, in them. These samples were tested for the presence of IgM antibody by ELISA method. The results showed 83 (32.8%) positive. This year (2013) a total of 68 samples with a history of fever, head ache, body ache, joint pain were referred to this laboratory for the detection of CHIKV infection, if any, in them. Of these 3 were tested for the presence of IgM antibody by ELISA method.

Studies on *Herpes simplex Virus Infection*

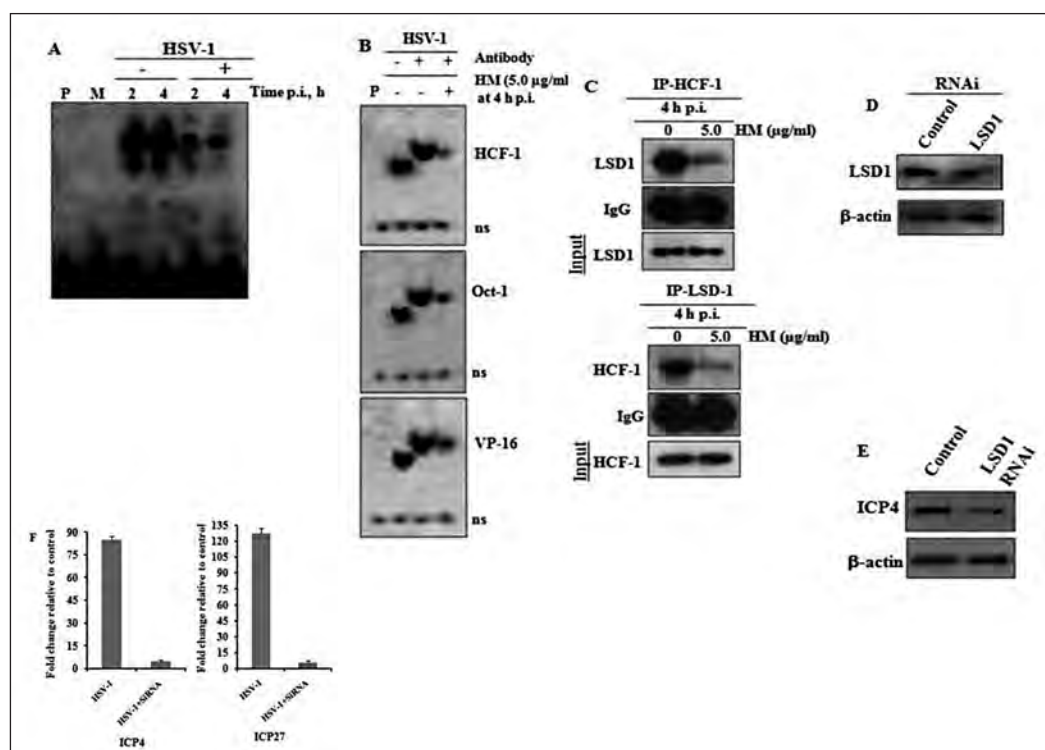
We have isolated an alkaloid from the bioactive fraction of an ethno-medicine (designated as HM-7, applied for Patent) as light yellow powder with melting point 229°C, molecular mass 214.3 g/mol. The compound is insoluble in water but soluble in DMSO. The MTT assay revealed that HM-7 is cytotoxic (CC_{50}) at 30 µg/ml; while its antiviral activity (EC_{50}) was observed at 1.1 ± 0.1 and 1.5 ± 0.1 µg/ml against HSV-1 and 2. The *Plaque reduction assay* showed that HM-7 at 5 µg/ml inhibit 99% of plaque formation of HSV; compared to 100% inhibition at 10 µg/ml by acyclovir. *Time of-addition assay* showed that HM-7 at 1.0 and 5.0 µg/ml exhibited highest inhibition against HSV within 2-4 h, i.e., during the early phase of virus multiplication (Fig.); but no inhibition before infection or during infection.



Plaque reduction assay of HSV-1 and HSV-2 (AB) and Time of addition assay (C)

Further, the *attachment and penetration assay* revealed that HM-7 is unable to block the virus entry, suggesting that HM-7 may interfere with the early replication of HSC. Then we studied the *expression of two major proteins ICP4 and ICP27 of immediate early (IE) replication* and found that both IE proteins were failed to express in HSV-infected HM treated cells, but well expressed in untreated one (Fig. C-D). Moreover, the qRT-PCR of both proteins showed significantly decreased level in a time dependent manner (Fig. E-F). Further study on the

effect of HM-7 on IE transcriptional events revealed a significant reduction of IE complex in treated cells at 4 h p.i. (Fig. A-B), indicating that HM-7 interfered with the recruitment of IE complex on ICP0 promoter, leading to the decreased viral transcription (Fig.).



Effect of HM on binding of IE complex on ICP0 promoter (A) EMSA; (B) Super Shift; (C) Co-immuno-precipitation; (D) Western blot of LSD1 and (E) Viral ICP4, (F) Quantitative real-time PCR of ICP4 and ICP27 in LSD1 transfected cells.

Thus, our results collectively demonstrated that HM-7 interfere with the binding of IE complex on ICP0 promoter and down-regulates the expression LSD1 or its association with HCF1 for its antiviral activity. (Fig.).

The *preliminary Toxicity and efficacy study in Balb/C mice* revealed that HM-7 is safe below 50 mg/kg dose with normal hematological, biochemical and histo-pathological features. The efficacy of HM-7 in mice vaginally infected with HSV-2 showed potent anti-HSV activity, as the virus lesion score and yields in the vaginal tissue and brain of HM-7 treated virus infected animals on day 2, 4 and 6 was reduced in a dose and time dependent manner. The histopathology of vaginal tissues of uninfected animals revealed intact vaginal epithelium; while the HSV-2G infected genital tissues showed extensive infection with acute inflammation and leukocytic infiltration. Interestingly, the HM-7 (0.5 mg/kg) or acyclovir (5 mg/kg) treated groups showed limited or no infection.

Studies on Human Cytomegalovirus Infection

Among the 400 HAART (Highly Active Anti-Retroviral Therapy) naïve newly diagnosed HIV/AIDS patients with CD4 count 100 and below, 147 renal transplant subjects and 10 autologous hematopoietic stem cell transplant patients with multiple myeloma at six months, their HCMV status was confirmed by performing HCMV specific Real-Time PCR with the serum to determine the HCMV Viral Load by using HCMV real time PCR kit provided by Shanghai ZJ Bio-tech Company Ltd., (China) using Real-Time PCR (ABI7000). Subjects found HCMV positive on Real-Time PCR were only included in the study. Our

objective was to investigate the changes in the protein level of expression of the HCMV viral glycoproteins gB and gH with genotypic variation (with respect to gB-gH genotype). Viral strains depending on gB and gH genotypes were determined based on standard protocols (study done in the previous academic year). Glycoprotein B (gB) and glycoprotein H (gH) are the two major HCMV envelope glycol-proteins that mediate viral entry into cells and are targets of neutralizing antibodies.

Our study explicitly proves that with genotypic variation a change in the expression of the two most important viral proteins (gB and gH) takes place. gB1 strain of the virus was found to express maximum concentration of gB viral protein followed by the strain types with gB3, gB4 and gB2 respectively irrespectively of the type of immune suppression (HIV/ AIDS, RTx or STx). Similarly, HCMV containing gH-1 genotype was found to express greater concentration of gH viral protein followed by the strain gH-2 type.

Desert Medical Research Centre (DMRC), Jodhpur

Dengue

Translational Research for Development and Testing of ICMR-DMRC Module of Dengue Control for Rajasthan

A comprehensive project aimed to generate early warning system of activity of dengue virus in all the 32 districts of Rajasthan. Based on the presence of vertically infected mosquitoes at household level in each district town of Rajasthan, warning points of virus activity have been communicated to state health department for controlling dengue vectors.

Malaria

Health Seeking Behavior towards Malaria among Tribal & Non-tribal Groups in Villages of Kotra, Udaipur

In Garasia tribe the prevalence of malaria was observed in 79.4% households, whereas, in non-tribal households 70.8%. Majority of the malaria cases (78.3%) from hamlets opted treatment from Bengali RMP private practitioners, whereas, from main village only 24.0% however, the non-tribal groups chiefly utilized CHC facilities (36.9%) for seeking treatment of malaria. Among tribal 29.8% malaria cases from hamlets and main villages opted treatment on the day of commencement of fever, however the non-tribal 47.9%. Bed net usage in tribals was reported low (5.7%) in comparison to non-tribal house-holds (16.5%). Majority of tribal in hamlets (92.6%) and main village (81.4%) used fumigation of cow dung and Neem leaves as personal protection measures against mosquito bites, whereas, in majority of non-tribal population combination of electric fan, mosquito coil & fumigation of cow dung & neem leaves.

Japanese Encephalitis

Mapping of Mosquito Breeding Habitats in North and Southern parts of Rajasthan for Emergence of JE virus using Space Technology (RS & GIS)

Studies have been conducted in five districts viz., Udaipur, Dungarpur, Banswara, Sriganganagar and Hanumangarh. Adults and immature stages of mosquitoes belonging to 14 species were sampled from cattle sheds and different breeding habitats respectively in order to determine presence of Japanese Encephalitis vectors. As many as 7 JE vectors viz., *Cx. tritaeniorhynchus*, *bitaeniorhynchus*, *Cx. fuscocephala*, *Cx. quinquefasciatus*, *Cx. pseudovishnui*, *An. subpictus* and *uniformis* were collected during March and May, 2013.

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A comprehensive project aimed to generate early warning system of activity of dengue virus in all the 32 districts of Rajasthan. Based on the presence of vertically infected mosquitoes at household level in each district town of Rajasthan, warning points of virus activity have been communicated to state health department for controlling dengue vectors.

Malaria

Health Seeking Behavior towards Malaria among Tribal & Non-tribal Groups in Villages of Kotra, Udaipur

In Garasia tribe the prevalence of malaria was observed in 79.4% households, whereas, in non-tribal households 70.8%. Majority of the malaria cases (78.3%) from hamlets opted treatment from Bengali RMP private practitioners, whereas, from main village only 24.0% however, the non-tribal groups chiefly utilized CHC facilities (36.9%) for seeking treatment of malaria. Among tribal 29.8% malaria cases from hamlets and main villages opted treatment on the day of commencement of fever, however the non-tribal 47.9%. Bed net usage in tribals was reported low (5.7%) in comparison to non-tribal house-holds (16.5%). Majority of tribal in hamlets (92.6%) and main village (81.4%) used fumigation of cow dung and Neem leaves as personal protection measures against mosquito bites, whereas, in majority of non-tribal population combination of electric fan, mosquito coil & fumigation of cow dung & neem leaves.

Japanese Encephalitis

Mapping of Mosquito Breeding Habitats in North and Southern parts of Rajasthan for Emergence of JE virus using Space Technology (RS & GIS)

Studies have been conducted in five districts viz., Udaipur, Dungarpur, Banswara, Sriganganagar and Hanumangarh. Adults and immature stages of mosquitoes belonging to 14 species were sampled from cattle sheds and different breeding habitats respectively in order to determine presence of Japanese Encephalitis vectors. As many as 7 JE vectors viz., *Cx. tritaeniorhynchus*, *bitaeniorhynchus*, *Cx. fuscocephala*, *Cx. quinquefasciatus*, *Cx. pseudovishnui*, *An. subpictus* and *uniformis* were collected during March and May, 2013.

In addition to this, Geo-coordinates of pig sties & roosting places of paddy birds were also recorded using Global Positioning System (GPS) for the purpose of satellite mapping. The study is ongoing.

Vector Control

Surveillance of Pyrethroid Resistance in Important Malaria Vectors of Western Rajasthan and Studies on Genetic and Biochemical Mechanisms of Pyrethroid Resistance in *An. stephensi*

The studies carried-out on the surveillance of pyrethroid resistance in important malaria vectors of western Rajasthan revealed that both *An. stephensi* and *An. culicifacies* were found susceptible to synthetic pyrethroid permethrin, and resistant/ partial resistant to DDT, however, against malathion, *An. stephensi* exhibited partial resistance and *An. culicifacies* found susceptible. In Bikaner district, *An. stephensi* was susceptible to synthetic pyrethroids viz., permethrin and cyfluthrin, resistant to DDT and partial resistant to malathion. In Jaisalmer district, *An. stephensi* was found susceptible to synthetic pyrethroid permethrin, either susceptible or partial resistant against malathion, however, against DDT, it was reported susceptible, partial resistant or resistant in the survey villages. Current susceptibility status of *An. stephensi* determined against temephos larvicide revealed that this species is susceptible to this larvicide in all the study districts, however, *An. culicifacies* in one village of Jaisalmer district exhibited intermediate resistance, which needs further verification. The results of the study have direct relevance to the national malaria control programme and the collected information is important for consideration while conducting indoor residual spray operations.

Current status of Susceptibility of *Ae. aegypti* and *An. stephensi* against Larvicides/ Insecticides being used in National Programme in Rajasthan

Under this intra-mural project the studies carried-out in 9 districts of Rajasthan state viz., Ajmer, Alwar, Barmer, Bikaner, Jaipur, Jaisalmer, Jodhpur, Pali and Udaipur, in urban localities, revealed that *Aedes aegypti* (Abate), a mosquito larvicide, in Alwar, Bikaner, and Udaipur districts and partial resistance in Jodhpur, Kota, Jaipur and Pali districts. The development of resistance in *Ae. aegypti* against temephos is a first report from the country and would help in judicious use of this compound against the vectors of dengue/DHF.

Synergistic Efficacies of some Plant Extracts with and without Some Insecticidal Formulations against Vectors of Malaria and Dengue in North- Western Rajasthan

This project was started in 2012. Synergistic studies on larvae of *Aedes aegypti* and *Culex quinquefasciatus* to the methanol extracts from yellow ripe fruits of *Solanum xanthocarpum* (SX)) and red fruits of *Withania somnifera* (WS) were carried out. Based on the above results synergistic Factor (SF) and Co-toxicity Coefficient (CTC) were determined which revealed that except the pairs SX:WS (1:2) & SX:WS (1:3) which showed antagonistic effects for *Cx. quinquefasciatus*, every other combination showed the synergistic effects to both the species.

Prevalence of Diabetes Mellitus and Impaired Glucose Tolerance in the Raika and other Communities with similar Life Style in Rajasthan

A total population of 12020 was covered from 135 villages of Ajmer, Barmer, Jodhpur and Pali district of Rajasthan, of which raika population was 10003 and non-raika population was 2017. The preliminary analysis of data showed that among raika population, 65.6% of raika subjects ever consumed camel milk whereas only 10.2% of non-raika subjects ever consumed it. The raika population had consumed camel milk during last 12 months was

7.9% as compared to 0.7% of the non-raika population. Only 0.2% raika and 0.5% non-raika individuals were having history of diabetes at the time of survey. The prevalence of impaired glucose tolerance (IGT) and diabetes mellitus among raika community consuming camel milk was 1.0% and 0.7% respectively while in raika community not consuming camel milk, the prevalence of impaired glucose tolerance (IGT) and diabetes mellitus was 0.5% and 0.4% respectively. Similarly, the prevalence IGT and diabetes mellitus among non raika community consuming camel milk was 1.5% and 2.1% respectively while in non raika community non consuming camel milk, it was 0.4% and 1.0% respectively.

Estimation of Zinc deficiency, Under-nutrition and Morbidities especially ARI, Diarrhoea and Fever in School Children of Rajasthan

Sampling has been done and data has been collected from 465 school children of 6 to 11 years belonging to 15 schools of Jodhpur district. Standardization of the techniques has been done for estimation of Zn by AAS- flame mode. Analysis of the serum zinc of 342 school children revealed that 72.5 percent school children were normal and 27.5 percent children were deficient in serum zinc *i.e.* serum Zn level was less than 0.65 mg/l. It was observed that serum zinc deficiency was more in early age group *i.e.* 31.5 to 32.8 percent in 6 to 7 years age group than 11 years age group (15.4%). It was observed that serum zinc deficiency was 28.4 percent in boys whereas 26.4 percent in girls. Analysis of 319 school age children according to Hb estimation revealed that only 26.6 percent children were non anemic ($Hb \geq 11.5$ g/dl) where as 53.9 percent children belong to mild category (10-11.5 g/dl) and 19.1 percent to moderate category (7-10 g/dl) of anemia. Underweight (Weight for age) in school age children observed 24.2 % and stunting 18.2%. Stunting was observed higher in females than males though statistically insignificant. School children suffering from Acute Respiratory infection, and Fever were 3.4 and 4.7 percent respectively.

Nutritional Status along with Morbidity & Mortality of under five children- A Follow up Study of Earlier Registered Infants up to 5 years in Jodhpur

The analysis of the children belonging to one & half years age group (N= 275) revealed that overall 34.6 percent children were under weight and 6.5 percent belong to severe category. Stunting (Height for age) was 63.6% with the prevalence of severe stunting 26.9 % and Wasting was 6.9%. Main morbidities observed were, ARI (21.5%), fever (16.4%), GIT (15.3 %) and Ear disease 4.4 percent. Fever and ARI observed higher in males (20.5% & 22.3%) in comparison to females (13.5% & 20.9%) whereas GIT was higher in females (17.2%) than males (12.5%). Regarding nutritional deficiency signs, discoloration of hair, a sign of PCM was observed to be high *i.e.* 57.1 percent and Marasmus was observed to be 0.4 %. It was observed that 96.7 percent of children belong to category of 'Breast feeding & Top Milk consumption' up to the age of 18 months. Out of 300 neonates registered earlier, 13 were died up to the age of one year and 10 were not available/ not co-operated. The children followed up at the age of 18 months were 278, out of which 3 died. Mortality between one year - one & half year age group was 10.8/1000 whereas Mortality up to one & half year age (0-18 months) was 53.3/1000

NNMB Rajasthan Unit: Assessment of Diet and Nutritional Status of Urban Population and Prevalence & Determinants of Hypertension and Diabetes among adults in India

The survey has been conducted in Jodhpur urban areas covering around 720 households and 1465 adults (≥ 18 years), 390 adolescents (12-18 years) and 190 infants (≤ 3 years) were covered for basic demographic data, anthropometric measurements, biochemical investigation, including total lipid profile, fasting blood glucose for adults and dietary survey.

Out of the surveyed individuals, 12.8 per cent were found to be hyperglycaemic and 15.2 per cent hypercholesterolemic.

Regional Medical Research Centre (RMRC), Belgaum

Chemotaxonomy and Pharmacological activity of "IP No. SAC-2012/PD/02"

The plant IP No. SAC-2012/PD/02 is traditionally used in folklore medicine for treatment of diabetes. The plant was taxonomically identified and leaves of five individual plants were collected in the interval of three months for a year from the same locality or cluster.

Out of five samples, three plants had the same signature or marker compositions with phenyl derivatives dominating in all collections in the year, while remaining two samples were completely different in composition with no marker composition and containing monoterpene hydrocarbons, oxygenated monoterpenes and oxygenated sesquiterpenes- rich constituents in different seasons of collection. This investigation revealed that, among the all collected samples, there were two chemogroups viz., phenyl derivative and terpenoid groups, despite being morphologically and taxonomically identical plants. Further genetic and phytochemical studies are in progress. The organic extracts of chemotypically and genotypically different plants of IP No. SAC-2012/PD/02 were studied in animals for screening anti-diabetic activity in healthy male Wistar rats. Extracts and fractions were found to be safe up to 2000mg/kg b.wt.

Phytochemical Screening and *in vitro* studies in *Ancistrocladus heyneanus* Wall. Ex Grah. and *Achyranthes aspera* L.

Achyranthes aspera L. var. *aspera* (Family: Amaranthaceae), is a perennial stiff erect herb widespread all around the world and is known for its range medicinal properties. like antibacterial, anti-inflammatory, abortifacient activity and produces reproductive toxicity in male rats. Its antidepressant, anxiolytic and antinociceptive activity are also reported.

Two sites were sampled with different geographical and seasonal distinction for phytochemical work. Various extraction techniques were employed using different parts of *A. aspera* to analyze optimum yield of Betulinic acid (BA) and Oleanolic acid (OA) and to study efficient extraction procedure. The extracts obtained were subjected to RP-UFLC analysis using standard methodology for its detection and quantification (Fig.). Similarly, standard methodologies for tissue culture studies were carried out in the plants under study. Contents of OA were lower than that of BA in all the extraction methods tested. Betulinic acid (BA) was detected and quantified for the first time in *A. aspera*. Its presence was confirmed using HPTLC analysis further comparison of standard and sample profiles of FT-IR analysis confirmed presence of BA in the sample (Fig.).

In tissue culture studies, callus initiation was significant with 100 % response on MS basal fortified with 2, 4-D. All concentrations of auxins IAA and IBA proved poor both response and growth wise. It was subjected to RP-UFLC analysis for detection and quantification of OA. 30 min ultra sonic exposure of dry weighed callus obtained from MS fortified with 2, 4-D 1.0 mg/L and BAP 3.0 mg/L yielded 4.36 ppm of OA. This yield was considered 50% lesser than that obtained in leaf extraction. Further stabilization studies are in progress.

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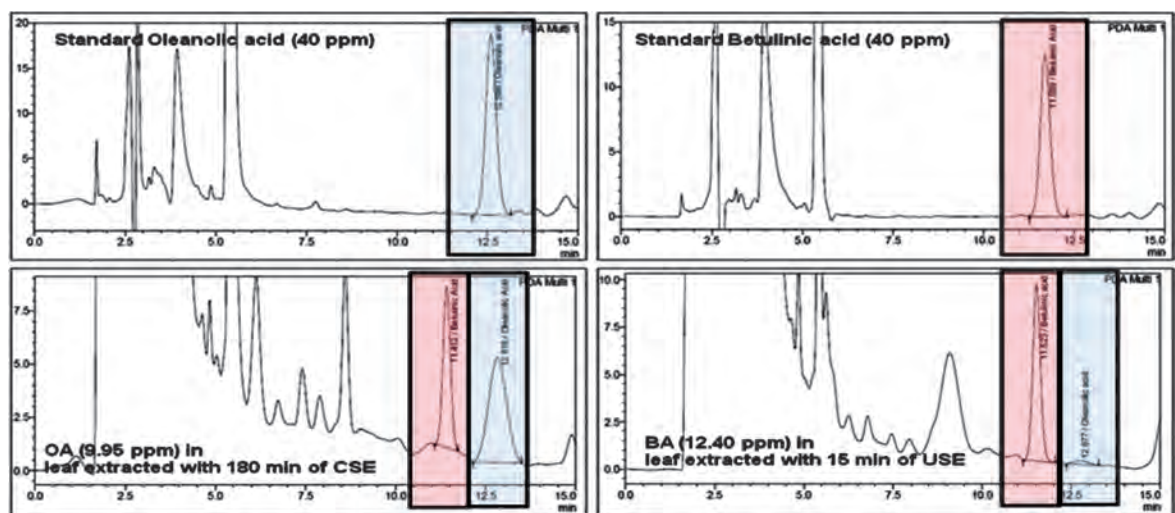
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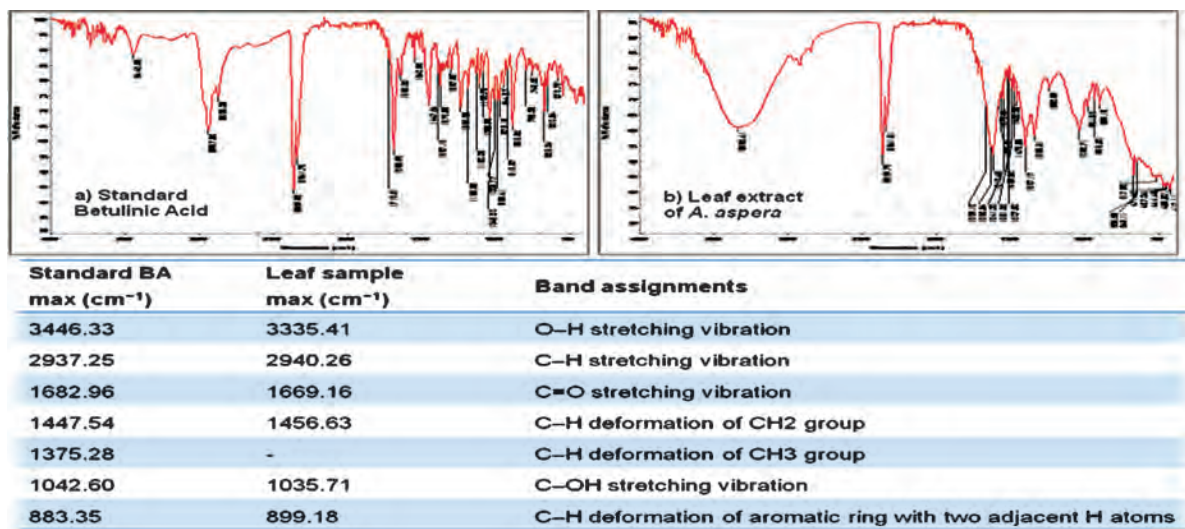
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RP-UFLC Profiles of Standards and samples

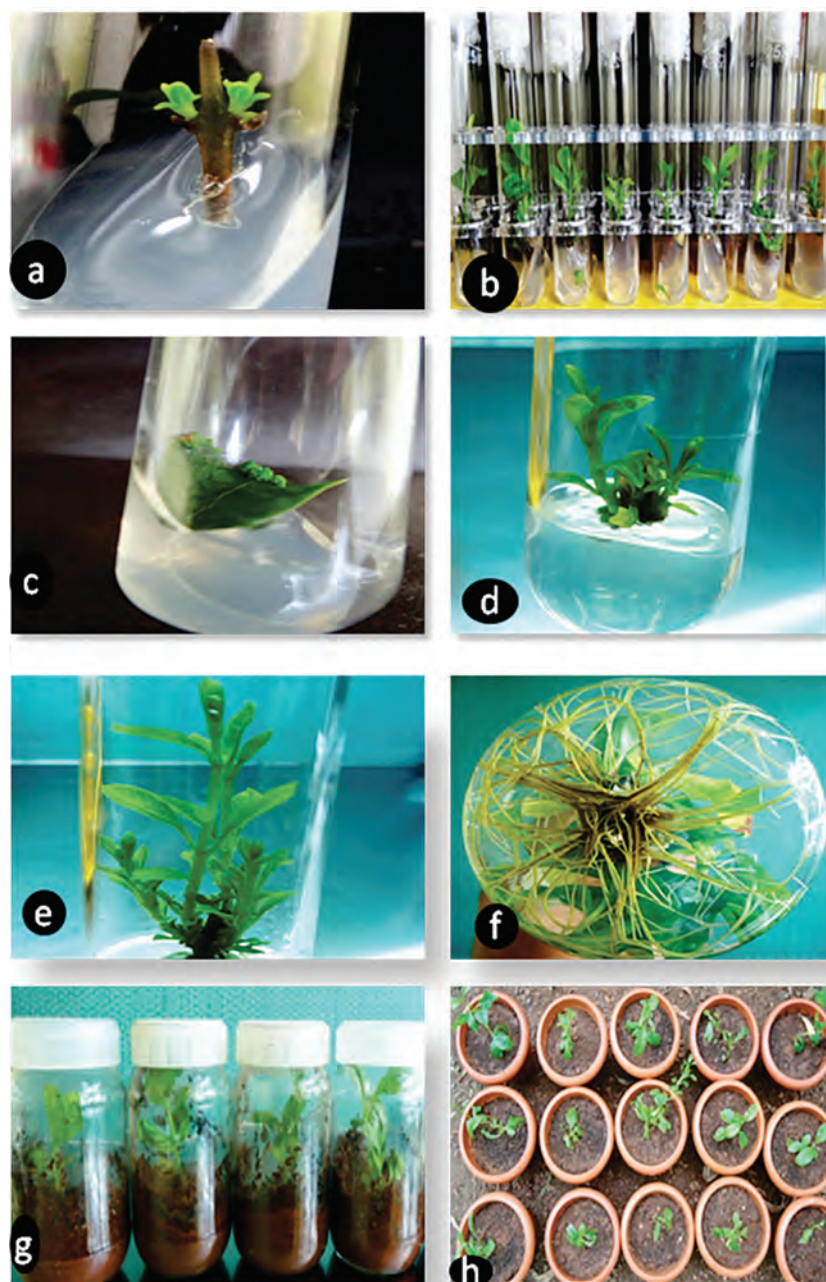


FT-IR profile of standard and samples

In vivo and in vitro* Production of Flavanoids in Selected Species of *Clerodendrum

Clerodendrum inerme (L.) Gaertn and *C. phlomidis* (L.) f. are well documented in traditional system of medicines for several formulations and used as folk medicines by various tribes. Over collection, unsustainable extraction for medicines and trade coupled with poor seed viability are the major factors for continuous dwindling of these species in natural habitat. A study was undertaken to: Establish an efficient protocol for rapid *in vitro* propagation and cell culture of *C. inerme* and *C. phlomidis*, enhance bioactive secondary metabolites (flavonoids; apigenin and luteolin) production in *in vitro* culture through elicitation and hairy root culture and compare the production of tissue vis-à-vis hairy root cultures and callus culture. The plants of *C. inerme* and *C. phlomidis* were collected randomly from two different geographical regions (Northern Western Ghat, Belgaum, Karnataka and Aravali Region, Jhalana Doongri, Rajasthan).

High frequency and direct plant regeneration was achieved from nodal explants of both *Clerodendrum* spp. Rooting of regenerated shoots was achieved on half strength MS medium supplemented with auxins (IAA+ IBA; 0.5 +1.0 mg/l). Further, acclimatization step is in the process.



Clerodendrum inerme (L.) Gaerten . (a-h) a: Shoot induction from nodal segment; b: Shoot on MS basal + BA+Kn (2+0.5 mg/l)+ 2ml/l PPM; c: Direct plant regeneration from leaf; d: Leaf regenerated shoot on MS basal + BA+Kn (2+0.5 mg/l)+ 1ml/l PPM; e: Callus obtained on MS basal +2,4-D+NAA+Kn (1+4+1.5 mg/l) and 2ml/l PPM.; f: Roots obtained on MS basal IAA+ IBA; 1+1 mg/l; g: An individual regenerate acclimatized on a soil mixture with sand: soil: peat: vermiculite mix (1:1:1:1; v/v) in a glass culture vessel; h: Acclimated plantlet on vermiculate substrate.

Services to State/District Health Units and Medical Colleges

The Centre has been providing services to the State Surveillance Unit and the District Surveillance Units of the Karnataka Government in identification and confirmation of bacterial pathogens and investigation of outbreaks during various epidemics. Similar services have been rendered to the Government Medical Colleges in the region like State Surveillance Unit, Bangalore; District Surveillance Unit, Bangalore (Urban), Bijapur and

Belgaum; Hassan Institute of Medical Sciences (Govt Medical College), Hassan; Karnataka Institute of Medical Sciences (Govt. Medical College), Hubli; Belgaum Institute of Medical Sciences (Govt. Medical College), Hubli and Jawaharlal Nehru Medical College, Belgaum.

RMRC helped the State Administration in identification of an outbreak of Hepatitis in Turmuri village on the outskirts of Belgaum in 2012. It also helped in identification and study of outbreaks of cholera in Harnal and Talikoti in Bijapur District. An upsurge of cases of diphtheria was identified in rural areas of North Karnataka.



Spot map of districts receiving services from RMRC

Regional Medical Research Centre (RMRC), Bhubaneswar

The Centre addressed some of the most important health challenges like vector borne diseases, diarrhoeal disorders, bacterial meningitis, encephalitis, tuberculosis, and non-communicable diseases like under nutrition, diabetes, hypertension and sickle cell disease. The network with the State Health Department, Medical Colleges and Hospitals of the region has been further strengthened. Two field units, one at Raygada District Head Quarter Hospital, Raygada and other at District Head Quarter Hospital Bhawnipatna of Kalahandi district have been established in collaboration with the state health department and started functioning for providing diagnosis for diarrheal disorders, drug resistant TB, nutritional assessment and transfer of technology to the state health services.

Filariasis: Lymphatic Pathology

The National Health Policy of Government of India aims to eliminate lymphatic filariasis from the country by 2015. To explore any sub-clinical pathology in prolonged silent phase that leads to full-fledged disease later, 102 children between 5 to 18 years of both sexes with evidence of infection (either microfilaremia or circulating filarial antigen) with or

Belgaum; Hassan Institute of Medical Sciences (Govt Medical College), Hassan; Karnataka Institute of Medical Sciences (Govt. Medical College), Hubli; Belgaum Institute of Medical Sciences (Govt. Medical College), Hubli and Jawaharlal Nehru Medical College, Belgaum.

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without symptoms were enrolled in to the study. Lymphoscintigraphy examination detected abnormality in the lymphatic scan among 74(72.5%) enrolled children at the baseline. While ultrasound examination using 11 megahertz probe indicated presence of adult parasite in same side lymphatic pathology detected. Symptomatic subjects demonstrated higher frequency (80%) of pathology. Amongst the enrolled children 52 were assigned randomly to annual and 50 to biannual dose of DEC + Albendazole and followed up 6 monthly for two years at different time points. Result shown improvement in lymphatic pathology in 71%, 94% and 85% of children at 6th, 12th and 18th month period respectively. Total reversal of Pathology was visualized in 65% at 24th month. MF clearance and adult worm clearance at 24th month (n=50) was 95% & 60% respectively. This indicates that it can serve as an effective tool for advocacy to improve the compliance rate of MDA in children as well as a tool to prevent morbidity by reversing early lymphatic pathology amongst asymptomatic cases in the community. Even the cases with early lymphoedema exhibited reversal.

Immunology of Filarial Infection

Filarial infection in mothers has been considered a risk factor for increased susceptibility to infection in the off springs. Elevated levels of IL-10 in anti-sheath negative cord blood and IFN- γ levels in anti-sheath positive cord blood irrespective of infection status of mothers provides an evidence that presence/absence of anti-sheath antibodies with the association of cytokines in the neonates skewed the filarial specific immunity to either Th1 or Th2 responses and can decide the natural history of filariasis during childhood. Another study has indicated increased population of apoptotic T cells among infected individuals compared to endemic controls along with increased Fas-L expression on the surface of B1 cells. Since FasL expressing B-1 cells are important mediators of CD4+ T-cell apoptosis, they may be responsible for hypo responsiveness in microfilariaemic individuals.

L3 stage specific RT-PCR assay for detection of infective stage *W.bancrofti* in vector was evaluated as a part of multi-centric project. The assay was found to be sensitive and specific and can be useful for monitoring of the nation LF elimination programme.

Malaria

Malaria survey conducted using molecular tool in Badampahar CHC (Mayurbhanj Dist) and Ghatgaon CHC (Keonjhar Dist) has revealed *P. malariae* mono infections in 11.6% of cases and mixed infections were 14.2% in Ghatagaon and 6% in Badampahar. Presence of *P. malariae* poses a difficulty, as the screening is performed by RDT alone. The species specific RDTs were not able to detect either the mono infection or the mixed infections of *P. malariae*. Therefore the molecular method can be used as a tool for surveillance to overcome such problems. Diagnosis by commonly used molecular tools i.e. polymerase Chain reaction may not be feasible in field condition. So an alternative tool using LAMP assay has been developed to detect different malaria parasite (*P.falciparum*, *vivax* and *malariae*). Primers have been designed and reaction conditions standardised. The efficacy has been shown to be comparable to PCR. It will be validated in field condition and observer variation will be checked before recommendation.

Treatment Seeking Behaviour

LLIN use and acceptance of IRS by the tribal communities was studied. Acceptance was seen to be high (around 90%) and 92% of the households were willing to purchase ITN/LLIN at subsidised cost. However, API was seen to be high (more than 14) in the studied villages of the two blocks in spite of good LLIN coverage. Hence, other factors need to be addressed.

Distribution of sibling species of malaria vectors and their role in transmission is being studied. Genetic sequence of ribosomal D3 and mitochondrial COII region of *Anopheles* mosquitoes were submitted to gene bank, NCBI; to which accession numbers assigned for use in public domain.

Cholera

To determine the feasibility, acceptability and costs associated with the introduction of the modified killed whole cell oral cholera vaccine in India when given in a public health setting, a pilot study has been instituted in Satyabadi block of Puri district during May –June 2011. The 1st dose of mass vaccination was received by 31551 and 2nd dose by 23751 individuals. The first dose coverage, based on population census was around 61% with a drop-out rate of 25%. A total of 46% of population received two (complete) doses of oral cholera vaccine during the mass vaccination campaign.

Etiology of diarrhoea in 3 tribal districts of Odisha was investigated. Bacterial pathogens, their molecular characterization and anti-biogram was described and reported to district public health system along with water sources identification of infection. Prompt investigation and early reporting could support public health action in preventing epidemics and diarrhoea case fatality.

The centre has carried out outbreak investigations of severe diarrhoea in tribal dominated areas; Mohana, Laxmipur, Dasmantpur and Kashipur blocks of Gajapati, Koraput and Rayagada districts from October, 2012 to June, 2013. Out of total 107 rectal swabs collected, 81 were culture positive (75.7%) from which 48 (59.2%) were *Esch. coli*, 16 (19.8%) were *Vibrio cholerae* O1 Ogawa, 11 (13.6%) were *Shigella* spp. and 6 (7.4%) were *Aeromona* spp, while no *V. cholerae* were isolated from water samples. The early reporting of cholera had helped the health authorities of the district to take adequate control measures which could check the spread of cholera epidemic in this region.

Sentinel Surveillance Unit at SVPPGIP, Cuttack

As a part of the preparations for the phased introduction of a pentavalent vaccine (DPT-Hep.B-Hib) by Government of India in selected states of the country in Universal Immunization Programme (UIP), a 24 hour sentinel surveillance unit has been established at SVPPGIP, Cuttack to find out the burden of the disease. During the period under report, 543 CSF and 250 blood samples were investigated from suspected meningitis cases between 1 to 59 months of age. Amongst them 16 samples were found to be latex positive (six for Hib, nine for *S. pneumoniae* and one for group B streptococcus), 3 CSF were culture positive for *Staphylococcus aureus* and 1 was positive for *Salmonella typhi* and 2 blood samples were culture positive for *Klebsiella pneumoniae* and 4 were positive for *Pseudomonas aeruginosa*. Real time PCR identified 21 cases of *Streptococcus pneumoniae* and 4 Hib. Antibiotic sensitivity testing supported case management in the hospital.

Virology

Investigation on viral diseases is on-going under ICMR virology grade 1 network laboratory project. From Jan to October 2013, a total number of 5412 samples from sporadic/ referral cases were received from different Govt. and Private Hospitals of Odisha for investigation. Amongst the total cases majority were with clinical suspicion of a viral disease i.e. for hepatitis (n=919), Viral diarrhea (n= 546), Rubella (n=444), Encephalitis (n=442), Dengue (n=103), Respiratory infection (n=97), Measles (n= 78), Chickenpox (n=72), Human Papilloma

Virus (n= 17) , CMV (n=11) , Mumps (n=6) , Fever and rash (HFMD, Parvo) (n= 4) and EBV (n= 1).

Outbreak Investigations

During this period one outbreaks of jaundice, 4 chickenpox, 4 measles, 2 rubella and 1 encephalitis out breaks covering 11 districts have been investigated along with state health department and total 39 different types of viruses have been detected .They were HSV I, HSV II, JE Virus, Dengue, CHIK, Rota, Astro, Adeno(Enteric), Noro G1, Noro G2, Coxackie, Measles, Varicella, Mumps, Rubella, Entero HAV, HEV, HBV, HCV, HDV, HPV, EBV, CMV, Adeno, Influenza A(FluA), FluA(H1N1), Flu B, HMPV A/B, Rhino, Para influenza 1, Para influenza 2, Para influenza 3, Para influenza 4, RSV A/B, Corona viruses(Cor63,Cor229,Cor43, HKU1), Parecho virus, Boca Virus (HBoV) and EV. The enteric virus, Rota, found during this year mostly belongs to G1, G9, G10, and G12 types and P8, P10 types. HAV infection were observed in 6-15 years of age group (42.8%) of patients while, HEV infection was high in adult population (56.8%). Amongst the respiratory infections Adeno virus was most common (22.2%) followed by Human Boca, Rhino and Corona virus.

During 2010 dengue serotype II was prevalent whereas in 2012-13 all four serotypes were reported with serotype II as the dominant type. In the northern region serotypes were I, II and III, whereas in southern regions serotype II and IV were reported. CHIKV circulating in Odisha, seen to be of IOL (Indian Ocean Lineage) strain within ECSA (East Central South Asian) genotype, originating probably from the Kenya 2004 strain (predecessor) and being transmitted by *Aedes albopictus*.

Neurotropic viruses causing acute encephalitis admitted to different hospitals were investigated and clinical manifestations described. HSV, Measles, Dengue and Varicella zoster virus were seen as the major causes of viral AES either as single or co-infection.

Aedes mosquito vectors in various parts of Odisha were investigated with reference to transmission of arboviral disease.It was revealed that the recent outbreaks of chikunguniya in Odisha have been caused by IOL group of ECSA-Genotype, which was postulated to be transmitted by *Ae. albopictus*, the most abundant vector in Odisha.

Tuberculosis

Under surveillance of drug resistance TB in Raygada district, 634 sputum positive tuberculosis cases were subjected for drug susceptibility testing with the four first line drugs, where mono resistance was seen in 35, i.e.to isoniazid in 14 cases & streptomycin in 21 cases and 3 isolates showed resistance to isoniazid and rifampicin (MDR). However MDR was not observed in any of the newly diagnosed TB cases (n=577).

The study undertaken in Kalahandi (Dharmagarh and Junagarh) and Raygada (Jamadehipentha) districts to assess the knowledge, attitude and behavior on reproductive health problems of adolescents, quality of care at Adolescent Friendly Health Clinics, accessibility and utilization of health care services by adolescents so as to devise plausible ways and intervene with package of services for improving utilization of adolescent health services indicates that adolescent females of Raygada(21.3-31.8%) are experiencing more premenstrual complains syndrome than the adolescent females of Kalahandi district. In both areas about 50% of the girls are maintaining menstrual hygiene practices, but only 4-12.7% are using sanitary pads. Similarly knowledge on RTI/STI and HIV/AIDS and level

of awareness about contraception and family planning methods is greater in Kalahandi as compared to Rayagada district.

Studies on Migratory Population

With respect to the access and responsiveness of the health system towards migratory population, the centre has found that migrant community usually experience common health problems like common cold & fever, gastritis, diarrhoea, abdominal pain, vomiting, dysentery, asthma and T.B. Around 45 % availed regular health services from government health facilities. The husband or elder person like mother in law / aunt are the decision maker for health issues. Among the pregnant women 80% opted for institutional delivery and 56% of them had gone for 3 visits of ANC and 90% have received more than 2 doses of injection TT in urban slums of Bhubaneswar MC. The individual component of primary MCH services indicates a good coverage. But when all components combined together, the coverage is very low (around 12.9%) only. Therefore an interventional package combining the approaches of inclusive partnership with government and non-governmental providers, CBOs, community participation and community mobilization for better health service utilisation has been developed for implementation.

Sickle Cell Disease

Neonatal screening for sickle cell disease was undertaken in Kalahandi district from March 2013. This included 635 cord blood samples. 110 cord blood samples were found to be SCD positive of which 8 were homozygous for the disease. A three monthly door-to-door follow-up and investigation of parents of 2 homozygous and 9 heterozygous SCD neonates confirmed their SCD status and information on parental morbidity pattern using a pre-designed questionnaire was collected. The percentage of SCD homozygous cases was found to be highest in M. Rampur block of Kalahandi district. No SCD related morbidity was detected in the newborns followed till date.

Translational Research

Under translational research the centre has taken effort to develop two PCR based tools for public health use. One is to monitor the information of vector prevalence, incrimination of vector for malaria transmission, identification of the sibling species of vector and chloroquine (CQ) sensitivity of the parasite ingested by the vector. This technique has been internally validated and the practical aspects of the technique has been demonstrated to the researchers of NIMR and programme personnel of the state NVBDCP in workshop held during 4th to 8th February 2013 at Regional Medical Research Centre, Bhubaneswar .

The other tool developed by the centre is to detect all different serogroups of *V. cholerae* causing cholera in a single PCR test. In-house validation of the technique has been done. Applicability of both the tools are now being field tested.

OPD Facility

As a service component, the centre is providing outpatient facility to patients of lymphatic filariasis and haemoglobinopathy at Capital Hospital, Bhubaneswar. The facility is being utilized for referral investigation, diagnosis management of suspected cases of filariasis and haemoglobinopathy from different parts of the state. Besides, the facility is providing treatment to acute and chronic filarial disease including decompression therapy for filarial lymphedema reduction.

Chronic kidney disease with high case fatality in two blocks of Cuttack district was raised as a public health concern by the district administration. Baseline investigation was undertaken in collaboration with district health system, SCB Medical College, Cuttack and NIN, Hyderabad. The initial survey points towards chronic tubule-interstitial disease, Possibility of heavy metals from water/food source, analgesic use or any other toxins are planned to be evaluated.

Tribal Health

An ongoing activity under tribal health research forum is being undertaken to develop a morbidity management strategy for febrile illness through syndromic approach in tribal population of Rayagada district. Baseline morbidity survey was undertaken in 5800 population covering 21 villages from 3 adjacent sub-centres. Prevalence of febrile illness was 9.5% and 1.8% of the surveyed population during a fortnight period of rainy and winter seasons respectively. Total morbidity including non-febrile disorders was 21.9% and 6.44% of the population during above seasons. Among the febrile illness, acute respiratory infections (62%), malaria (22%) & diarrhoeal disorders (10%) were common during rainy season, while in winter, URTI was commonest. Both the extremes of ages (<5 yrs & more than 60 yrs) were predominantly affected. Bacterial infections (*S.pneumoniae*, *H.influenzae* & *Staph aureus*) were identified as the cause of ARI in 75% cases followed by viral infections (Corona & Para influenza) in 20% of ARI cases. *P. falciparum* was the dominant (87%) malaria parasite. Diarrhoeal disorders were associated with *Esch.coli* in 30% & Rotavirus in 10% of cases. Under-nutrition in childhood was found as an underlying risk (71.4% in under 5). The population demography showed a distorted pyramidal structure with low population in higher age group (>55yrs) compared to normal population. To answer the above distortion, cause of death was analyzed by verbal autopsy procedure, covering 52 deaths in past 1 yr. The common causes of death noted were cardiovascular diseases, pulmonary tuberculosis, liver diseases and malaria. CVD deaths were corroborated with hypertension prevalence of 24.6% in adults.

Baseline assessment of health system, grass-root level health providers and the community has been undertaken to frame a strategy for intervention which included community awareness and participation, training/reorientation of health providers and strengthening logistics, supplies and monitoring/supervision.

Genetics and Hypertension

A study on host genetic factors of essential hypertension among the natives of Odisha was undertaken including 246 hypertensives and 274 normotensive controls. Different genes associated with hypertension like eNOS, 11 β HSD2, CYP11B2, AGTR1, AGT were investigated. The study has shown that in the study population, the CYP11B2 -344T/C, eNOS VNTR 4a/b, ANG G-6A polymorphisms are associated with hypertension in males and AGTR1 A1166C, eNOS VNTR 4a/4b and eNOS E298D polymorphisms are associated with hypertension in females.

Field Units

Two field units in tribal dominated districts (Rayagada and Kalahandi) established in collaboration with State Health Department are operating with the goals to improve the health parameters of the region with emphasis on tribal population. Technology transfer, alternative health care strategy and application of advanced diagnostic techniques at district headquarters level are being focused to achieve the goal.

Regional Medical Research Centre, NE (RMRC), Dibrugarh

The focus of research work of RMRC, Dibrugarh during the year was on cancers, cardiovascular disease and diabetes, among the non-communicable diseases; and vector borne diseases, viral diseases and bacterial diseases among the communicable diseases.

Cancers

During this year a total of four studies were pursued on breast and oesophageal cancers. The case-control study on Genetic and molecular epidemiology of breast cancer in urban and rural areas of Mizoram and Tripura, involving 286 cases and 605 controls in Tripura and 101 cases and 356 controls in Mizoram, was completed. The betel nut consumption increased the risk of breast cancer about 2.5 times (odds ratio, 2.47; 95% CI 1.8 – 3.5; $p < 0.001$) and the risk was twice in females who consumed betel nut with tobacco (odds ratio, 5.3; 95% CI 3.3 - 9.4; $p < 0.001$) in Tripura but not in Mizoram. Carriers of mutations in XRCC1 gene significantly increased the risk of breast cancer in Tripura but not in Mizoram. On the other hand mutations in XRCC3 gene significantly increased the breast cancer risk in Mizoram but not in Tripura. The other study on Genetic and molecular epidemiology of breast cancer in Assam and Meghalaya is near completion. Epidemiological information from study subjects in two studies in case-control mode on oesophageal cancer viz. Genome-wide analysis of genetic alternations in patients of oesophageal cancer from north-east India using single nucleotide polymorphism arrays and Epigenetic studies in oesophageal cancer in high risk region of north-east India were collected and molecular work initiated. Estimation of cancer disease burden through 12 population based cancer registries in north-east India was continued.

Cardiovascular Disease

The community based *intervention study to assess reduction of blood pressure in tea garden population by dietary salt restriction* was pursued in two tea gardens (1 intervention garden and 1 non-intervention garden) of Dibrugarh district, Assam. In the stage I of the study, prevalence of hypertension (SBP ≥ 140 or DBP ≥ 90 mm Hg or on antihypertensive treatment) among the study subjects, estimated cross sectionally covering 916 subjects, was found to be 48.8%. In the stage II, community based dietary salt restriction intervention restricting the salt intake to 6 gm/day, covering 605 subjects (270 intervention group and 335 non-intervention group) has been implemented in the intervention garden.

Diabetes

Phase I of the *ICMR-India Diabetes (INDIAB) study, NE Component* was completed in the states of Assam and Mizoram. In Assam, surveys were undertaken in 99 primary sampling units (49 urban, 50 rural), covering 3920 households whereas in Mizoram 102 PSUs (50 urban, 52 rural) were covered involving 4074 households. Age standardized prevalence of diabetes was found 5.3% in Assam (already known



Capillary blood glucose collection
ICMR-India Diabetes (INDIAB) study field work in Tripura

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diabetes 3.0%, new diabetes detected 2.3%) and 3.8% in Mizoram (already known diabetes 1.7%, new diabetes detected 2.1%).

Mosquito-borne Diseases

A total of 10 studies on malaria epidemiology, malaria vectors and control were pursued during the year. The Indo-Myanmar-UK collaborative study *to determine geographical and genomic barriers to gene flow in Anopheles baimaii* was completed. Phylogeography study revealed that in the north-east India population expansion in *An. baimaii* started about 0.21 million years before present during the late Pleistocene period which is still continuing, thus, raising its effective population size to 2.5 times. Analysis of 3197 restriction site associated digestion (RAD) loci in 147 *An. baimaii* individuals (from north-east India and Myanmar), four tightly linked Linkage Disequilibrium Clusters (LDCs) comprising of 15-33 loci associated with 4 inversions were found. All the LDCs displayed exceptionally high geographic structure, relative to putatively neutral loci outside of LDCs, indicating inversions acting as a stronger barrier to gene flow.

The exploratory study on *malaria surveillance using mobile platform* piloted in collaboration with C-DAC, Pune was continued. In this study, real time malaria surveillance is being carried out in the 5 sub-centre areas of Tengakhat PHC in Dibrugarh district, Assam through cell phones loaded with the MosQuit software, developed by C-DAC, Pune. This MOSQUIT system has the capability of reducing the lag time from fever case detection to institution of antimalarial therapy to 2-3 days as against 2-3 weeks taken during the conventional surveillance system. The *Phase II evaluation results of DRDO Developed Defender nets*, a long lasting insecticide treated net, on mosquitoes in Assam following ICMR revised common protocol (2012) was carried out during the year. A total of 3 collaborative studies with Gauhati University and Dibrugarh University were pursued on *antimalarial screening of ethnomedicinal plants of NE and synthetic hybrid compounds*. In these studies 57 crude extracts belonging to 26 plants and 40 synthetic compounds were screened for *in vitro* antimalarial activity against chloroquine sensitive and resistant strains of *P. falciparum*.

In case of lymphatic filariasis 3 studies were pursued of which two multicentric studies entitled (i) National network for genotyping of human lymphatic filarial parasite *Wuchereria bancrofti* from different endemic areas; and (ii) Multi-centric evaluation of L3 stage specific RT-PCR assay for the detection of infective stage (L3) *Wuchereria bancrofti* in vectors were completed. Evaluation of the RT-PCR assay, developed by VCRC, Pondicherry, in the latter study revealed that the assay was more sensitive than conventional mosquito dissection technique. In the study on development of filaria risk maps in the Tripura state of northeast India so far, surveys have been completed in 5 gram panchayats and 50 randomly selected households in each gram panchayat in Tripura.

Evaluation of safety and immunogenicity of single dose of live attenuated Japanese Encephalitis Vaccine SA 14-14-2 in adults in Assam was completed in Demow block of Sibsagar district, Assam. This study documented effectiveness and safety of the vaccine in both seropositive and seronegative subjects. Fourfold rise in antibody titres in sero-negatives and moderately seropositive adults was seen. All subjects showed an increase in GMT at ~28 days' post vaccination which persisted to protective levels till 12 months. The vaccine was found safe and acceptable to the study community and its efficacy was found to be 90.1% (95% CI 55.5 – 97.8). Under the ICMR Task Force study on Aetiology of acute encephalitis syndrome in India and establishment of ICMR sample bank of AES cases so far, 784 blood and CSF samples have been collected from the suspected AES patients from different parts of NE

India. Screening of these samples revealed 44.8% (351/784) positivity for JE. Among the 433 JE negative samples, 2.7% (1/37) positivity for Chikungunya, 18.2% (20/110) for *Leptospira*, 4.2% (1/24) for Scrub typhus, 1.9% (2/106) for Rubella, 5.1% (3/59) for Measles, 6.4% (3/47) for Mumps, 12.3% (8/65) for HSV-1 and 3.6% for HSV-2 was detected. The study on GIS mapping of mosquito vector borne diseases in NE India was completed during the year with the preparation of GIS maps for malaria, JE, West Nile, dengue and chikungunya in the region.

While the exploratory study in visceral leishmaniasis endemic areas of Assam was continued, two new studies on the epidemiology of emerging vector borne diseases in the north-east India i.e. west Nile and scrub typhus were initiated during the year.

Microbial Diseases

A total of 5 studies on various viruses and 2 on bacterial diseases were pursued during the year. In the ongoing *Phase II multisite monitoring of human influenza viruses* study in Dibrugarh district 10.9% (26/238) samples were found PCR positive for influenza Type-A/H3N2 and 1.3% (3/238) for influenza Type B-3. In influenza negative samples from children Human Respiratory Syncytial Virus (RSV) was detected in 7.9% (39/493) cases with NA1 and GA1 circulating genotypes in another study. In the multicentric *prospective study of hepatitis B virus infection and its genotypes in the north-eastern India* 392 cases were screened for HBV. The prevalence of HBV (HBsAg) was 1.3% among blood donors, 1.8% among health care workers, 14.6% among acute viral hepatitis, 40.6% among chronic active hepatitis, 40% among fulminant hepatic failure, 16.6% among hepatocellular carcinoma and 9% among cirrhosis cases. Genotype C in 38.6 %, genotype A in 34.6%, genotype D in 11.5%, mix genotype C/A in 11.5% and C/D mix in 3.8% persons was detected.

Study of Host innate immunity and hepatitis B Persistence was initiated during the year to study the expression levels of Pattern Recognition Receptor adaptors and proinflammatory cytokines in peripheral blood mononuclear cells in chronic hepatitis B and spontaneously cleared hepatitis B infections in adults.

In the ongoing Task force study entitled *Surveillance of Infection in neonates (0-28 days)* 58 culture positive samples (14 gram negative bacilli and 44 gram positive bacteria) were processed. Among the gram positive isolates, 75% (33/44) were of *Staphylococcus aureus* with detection of *mecA* gene in 42.4 % (14/33) isolates. 33.3% isolates (3/10) of gram negative bacilli revealed extended-spectrum B-lactamase (ESBL). A new Task Force project entitled *National Hospital Based Rotavirus Surveillance Network* was initiated. The prevalence of rotavirus group A was found to be 26.6% with higher prevalence amongst females (31.4%) compared to males (24.2%) after screening 142 indoor diarrheal samples from patient less than 5 yrs of age using detection of rotavirus VP6 antigen in stool by ELISA. The prevalence was higher (29%) in infants compared to in above 1 year age group (25%). The subtype of rotavirus A detected were G2 P[4]-70% and G1 P[8]-30%.

A new study on *neonatal meningitis in a tertiary care hospital* was initiated during the year. In this study CSF samples of 100 neonates aged 0-28 days with suspected meningitis/sepsis were processed which yielded 28 culture positive samples for *Neisseria meningitidis* (n=3), *Acinetobacter* (n=2), *Leptotrichia amnionii* (n=1), *Enterococcus faecium* (n=2), *Lysinibacillus sphaericus* (n=1), *Pseudomonas putida* (n=1), *Pseudomonas stutzeri* (n=1), *Brevibacterium linens* (n=1), *Klebsiella* (n=1), *Staphylococcus scurii* (n=1), Coagulase negative *Staphylococcus* (n=2), unspciated gram negative organism (n=6), unspciated gram positive organism

(n=2), yeast (n=1), and mixed (n=3). ICMR Task Force study on *cultural epidemiology of leprosy* was continued wherein 158 interviews [77 Leprosy (41-RFT & 36 -UT) cases, 38 tuberculosis cases, 17 malaria cases, 12 family members of the patients & 14 Govt. health staffs] were completed.

Miscellaneous Studies

Other than the regular research activities, the Centre investigated outbreaks of acute RTI and gastroenteritis in China bordering area of West Siang district, Arunachal Pradesh and Hepatitis A virus (HAV) outbreak in Lakhimpur district, Assam. Centre also participated with NIH&FW, New Delhi in two studies viz. Clinical, Anthropometrical and Biochemical (CAB) Component of District Level Household Survey-4 (DLHS-4); and Clinical, Anthropometrical and Biochemical (CAB) Component of Annual Health Survey. Centre organized two weeks orientation training for the newly appointed 32 Malaria Technical Supervisors of Assam was conducted. Five students working in the Centre were awarded Ph.D. degree.

Regional Medical Research Centre (RMRC), Port Blair

Support to National Control Programmes

Revised National Tuberculosis Control Programme (RNTCP)

RMRC is accredited Intermediate Level Reference Laboratory for *Mycobacterium tuberculosis* culture and Drug Susceptibility Testing (DST). The Centre is extending diagnostic support to the RNTCP for monitoring drug resistance and emergence of Multi Drug Resistance (MDR) tuberculosis for strengthening the implementation of DOTS plus strategy under RNTCP. During the period under report 44 MDR TB suspects sputum specimens were referred to the center for laboratory confirmation. All these samples were processed and 20 patients were confirmed to be MDR TB by isolation of *M. tuberculosis* and conventional drug susceptibility test. The results are being communicated to the State TB officer in time for initiation of specific treatment.

Support to National Vector Borne Diseases Control Programme (NVBDCP)

Identified a wide array of manmade, natural and artificial habitats supporting *Aedes* spp breeding in South Andaman District. Overall a total of thirty species belonging to thirteen genera viz. *Aedes*, *Culex*, *Anopheles*, *Armigeres*, *Toxorhynchites*, *Verrallina*, *Uranotenia*, *Stegomyia*, *Lutzia*, *Tripteroides*, *Malaya*, *Heizmania* and *Christopersiomyia* were observed from the three tehsils of South Andaman district. Preliminary observations indicate the invasive behaviour of *Aedes albopictus* into human inhabitations. The information generated has been communicated to the programme officer NVBDCP.

Identified high levels of *Aedes* infestation in Car Nicobar. This is the first systematic effort to assess the prevalence of the vectors of dengue/chikungunya virus in the villages of Car Nicobar Island, in view of the various post tsunami developmental activities. Findings have implications on the control measures and augur well for a community centered approach.

Highlighted the role of drug distributors for educating the community at risk of acquiring filarial infection about the side reactions in the ongoing LF elimination programme.

Support to the Directorate of Health Services, A & N administration

The following support was extended to the local health administration.

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Support to the Directorate of Health Services, A & N administration

The following support was extended to the local health administration.

Extending diagnostic support for confirmation of the leptospirosis, characterization of leptospiral isolates and assessing antibiotic susceptibility pattern of isolates recovered from patients with various clinical syndromes.

Extending diagnostic support as a part of the ICMR National virology network to various infections suspected of viral etiologies (about 29 diseases of viral etiology, with particular emphasis on dengue, Chikungunya, Japanese encephalitis, Hand Foot and Mouth Disease, novel H1N1 influenza, respiratory syncytial virus (RSV), other enteroviruses, norovirus, astrovirus and sapovirus, adenovirus, human metapneumovirus, parvovirus B19, and childhood rotaviral diarrheas).

Monitoring of childhood diarrheas with suspected etiology of *Shigella*, *E. coli* and *Salmonella* and with rotaviral etiology.

Drug susceptibility monitoring of various bacterial agents of childhood diarrheas and urinary tract infections.

Monitoring CD4 and CD8 counts in patients under anti-retroviral therapy of HIV/AIDS patients for about 120 patients referred by the Andaman AIDS control society.

Local Public Health Problems – Efforts undertaken for Risk Reduction

Leptospirosis

Leptospirosis is an important public health problem in A & N islands. Studies in the 1990s showed an incidence as high as 750 cases/100,000 population. The incidence of severe cases requiring tertiary care treatment was about 30/100,000 and the specific mortality was 7.5/100,000. The terminal events in most patients presenting haemorrhagic pneumonitis were massive haemorrhages into the tracheo-bronchial tree resulting in acute respiratory distress. Case fatality ratios were in the range of 10 – 30 %. Although there were no organized effort from the part of health, veterinary and agricultural sector to systematically address the issue, collective efforts were made in all these sectors. These measures that targeted domestic animals, environment and humans with special emphasis on early diagnosis and prompt treatment appeared to have paid off. The situation has improved substantially and drop has been observed during recent past (2011- 2013) in the incidence of leptospirosis as well as severe leptospirosis and specific mortality due to leptospirosis. The severe leptospirosis dropped from 31/100,000 to around 15/100,000 and specific mortality from 7.5/100,000 to around 1/100,000.

Tribal Health

Tuberculosis is one of the significant public health problems among the Nicobarese tribe of Car Nicobar Island. In 1986, the prevalence of sputum positive cases of pulmonary tuberculosis was 410/100,000 population and that of sputum negative radiologically active cases was 788/100,000. This prevalence of sputum positive cases had gone up to 735/100,000 by 2001-02. RNTCP was introduced in 2005 and DOTS+ strategy in 2012. Preliminary surveys for assessing the current situation indicates that the sputum positive cases are 87/100,000 indicating a significant reduction of the pulmonary tuberculosis among this marginalized population group.

In India, diurnally sub-periodic form of filariasis caused by *W. bancrofti* is prevalent only among the Nicobarese tribe of Nancowry group of islands. The disease is transmitted by a day-biting mosquito *Downsiomyia nivea* that breeds in tree holes in forests. The overall prevalence of microfilaria (mf) was about 12% during the pre-MDA period and mean

parasite load per microfilaraemic was 27.30. Disease prevalence is about 5.2%. The overall endemicity rate was 16.2%. Assessment undertaken post six rounds of MDA by the Centre indicate persistence of microfilaraemia with an overall (i) prevalence of 5.3% in Nancowry group of islands.

Support to World Health Organization (WHO)

Evaluation of Rapid Diagnostic kits for Leptospirosis

The Govt of Thailand requested through WHO for evaluation of the Immuno-Chromatography Test (ICT) developed by the Ministry of Public Health, Govt. of Thailand. The Centre evaluated the test and found that it can be performed at peripheral health care centres and is easy to perform and read. The test results can be obtained within 15 minutes. The sensitivity and specificity observed was 90% and 88% respectively, which was in the acceptable range. The reagent can be stored at ambient temperature hence does not require any cold storage facility.

Establishment of Reference Laboratories in the South East Asian region

As one of the mandates as a WHO referral Centre for diagnosis, research, reference and training, the centre has extended technical support to Indonesia in order to develop leptospirosis reference laboratories.

Basic Research

Anti-malarial and Anti-bacterial Potentials of Medicinal Plants, Sponges and Sea Weeds Endemic to these Islands

The centre has generated information on traditional knowledge of the indigenous tribal communities on herbal medicine and health care practices. In continuation the centre carried out studies to assess antimicrobial properties of plants/seaweeds/sponges. 22 sponges were collected from different parts of these islands. From these 22 sponges, 84 associated bacteria were isolated, from which 15 secondary bacterial metabolites were tested and two was found to be effective against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia*. Out of the 22 sponges collected, crude extracts from 16 sponges were tested of which nine showed inhibitory effects against various bacterial pathogens.

Development of New Control Strategies for the Prevention and Control of Leptospirosis

Laboratory and field based studies on leptospiral bio film, demonstrated bio film formation in the field conditions. The bio film formation with other bacteria enables them cope the environmental stress and facilitates prolonged survival. The information could facilitate in developing control strategies with particular reference to the agriculture workers, who are at higher risk of acquiring leptospiral infection. Studies so far conducted indicates that two bio fertilizers being used could have inhibitory/cidal effect on leptospires. These bio fertilizers could be modified and may be used for the control of leptospirosis.

Infrastructure Development

Establishment of new BSL3 has been completed. Construction of the Phase II of the Centre's building has been accomplished. Renovation and modernization of laboratories, and putting in place a state of art auditorium and conference hall have been completed (Figs.).



Hon'ble Lt Governor A & N Islands, Bhopinder Singh, PVSM, AVSM along with Dr V M Katoch, Secretary, DHR, GOI & DG ICMR and Shri Anand Prakash, IAS, Chief Secretary along with secretaries and officers of A & N administration at the inaugural function of BSL-3 facilities at the Mahatma Conference Hall, RMRC, Port Blair



Hon'ble Lt Governor A & N Islands, Bhopinder Singh, PVSM, AVSM addressing the audience at the inaugural function. Towards the right is seated Dr V M Katoch, Secretary, DHR, GOI & DG ICMR and left is Shri Anand Prakash, IAS, Chief Secretary, A & N administration.



Hon'ble Lt Governor A & N Islands, Bhopinder Singh, PVSM, AVSM unveils the inaugural plaque. Accompanying the Hon'ble Lt Governor is Dr V M Katoch, Secretary, DHR, GOI & DG ICMR and Shri Anand Prakash, IAS and in the rear is Shri Sudhir Yadav, DGP, A&N administration



Hon'ble Lt Governor A & N Islands, Bhopinder Singh, PVSM, AVSM along with Dr V M Katoch, Secretary, DHR, GOI & DG ICMR, Shri Sudhir Yadav, DGP, A&N administration and Dr P Vijayachari, Director, RMRC, Port Blair and to the left is Anand Prakash, IAS Chief Secretary, A & N administration

Regional Medical Research Centre for Tribals (RMRCT), Jabalpur

Vector Borne Diseases

Malaria

To determine the Effectiveness of Intensive Intervention Measures on Malaria Prevalence in Tribal District, Dindori, Madhya Pradesh (MP)

A study was undertaken to evaluate new intervention measures for developing a suitable model for malaria control in collaboration with State Vector Borne Disease Control Programme. Malaria control measures in this area included mainly indoor residual spraying (IRS) with a synthetic pyrethroid (alphacypermethrin), Long lasting insecticide nets (LLINs), Rapid diagnostic tests (RDTs) and Artemisinin based combination therapy (ACT). Monthly cross sectional fever surveys were carried out door-to-door in study villages. Indoor resting *Anopheles* mosquitoes (per man hour), Pyrethrum spray catches (PSC) were sampled once in a month. *An. culicifacies* and *An. fluviatilis* were tested for species specific malaria parasite and their sibling species was identified using polymerase chain reaction (PCR). Out of total 1679 fever cases, 98 (86 Pf, 12 Pv) cases were found malaria positive. The Slide Positivity Rate (SPR), Slide Falciparum Rate (SFR) and *P. falciparum* percentage were 5.8, 5.1 and 88% respectively. All indices showed a sharp decline as compared to 2011- 2012. Precisely > 50% reduction in overall malaria slide positivity rate and 65% in *P. falciparum* was observed. Spleen rate reduced to only 5%. While sporezoite rate also showed 0.45% decline as compared to previous years.

Assessment of the Effectiveness of Intensive Intervention Measures on Malaria Control Programme in Tribal District, Balaghat, Madhya Pradesh

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Hon'ble Lt Governor A & N Islands, Bhopinder Singh, PVSM, AVSM along with Dr V M Katoch, Secretary, DHR, GOI & DG ICMR, Shri Sudhir Yadav, DGP, A&N administration and Dr P Vijayachari, Director, RMRC, Port Blair and to the left is Anand Prakash, IAS Chief Secretary, A & N administration

Regional Medical Research Centre for Tribals (RMRCT), Jabalpur

Vector Borne Diseases

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During the period under report, a total of 3260 fever cases were screened, of which 1374 were found positive for malaria (231 *P. vivax*, 1122 *P. falciparum*, 5 *P. malariae* and 16 mixed). The Slide Positivity Rate (SPR), Slide Falciparum Rate (SFR) and *P. falciparum* percentage were 42.1, 34.9 and 83% respectively. The spleen rate in children was 43.8% and average enlarged spleen was 1.99 (95% CI 1.94-2.04). ZeroVector® Durable Lining (ZVDL) was installed in 6 villages in Jan 2013. Initial results revealed a decline in SPR and SFR although not significant statically. So far out of 2043 *An. culicifacies* for malaria parasite, 8 were found positive for sporozoite (sporozoite rate 0.35%) 2 for Pf and 6 for Pv represented sibling species C, D and E (GenBank database accession numbers KC494261, KC494262 & KC494264). Out of 215 *An. fluviatilis* was tested 1 was found positive for Pv (sporozoite rate 0.47%) represented sibling species S (GenBank database accession numbers KC345546).

Evaluation of Biomarkers to Assess Malaria Severity due to *P. falciparum* Malaria in Central India

Different cytokines IL-1ra (interleukin 1 receptor antagonist), VEGF (vascular endothelial growth factor), sTNFR1 (soluble tumor necrosis receptor 1), sTNFR2 (and soluble tumor necrosis receptor 2), sFas, Fas L and additionally sICAM-1 (soluble intercellular adhesion marker) and MIF (macrophage migration inhibitory factor) were tested for their role as prognostic marker in different severe forms of malaria. Data was analyzed for 141 samples at the time of admission (Healthy controls = 19, mild to moderate malaria = 34, non cerebral severe malaria = 20, cerebral malaria survivors = 44 and non survivors = 24) for individual/ combinational markers of prognosis).

Plasma levels of IL-1 ra were 69% sensitive and 62% specific to distinguish Cerebral Malaria (CM) survivors from non survivors at cutoff of 168 pg/ml ($P < 0.001$). For combinational biomarker analysis we have selected IL-1ra, sICAM-1 and MIF in a pool of 72 CM cases out of which 25 died. IL-1ra, sICAM-1 and MIF in combination were 88% sensitive and 70% specific to predict bad prognosis of the patients at the time of admission.

Clinical and Molecular Surveillance for Monitoring the Emerging Resistance to Anti-malarial Drugs in *Plasmodium falciparum* in Central India

A study aims to monitor therapeutic efficacy of Artemisinin-based combination therapy (ACT) for the treatment of uncomplicated falciparum malaria and molecular markers of drug resistance. Therapeutic efficacy study was carried out with ACT (orally three day) over a period of 28 days follow-up. The parasite DNA was extracted from blood samples collected on filter paper and dhfr dhps gene was amplified and sequenced.

Of the 92 patients enrolled, the outcome was determined among 47 patients only as forty five patients did not complete the study. Over all therapeutic efficacy showed 100% adequate clinical and parasitological response. Sixty eight samples were analyzed for *dhfr* mutations at five codons (16, 51, 59, 108, 164). Parasite population with mutant *pf dhfr* $A_{16}N_{51}C_{59}N_{108}I_{164}$ (45.6%) and $A_{16}N_{51}R_{59}N_{108}I_{164}$ (36.8%) was prevalent followed by wild type *pf dhfr* allele $A_{16}N_{51}C_{59}S_{108}I_{164}$. The five codons (436, 437, 540, 581, and 613) for *dhps* mutation were analyzed. Parasite population with wild type *pf dhps* allele $S_{436}A_{437}K_{540}A_{581}A_{613}$ was prevalent (66%), single mutant *pf dhps* genotype $S_{436}G_{437}K_{540}A_{581}A_{613}$ (23%) and double mutant *pf dhps* genotype $S_{436}G_{437}E_{540}A_{581}A_{613}$ (11%) were also recorded.

Molecular Epidemiological Study of *Plasmodium falciparum* Field Isolates and the Incidence of Malaria in Endemic Regions of Central India

A molecular epidemiological study was continued to provide a better understanding about the invasion characteristics/phenotypes, genotypes of *P. falciparum* field isolates from endemic regions as well as to study the development and maintenance of immune responses against *P. falciparum*. Fifty four *P. falciparum* field isolates were collected and cultured in the laboratory for further experimentations. Out of 54 field isolates 22 isolates were successfully adapted for *in vitro* culture and rest of the samples failed to grow due to low parasite density at the time of collection or due to contamination. The glycerol stocks were made and frozen for future invasion assay. The assay has been standardized with *P. falciparum* laboratory clones, 3D7, 7G8 & Dd2 as a mock to estimate erythrocyte invasion phenotype for field isolates.

IEC on Malaria in Baigachak Area of Dindori district of Madhya Pradesh

Traditional beliefs and practices in tribal area, their traditions, inaccessibility to health posts and their backwardness both educationally and economically, risk their life to malarial infection. The centre has made an attempt to establish a ground communication mechanism to sensitize the Baiga tribal people in Dindori district of Madhya Pradesh on preventive aspects of malaria by roping in local school going children as agent of change and using the tools of communication such as theatre camping, using local folk, rallies, storytelling using hand masks, wall posters and community meetings, etc. Several sensitization workshops with the participating children were conducted with the help of a Kolkata based NGO- i-Land Informatics Ltd. Evaluation of (Information, Education & Communication) IEC strategy within a four months of initiation reveals 23% enhancement in the level of awareness on malaria among the masses in the target area. During the period under report these children were brought to RMRCT, Jabalpur for exposure to malaria laboratory, sensitization and also they were examined clinically and pathologically using our resources and provided treatment. The children also performed at the centre the IEC activities they were trained. The study is in progress.



Samples taken for pathological examination



Baiga tribal youth exposed to microscope

Detection and Molecular Confirmation of *Plasmodium ovale*

A malaria clinic of RMRCT has been established in a tertiary health care facility (Maharani Hospital and associated medical college, Jagdalpur) of South Bastar where case fatality rate was found to be >25%. Out of 256 cases of confirmed malaria, *P. ovale* was detected in 3 cases (1.2%) by species specific nested PCR and sequencing. Of these 3 cases, one had cerebral malaria and another had severe malaria anaemia. In both of these cases *P. ovale*

was mixed with *P. falciparum*. While in third case the infection was mixed with both *P. falciparum* and *P. vivax*. Phylogenetic analysis revealed that these isolates showed closed homology with West African genotypes. All 3 patients were from remote inaccessible forest villages and never moved out of their residence. Because of prompt diagnosis and treatment all 3 patients recovered.

Tuberculosis

Estimation of TB Disease Burden, Risk Factors Assessment and IEC Intervention to Improve KAP related to Tuberculosis among Saharia Tribe

IEC intervention study to improve KAP related to tuberculosis among Saharia tribe is in progress in Shivpuri district of Madhya Pradesh. It is being carried out in three phases - Baseline survey (phase I), IEC intervention (phase II) and the endline survey (phase III). The baseline survey comprising of TB disease survey, risk factor and KAP assessment has been completed. The baseline prevalence in this area was found to be 3000 per 100,000 population. In addition, the findings highlighted their poor knowledge and perception about tuberculosis.

A study to estimate the prevalence of pulmonary tuberculosis and to identify the risk factors has also been undertaken among Saharia tribe of Gwalior district. The findings of the study show very high prevalence of pulmonary tuberculosis (3000 per 100,000 population) among the community. The major risk factors for TB viz. tobacco use, alcohol consumption, under-nutrition, indoor air pollution are also found prevalent amongst them.

Drug Resistance Survey for Tuberculosis in Sahariya Tribe of Guna and Gwalior Districts

The study was undertaken in TB patients belonging to Sahariya tribe in 2 districts; Guna and Gwalior where prevalence of TB is very high. Both new and retreatment cases attending the designated microscopy centres for treatment of tuberculosis were included in the study. Total of 102 TB patients were registered for the study of which 88 individuals were culture positive. Fifty one isolates were susceptible to all the four drugs. Monodrug resistance was seen in 12 isolates with the maximum of 9(10 %) being resistant to Streptomycin. Nineteen MDR isolates were detected of which 15 (17%) were in retreatment cases while 4 (4.5%) were from new cases. In spite of high TB prevalence among this indigenous population of M.P the drug resistance for TB is not different from national figures.

Virology

The diagnosis for 15 different viruses is made available to the government and recognized hospitals in Madhya Pradesh. This year more than 3700 samples were tested for viral infections using molecular and serological tools and timely & accurate diagnosis was provided.

Dengue

A total of 1235 samples were tested by ELISA, RDT or nRT-PCR this year. Of these 429 i.e. 35.5% samples were positive for dengue infection. This year the laboratory could detect dengue virus 2 from district Mandla, Jabalpur, and Rewa, Dengue 3 was detected from Narsinghpur, Jabalpur and Mandla. A major outbreak of dengue 2 was investigated in tribal district Mandala where 46% of suspected cases had dengue infections and 10 deaths were attributed to dengue. This laboratory also assisted in identification of serotype outbreak of Ahiwara (Durg), district in Chhattisgarh (CG) and Dengue virus 1 was found to be causative agent. Further the molecular studies conducted on the dengue samples collected last year

revealed that the dengue virus 1 a causative agent of outbreaks in MP and CG belonged to genotype III.

Influenza

During period of report, a total 591 samples of Category-C patients were referred to this laboratory and 109 (18.1%) samples were diagnosed positive Influenza A (H1N) pdm09 and 11 samples were positive for Influenza A H3N2. A retrospective study also revealed that 38.1% of the children (less than 2 years) admitted to hospital suspected of influenza had Respiratory Syncytial Virus (RSV) infections and is a major cause of hospitalization.

Hepatitis

More than 1000 samples were tested for four hepatitis (HAV, HBV, HCV and HEV) viruses in this period. Antibody capture ELISA for Hepatitis A on 218 samples was done and 38 (17.4%) were detected positive. Phylogenetic analysis was done on the samples collected earlier and the analysis showed that the virus belonged to genotype IIIA. The screening of samples for Hepatitis B surface antigen by ELISA revealed that 66 were positive out of 525 tested. The sequencing analysis demonstrated prevalence of genotype D in the samples collected from this area. Hepatitis C infection was detected by antibody IgM capture ELISA. Total 177 samples were tested and 5 were diagnosed positive. Serological diagnosis of hepatitis E virus on 339 samples suspected for HEV infection out of which 95 (28%) were positive.

Community Health

Health and Nutrition Survey of Baiga Tribe of Dindori District, Madhya Pradesh

Baigas are one of the aboriginal tribe and are classified as one of the particularly vulnerable tribe of Madhya Pradesh. In this study a total of 2319 individuals from 542 households were surveyed. One thousand eighty three blood samples out of 2319 individuals were collected for estimation of haemoglobin levels. Moderate type anemia was 43.3% and severe anemia was 12.5.% among Baiga population. Two hundred stool samples were also collected from school going children for assessing parasitic infections and 49.5% were found to be positive. Round worm (10%) was the most common worm infestation. A total of 319 pre-school children were clinically examined for various morbidity. It was found that acute respiratory infection was 25.1% followed by scabies (7.7%) and ear discharge (3.1%). Nutritional status among the pre school children (0-6 years) was vulnerable. It is found that about 28.4% male and 32.1% female children were severely underweight.

EXTRAMURAL RESEARCH & OTHER PROGRAMMES

During 2013-2014, ICMR supported 1114 Extramural Projects in open competitive mode. These included 481 new projects. Support was also given for 226 fellowship programmes.

Communicable Diseases

In the area of Epidemiology and Communicable Diseases, adhoc and Task Force extramural research projects were supported in areas of Antimicrobial Resistance, leprosy, Tuberculosis, HIV/AIDS, diarrheal diseases, viral infections, other microbial infections, immunology of infections and Zoonoses. The Division has established 6 Nodal centres for AMR {(AIIMS-1), (PGIMER-2), (JIPMER-1), (CMC-2)} in six specific pathogens and 5 new viral diagnostic laboratories.

Anti-Microbial Resistance Network

In order to strengthen the surveillance of antimicrobial resistance a National Anti Microbial Resistance Surveillance Network (AMRSN) has been initiated to enable compilation of National Data of AMR at different levels of Health Care, detailed understanding of underlying mechanisms of resistance and genetic molecular studies. AMR Surveillance Networks as proposed will have six National centers (NCs) which would focus on (i) Diarrhoeagenic bacterial organisms, (ii) Enteric fever pathogens, (iii) Enterobacteriaceae causing sepsis (iv) Gram negative Non-fermenters (v) Gram positives including MRSA (vi) Fungal infections (vii) Respiratory pathogens. The NCs will focus on the identified resistant organisms & will exchange organisms amongst each other according to their expertise for in depth molecular studies of the group of pathogens for which they are responsible. ICMR is in the process of identifying 20-25 medical colleges across the country to act as regional centers (RCs) to work with National Centers. A web based portal has been developed for a real time data collection data collection monitoring and analysis.

The ICMR in collaboration with the Public Health Foundation India (PHFI) and the London School of Hygiene & Tropical Medicine (LSHTM) organized a workshop on "Pathogen Diversity : Exploiting Pathogen Genetics for New Control Strategies". The conference programme included 16 expert speakers and approximately 50 delegates. The workshop led to scientific deliberations on (i) methods of pathogen identification, (ii) challenges for vaccine, drug and diagnostic development and (iii) surveillance and monitoring. The workshop was aimed to establish closer interactions between research scientists working on pathogens in UK with those in India through sharing of new knowledge and methodologies on pathogen diversity, through the development of links and collaborations in areas of common interest leading.

Diarrhoeal Diseases

A study at RMRC, Port Blair explored the microbiological, clinical and epidemiological determinants of childhood diarrheas in hospitalized patients. 91 enteric bacterial pathogens were isolated from 698 patients with 13% proportional morbidity for bacterial diarrheas. The most frequent G/P genotype combinations detected were G2P [4], G1P [8], G9P [4] and G1P [4] respectively. The sudden emergence of resistance to several new drugs is a cause of great concern.

A study at PGIMER, Chandigarh studied the drug resistance mechanisms and molecular epidemiology of ciprofloxacin resistant *Shigellae*. The researchers reported a very high

fluoroquinolones resistance of 46% in *S flexneri*. The findings also suggested that *acrAB* over expression is an indicator of fluoroquinolone resistance. New mutations (*parC* at position 93, to the best of knowledge being reported for the first time) were reported.

Another study from AIIMS, New Delhi examined newborns with neonatal rotavirus (RV) infection and RV diarrheal children (< 5 years). Rotavirus antigens were detected in 30.07% of children with severe diarrhea and 1.54% newborns. Rotavirus vaccine that is currently in development in India (116E, G9P[11]) is having a monovalent formulation like Rotarix® and it is important to continue careful monitoring of the strains to gauge the impact of vaccines on strains and help understand the effect of strains on efficacy of the vaccine.

Immunology

A study completed at JSS Medical College, Mysore revealed that the most powerful predictor to differentiate between the non-infected and infected neonates before antibiotics, 24 hours and 48 hours after antibiotics was CRP and sCD163. The most powerful predictor to differentiate between the control and non-infected neonates before antibiotics were IL-6 and TNF- α and at 24 hours after antibiotics was CRP.

A study on effect of maternal infection on neonatal immune responses in bancroftian filariasis completed at RMRC, Bhubaneswar showed an increased level of IL-10 (Th-2) and down regulation of IFN- γ (Th-1) has been detected in cord blood of children born to filarial infected mothers. High level of T-Regulatory cells and increased production of IL-10 in cord blood from infected mothers indicate that increased T-regulatory cells could down regulate inflammatory responses and may be associated with parasite survival.

To examine whether the increased expression of MMPs (-2,-7,-9) and TIMPs (-1,-3) in the CNS of JEV infected BALB/c mice model is mirrored in the peripheral venous blood, the expression of these specific MMPs and TIMPs has been studied in the mice sera by ELISA at SGPGIMS, Lucknow. The study shows that MMP-2, MMP-7 and MMP-9 levels were up regulated in the mice sera after IC JEV challenge, while TIMP-1 and TIMP-3 levels were substantially down regulated with the disease progression, increased viral load and tissue pathology. The study provides preliminary evidence for a pattern of TIMP response in JEV infection distinct from that seen in acute inflammatory CNS conditions in JE.

HIV/AIDS

A study completed at National Institute of Research in Tuberculosis, Chennai assessed the effectiveness of the model study intervention through a randomised controlled trial to provide evidence for policy makers. There was a greater reduction in the number of unprotected anal sex acts from baseline to 3rd month in the intervention group.

A study completed at AIIMS, New Delhi showed that the impact of Antiretroviral Therapy (ART) on lipid profile among Human Immunodeficiency Virus (HIV) patients receiving ART different regimen. In this study, 3 drugs combination ART was given and 30% (40) of the these patients were receiving Stavudine based ART regimen (d4T+3TC+NVP/EFV), 70% (95) Zydovudine based regimen (AZT+3TC+NVP/EFV). Overall incidence of dyslipidemia (high total cholesterol >239 mg/dl) was detected among 25% patients. However in the study Stavudine based regimen was found to have 15% incidence of dyslipidemia.

A study done at Maulana Azad Medical College and Associated Hospitals, New Delhi revealed that the clinical profile of AIDS in India tends to be different from the developed world. A decline in type-1 cytokines (IFN- γ , IL-2) and rise in type-2 cytokines (IL-4, IL-10) was observed in patients with HIV infection suggesting a shift from Th1 to Th2 type cytokine

response, more pronounced in presence of opportunistic infections suggesting a more severe immunosuppressant and a prompt recognition and treatment of these infections is essential to prevent the progression to AIDS.

A study was done at NARI, Pune to show that in the recent years, 2, 3-diaryl-1, 3-thiazolidin-4-one has emerged as an important chemical scaffold having promising anti-HIV activity. The study concludes that 4-Thiazolidinones have potential to inhibit HIV. The QSAR and molecular modeling of the four lead NCEs may help in developing more effective NCEs.

In a study completed at Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore showed that the viral antigen Tat is a potential vaccine candidate given that immune responses to Tat are negatively correlated with disease progression and/or viral load, suggesting a protective role. Optimizing Tat vaccines could be critical to formulate multi-component HIV vaccines that are likely to generate cross-clade protective immune response. This data ascertains the role of Tat as a potential HIV vaccine candidate.

Leprosy

Knowledge, Attitude & Practice (KAP) survey of low endemic districts in West Bengal were found much less (64% unaware) as that of high endemic one & more proportion of MB cases (35%), warranting stringent IEC at community level with appropriate channels of communication. A high proportion of patients with disability were found 42.16% in high prevalence and 76% in low prevalence area. The study identified the priority areas like prevention & appropriate management of the disability that needed urgent & timely attention. Concerted and focused research on pertinent areas like childhood leprosy, disability due to leprosy-its prevention, management & rehabilitation, community survey in low endemic district to identify their perception & practices, and searching for hidden cases, is urgently needed.

In a multicentric study entitled 'Search for Prevalence of MDR - *M. leprae* From Clinical Isolates of Leprosy Patients' completed at Kolkata has demonstrated that the Multiplex PCR developed not only would help early diagnosis of leprosy (untreated, treated, relapsed, reinfection, treatment failure) cases, but Drug Resistance Surveillance is essential to keep a vigil on the drug resistance scenario at many vulnerable settings in spite of the declining leprosy trend and thereby attaining the success to the final goal of leprosy elimination as a public health problem.

Microbial Infections

A molecular epidemiological study of Group A streptococci (GAS) infection conducted in the All India Institute of Medical sciences, New Delhi showed that the isolation rate of GAS was 75%, with high exotoxins and resistant genes which may result in more resistant and virulent strains. GAS vaccine coverage and control of GAS infections will need to take these local factors and strain differences into consideration.

A study funded in PGIMER, Chandigarh characterized the isolates of *Campylobacter* at the molecular level and showed that *C. jejuni* was most commonly isolated *Campylobacter* species followed by *C. coli*. In all poultry isolates were *C. jejuni* with *C. coli* co-infection in 19.2%. *C. lari* and *C. upsaliensis* were not found in patients or poultry. *Campylobacters* from patients were sensitive to nalidixic acid (56.6%) and ciprofloxacin (73.3%). Similarly, 63.6% of isolates from poultry were sensitive to nalidixic acid and 65.4% to ciprofloxacin.

National (Hospital Based) Rotavirus Surveillance Network (NRSN)

A National Hospital Based Rotavirus Surveillance Network in 4 zones North, East and West and south has been established with the objective of the study is to assess epidemiological aspects of rotavirus disease in India and provide essential information before and during introduction of new interventions against rotavirus. In the South zone there are 1 Referral centre, 1 Quality Control centre, 1 Coordinating/ Monitoring centre, 1 Regional centre with 9 peripheral sites started in July 2012. Other 3 zones (North, East and West) are started this year. In the west zone there are 1 Referral level, 1 Regional level and 6 Peripheral sites. In the east zone there are 1 Referral centre, 3 Regional level with 6 Peripheral sites. In the North zone there is 1 Referral centre with 9 peripheral sites. South zone has completed one year of study. The study is coordinated by NIE, Chennai. Study manual for national hospital based rotavirus surveillance network (NRSN) was prepared to be used at all the sites uniformly.

The project will facilitate expansion of the multi- centric network by adding new centres and sites and will provide training to peripheral sites, enabling transferring of technology for antigen detection to peripheral sites and building basic capacity in clinical research.

Projects Supported in North Eastern States

A study has been concluded at RMRC, Dibrugarh, which revealed the prevalence of smear positive TB in tea garden workers to be 1.93 per thousand. However, about 65.07% of cases were not aware that they had TB as indicated by the active surveillance in 12 tea gardens. Implementation of active surveillance will be important to control spread of TB. This study has shown that the prevalence of MDR is 1.61% among new smear positive cases and about 13.6% among previously treated cases.

Translational Research

VCRC, Pondicherry optimized production and down-stream processing for the improved yield of Thrombinase enzyme from *Bacillus sphaericus* (Strain No. NRRL B18949). Selection of production strain of *Bacillus sphaericus* (VCRC B42), media optimization, optimization of production at pilot scale level, downstream process and purification of the fibrinolytic enzyme have been carried out. Compared to the earlier method of downstream process which involved 7 steps, the new method involves only 5 steps. The time taken for final purification of thrombinase by old method was 96 h while that taken by the new method is 72 h. Further the yield of the enzyme was 5 mg/l by the earlier method. The improved method yielded 7 mg/l. Thus the improved method resulted in the decrease in the number of steps and time involved in purification of thrombinase and a marginal increase in the yield.

Tribal Health & Tribal Sub-Plan

A Remote Sensing and GIS based study was initiated in Ranchi district, Jharkhand to map malaria receptivity along with identification of risk factors at NIMR, New Delhi. On the basis of average API of 10 years, two PHCs namely Bundu and Angara with high and medium malaria endemicity were identified. Eleven risk factors were identified and mitigating measures for vector control were suggested. Streams emerged as major risk factor responsible for high endemicity in Ranchi district. Area was found to be more receptive for malaria in Bundu PHC in comparison to Angara due to migratory population settlement from endemic areas around stone quarries; higher length of perennial streams; more area under rocky terrain leading to formation of rocky terrain based pools; more number of hamlets affected by water logging in low lying areas during rains; less Insecticide treated net (ITN) coverage in comparison to Angara PHC; and higher vector density.

The School of Environmental Sciences, Bharathidasan University & CRME, Madurai collaborated to initiate a major project concerned with the identification of vector borne disease and surveillance of vectors in tribal areas by RS and GIS, and to explore the various control strategies. Entomological survey and spatial analysis revealed a total of 2533 female mosquito specimens contributing to 19 species belonging to 7 genera. The abundance map indicated the highest and lowest abundance of vectors in Sitheri hills such as *S. ammapalayam* and *S. suriyakadai* respectively. The vector surveillance map also revealed the highest and lowest percentage of dengue and chikungunya surveillance in Sitheri hills.

Results of study by NIMR on *fluviatilis-minimus* group in 22 malaria endemic tribal districts revealed that *An. fluviatilis* species S was prevalent and predominant in forest areas of study districts in Andhra Pradesh, Chhattisgarh and Odisha states. *An. culicifacies* found co-existing with *An. fluviatilis* in study districts and comprised sibling species B and C which were primarily zoophagic. *An. culicifacies* was found resistant to DDT and in some districts it was resistant/ tolerant to Malathion and deltamethrin. In study districts of north eastern region only *An. minimus sensu stricto* (formerly species A) of *Minimus* Complex was found prevalent in study districts and *An. harrisoni* (Minimus C) was not encountered. Since this species is highly anthropophagic personal protection measures (use of repellents, coils and vaporizers) would supplement the major intervention tool in decreasing the man-mosquito contact.

Two field units one at Raygada and another at Kalahandi have been opened on request from the state health department for improvement of the health indicators of the tribal people of these areas. It will target operational and health system research activities to increase utilization of the current health programme. Studies will be undertaken to find out the prevalence of drug resistant TB, RTI and HIV/STDs infections and activities will be done to reduce the under-five child mortality by giving intervention for acute diarrhea, acute respiratory infections and under-nutrition in this district in the first phase. This will help in capacity building through transfer of improved technology and disease control strategies to augment ongoing state health programmes.

The sub-plan undertakes research on health problems of the tribal people. Under this sub-plan two studies have been completed in this year.

A study entitled "Mapping of sibling species of malaria vectors and their bionomics in Madhya Pradesh" was undertaken by Regional Medical Research institute, Jabalpur. In all 24151 specimens of anopheline were caught which belong to 12 species. In Shivpuri district number of anopheline species was 9 while in Balaghat and Sindhi district 11 & 12 species were recorded. *An. fluviatilis* was recorded mainly in post monsoon and winter season only. Proportion of *An. culicifacies* was only 12.2% while *An. subpictus* constitutes around 56.1% of all the anophelines. Overall man hour density of anophelines, *An. culicifacies* and *An. fluviatilis* was 56.1, 11, 0.5 respectively. 486 specimens of *An. culicifacies* were identified for sibling species composition by polytene chromosome preparation method. Overall, species C was the predominant species (80.5%) followed by species B (10.3%) 804 specimens of *An. culicifacies* were identified by PCR method. By this method specimens were classified into two groups X-A representing species A and D and X-B representing species C and D. 88.4% of the specimens that were identified as X-B were B and C and 14 specimens that were identified as X-A were species A and D.

A study entitled "Studies on distribution and biological characteristics of the members of fluviatilis - minimus group for effective vector control strategies in tribal areas of India" has been completed by National Institute of Malaria Research, New Delhi. Study has been carried out in 22 malaria endemic tribal dominated districts of 10 states in east- central,

north-eastern and peninsular India to map the distribution of the members of the *fluviatilis* - *minimus* group and study their biological characteristics in terms of resting and feeding preference, vectorial potential and response to insecticides used in public health. Results revealed that *An. fluviatilis* species S was prevalent and predominant (72-99%) in hilly and foot hill forest areas of study districts in Odisha, Chattisgarh and Andhra Pradesh states. Species S was found to be highly anthropophagic (HBI >0.9) with preference to rest in human dwellings and was detected harbouring sporozoites of malaria parasites in districts Keonjhar, Deogarh, Dantewada, Bastar, Vishakapatnam and Vizianagaram (sporozoite rate ranging from 1.56-2.51). Insecticide susceptibility tests revealed that resistance/tolerance to DDT has precipitated in *An. fluviatilis* in species T dominated areas (districts Gumla, Simdega and Surguja) where % corrected mortality observed ranged from 70% to 77.6% but this species was found completely susceptible to malathion 5% and deltamethrin 5%.

Tuberculosis

A study completed at Sawai Man Singh (SMS) Medical College and Hospital, Jaipur showed that 32.62% samples were culture positive, of which 2.5% were Non Tubercular Mycobacteria (NTM). RAPD is a simple rapid method which takes few hours but is not reproducible and has low discriminatory power.

A study conducted at Central India Institute of Medical Sciences, Nagpur showed that Tuberculous meningitis (TBM) caused by *Mycobacterium tuberculosis* (MTB) continue to be a major cause of morbidity and mortality. In summary, increased levels of Hsp 65 was found in clinical samples and in *in-vitro* cell line model thus indicating MTB Hsp 65 as a potential biomarker for the diagnosis and in understanding pathogenesis of TBM.

In a study completed at NIRT, Chennai, transitmycin (Tr), a novel antibiotic from marine *Streptomyces* sp, isolated from sea sediment off Rameswaram coast, was tested against standard strains and clinical isolates of *M. tuberculosis* and HIV to study its antitubercular and anti HIV property. Dose response of Tr indicated that compared to INH, Tr showed better killing at 1uM concentration; compared to Rif killing effect of Tr was equivalent at 10uM concentration and inhibited 16 out of 18 MDR TB isolates at 5ug/ml concentration.

Vector Borne Disease Science Forum (VBDSF)

Under the Forum, 12 new adhoc studies have been initiated in the year 2013. Three studies have been completed.

A study entitled "Multi-Centric Evaluation of L3 Stage Specific RT-PCR Assay For The Infective Stage (L3) *Wuchereria Bancrofti* was completed at Vector Control Research Centre, Indira Nagar, Pondicherry Overall the results of the evaluation of RT-PCR based assay for the detection of infective (L₃) stage larvae of lymphatic filarial parasite, *W. bancrofti*, in vector mosquito *Cx. quinquefasciatus* from the four participating centres indicated that the assay is as sensitive and stage specific as the conventional mosquito dissection technique.

A study entitled "Studies on *Aedes* mosquitoes to determine vectors of Dengue and Chikungunya virus in Alappuzha and Kottayam districts of Kerala" was completed by National Institute of Virology, Kerala unit, Alappuzha Kerala. Entomological studies were conducted in Alappuzha and Kottayam district of Kerala state, from March 2012 to January 2013, to identify the *Aedes* mosquitoes responsible for the Dengue and Chikungunya virus transmission. The three most productive containers generate most pupae such as cement tank, discarded plastic waste, and plastic sheet yielded 80% of total pupae. Targeting these most common containers would bring about a similar reduction in pupae production.

A study entitled “Seasonal Abundance of *Aedes (Stegomyia) albopictus* and *Aedes (Stegomyia) aegypti* in Guwahati Metropolis and Suburban Settlements, Assam Northeast India was completed by National Institute of Malaria Research (ICMR) Assam among *Ae. albopictus* subgroup of species prevalent in India, all mosquitoes dissected for male genitalia were confirmed to be true breeding *Aedes (Stegomyia) albopictus* (Skuse), the only member species of the *Ae. albopictus* subgroup that is prevalent in Guwahati and suburbs. It was observed that both *Ae. aegypti* and *Ae. albopictus* were resistant to DDT (4%), but fully susceptible to malathion (5%) at given diagnostic concentrations. However, both these species exhibited varied response to pyrethroids (deltamethrin and permethrin). *Ae. aegypti* was observed to be resistant to deltamethrin (0.05%) as well as permethrin (0.75%), but *Ae. albopictus* was susceptible to deltamethrin, and for permethrin the status was border line susceptibility (verification required). However, larval populations of both these mosquito species were susceptible to all three larvicides including malathion (1.0 mg/l), temephos (0.02 mg/l) and fenthion (0.05 mg/l) at much lower dosages than given diagnostic concentrations. The study results have direct relevance for benefit of the state dengue control programme in scaling up interventions and averting disease outbreaks and spread.

Vector-Borne Diseases

A study at CDRI, Lucknow explored the application of DNA-based tools for antimicrobial drug screening against *Plasmodium falciparum* and studies with modified (RPNI) medium. The findings revealed, that the MSF assay being a one-step method, and many times cheaper than the (3H) Hypoxanthine incorporation assay, is more convenient and suitable for bio-evaluation of antimalarial activity of new molecules, including synthetic and plant extracts.

A study at Osmania University undertook epidemiological, immunological and genetic studies in Lymphatic filariasis. The comparison of socioeconomic factors in endemic controls and Lymphatic filariasis patients revealed a significant variation with regards to household structure. A significant association of B blood group antigen with lymphatic filariasis was observed. The complement assay revealed that the differential capacity of function and binding of ‘S’ allele of C3 complement encoded protein may contribute to the increased predilection to lymphatic filariasis.

A study from Punjab University investigated the immune-prophylactic potential of 63 kDa and 70kDa genetic and protein vaccines against murine visceral Leishmaniasis. The same research group also successfully concluded another project to analyze the protective efficacy of recombinant 78 kDa antigen of *Leishmania donovani* in combination with two adjuvants, i.e., cationic liposomes or MPL-A against visceral leishmaniasis in BALB/c mice. The study proves that r78 in combination with suitable adjuvants is a potential vaccine candidate and may be instrumental in control of visceral leishmaniasis.

Another study from AIIMS, New Delhi aimed at elucidating the biochemical, immunological and genetic traits associated with the susceptibility and severe complications of falciparum malaria. Screening of patients from this region may help timely management of patients with *pf* malaria to prevent fatal end due to severe complications.

Viral Diagnostic Laboratory (VDL) Network

From its various experiences in handling epidemics due to viruses, an urgent need was felt to (i) strengthen infrastructure and capacity for handling viral diseases in the country in terms of early and correct diagnosis, (ii) development of tools to predict viral disease outbreaks beforehand, (iii) continuous monitoring and surveillance of existing as well as new viral strains

and (iv) handling viruses with a potential to be used as agents of bioterrorism. Surveillance on commonly occurring viral diseases can help Government in planning proper strategies for prevention and control of viral outbreaks. In view of this, ICMR took the initiative to establish facilities for the diagnosis of viral infections in all regions and states of the country in a Task Force mode for a period of five years, with a vision that eventually this programme will merge and synergize with activities of the DHR. During the reported period, DHR/ICMR established 5 new virus diagnostic laboratories in different states of the country:

- Two Regional labs have been approved to be established at PGIMER, Chandigarh and RMRC, Dibrugarh.
- Four State Level Labs have been established at Sher-i-Kashmir Institute of Medical Sciences, Srinagar, J & K, Indira Gandhi Medical College, Shimla, HP, BJ Medical College, Ahmedabad, Gujarat and NEIGRIHMS, Shillong, Meghalaya.
- Eight Medical College Level VDLs were established at Osmania Medical College, Hyderabad, Govt. Medical College, Jammu, Patna Medical College, Patna, IGGMC, Nagpur, S.N. Medical College, Jodhpur, Govt. Medical College, Amritsar, Pt. BD Sharma Post Graduate Institute of Medical Education & Research, Rohtak and MP Shah Medical College, Jamnagar, Gujarat.
- Total Expenditure incurred is 29.8 crores till end of 2013.

Viral Diseases

A project entitled “Role of Hepatitis E virus infection in acute viral hepatitis and fulminant hepatitis during pregnancy” was recently completed at Maulana Azad Medical College, New Delhi. Comparison was made to correlate HEV viral load with disease severity in acute viral hepatitis (AVH) and fulminant hepatic failure (FHF) in pregnant and non-pregnant women. Human placenta was found to be an extrahepatic site of replication of HEV.

A project entitled “Tracing the dynamics of host-virus interaction in different phases of e-antigen negative chronic hepatitis B infection” was completed at Institute of Post Graduate Medical Education and Research, Kolkata. A new subgenotype (D9) of HBV of genotype D, resulting from a novel recombination between genotypes D and C and carrying high frequency of cancer-related A1762T/ G1764A mutations within the genome, had been identified among chronic e-negative patients of Eastern India.

A project entitled “Hepatitis C Virus (HCV) infection: Prevalence, characterization, and health-related risk behavior in injecting drug users attending a de-addiction centre in northern India” was completed at Post Graduate Institute of Medical Education And Research (PGIMER), Chandigarh. The IDUs had higher risk behaviours than the NIDUs both in terms of injecting behavior but also other risk exposures such as sexual behavior (multiple partners; commercial sex workers; sex with strangers), tattoo/piercing of body, and blood transfusions. Injection of illicit drugs, especially with needle sharing at a young age was the

strongest predictor of acquiring HCV infection in the substance users.

Non Communicable Disease

Cancer Management Guidelines

A Task Force on review of cancer management guidelines has been initiated to review and understand the appropriateness of published literature on management of common cancers under Indian conditions.

Centre for Advanced Research on Environmental Health: Air Pollution

A total of 480 pregnant women and 850 adults were enrolled in Mother-Child (M-C) and Adult cohorts this year, bringing the total to 1083 pregnant women, 688 babies and 1200 adults for follow up. Permissions have been accorded to access the PICME data of the Government of Tamil Nadu which will allow important insights into using such existing databases for the current and future projects. GIS-based analyses have been initiated using relevant maps (procured from Survey of India) and software (Arc-GIS).

Diabetes

ICMR-Indian National Diabetes Study (ICMR-INDIAB)

The ICMR-INDIAB study (Phase I) has been completed and in the NE region two states Assam and Mizoram have been surveyed. The data analysis is ongoing.

Registry of People with Diabetes with Young Age at the Onset

The Task force project on, "Registry of People with Diabetes in India with Young Age at Onset," is continuing at eight centres with aim to understand magnitude of problem, disease pattern or types, geographic variation and incidence and prevalence rate of complications. The data sets from approximately 5,000 subjects have been collected which includes information on diabetes types prevalent, complications, types of treatment, etc. Draft report of phase I has been formulated. A majority of the subjects were with type 1 diabetes followed by type 2 diabetes. The neuropathy was reported as the commonest complication followed by retinopathy. Majority of the subjects were on insulin treatment. The phase II of the project was initiated in September 2012 and is ongoing at ten centres.

Diabetes-Genetic Susceptibility in the Asian Indian Population

The study identified methods and populations for the study of genetic susceptibility to type II diabetes in an Asian Indian population. Initially, the effort was directed at the development of methods for performance of a GWA study. However, this effort was refocused slightly on the basis of recent developments in the field of type 2 diabetes and the availability of new technology in a fast moving field. Through the UM-ICMR program a pilot project was completed utilizing the full complement of the new technology and available population. The project involved not only new technology (NGS), and an innovative procedure (pooling) for the sequencing of a large number of subjects (200) at the University of Minnesota, but also a significant recruitment effort at MDRF, India. The project was very successful with not only an excellent application and development of the technology for the project, but also finding an association between several genetic variants with early-onset type 2 diabetes.

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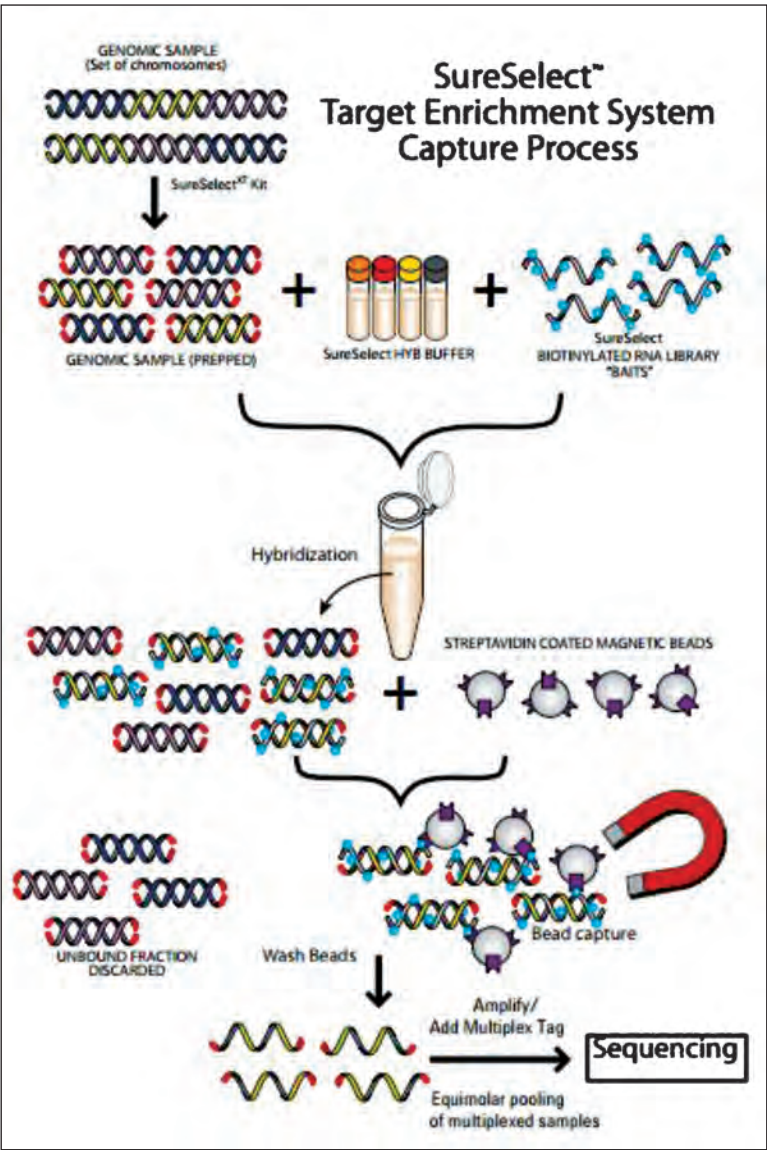
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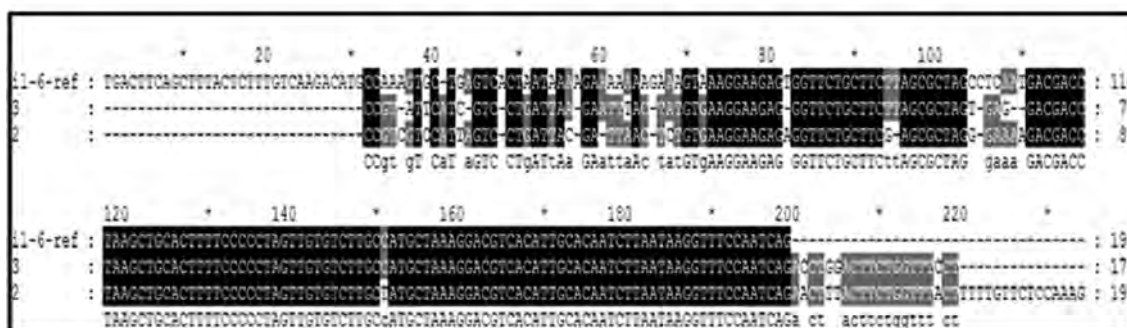
Sure Select Target Enrichment System Capture Process

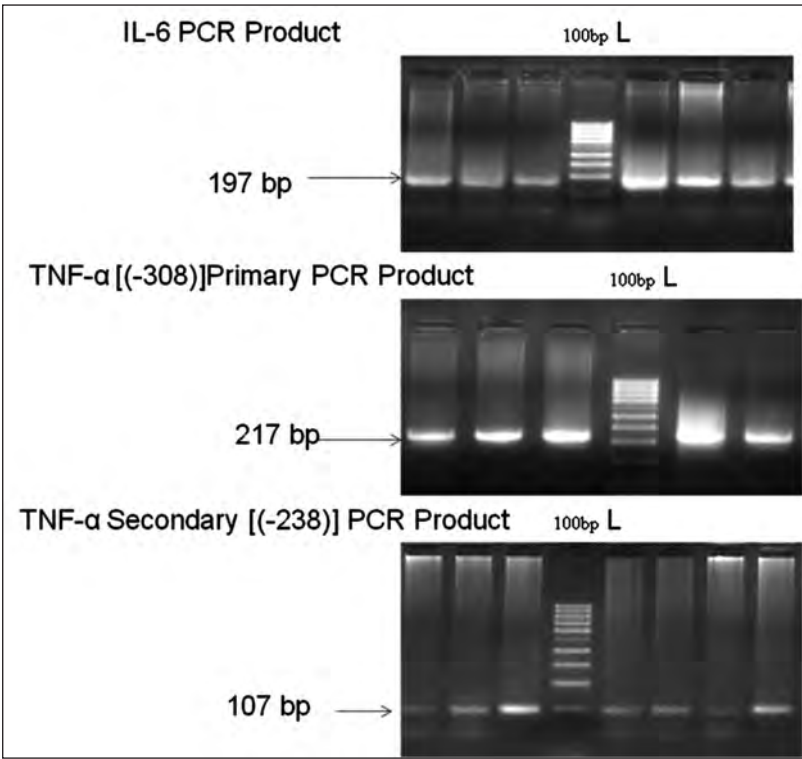
The scientists from MDRF received training in the various aspects of the project and received hands-on experience in the methods of DNA pooling, preparation for sequencing and data analysis. The pilot project was designed as a two-stage project.



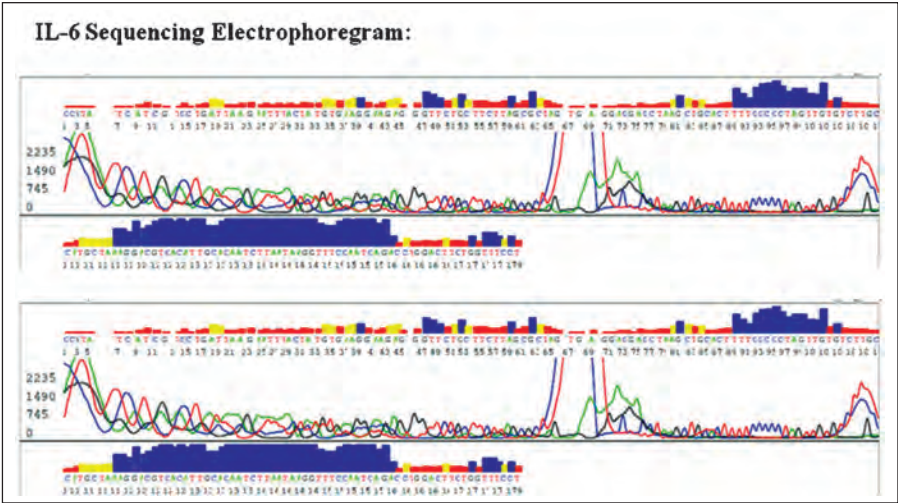
Illumina HiSeq 2000

Association of Obstructive Sleep Apnea (OSA) with Metabolic Syndrome, Insulin Resistance and TNF- α , IL-6 and ACE Gene Polymorphisms- Community-based Case-Control Study: 550 patients were screened with polysomnography studies. Of these, 450 patients (150 apnoeics and 300 non-apnoeics) were finally enrolled in the study. Apnoeics had significantly higher BMI ($p < 0.001$). The proportion of patients with diabetes mellitus and hypertension was not significantly different between two groups. ΔSaO_2 (basal minus arterial oxygen saturation) during sleep differed significantly between apnoeics and non-apnoeics ($p < 0.001$). Fasting blood sugar was found to be significantly different between apnoeics and non-apnoeics. Other variables of serum lipid profile (triglyceride, total cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL, HDL: total cholesterol ratio, LDL: total cholesterol ratio) did not differ between the two groups. Plasma insulin levels ($p < 0.004$), HOMA-IR (Homeostatic Model Assessment for insulin resistance) ($p < 0.002$), Interleukin-6 ($p < 0.001$) and TNF- α ($p < 0.001$) were significantly different between apnoeic and non-apnoeic groups. Serum angiotensin converting enzyme (SACE) levels were significantly lower in apnoeics ($p < 0.001$). G allelic frequency ($p < 0.001$) and GA genotype frequencies ($p < 0.001$) of TNF- α (-308 G/A) showed significant difference in apnoeic and non-apnoeic groups.





IL-6 reference sequence alignment



IL-6 Sequencing Electrophoregram

G allelic frequency of IL-6 gene in apneic group differed significantly as compared to non-apneic group. Analysis of angiotensin converting enzyme (ACE) (I/D) polymorphism did not show a significant difference between apneic and non-apneic groups. On multivariable logistic regression, male gender, age (taken as continuous variable), BMI, neck circumference and TNF-α GA genotype were independent predictors of OSA. OSA and atherosclerotic cardiovascular disease have several common risk factors. Previous studies have shown that OSA is a common public health problem in India; however, its awareness among public and practicing physicians is low. Untreated OSA is a huge social and economic burden because undiagnosed OSA, with or without symptoms, is associated with increased likelihood of hypertension, insulin resistance, and metabolic syndrome. This predisposes to consequences

such as stroke, myocardial infarction, and heart failure resulting in diminished quality of life. Study found that metabolic syndrome and insulin resistance are independently associated with OSA in the Indian population.

Genetic, Molecular and Biochemical studies of Post Transplant Diabetes Mellitus following treatment with Immunosuppressive Drugs: Study enrolled 201 non-diabetic end stage renal disease (ESRD) patients who received a renal transplant and were on immunosuppressive therapy were included. 76 % of the cases were males and 24% were females, both belonged to a similar age and weight range. All cases were maintained on CI, 41% of these were on CsA, while 59% on Tac. ABCB1 C3435T polymorphism (rs#1045642) showed 16.41% of CC, 43.28% of CT and 40.29% TT genotypes in renal transplant patients. Individuals with TT genotype showed high mean CsA drug level (1033.97 ± 284.37 ng/dl) in blood when compared to CC genotype (846.37 ± 310.17 ng/dl). Blood C2 levels and dose ratio was also significantly elevated ($p < 0.05$) in patients having TT genotype when compared to CC and CT genotypes. Renal transplant patients on Tac which were assessed for the same polymorphism showed that C2 levels altered with genotype with individuals TT genotype having high C2 levels / dose ratio (2.92 ± 1.70 ng/dl), when compared to the other genotypes ($p < 0.05$). The data indicates that ABCB1 T allele is inefficient for CI extrusion from intestine in a dose dependent manner, resulting in increased blood levels of both CsA and Tac. CYP3A5 A6986G polymorphism (rs#776746) evaluation in renal transplant patients showed that 23.88% had AA, 49.75% AG and 26.36% GG genotypes. Individuals having GG genotype showed increased CsA C2 levels in blood (1171 ± 319.02 ng/dl), which was significantly different from individuals with AA genotype ($p < 0.05$). Similarly GG genotype had high Tac blood levels (9.85 ± 3.71 ng/dl) and C2 levels/dose ratio (3.36 ± 1.51) compared to AA genotype. When the patients were grouped according to both ABCB1 and CYP3A5 genotypes there was a significant difference in both CsA and Tac drug levels/drug ratio, however, there was no significant difference between mean age, weight and drug dose between three genotypes. However, when the patients were grouped based on CsA blood drug levels into three categories, which are high, intermediate and low. It was observed that 50% of individuals had increased drug levels and 5% decreased, while 45% were in the recommended drug level range. The ABCB1 T allele and CYP3A5 G allele appear to be responsible for the high blood levels in 92% of the cases with >1000 ng/dl CsA, where as none of the cases with low blood levels (<500 ng/dl) had the TT and GG genotypes. Similarly patients on Tac were categorized into 3 groups based on >10 , 4 to 10 and <4 ng/dl of the blood drug level. It was observed that 23% of individuals had increased drug levels and 8% decreased, while 68% were in recommended drug level range. The ABCB1 T allele and CYP3A5 G allele were present in higher percentage of the cases with >10 ng/dl Tac levels but the striking absence of TT and GG genotype seen with CsA was not observed here. When gene-gene interaction was evaluated it was observed that ABCB1TT and CYP3A5GG genotypes showed the highest blood levels of Tac, however, in case of CsA CYP3A5GG genotype is responsible for higher blood levels, irrespective of the ABCB1 genotype.

Study of Factors Influencing Host Defense against Infection in Diabetic Foot with Special Reference to vitamin D Deficiency: Sixty-two diabetic foot cases (male: female ratio = 42:20) were included in this study. The mean age of cases was $52.4 (\pm 11.6)$ years. The duration of diabetes ranged from less than a year to 20 years with a mean duration of $5.9 (\pm 5.5)$ years. The duration of diabetic foot ulcer varied from five days to one year and the cases enrolled were of Wagner's grade 2 to 4. Among 62 cases, 27 (43.5%) had mono-microbial infection, 22 (35.5%) had poly-microbial infection, and 13 (21%) had sterile culture. Altogether 82 bacteria were isolated from 49 cases. Among 82 bacterial isolates, 56 (68.3%)

were Gram negative while 26 (31.7%) were Gram-positive bacteria. *Escherichia coli* was the most common pathogen isolated followed by *Staphylococcus aureus*. Other commonly isolated bacteria were *Pseudomonas aeruginosa*, *Streptococci*, *Proteus mirabilis*, *Citrobacter* sp., *Proteus vulgaris*, *Klebsiella pneumoniae*, *Bacillus* sp., *Morganella* sp., *Acinetobacter* sp., *Enterococcus faecalis*, *Klebsiella oxytoca*, *Enterobacter aerogenes*, Coagulase –ve Staph, *Pneumococcus*, *Enterococci*. Co-infection with *Candida* spp. was also found in one case with Gram-negative infection (*E. coli*). In another case with a sterile culture report, the wound was foul smelling and full of maggots. Gram-negative infection was most common (74%) in mono-microbial infections, whereas both Gram-positive and Gram-negative were high (63.6%) in cases with poly-microbial infection. Diabetic foot patients with poly-microbial infection had a comparatively higher total leukocyte count ($16,928 \pm 9,642$ versus $14,593 \pm 6,687$; $p = 0.4$) and significantly lower haemoglobin (7.9 ± 2.4 versus 9.2 ± 2.2 ; $p = 0.02$) than the mono-microbial infections, whereas HbA1C in both the groups was similar (9.9% versus 9.5%; $p = 0.1$). Patients infected with Gram-negative bacteria also had significantly lower Hb (8.5 ± 1.9 versus 11.1 ± 2.2 ; $p = 0.01$), higher TLC (16280 ± 6806 versus 9771 ± 3243 ; $p = 0.03$), and a higher percentage of neutrophils (77 versus 67; $p = 0.03$) than those infected with Gram-positive bacteria. Patients infected with both Gram-positive and Gram-negative bacteria had significantly lower Hb (7.6 ± 3.2 versus 11.1 ± 2.2 ; $p = 0.003$) compared to those infected with only Gram-positive microbes; however, the difference was insignificant when compared to patients infected with only Gram-negative bacteria. On the other hand, diabetic foot patients with sterile culture reports were clinically found to have some evidence of persistent infection. Their wounds were foul-smelling and they had raised TLC (12233 ± 3469 cells/mm³), lower mean hemoglobin (9.5 ± 1.8 mg/dl), and HbA1C of 9.5%. The mean age, duration of diabetes and duration of diabetic foot of the cases were $52.08(\pm 9.12)$ years, $7.91(\pm 6.62)$ years and $2.11(\pm 3.64)$ months respectively. Among 56 cases, 7 (13.4%) were culture sterile and 19 (33.9%) were PCR negative for all the three selected genera of anaerobes. Thirty two (57.1%) were aerobic and anaerobic positive, 17 (30.4%) were aerobic positive and anaerobic negative, 5 (8.9%) aerobic negative and anaerobic positive, and 2 (3.6%) were negative for both. Only 5 patients were culture positive for anaerobes. Altogether 55 aerobic and 61 anaerobic bacteria were identified. *E.coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Citrobacter freundii* and *Micrococcus* sp. were commonly isolated aerobes whereas prevalence of anaerobic isolates were *Clostridium* [28 (45.9%)] *Bacteroides* [19 (31.1%)] and *Peptostreptococcus* [14 (23%)].

Conventional culture technique fails to identify anaerobic infection in diabetic foot. Analysis of anaerobic infection in diabetic foot is possible by molecular technique like PCR. This may have implication in diabetic foot infection.

Indigenous, and Affordable Glucose Sensing Device Development Supported by ICMR:

ICMR supported biomedical and engineering institutions for development of Glucose sensing device which is indigenously developed so that cost can be made affordable. The technology is imported currently, hence to make large screening of diabetes drive cost effective. As a result of these efforts two such technologies are already launched on 13.01.2014.

“QuickcheQ”- Blood glucose sensing system under the project “Developing a Low cost Point of Care (POC) device for detection of blood glucose levels” by a senior faculty at, BITS-Pilani, Hyderabad campus. Two different modes of measurement have been standardized in the laboratory. This equipment works on “Optical sensing of chromogenic end point”. With the advent of microfluidics and miniaturized platforms point-of-care devices are becoming

increasingly realizable in replacing conventional laboratory-based analysis. The small sample volume employed in microscale assay techniques not only increase patient comfort, convenience, and compliance by minimizing the amount of blood required to be drawn, but also allow the analysis to be carried out precisely at a fraction of the present cost and time.

“**Suchek**” is an indigenous, accurate, low-cost glucometer developed by Biosense Technologies Pvt Ltd in collaboration with Indian Institute of Technology, Bombay supported by the Indian Council of Medical Research. Suchek reagent strips are as accurate as conventional glucometers, at a fraction of the price. Along with the glucometer, the companion Suchek mobile application helps you save, trend and analyze blood glucose levels at an individual level or track response to treatment at a Unity. This instrument is a Reflectance photometer working on Colorimetric Transduction.

Environment

Ocular Health vis-à-vis Climatic Changes

Multicentric Collaborative study on impact of Global warming and ultra violet radiation (UVR) exposure on ocular health in India is ongoing at AIIMS New Delhi, National Physical Laboratory, New Delhi, Guwahati and Hyderabad to study the effect of environmental factors and UVA & B radiation on eye diseases. Separate measurements at Delhi showed that of the total UV flux received at surface, the UVA contribution is about 97-99% and the UVB flux constitutes only 1-3%.

Neurological Sciences

Population Based Urban Stroke Registry

Out of 3126 patients identified in the year 2012-2013, 1497 were from Ludhiana city. The annual incidence rate is 140/100,000 (95% confidence interval: 132.90, 147.09). The age adjusted incidence rate based on WHO standard world population is 181.67/100,000 (95% confidence interval (CI): 172.44-190.89). The case fatality rate was 12.2%. 3126 first ever stroke patients were identified. The mean age of the stroke cases was 58.9 ± 15 years. Majority of patients 66% had ischemic stroke. Limb weakness was the common presenting symptom in these patients. Hypertension was the most common risk factor. In 833 patients, disability assessment using mRS was done at the time of discharge and 410 (49%) patients had a poor outcome (mRS > 2) at the time of discharge and 7.2% died when followed up after 28 days of the acute event.

Population Based Rural Stroke Registry

The research on “Establishment of population based rural stroke registry - A pilot study was initiated on 1 March 2012 in a population of 293393 in 400 villages of Chinthamani Taluk, Chikkaballapur District, Karnataka. Data of first ever stroke cases reported during six months of recruitment indicates incidence of first ever stroke to be 55.9 per lakh population. 68% of the cases from the community were male. Only 8.5% of the cases were reported from hospitals/health centers/practitioners of the area. Place of first contact to project team was home in 87.8% instances and 12.2% constituted those below 45 years. Only 34.2% had CT or MRI or both reports. Allopathy, Traditional medicine, Ayurveda constituted first contacts of care in path way of care. Interestingly 78 out of 82 cases had approached traditional healers too. Lack of money (12.7%), symptoms being very serious (34.9%), lack of transportation (9.5%), no male member (decision maker) (14.3%) feeling that it is not worth spending time/money (11.1%), no faith in allopathy (23.8%), faith in other systems (11.1%) and other

causes (15.9%) constituted reasons for not seeking health care within 4 hours of stroke. Important risk factors were hypertension, smoking, other forms of tobacco, alcohol, diabetes mellitus and family history of stroke.

Obesity and Metabolic Syndrome

Under the MoU of ICMR with the Canadian Institutes of Health Research (CIHR), two proposals have been funded and are ongoing on the collaboration on Childhood Obesity.

- **Understanding the Determinants of Adiposity among Newborns of Indian Ancestry in Canada and India: The South Asian Birth Cohort**

Among three birth cohorts: rural India, urban India, and S. Asian from urban Canada, the objectives of this study are to understand the effect of diverse environments on the development of adiposity among newborns and the growing offspring during the first three years of age. Rural pregnant women weighed lesser and had lower BMI at recruitment compared to the urban women. No significant differences found in the anthropometric measurements among the groups. The rural women had lower fat free mass as compared to the urban pregnant women.

- **Overweight and Obesity in Asian Indian children in India and Canada: Multi-level Determinants, Functional Consequences and Novel Mechanisms**

The overall goals of this school-based cross-sectional study are to describe the differences in body composition of Indian children and youth in 3 distinct settings which represent diverse environments: rural India, urban India and urban Canada, and to identify characteristics at the individual, family, school and community level that are associated with adiposity and its metabolic consequences. There were 13.8% in urban and 7.1% rural overweight/obese females and 16.1% urban and 6.1% rural overweight/obese males. Information on perceive barriers and food consumption were also studied.

Oncology

National Cancer Registry Programme (NCRP)

The Twenty Eighth Population Based Cancer Registry was commenced at Nizam's Institute of Medical Sciences, Hyderabad. A project on "Development of Stroke Registry in India" was also commenced. Fifty one centres across the country have so far registered under this project. The web page on National Stroke Registry Programme on the NCDIR website facilitates the centres to register under this project and centres can download the Population Based Stroke Registry Core Form from this web site.

Under the project on "Development of An Atlas of Cancer in Punjab State", training cum review workshops were held at Shri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, at Jalandhar and at Mohan Dai Oswal Multispeciality and Cancer Hospital, Ludhiana. Another conference / meeting was held in Ludhiana exclusively for all the Civil Surgeons to request them to proactively and personally visit the hospitals / laboratories under their jurisdiction and ensure that information on all cancer cases registered and / or diagnosed in the specified hospitals are abstracted in the prescribed form and transmitted on-line. Registration forms were sent to the empanelled hospitals in Punjab State which had not registered earlier. Punjab Cancer website has been added with a map of Punjab with the title "Online and Dynamic E-monitoring of Data Capture - Coverage of Cases". With the click on a district on the map, more specific district wise tables are dynamically generated. As of now there are 154 centres that have registered (141 centres from Punjab State, 3 from

Chandigarh 2 from Haryana State and 1 from Jammu & Kashmir, 4 from Delhi State and 3 from Rajasthan).

With the development of software modules, 61 centres have started using the Hospital Based Cancer Registry Data Management Programme. The number of Centers and data sets under the Network of the NCRP as of October 2013 is given below:

Sl. No.	Type	Centres		Data Sets
1	PBCRs	28	260	27
2	HBCRs	07		07
3	POCSS (incl. 5 HBCRs)	18		47
4	Cancer atlas NE	17		17
5	HBCR-DM-SW	92(61)		41
6	Punjab Cancer Atlas	154		60
7	Kerala Cancer Atlas	(8)		0
	Total	227		199

Ophthalmology

Study on Anophthalmia/Microphthalmia

A Task Force Project on epidemiology of anophthalmia and/or microphthalmia in children aged 0-5 years in selected districts of Bihar has been initiated from 1st March 2011 for a period of 2 years. In phase I identification and mapping of cases of Anophthalmia and/or Microphthalmia from the primary health centres and subcentres of the districts of Bhojpur, Buxar and Rohtash has been done. The findings reports so far show only fever due to some infection and night blindness as significant factor. Preliminary analysis in these subjects has revealed that 78% were reported from Bhojpur district. It was found that not attending ANC unit had an odds ratio of 1.95 with a 95% CI of (0.9476 to 4.0475, $p=0.06$). Fever had an odds ratio of 6.1 (95% CI (2.37-15.57, $p=0.002$) and Night-blindness had an odds ratio of 30.76 (95% CI 3.96-238.65, $p=0.001$). Both these factors have a positive association with the disease. Analysis of trace elements revealed that more cases were proportionately deficient for zinc as compared to controls (Cases -72%, Controls- 50%).

Research on Chronic Diseases

Oral Precancer

The project "A study on association of Oral Precancer with use of Pan Masala" aims to generate evidence on the health effects of use of Plain Pan Masala and establish the role of plain pan Masala in occurrence of oral precancer. The study was conducted in Lucknow city (Cis Gomati area), Uttar Pradesh in which 4,53,823 persons were contacted, and the final analysis was done on 4,02,669 persons (males and females aged 15 years and above). There were 108236 persons who reported using tobacco and non-tobacco arecanut products, of which 1.1% were users of plain pan masala. The prevalence of oral cancerous lesions was found in 64 per 1000 users. The odds ratio for oral precancer for users of plain pan masala was 18.56 (95% CI 15.52-22.20).

The project "Development of a Model for Strengthening of existing health system to address Non Communicable Diseases in India" is ongoing at 3 sites Ballabgarh, St. Stephen's Hospital Delhi and AHEAD, Delhi. The project aims at assessing the existing health system's ability to carry out NCD screening, prevention and control activities. The trained lay health workers

in all the agencies carried out NCD Risk Factor assessment of the adult members of the Families allocated to them and counseled them to change risk behaviours. The workers also carried out a modified form of Community Health Environmental Scan Survey. Retraining of all lay health workers was carried out and their knowledge was reassessed. The workers were also trained to develop case studies from the families among whom they had conducted risk assessment and counseled.

Reproductive and Child Health

Adolescent Health

- Determining Prevalence of PCOS among Adolescents and Young Girls in Mumbai:** Polycystic Ovarian Syndrome is slowly becoming a public health problem among girls with its onset in adolescent age. Using a systematic multistage random sampling method, 1212 young girls and women belonging to lower middle class were enrolled. Adolescent girls who had attained menarche for not less than 2 years, who were unmarried and were willing to participate in the study were included. To assess symptoms of PCOS an instrument containing sections on demographics, menstrual history, history of acne, hirsutism, obesity, any skin discoloration, any menstrual problems in mothers/siblings, sexual history and any treatment sought for the above complaints, was used. All enrolled participants were required to undergo clinical examination by a doctor, biochemical investigations, and abdominal ultrasound performed by a trained gynaecologist. At present there are three different criteria followed for diagnosis of PCOS – the NIH criteria, Rotterdam criteria, and the AES criteria (2). Diagnosis of PCOS after ruling out Differential diagnosis based on these criteria is summarized below:

Diagnostic Criteria for PCO on Ultrasound

The PCO should have 12 or more follicles measuring 2–9 mm in diameter with or without increased ovarian volume ($>10\text{ cm}^3$).

Abdominal ultrasound of a participant with bilateral PCO



PCO was seen in 19.7% (118) cases, in 18.5% (111) both enlarged ovary/s and PCO picture was seen, and 6% (36) cases had only enlarged ovary/s. Ovarian cyst (simple/ hemorrhagic/ complex) was seen in 6.5% (39) cases

PCOS prevalence among 600 subjects that fulfilled the diagnostic requirements was estimated to be 24% by Rotterdam and 12.7% by AES criteria. Only 5 cases of hypothyroidism were diagnosed and ruled out as differential diagnosis. Lean PCOS were most common

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(73.6%). Phenotype J (oligo anovulation and PCO on USG) was found among 76.4% followed by I (biochemical hyperandrogenism and PCO on USG) among 28.5%, H (clinical hyperandrogenism and PCO on USG) among 27% and D (biochemical hyperandrogenism and oligo anovulation) among 25.7% of PCOS cases. The study showed high prevalence of PCOs among lean adolescents. The Project Review Group (PRG) recommended forming a Task Force with multispeciality expertise and conducting multi centric studies in rural and affluent urban population on infertility and treatment aspects.

Child Health

- **Causes of perinatal deaths:** 477 respondents experiencing events were identified till August 2013, 305 were still births and 172 were early neonatal death. Major causes of deaths were unexplained asphyxia(114), prematurity(100), specific infant condition(105).
- **Surveillance study in Child health for estimating burden of disease:** A multicenter study is ongoing in six secondary level hospitals in six states to identify etiological agents causing neonatal sepsis and their antibiogram. A total of 1524 cases of suspected sepsis have been enrolled out of which 411 were culture positive. Major organisms identified were Staphylococcus aureus, Klebsiella, CONS, E.coli and NFGNB(non fermenting gram negative bacteria).
- An attempt is being made **to identify and characterize the receptor for yersiniabactin** in Klebsiella pneumoniae 43816 The presence of high pathogenicity island was confirmed on the basis of LC-MS analysis as well as by PCR that identified *fyuA* gene. These results showed that this strain has the ability to produce siderophore, yersiniabactin. In order to identify the yersiniabactin receptor, the organism was grown in presence and absence of iron and the outer membrane proteins isolated from these organisms were separated on SDS-PAGE gel. A 75 kDa protein was identified in the outer membrane proteins of cells grown in iron deprived medium. As per literature this might be the yersiniabactin receptor and hence the attempts are being made now to purify and identify this protein so as to confirm that it is the yersinabactin receptor.
- **Acute Lower Respiratory Infection (ALRI):** A novel multiplex real time PCR assay using Taqman chemistry was employed in a study to determine the viral aetiological agents causing ALRI among children under 5 years of age who presented to the tertiary care hospital of Christian Medical College, Vellore, South India. A total of 734 patients were recruited on this study. In addition to collecting respiratory samples from the recruited subjects, we also performed a detailed clinical evaluation and obtained information on clinical course and outcome of the illness. Samples were screened by the multiplex realtime PCR assay and it was found that a viral agent was detected in about 71% of samples. Mono-infection were the most common (55%) followed by dual- (13.3%) and triple infections (2.0%). The most common agents detected were RSV-A (18%), Rhinovirus (16.0%), Adenovirus and Metapneumovirus (12.3%), respectively. Dual and triple infection resulted in a more severe infection and resulted in a poorer outcome of illness. **Conclusion:** Respiratory viral infections cause a significant proportion of ALRI in this setting and presence of multiple agents results in more symptomatic disease and poorer outcomes. This study outlines the need for more comprehensive studies on viral ALRI and the development and testing of vaccines for viral agents should be accorded high priority to enable reduction of disease burden among children under 5 years of age.

- **Vitamin D Supplementation for Severe Pneumonia in Under-five Children:** A Double Blind, Randomized Placebo Controlled trial is ongoing to evaluate efficacy of single mega-dose of vitamin D supplementation on time to resolution of severe pneumonia and its effect on prevention of episodes of pneumonia in next six months. Children aged between 6 months to 5 years presenting to the Pediatric Emergency Department or outpatient department of GTB hospital, Delhi with a clinical diagnosis of WHO/ IMCI defined 'severe pneumonia. Ninety one cases have been enrolled till March 2013. Study is in progress.
- A study is ongoing to evaluate the role of neurobiochemical markers in diagnosis and prediction of outcome of pediatric meningitis in children. On comparing the cytokine markers, significant differences were observed in the levels of S-100B on Day 1 and Interleukin-6 on Day 1 and 5 in the bacterial & aseptic meningitis group. In addition, the preliminary follow –up data revealed that the levels of Neuron specific enolase and S-100 recorded on Day1 had a role in predicting the outcome and neurological status at discharge.

Infertility and Assisted Reproductive Technologies

The draft Assisted Reproductive Technology (ART) (Regulation) Bill & Regulations – 2013:

Based on the recommendations of the Ministry of Law and Justice, Govt. of India the draft ART (Regulation) Bill and draft Cabinet Note has been circulated to all the concerned Ministries and Departments of Govt. of India for their comments. The comments from all the concerned Ministries and Departments of the Govt. of India have been received and the response of the ICMR/DHR has been prepared which will be sent to the Ministry of Law and Justice for their consideration.

National Registry of ART Clinics and Banks in India: About 1272 ART Clinics and Banks have been identified under the National Registry through various sources. Out of that 643 ART Clinics and 108 ART Banks (751) have confirmed their contact details and about their task & work as per the ART Bill. Out of 643 ART Clinics, 521 ART Clinics have submitted their information on minimum infrastructure facilities, trained manpower and procedures being under taken at these ART Clinics through a prescribed proforma. Out of 521 ART Clinics, 180 ART Clinics have the got the facilities as per the provision of the ART Bill and hence, has been enrolled under the National Registry. The detailed information about the 180 enrolled ART Clinics is available on ICMR Website.

Other interventions for Neonatal and Child Survival

- **Distribution and management system of child survival interventions:** A study is ongoing to describe the existing procurement, distribution and management system of child survival interventions namely zinc dispersible tablets, IFA tablets/liquid and Vitamin A supplements under Diarrheal Disease Control Programme, NACP and NP-PNB programmes in Uttar Pradesh, Maharashtra, Himachal Pradesh, Kerala and Rajasthan states of India, identify bottlenecks and suggest optional measures to overcome the identified problems. Preliminary findings indicate that GOI supply of sub center kit A, IFA tablets, zinc suspension varied among the states, there was delay in supply, variation in quantity of supply, and inadequate supply of IFA were received by the states. Translation potential: The findings will help in identifying bottlenecks and plan/ improve strategy to bring improvement in supply management system.

Reproductive Health in Adults

Expanding Contraceptive Choices for Men and Women

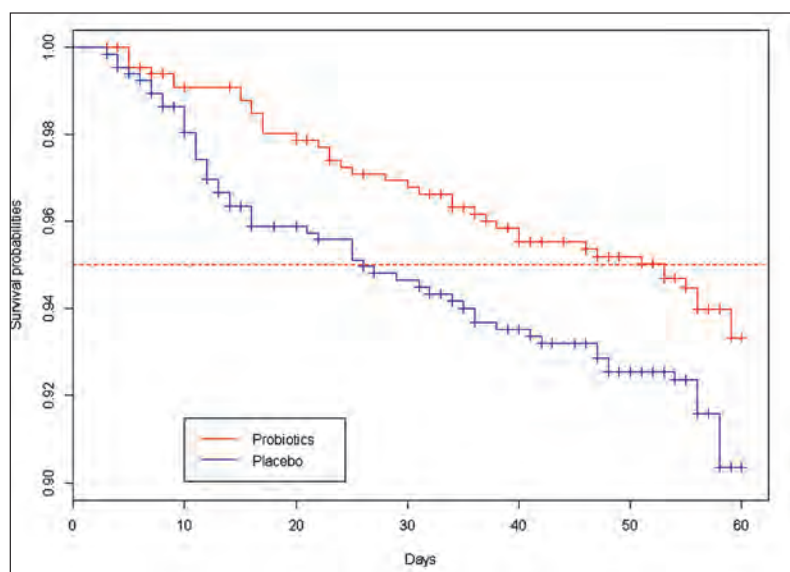
Phase-III Clinical Trial with an Intravasal Injectable Male Contraceptive – RISUG®: A Phase-III Clinical Trial is going on at five centers in the Country and few more centres are in process of inclusion under the Trial. Total around 133 subjects have received RISUG injection and all these subjects have been followed for their efficacy and safety. No side effects have been noticed in any of the subjects post RISUG injection. All subjects are maintaining the clinical efficacy of the drug. A new prototype of RISUG Syringe which was developed and approved by the Monitoring Committee has been sent to participating centers for use on new subjects. The centers have initiated enrolling new subjects and started using the new syringe.

Evaluation of a Progesterone Vaginal Ring (PVR) as a New Contraceptive Option in India: The results of this ongoing non-randomised comparative study at 20 sites with PVR (progesterone vaginal ring) as a user control method and CuT 380A IUCD as a provider control method and a comparator in the study which is available in the National Family Welfare Programme (NFWP) indicates that the relative acceptability of PVR and CuT 380A (T-Care) was 5% and 4% respectively when these methods were offered through an informed choice in stringent clinical trial settings. PVR is said to act by prolongation of lactation amenorrhoea, it is therefore necessary for women to continue breast feeding with minimum of 4 feeds per day to ensure contraceptive efficacy of PVR. The profile of enrolled women indicates that majority of the acceptors were primi-parous and the last pregnancy outcome was normal delivery. At enrolment which was 6-9 weeks post delivery, more that 75% women were in lactational amonorrhea and it was reassuring to note that women with more than one living child, majority (>80%) of them gave history of previous child being breastfed. Of the 458 and 291 PVR and CuT users respectively enrolled till date have been observed for a total of 3266 and 2547 woman months of use and 199 and 165 women have completed 9 months of use giving a continuation rate of 65.5% and 85.4% with PVR and IUCD respectively. One pregnancy /method failure has been reported with PVR till date. CuT 380A IUCD being a provider controlled method as compared to PVR which is a user controlled method; it was observed that use related discontinuations including ring expulsion were more with PVR and discontinuations due to menstrual problems was more in the CuT IUCD group especially in the initial 3 months of use. User acceptability indicated that majority of the PVR users found the method easy to use and women in both groups were satisfied with the method they were using.

Role of Probiotics in Child Health

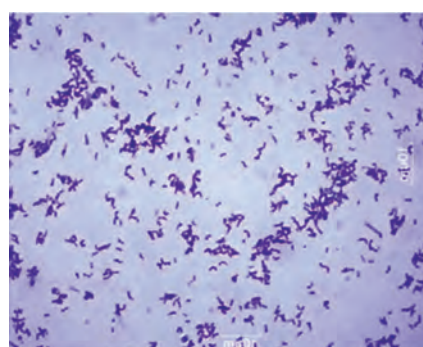
- A multicentre randomised, double-blind, placebo-controlled trial involving LBW infants weighing 1500 - 2500 grams was initiated to find out the efficacy of probiotics VSl#3, in preventing neonatal sepsis. Eligible infants were enrolled in the hospitals and randomly assigned at 3 days of age to receive either daily oral probiotic (#VSL3) or placebo for 30 days. The subjects were followed up in the community for a period of two months. The primary outcome was possible serious bacterial infection as per Integrated Management of Neonatal Childhood Illnesses (IMNCCI) algorithm, diagnosed by the field workers/ physicians.
- A significant reduction in the risk of PSBI (RR 0.29; 95% CI 0.10, 0.84) was observed among infants with birth weights 1.5-1.99 Kg in this study along with a non significant 21% reduction in the overall risk of possible serious bacterial infection (PSBI) in the probiotics group (RR 0.79; 95% CI 0.56, 1.03) in intention-to-treat analysis. Probiotics

intervention reduced the need for hospitalization (29 infants in the probiotics and 44 in the placebo arm ($p=0.038$)) and mean number of days of hospitalization (4.6 ± 4.4 in the probiotics, versus 6.9 ± 5.6 ($p<0.0001$) in the placebo arm. The Kaplan Meier survival analysis showed the onset PSBI in 10 % of study subjects in the probiotic arm on 40th day as compared to 25th day in the control arm ($p=0.063$). The results show a significant reduction in PSBI rates in Probiotics group among infants weighing 1.5-1.99 Kg. A larger study with better outcome measures is being planned.



Kaplan-Meier Survival Curve for difference between event rates in probiotics and placebo groups

- **Studies on identification of *Bifidobacteria* in Breast Milk of Indian Women by various Molecular Tools and their Bioproducts:** The study aims to isolate and identify Bifidobacteria in human milks of Indian origin, and to Bio-prospect Bifido bacterial species which can be further employed as probiotics.
- During the period under study a total of 60 breast milk samples were collected from lactating women from Gandhi Hospital, Secundrabad. The collected milk samples were subjected to microbiological investigations for the isolation and identification of bifidobacterial sps apart from conventional techniques we have established specific Biochemical test i.e. Fructose -6-Phosphate Phospho Ketolase (F6PPK) for the identification of Genus .
- We have also established and standardized the PCR protocol for rapid identification of this species.



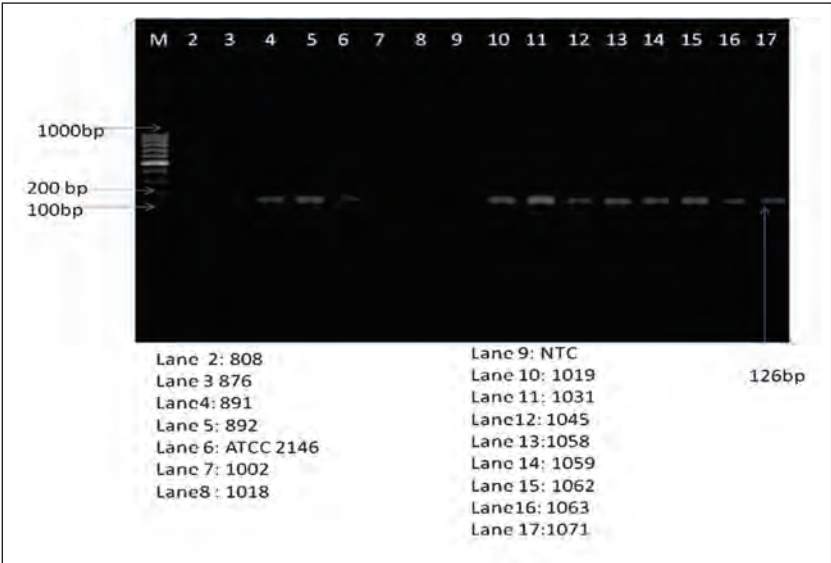
Photograph showing pure culture of Bifido bacterium isolated from human Breast milk



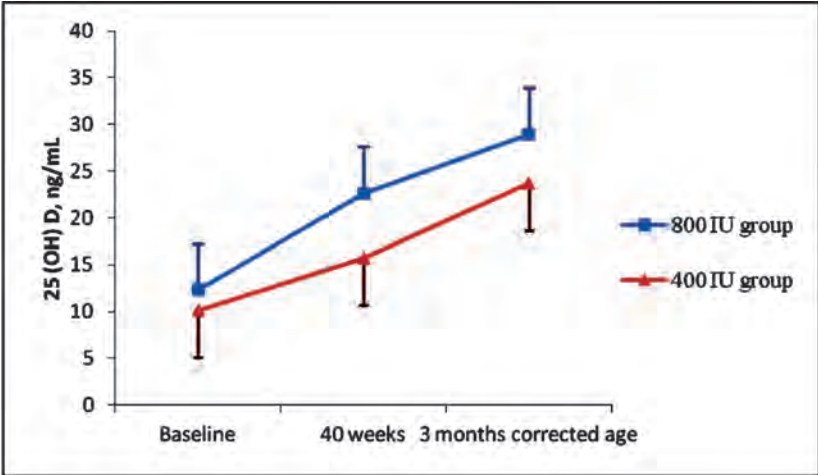
Plate showing confirmation of Bifido bacterial genus by F6PPK test indicated by brick red colors.

- Center for Advanced Research for Newborn Health** was established to generate quality evidence of clinical/programme relevance on key neonatal health issues. A neonatal sepsis reference centre/registry has been developed. Molecular epidemiology study of bacterial isolates from participating centers and their antimicrobial resistance pattern are being studied. Analysis of data from 9372 inborn neonates (3 sites) and 1097 extramural infants (one site) showed that, about 16% of the enrolled infants (intramural sites) had at least one episode of sepsis – culture positive and/or culture negative – during the initial hospital stay. The proportion of infants with sepsis was much higher in the outborn neonates (62.2%). The rates were higher in VLBW infants in both the intramural and extramural sites. Culture positive sepsis rates were lower in both intramural and extramural study sites - it contributed to about 40% of any sepsis among the intramural infants and about 22% in the outborn neonates. Any sepsis contributed to nearly a quarter of total deaths in the inborn units; whereas in the outborn unit, it accounted for more than half of total deaths. Among the intramural neonates, the most common organisms isolated were *Klebsiella* (135; 19%), *Acinetobacter* (125; 18%), coagulase negative staphylococci (110; 15%), *Staphylococcus aureus* (101; 14%), and *E coli* (96; 13%); among the outborn neonates, *Candida* was found to be predominant organism causing sepsis. Coagulase negative staphylococci, *Klebsiella* and *Acinetobacter* were the commonest bacterial pathogens. Majority of the CoNS isolates from both intramural and extramural sites were resistant to methicillin; in contrast, only about one-third of the isolates of *Staphylococcus aureus* were methicillin resistant. None of the Gram positive organisms were resistant to vancomycin. Among Gram-negative organisms, *Acinetobacter* showed an alarmingly high degree of resistance to all the commonly used antibiotics. Most isolates of *Klebsiella* from both the intra- and extramural centers showed high resistance to cefotaxime, gentamycin and piperacillin-tazobactam; the second line antibiotics (meropenem and cefoperazone-sulbactam) also showed up significant resistance

The molecular mechanisms of antimicrobial resistance done in 47 strains including those who were sensitive to carbapenems by phenotypic methods were found to harbor the NDM-1 gene (Fig.).



Gel picture showing PCR amplification of NDM-1 gene of Klebsiella strains



Vitamin D levels at different time points

Centre for Advanced Research in Evidence Based Child Health: The broad objectives of the centre are to conduct systematic reviews in order to answer specific research questions related to child health, to build capacity in chosen peripheral centres (NEIGRIMS Shillong, RPGMC Tanda) to conduct systematic reviews and to promote practice and teaching of Evidence Based Health Care in children and to analyze and interpret information from systematic reviews for Evidence informed policies for child health. (Fig.) The centre has completed two systematic reviews: 1) Effectiveness of pneumococcal conjugate vaccine for pneumococcal disease in children under 5 years of age in India: A Systematic Review, 2) Effectiveness of Hib conjugate vaccine in reducing mortality in under 5 years of age: A Systematic Review. Use of I/M gentamicin in management of neonatal sepsis in community: Apart from these reviews the centre has finished two additional reviews on the disease burden.

The centre has conducted five capacity building courses and workshops “How to practise Evidence Based Child Health and “Protocol Development and Review Completion during the first year of existence at Satellite centres in Shillong, Tanda, Shimla and Chandigarh.

Child health in tribal areas: Most under-five deaths takes place in children from tribal areas. To improve health of children in tribal areas concept proposals were invited . Of the 66 concept proposals received 15 were approved for developing into full length proposals, eleven of them have been approved in principle with suggestion for modification.

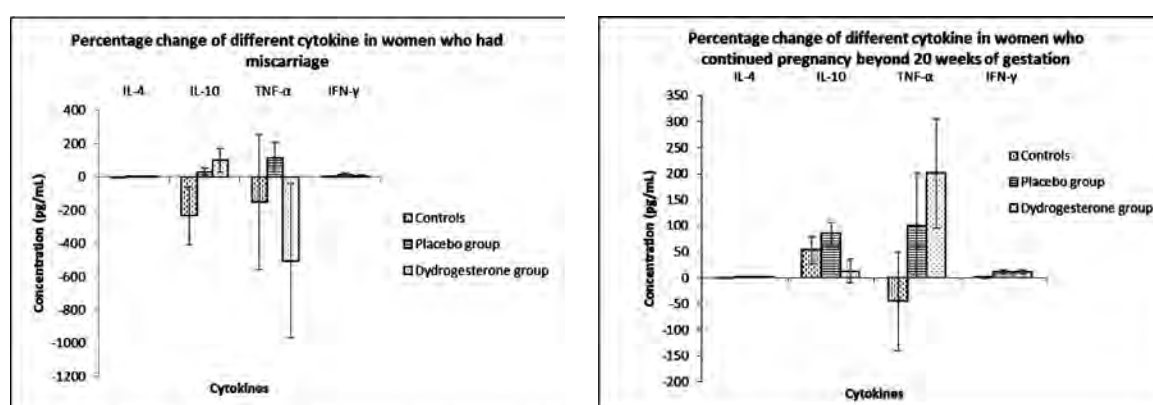
Capacity building for health research in North Eastern States: Seed Grant scheme is ongoing for North east states in which a grant upto Rs. 10,00,000 is provided to young and mid level faculties to build capacity for undertaking research activities to address local health problems. During the year a total of 18 projects have been awarded.

Studies on Pediatric HIV

- Study to assess the effect of highly active antiretroviral therapy on the B cell sub populations (immature transitional B cells, exhausted B cells, activated mature B cells and memory B cells) in HIV-1 infected children of age less than 5 years is ongoing at all India Institute of Medical Sciences. 14 children HIV infected (mean age: 2.5 years) have been enrolled till September 2013 and followed up as per protocol. The mean CD4% in these patients is $19.4 \pm 9\%$. The mean CD4 count in these patients is 1316.5 cells/ μL The mean CD19 count in these patients is 966 cell/ μL HIV-1 viral load quantitation has been done for 11 children. The mean viral load in these children at enrollment was 1001050 copies/mL
- A study is being conducted on pneumonia prevention in families affected by HIV. A prospective interventional study looking at the impact of the Hib conjugate vaccine on nasopharyngeal colonization in children and their mothers affected by HIV is in progress. One hundred and twenty children with HIV infection have been inoculated with two doses of the Hib vaccine. Eighty child and mother pairs have completed six month follow up. There has been a drop in baseline carriage with Hib following immunization in the children and also in their mothers. It is being observed that HIV infected children do not have immunity to Hib at baseline, but mount an immune response following two doses of the vaccine.

Women's Health

- **Recurrent pregnancy loss:** A double-blind, prospective randomized, placebo-controlled study was carried out to study the modulation of cytokine production and pregnancy outcome in 360 women with recurrent pregnancy loss (RPL) when supplemented with a daily dose of 20 mg dydrogesterone (a synthetic progestogen) up to 20 weeks of gestation. Blood levels and variation of cytokines (IL-4, IL-10, IFN- γ and TNF- α) were estimated using commercially available ELISA kits at the time of enrollment and again at 18-20 weeks of gestation or at the time of abortion. It was found that at baseline (4-8 weeks of gestation) the serum IL-4 & TNF- α levels were significantly lower ($p < 0.0001$) while IFN- γ level was significantly higher ($p < 0.0001$) in RPL group as compared to healthy pregnant control group. However, in women who continued their pregnancy beyond 20 weeks of gestation, it was found that the serum level of IL-4 was significantly lower ($p < 0.05$) in the dydrogesterone group compared to placebo group. The percentage change in level of IL-10 was found to be significantly higher in women with RPL as compared to healthy pregnant control ($p < 0.05$). For women who continued their pregnancy beyond 20 weeks of gestation, the percentage change in the level of IL-4 was found to be significantly higher in placebo group as compared to healthy pregnant control ($p < 0.05$) (Fig.).



Percentage change of cytokines (Mean \pm SE) in women who had miscarriage and women who continued the pregnancy beyond 20 weeks of gestation.

The occurrence of having another abortion after three consecutive abortions was significantly higher in women with RPL as compared to healthy pregnant control. It was observed that there was significant decrease in the proportion of miscarriages in dydrogesterone group as compared to placebo group (Table).

The study concluded that dydrogesterone supplementation in early pregnancy reduces the chances of spontaneous miscarriage in women with unexplained RPL but these outcomes may not be influenced by cytokine production.

Table: Comparison of pregnancy outcome between the placebo and dydrogesterone group

Pregnancy outcome	Healthy pregnant control	Recurrent pregnancy loss		p value	
	Controls (1) N=168	Placebo (2) N=144	Dydrogesterone (3) N=163	1&2	2&3
Abortion N (%)	06/174 (3.45%)	29/173 (16.76%)	12/175 (6.86%)	0.0001*	0.004*
Mean \pm SD gestation at abortion (weeks)	9.83 \pm 4.67 (6-18)	10.48 \pm 3.73 (6-18)	10.75 \pm 4.03 (6-18)		
Mean \pm SD gestation at delivery (weeks)	38.15 \pm 3.21 (35-40)	37.23 \pm 2.41 (34-39)	38.01 \pm 1.96	0.005*	0.002*

- Reproductive morbidities among adolescents:** A cross sectional study was carried out in Thiruvananthapuram district using systematic sampling procedure to assess reproductive health status of adolescent girls. A total of 3932 adolescent girls (ten to sixteen years) were screened. Mean age at menarche was 12.48 years (SD \pm 1.23 years). Out of total 2797 girls who have attained menarche, 6% were diagnosed with premenstrual dysphoric disorder (PMDD) while 5.3% girls had moderate to severe premenstrual syndrome (PMS). About one third of the adolescent girls with dysmenorrhoea reported absenteeism from school and 14% limited or restricted their activities. Reuse of clothes used during menstruation was almost universal (95.6%). Self reported symptoms based on the screening questions indicated that 36% adolescent girls had menstrual problems, 8.4% had symptoms of reproductive tract infections (RTI), 2.3% had symptoms of urinary tract infection and 6% had symptoms of polycystic ovary. Clinical examination of 260 screen positives

and equal number of screen negatives for RTI indicated candidiasis in 38.6%, bacterial vaginosis in 4.6% and trichomoniasis in 0.8% adolescent girls. However, laboratory tests on samples collected from the same cases showed the presence of Candidiasis in 22.7%, Bacterial Vaginosis in 2.1%, intermediate BV in 1%, both BV & Candidiasis in 0.8%, *Staphylococcus aureus* in 1% and *Klebsiella* in 0.4% samples.

- **Metabolic Syndrome in Pre and Post-menopausal Women**

The effect of genetic variants of different markers associated with metabolic risk factors, adipokines level, hormonal levels, adipokines, mRNA expression and effect of yogic practices on metabolic syndrome was studied among 225 premenopausal and 230 postmenopausal women with metabolic syndrome (cases) and without metabolic syndrome (controls). Most of the anthropometrical and biochemical parameters were significantly different ($p < 0.05$) in study group than the controls. Adipokines (TNF- α , IL-6, Resistin & leptin) serum and tissue level were higher ($p < 0.05$) among cases than controls. IL-6 mRNA expression was observed to be higher in visceral adipose tissue (VAT) and IL-6, Resistin mRNA expression was significantly higher in subcutaneous adipose tissue (SAT) of premenopausal women with metabolic syndrome. Frequency of IL-6 174-CC and C allele, TNF- α 308-AA and A allele, Resistin 420-GG and G allele & 181 AA and A allele, Leptin 2549-AA and A allele, Adiponectin 45GG and G allele & 276TT and T allele & 517 CC and C allele were observed to be higher in women with metabolic syndrome. Mutant genotype of adipokines gene (TNF- α , IL-6, resistin, leptin, adiponectin) in pre and postmenopausal women with metabolic syndrome were responsible for increased secretion and synthesis of adipokines (TNF- α , IL-6, resistin, leptin, adiponectin). So the presence of the mutant genotype in women increase risk for development of metabolic syndrome. Practice of yogic exercises for a period of 3 months showed a beneficial effect on metabolic risk markers like BP, BMI, WHR, TG and increase in HDL in pre as well as in postmenopausal women with metabolic syndrome.

- **School and Community-based Sexual and Reproductive Needs, Counselling and Services – An Operational Research in Rural Gujarat**

An Operational Research (OR) study with quasi-experimental design was undertaken among adolescents and youths of District Baroda to address the sexual and reproductive health needs. The specific objective was to develop and test a model for ensuring positive behavioural change, provide Youth Friendly Sexual and Reproductive Health Services and network with local service providers and gatekeepers. Intervention mainly included counseling to adolescents and youths after sensitizing the gatekeepers through peer educators. Drop-in centers were set up in each village, in which Sexual and Reproductive Health Services through weekly clinics were provided to adolescents and youths. Approximately 2234 adolescents and youths were counseled and 2196 adolescents and youths received treatment through mobile clinic. In all, more than 600 children and 1100 people viewed street play that addressed the study issues. The study intervention contributed to providing information regarding sexual and reproductive health issues. Among the total youths interviewed during endline in the experimental area, 72 percent boys and 62 percent girls had participated in the intervention. Operational Research activities facilitated them in increasing their awareness and knowledge regarding menstruation, contraceptive, RTI/ STI and Anemia. Around ten percent had awaited

services for the same from mobile clinic. Almost all (97 %) opined that the services should continue in the village.

- **Modeling the Impact of Stigma on Depression and Sexual Risk Behaviours of Men who have Sex with Men (MSM) and Hijras/Transgender (TG) people in India: Implications for HIV and Sexual Health Programs**

A sequential explanatory mixed methods design using Meyer's minority stress model was used to examine the influence of sexual stigma (SxS)/gender non-conformity stigma (GNS), transgender identity stigma (TGS) and HIV-related stigma (HIVS: vicarious, felt normative, enacted and internalised) on mental health (depression) and sexual risk (unprotected anal sex) among men who have sex with men (MSM) and hijras/transgender people in India. A cross-sectional survey on 300 MSM and 300 hijras/TG recruited from 3 urban (Mumbai, Delhi and Kolkata) and 3 rural (Sangli, Kancheepuram and Kumbakonam) sites was followed by in-depth interviews with 20 confirming cases (MSM=10; TG=10) and 19 disconfirming cases (MSM=10; TG=9) from the survey sample. A significant proportion of MSMs reported moderate (21%) or severe (15%) depression scores (Mean=5.12, SD=4.1); and moderate (55%; n=113/205) or severe (7%; n=15/205) GNS. Whereas A majority of Hijras/TG reported moderate (57%) or severe (24%) depression scores (Mean=5.9, SD=4.2) and moderate (53%) or severe (33%) TGS (Mean=38.6, SD=7.1). Among those who engaged in anal sex, about one-fourth of MSM (27%; n=80/294), and one-third (32%; n=95/293) of TG did not use condom in last anal sex. Hierarchical linear regression models for the influence of stigma on depression indicated that among MSM, SxS/GNS, and HIVS were significant predictors of depression. Resilient coping and social support too were significant at the final step. Among hijras/TG, TGS was a significant predictor of depression. Resilient coping was significant at the final step. Multivariate hierarchical logistic regression modelling of sexual risk behaviours indicated that sexual minority stigma (gender non-conformity stigma/sexual stigma or transgender identity stigma) was not found to be significant predictor of sexual risk among MSM and hijras/TG. However, among MSM, HIV-related stigma was found as a significant predictor for sexual risk in last anal sex (MSM with high levels of HIV-related stigma were more likely to not use condom in last anal sex). Among both MSM and hijras, social support acted as a buffer against sexual risk with male paying partners, but not with male regular partners. Among hijras, resilient coping was not a significant predictor of sexual risk with any type of male partners. However, among MSM, those with high levels of resilient coping were less likely to be inconsistent condom users with male regular, paying or casual partners, and less likely to engage in unprotected sex in last anal sex encounter.

Structural Equation Models (SEM) of the influence of stigma on depression were highly fit and provided evidence that the minority stress models for MSM and hijras/TG cannot be rejected. Qualitative findings indicated that societal stigma contributed to internalised homo/transphobia; discriminatory incidents based on sexuality, gender identity or HIV-positive status seemed to have a cumulative effect on the mental health - resulting in depression and alcohol use, which in turn influenced sexual risk.

Nutrition

Adhoc Studies

The projects being undertaken range from community based studies on assessment of nutritional status to supplementation trials and molecular level studies.

- (i) A randomized trial to assess the effect of music on prehypertensives and stage-I hypertensives was undertaken in Karnataka (Bangalore). Under the study, one group received music and lifestyle intervention, while the other received only the lifestyle intervention. After three months of intervention, the study revealed that diastolic blood pressure decreased significantly in the group receiving the music intervention. Also, the noradrenaline, dopamine and rennin also showed a significant decline. The investigators concluded that music can be included as an adjunct therapy along with conventional lifestyle modifications recommended for the control of blood pressure in hypertension.
- (ii) A recently concluded study in Tamil Nadu, on the differential effects of soyprotein, casein and egg albumin on insulin sensitivity, glucose metabolism, adipokines, inflammatory markers etc in fructose fed insulin resistant rats reported that the vegetable protein, soy emerged as the most effective protein among the three in improving insulin sensitivity and lipid abnormalities. The study also revealed that soy protein improves insulin sensitivity by regulating the PI3K-Akt signaling.
- (iii) A study on resolution of Bitot's spots following mega-dose Vitamin A supplementation in children between 1 and 5 years of age reported that at six months of follow up, 51.1% (95% CI, 45.3% to 57.3%) subjects were classified as cured. The corresponding figures at one year were 59.9% (95% CI 54.1% to 65.9%). Amongst those cured at six months, about half and three-fourths had resolution at two and three months, respectively.
- (iv) A double blind randomized clinical trial was undertaken among anaemic adolescent girls (11-18 years) in a slum of Delhi to assess the impact of weekly iron and folic acid (IFA) supplementation with or without Vitamin B12 on hemoglobin levels. Anaemic subjects were identified and randomly allocated to 2 groups, i.e. Group A (n=222) in which IFA and placebo was supplemented and Group B (n=224) in which same dose of IFA along with cyanocobalamin was supplemented once weekly for 26 weeks. The overall prevalence of anaemia reduced by 37.8% (35.9% in Group A and 39.7% in Group B). The results in the two groups were found to be similar ($p>0.05$). Prevalence of Serum ferritin deficiency reduced more significantly ($p=0.010$) in Group B (from 36.5% to 6.4%) than Group A (from 39.1% to 15.2%). The findings of the study revealed that iron folic acid supplementation is an effective strategy to control anaemia among adolescent girls. Addition of Vitamin B12 resulted in significantly better ferritin status, indicating towards possible role of Vitamin B12 in regulating ferritin mechanism in the body.
- (v) Another study was carried out with the objective to assess the nutritional status of third trimester pregnant women residing in a slum of Delhi and assess its correlation with birth outcome measured in terms of anthropometry of infant. The study revealed that a total of 84.6% pregnant women were anaemic. A total of 36.2%, 68.1%, 63.8%, 31.4%, 25.5%, 8.5%, 43.1% and 19.7% pregnant women were found to be having deficient serum levels of folic acid, vitamin B12, ferritin, iron, vitamin A, vitamin C, zinc and protein respectively. The mean dietary adequacy for energy and protein was 63.4% and 52.3% respectively. Further less than 80% of pregnant women were meeting two thirds of the

RDA for energy, protein, calcium, iron, zinc, retinol equivalent, vitamin B-12 and folic acid. A total of 37% of infants were low birth weight. Maternal green leafy vegetable intake, weight; serum protein and gestational age were found to be significantly related to birth weight.

Centre for Promotion of Nutrition Research and Training with Special Focus on North-East, Tribal and Inaccessible Population

During the year under report, the Centre carried out the analysis of over 11,000 samples for hemoglobin, glucose and lipid profile under the multicentre intervention study on hypertension. Further, around 1200 samples for various biochemical parameters like serum retinol, retinol binding protein, hsCRP, hemoglobin, vitamin B-12, folic acid, ferritin, *etc* have also been analyzed under various small collaborative projects with the aim to facilitate researchers/ students for their degrees and providing assistance to medical colleges/ universities where adequate facilities for research are not available. In the current year, two Ph.D and two M.Sc students have submitted their thesis whereas two Ph.D and one M.Sc students are currently enrolled with the centre.

National Nutrition Monitoring Bureau (NNMB)

The Indian Council of Medical Research (ICMR) established National Nutrition Monitoring Bureau (NNMB) in 1972 in the States of Kerala, Tamil Nadu, Karnataka, Andhra Pradesh, Maharashtra, Gujarat, Madhya Pradesh, Orissa, West Bengal and Uttar Pradesh. The DG, ICMR and Secretary, DHR, GoI, has sanctioned 6 more new NNMB units in the States/UTs of Assam, Andaman & Nicobar Islands, Bihar, Delhi, Rajasthan and Pudhucherry in the year 2012.

The Bureau, since its inception, has been carrying out diet and nutrition surveys on a regular basis and time trends in the rural and tribal areas only. The results are being published as NNMB Technical Reports (1-26) and the same are hosted in the NNMB website (www.nnmbindia.org).

Since, data on diet and nutrition status at country level is not available for urban population, which is very essential for policy and development of various intervention strategies in the country. Therefore, diet and nutritional status of urban population and prevalence and determinants of obesity, hypertension, and diabetes among adults' was initiated in the year 2013 in all the 16 NNMB states, including 6 new NNMB states.

The study was aimed to assess food and nutrient intakes of different age/ gender/ physiological/ activity groups of urban population, to assess the nutritional status in terms of anthropometry and clinical examination for nutritional deficiency signs, to assess the infant and young child feeding practices of mother of <3 year children, to assess the prevalence and determinants of obesity, hypertension, and diabetes mellitus among adults, to assess body composition using fat fold thickness and BIA among adults, and to assess knowledge and practices with reference to hypertension, and diabetes and lifestyles and risk behaviours of adults.

As on 30th November 2013, all the NNMB state units have completed the above survey in about 400 wards as against the total of 1200 wards. Report will be submitted at end of project by March, 2015.

Nutritive Value of Indian Foods (NVIF)

A nationwide food sampling plan was drawn up to provide the best estimates of the nutrient profile or the nutrient means for each food in the food supply in order to accurately represent

what is currently being consumed by the population. A prioritized food list was developed using the Key Foods approach, where food consumption surveys are combined with nutrient data to determine a food's relative nutrient contribution to the Indian diet. Key food lists of 240 foods that contribute to 80% of the Indian rural diet was prioritized to be taken up for analysis in the first phase.

Four rounds of nationwide food sampling covering 107 sampling points in the country have been carried out so far. Overall, a total of 200 different food items have been sampled for six regions of the country and analysed.

During the current year, a total of 50 different foods have been sampled. The food items sampled included cereals and cereal products (2), grain legumes and pulses (2), Green leafy vegetables (16), roots and tubers (2), vegetables (9), nuts and oilseeds (5), spices and condiments (2), fruits (10) and dairy products (2). The composite samples of 50 different foods have been analysed for more than 200 nutrient and bioactive substances for six regions of the country.

The Indian food composition database will provide the much needed data in specialized fields such as planning, health, agriculture, trade, food science, environmental sciences and economics.

Special Activities

Interagency collaborations: Under the ICMR-ICAR-FSSAI Joint Committee for Research on Food safety, five research projects have been completed on the extent of use of artificial ripening agents and oxytocin in fruits and vegetables, effect of oxytocin injection on vegetables, *in vivo* and *in vitro* digestibility of oxytocin and effect of oxytocin ingestion on reproductive health of animals. The findings of these studies will help address public concerns regarding safety of food being consumed. Various other interagency collaborative efforts includes formulation of a committee of secretaries to address various issues related to development and marketing of GM foods and an interagency group on micronutrients involving various Departments to develop strategies to combat micronutrient deficiency in India following an interdisciplinary approach.

Basic Medical Sciences

Anthropology

Health Status and Health Behaviour of Santals: Comparison Between Urban And Rural Groups

A study was carried out at Indian Statistical Institute, Kolkata to study primarily the health status as well as health behaviour of Santals residing in urban and rural areas of West Bengal. Greater socio-economic disparity between urban and rural groups (Santals) in terms of education, occupation and household expenditure was found. Urban group showed relatively lower fertility and mortality rates but higher BMI values compared to rural group. Findings consistently indicated differences in most of the health traits; this may be due to differential socio-economic condition. Little differences existed in health behaviour traits because of the fact that both urban and rural groups live in close proximity with other ethnic groups and are exposed to several modern amenities that may influence their health behaviour.

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Bioethics

Capacity Building for Institutional Ethics Committees

Under a major initiative to strengthen the status and functioning of the ethics committees in India and to assist them in raising their standards to the International level, the Council has conducted several training workshops, namely Human Subject Protection Course (HSPC) and Standards Operating Procedures (SOP) Training and Survey of Institutional Ethics Committee Trainings at National Institute for Research in Tuberculosis, Chennai involving participation of several ethics committees from Chennai. The courses were organized by the Council in association with Forum for Ethical Review Committees in Asia and Western Pacific Region (FERCAP) for in-depth training and capacity building of ethics committees. National Institute of Research in Tuberculosis (NIRT) has received International acclaim and recognition certificate from International Organisation SIDCER, during the FERCAP Conference in Bali, Indonesia during November, 2013.

Hematology

- A study was carried out at Rajiv Gandhi Proudyogiki Vishwavidyalaya institute for carrier detection and molecular diagnosis of beta globin gene mutations in Bhopal. The study assessed the prevalence of thalassaemia and other haemoglobinopathies in the general population and determination of frequency of different mutations in ethnic groups. Overall this study gives a clue to the fact that besides the five common Indian mutations, there are mutations of the beta globin gene that form around 15% of the mutation spectrum.
- Another study was carried out in Assam on haemoglobinopathies at Dibrugarh Hanumanbux Surajmal Kanoi (DHSK) College to examine if any significant difference exists between different Hb genotypes with regard to reproductive performance and to estimate the Hb concentration of the subjects with regard to different Hb genotypes in the state of Assam. It was concluded that in populations with frequent Hb E, high incidence of Hb E induced anaemia showed increase spontaneous abortion and infant mortality in AE (Hb E carrier), and EE (Hb E disease) mothers.
- At University College of Science & Technology, Kolkata, a study was carried out to study how microRNA expression profile in erythroid cells is modulated and its effect on the physiological changes associated with thalassemia major. The study showed the expression level of hsa-miR-503 decreased with increase of severity of the disease and increased the rate of growth of erythropoietic progenitors in a statistically significant way.
- Molecular Screening of Fanconi Anemia Complementation groups in Indian population were carried out at National Institute of Immunohaematology, Mumbai. The objectives of the study were to differentiate Fanconi anemia from idiopathic aplastic anemia and screen complementation groups mainly FANC D2, FANCA, C, G and BRACA 2 and its clinical correlation. The FA complementation groups, A, C, G are reported to be frequently associated with the phenotype. FANA gene defect is detected in 70% of the cases.
- At Amrita Institute of Medical Sciences, Kerala, a study was carried out to identify novel molecules of pathogenic significance in central nervous system leukemia. Though 80% of childhood leukemia is curable, relapse occurs in the remaining 20%. Identification of novel molecules that differently react to leukemia CSF is a major finding. The potential

of these findings lies in the development of a prognostic marker as well as understanding why the differential reactivity observed during relapse and remission of CNS leukemia is immense.

Human Genetics

- A clinical, biochemical and molecular analysis of common and rare lysosomal storage disorders was carried out at **Centre for DNA Fingerprinting and Diagnostics**, Hyderabad. This study helped to establish mutation testing which has helped more than 150 families for diagnosis, prenatal diagnosis and genetic counseling.
- A study was done at Vasavi Medical and Research Centre, Hyderabad to study the molecular genetics of β Amyloid Precursor Protein (APP) in different neurological disorders like Alzheimer, Down's syndrome, Autism and Fragile syndrome. ELISA results suggest the ratio of the APP peptides is significantly different in Alzheimers patients as compared to others which shows it is an important gene in neurobehavioral disorders rather than mental retardation.
- Another study was carried out at Chhatrapati Shahuji Maharaj Medical College (CSMMC), Lucknow to find out the association of polymorphisms in the genes of Fat mass- and obesity-associated (FTO) gene, Insulin-induced gene 2 (INSIG2), Ectoenzyme nucleotide pyrophosphate phosphodiesterase (ENPP1) gene and Glutamate decarboxylase 2 (GAD2) gene in individuals with obesity and non-obese healthy individuals and to analyze the association of haplotypes in susceptibility to obesity and obesity related diseases. Thus, hyperleptinemia is not just a marker of obesity but may be a counter regulatory response to underlying insulin resistance. On the other hand, adiponectin may constitute an early biomarker to identify obese at high risk for the future development of obesity associated co-morbidities.
- At Manipal University, Karnataka a study was carried out to genetically evaluate patients with intellectual disability (ID) in Udupi and Dakshin Kannada Districts of Karnataka. The finding from the study reflects the importance of screening children with ID with a normal karyotype at a submicroscopic level. It proposes the implementation MLPA as a first line of screening for these patients in addition to conventional cytogenetics. The study can thus be translated into a clinical genetic testing platform based on individual, family and community centered approaches.
- A study at Postgraduate Institute of Medical Education and Research, Chandigarh was done to screen amino acid disorders in high-risk infants in a hospitalized population to find out the frequency of aminoacidopathies and urea cycle defects. One out of twenty high-risk children has a possible IEM. The results of the study provide a strong lead to help in prevention of irreversible damage and/or attenuation of clinical severity of the disorder by way of an early recognition and therapeutic intervention.
- Mutation analysis of COL1A1 and COL1A2 genes in Indian patients with Osteogenesis Imperfecta (OI) was carried out at Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow. These results helped in genetic counseling and can provide prenatal diagnosis to these families for prevention of recurrences.
- A study to identify the susceptibility genes associated with non-syndromic cleft lip (CL) with or without cleft palate (CP) in Indian population was carried out at Sri Ramachandra University, Chennai. The study has identified novel genomic regions on 2p11.1, 4p12 and 6q15 that harbors a risk variant for cleft lip and palate in the south Indian families.

- Another study was carried out at Postgraduate Institute of Medical Education and Research, Chandigarh to identify and characterize Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) mutations and micro deletions in human Y chromosome AZF gene in male infertility. Results of this have a direct application for developing faster and economical screening tools of CFTR gene in CAVD males opting for assisted reproductive technique (ART).

National Task Force on Inborn Metabolic Disorders – Newborn Screening for Congenital Hypothyroidism and Congenital Adrenal Hyperplasia: A Multicentric Study

A National Task Force (NTF) using a common multicentric study protocol for pilot study on newborn screening of more than 1 lakh newborns was carried out at 5 centres (Delhi, Mumbai, Hyderabad, Kolkata, and Chennai). This NTF study aimed to explore the feasibility of introducing 'universal newborn screening' in the country. All newborn infants taking birth in the collaborating hospitals with Gestational age more than or equal to 34 weeks were included after informed consent and counselling. In addition there were centres for high risk screening (Hyderabad and Bangalore), Quality Control (Hyderabad), Data coordination, and Central Coordination (New Delhi). Heel prick samples were collected for biochemical genetic screening at 5 regional laboratories. The final report released during the International Society of New Born Screening (ISNS) conference at AIIMS in September 2013. Details of achievements are given in following table:

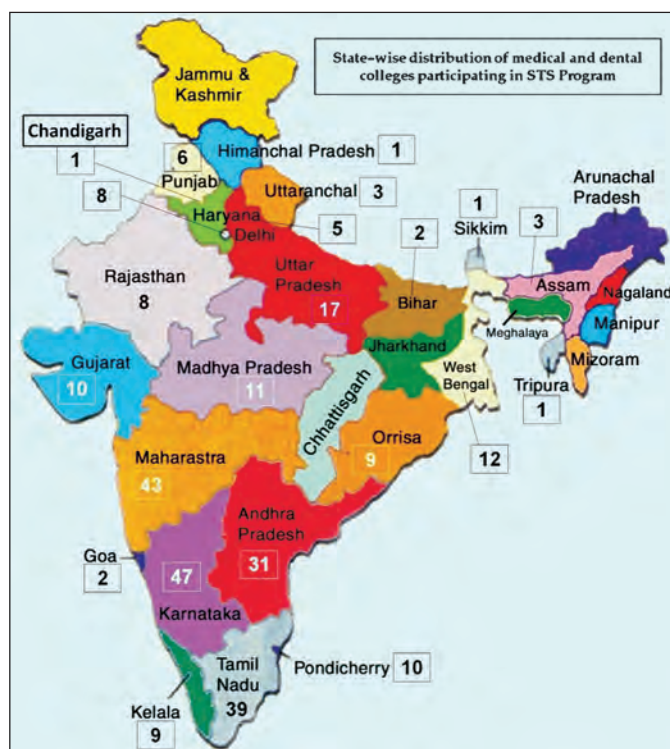
S. No.	Type	Details of Achievements
1	Clinical	<ul style="list-style-type: none"> • Standardization of heel prick method for sample collection on filter paper in rural/urban settings • Training in informed consent and genetic counselling.
2	Laboratory	<ul style="list-style-type: none"> • Standardization of lab protocols • On-site training & preparation of lab SOP's
3	Trainings/ Workshop	<ul style="list-style-type: none"> • Hands-on Workshops on clinical, Laboratory, Data Entry for investigators & research staff • Workshop on Quality Control Methods
4	Website	<ul style="list-style-type: none"> • Launch of a website (www.icmrmetbionet.org) as an Online Resources for Biochemical Genetic Testing in India for both patients and clinicians.
5	Data Coordination	<ul style="list-style-type: none"> • Creation of centre specific sample coding methods • Development of data collection cards • Online software program- biweekly reporting & analysis
6	Quality Control	<ul style="list-style-type: none"> • Quality Assurance Certification of 6 labs (CDC Atlanta, USA) • Protocols for external & internal Quality Control.
7	Advocacy Material	<ul style="list-style-type: none"> • Logo for ICMR TF-IMD on NBS finalized. • Advocacy material - posters, banners, charts, informed consent forms, patients information sheets in 7 languages (Hindi, English, Telugu, Marathi, Bangla, Urdu, Tamil)
8	Publications	<ul style="list-style-type: none"> • Printing & release of 'Work Book' with common SOPs. • Priced publication-'Clinical Manual on Inborn Errors of Metabolism' (Editors: Dr. V Kalra, Dr. M. Kabra, Dr. S. Kapur) costing Rs. 250/-.

National Task Force on ICMR Research Oriented Medical Education (NTF-ROME)

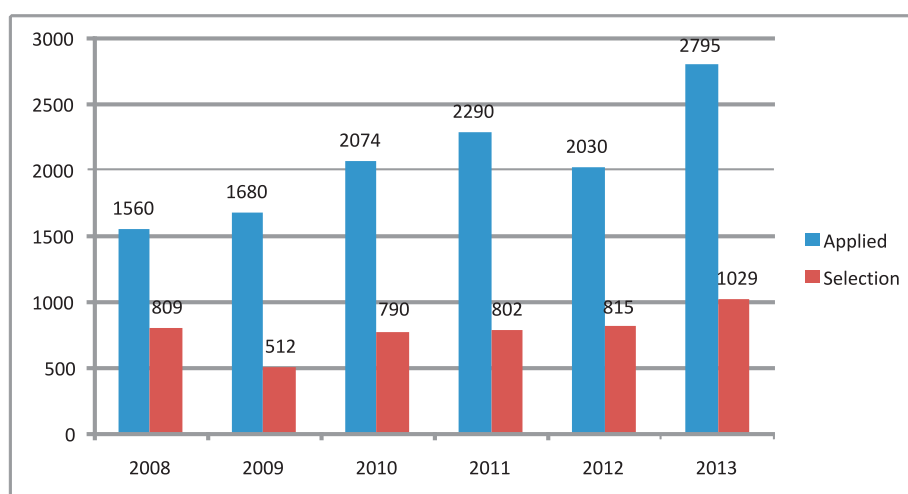
To promote research culture in the undergraduate medical students, the Council is supporting a National Task Force study to provide an opportunity to the recipients of Short term studentship to further enhance their skills and learning in research methodology by attending intensive short term trainings. In addition short term workshops and courses on research methodology were conducted for faculty members especially the young faculty, postgraduate students in both clinical research as well as lab medicine. This task force is being centrally coordinated by Moving Academy of Medicine and Biomedicine, Pune. Regional hands-on workshops in different aspects of clinical research (both hospital and field based), laboratory medicine, clinical trials, medical ethics, data analysis & communication *etc* were held. In addition national/ regional medical students' research conferences were organized with the aim to improve quality of research in medical colleges. During 2013, six undergraduate foundation workshops were held in Sevagram, Nagpur, Gwalior, Mumbai, Jodhpur and Karad. In addition one UG Medical Student Regional Research Conference was held in Nagpur. For PG Students and faculty members' two hands on Workshops were held in Pune. The program is helping in providing training and building capacity for conducting biomedical research in medical colleges.

Short Term Studentship (STS)

Application and proposal submission and its review and evaluation by experts are done online. During 2013 a total of 4511 registrations were made and 2795 proposals were evaluated online by 116 subject experts from different institutes in India. More than 1029 proposals have been approved, who have completed their research during summer vacations and 874 reports have been submitted. Proposals were received from 232 medical colleges and 47 dental colleges from all parts of the country and were categorized in 37 subject categories. The program has helped to create a pool of young medical scientists in the country.



Map showing the number of medical colleges from each State from where medical students have participated in STS Program



Bar Diagram to show year wise figure of STS

International Health

The International Health Division (IHD) in ICMR co-ordinates international collaboration in biomedical research between India and other countries as well as with national & international agencies such as Ministry of Science & Technology, Indian and foreign missions and WHO etc. There are few specific agreements signed by the Ministry of Health and Family Welfare with other countries and rest are those signed directly by ICMR/DHR with international organizations/ institutions such as INSERM in France, German Federal Ministry of Education and Research (BMBF) and Helmholtz Association (HGF) in Germany, National Institutes of Health (NIH) in USA, Canadian Institutes of Health Research (CIHR) in Canada, University of Sydney and George Institute for International Health in Australia, Karolinska Institute (KI) in Sweden, London School of Hygiene and Tropical Medicine (LSHTM) and Medical Research Council (MRC) in UK, Academy of Finland (AF) in Finland and Global Alliance for Chronic Diseases (GACD). Recently, the Department of Health Research (DHR) has signed a Memorandum of Understanding with National Institute of Health & Care Excellence (NICE) UK.

The purpose of these Memoranda of Understanding (MoU) and Joint Statements has been for exchange of scientific information; exchange of scientists/technicians; joint execution of scientific projects and organization of joint scientific meetings, seminars, workshops and symposia in identified areas of cooperation.

Exchange Visits

The IHD supports and coordinates the international travel of Indian scientists engaged in approved bilateral collaborative research projects under various MoUs and joint statements with other countries. A total of 16 exchange visits of scientists / officials to and from India were arranged under various international collaborative programmes / projects.

Health Ministry's Screening Committee (HMSC)

The 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 (HMSC). The International Health Division of ICMR acts as the Secretariat for HMSC. The projects are peer reviewed by the concerned

Technical Divisions at ICMR and then placed before the HMSC for consideration and decision. During the year 2013-14, three meetings of Health Ministry's Screening Committee were organized (till 31st December, 2013) wherein 114 projects were considered and out of which 67 projects were approved for international collaboration / assistance with agencies from USA, Germany, France, Canada, Australia, UK, WHO, European Union and several other foundations and foreign universities.

The IHD prepared the document entitled "An overview of International Collaborative Research Projects in Health Research approved by HMSC Volume II January, 2008 to December, 2012" which was released during the HMSC meeting held on 6th June, 2013, by the Secretary, DHR & DG, ICMR. The document provides the digest on the international collaborative research projects approved by HMSC during the period with brief account on Indian PI, Indian intuitions, funding agency *etc.*

The IHD also prepared and submitted the "Report on Outcome of International Collaborative Research Projects approved by HMSC and funded by ICMR during January,, 2008 to December, 2012". This report was presented to the committee members during the HMSC meeting held on 16th September, 2013.

Indo-German Science Centre for Infectious Diseases

The mission of the virtual Indo-German Science Centre for Infectious Diseases (IG-SCID), 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 with IHD. Under this programme four collaborative projects were approved, funded and completed. The IGSCID was extended upto December, 2013 by both HZI, Germany and ICMR, New Delhi.



ICMR – MRC JSC meeting Co-chaired by Secretary, DHR & DG, ICMR held on 13 – 14th June 2013 in London, UK



DHR-National Institute for Health and Care Excellence-MoU co-signed by Secretary, DHR and DG, ICMR in London, UK on 14th June, 2013



Tenth ICMR –INSERM Joint Working Group (JWG) meeting Co-chaired by Secretary, DHR & DG, ICMR held on 22nd October 2013 at the ICMR Headquarters in New Delhi

International Fellowship Programme

The ICMR International Fellowship Programme 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. The ICMR International Fellowships have been awarded to six Senior and twelve Young Indian scientists during the year 2013-14.

The reports of 19 Young and 10 Senior ICMR International Fellows who had undertaken the Fellowship during the years 2011-12 & 2012-13 have been placed on ICMR website.

International Visitors/Dignitaries

The Division also organized visits by various visitors to ICMR from foreign countries / agencies such as MRC, UK; BMBF, Germany; Institute of Merieux, France; ICAV, Canada; Bill & Melinda Gates Foundation (BMGF), USA; Messey University, New Zealand; Sheffield, Children's Hospital, UK; LSHTM, UK; CSIRO, Australia; University of Texas, USA; EMBL, Germany; Mozambique RCN, Norway; Simon Fraiser University, Canada; IVI, South Korea etc.

International Workshops held under Bilateral Programmes

Indo-Norway Workshop on Anti Microbial Resistance (AMR) was held in Norway in September, 2013.

The following MoUs have been signed during this period:

1. DHR-National Institute for Health and Care Excellence-MoU signed by Secretary, DHR and DG, ICMR in UK on 14th June, 2013.
2. Dialogues initiated and documents forwarded for Govt. of India for approval of Indo-US Joint Statement on Environmental and Occupational Health; Maternal and Child Health; ICMR-International AIDS Vaccine Initiative, USA and ICMR-University of Sydney/George Institute, Australia and NHMRC, Australia. Approval of GOI is awaited.

Proposed MoUs with Govt. of Saskatchewan, Canada; Bill and Mellinda Gates Foundation (BMGF), USA; German Research Foundation (DFG), Germany; International Consortium on Anti Virals (ICAV) Canada and Drugs for Neglected Diseases Initiative (DNDi) are under negotiation/consideration.

In addition to these meetings, the International Health Division has also represented ICMR in various bilateral/multilateral Joint Committee meetings coordinated by MEA, DST and Ministry of Health & Family Welfare, Govt. of India for cooperation with various countries such as IBSA, Canada, Germany, Sweden, European Union, South Africa, Australia, Tunisia, Mozambique etc.

Joint Working Group (JWG) and Joint Steering Committee (JSC) Meetings

The regular meetings of Joint Working Group (JWG) or Joint Steering Committee (JSC) with various countries/international institutes/organizations are organized to review, develop and finalize joint collaborative programmes, decide future plans of action and identify priorities for bilateral cooperation.

Following JWG/JSC meetings with various MoUs and Joint Statements have been held:

1. ICMR – MRC JSC meeting chaired by Secretary, DHR & DG, ICMR from Indian side held in London on 13 – 14th June 2013 (photo enclosed).
2. Indo-EU Group of Senior Officials (GSO) meeting was held through Video Conference on 8th October, 2013.
3. ICMR-INSERM JWG meeting held in New Delhi on 22nd October, 2013 (photo enclosed).
4. Working level meeting between officials of ICMR & MRC, UK was held in New Delhi on 11th November, 2013.

Publication, Information and Communication

Hindi Publications

ICMR Patrika

The publication of *ICMR Patrika*, a monthly in-house Bulletin in Hindi continued. The articles published in the *Patrika* included : *Atiraktadab: Ek Gambhir Swasthy Samasya, Swasthya Bigadate Dhuanrahit Tambaku Utpaad, Dainik Jivan mein Vayu Pradushan ke Prabhav, Rheumatic jvar aur Rheumatic Hriday Rog: Karan aur Nivaran, Swasthya Anusandhan Vibhag : Jana Swasthya ke hit mein Nirantar Karyarat, Bharat mein Ubharte evam Punah Ubharte Sankraman, Jaiva Ayurvedigyan ke kshetra mein Utkrisht Shodh Karya ke lie Vaigyanikon ko ICMR Puraskar, Bharat mein Iodine Alpata Vikaron ka Niyantran, Vishwa AIDS Diwas ka Ayojan : Jan-jagrukata Badhane mein Mahatvapurna, Mansik Swasthya aur madak Dravy Vyasan : Vriddhkon ke Samaksh Chunautiyan* .

Hindi version of Citations of ICMR Awards (2009 & 2010): Prepared the Hindi version of 50 Citations of ICMR Awardees for the years 2009 & 2010.

Hindi Day Lecture: Organized a lecture in Hindi on the topic “*Badalte vishwa mein Avasad ki Chunautiyan*” by Dr Jitendra Nagpal, Department of Psychiatry, Moolchand Hospital, New Delhi on 29th Oct., 2013.

Information and Communication

Library & Information Services: The subscription for the e-journals Lancet, Science, Nature, and NEJM for all ICMR Library & Information Centres has been continued in consortia mode. Subscription for full text electronic data base ProQuest Health & Medical Complete including ProQuest Medical Library (covers about 3000+ journals) has been renewed for one more year for six ICMR institutes including ICMR Hqrs.

The subscription to J-Gate Plus has also been renewed for one year. J-Gate provides access to millions of journal articles available online offered by 11,419 Publishers. It presently has a massive database of journal literature, indexed from 36,709 e-journals with links to full text at publisher sites. J-Gate offers two types of products/services: J-Gate Portal: a. Table of Contents (TOC)- For 36,709 e-journals. b. Database - A comprehensive searchable database with 36,569,422 articles, with 10,000+ articles added every day. J-Gate Customized Services: a. J-Gate Custom Content (JCC)- Local Intranet /Internet solution to libraries, providing e-access for subscribed journals. b. J-Gate Custom Content for Consortia (JCCC) - JCC extended to a homogeneous group of libraries for sharing “subscribed” journal resources.

Subscription to DELNET institutional membership has been renewed. The following databases are available from DELNET which can be accessed through online by the institutional members.

1. Union Catalogue of Books (1.28 crore bibliographic records)
2. Union Catalogue of Periodicals (33.9 thousand records)
3. Database of Periodical articles (9.22 lakh records)
4. CD-ROM Database (22 thousand records)

Publications

Indian Journal of Medical Research

The Indian Journal of Medical Research (IJMR) has successfully completed one hundred years of its existence in July 2013. During the Centenary year several new initiatives were taken. The Journal was published with a new get-up and a new section on "Clinical Images" was started. During the Centenary year (July 2012 to July 2013), a centenary special review article, and an IJMR Classic were published in each issue. In addition, 13 most cited IJMR articles published during the last 50 years were also selected and published in each issue. The IJMR continued to publish quality original research articles in the area of biomedical research as well as review articles (both solicited and unsolicited) on topics of contemporary biomedical interest. A special issue on "Translational Immunology in Health & Disease" was brought out in November 2013 with Dr N. K. Mehra as Guest Editor. A special section on "Nutrition & Food Security" was brought out in September 2013 with Dr Prema Ramachandran as guest editor. The Impact factor of the IJMR for 2012 was 2.061.

Annual Report: Annual Report (both English and Hindi) of the ICMR as well as the Department of Health Research were brought out during the year under report.

Other Publications: The ICMR brought out one publication entitled "Regulatory requirements for Drug Development and Clinical Research" edited by Dr. Nilima Kshirsagar, *et.al*.

Scientometric Studies

Annual Research Output of ICMR Institutes

The annual document '2012 Research Output of ICMR Institutes' with analysis of publications from all the institutes including Regional Medical Research Centres has been brought out. A total of 633 papers were published by the ICMR institutes during the calendar year 2012. The National Institute for Research in Tuberculosis (NIRT), Chennai topped the tally with 75 papers followed by the National Institute of Nutrition (NIN), Hyderabad (68), National Institute of Cholera and Enteric Diseases (NICED), Kolkata (67), National Institute of Malaria Research (NIMR), New Delhi (52) and National AIDS Research Institute (NARI), Pune (39). Of the 331 journals used for publishing 633 papers, 188 journals had an impact factor (IF) 2012 equal to or greater than 1.000. The average IF / paper of the Council for the calendar year 2012 was 3.096.

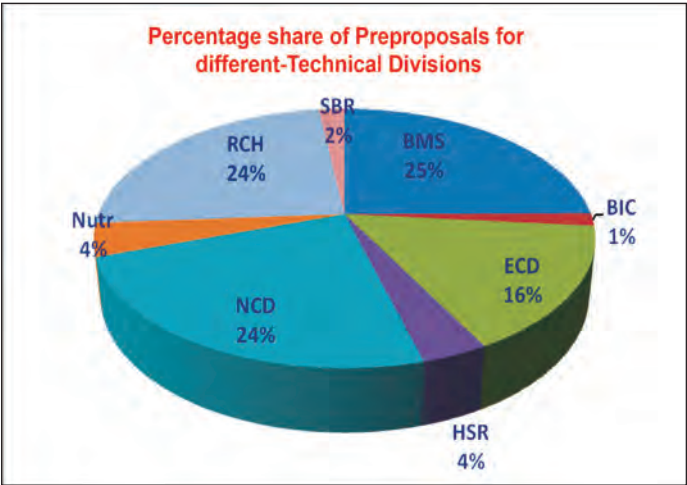
Human Resource Development in Biomedical Communication: Scientist of the Division of P&I acted as a resource person to cover topics related to biomedical communication in various Workshops organized during the period under report : Workshop on Biostatistics & Research Methodology (Institute of Cytology and Preventive Oncology, NOIDA); Workshop on Biostatistics & Research Methodology (PGIMER & Ram Manohar Lohia Hospital, New Delhi); and ICMR Workshop on Research Methodology (Govt. Medical College, Srinagar, J&K).

Web-based Extramural Project Management System

The ICMR has shifted from manual receipt processing and management of extramural projects to web-based interactive system. The council has decided to adopt an online and two stage processing of extramural projects. Initially the investigators are required to submit a pre-proposal only, not exceeding three pages. The pre-proposals received within a month or on deadline are scrutinized and evaluated by the Council within a fixed time period and decision is communicated to investigators for both selected and non-selected proposals.

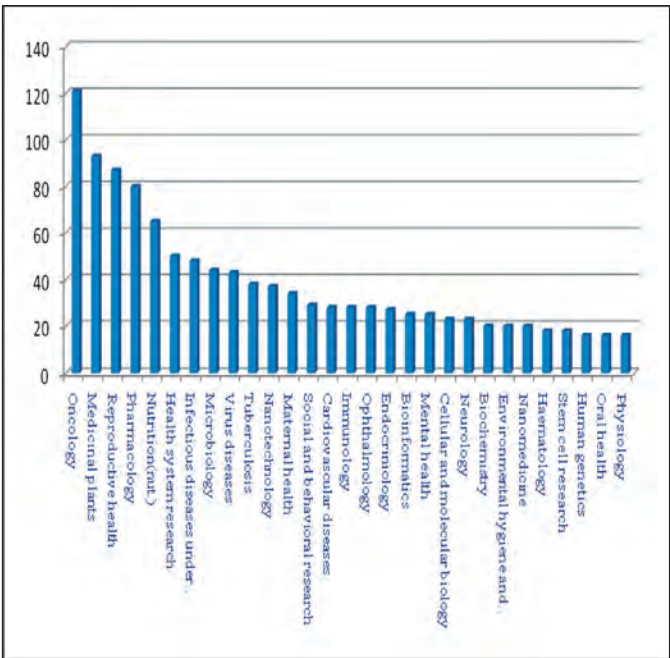
The Principal investigators (PIs) of the selected pre-proposal only are asked to expand their pre-proposal into detailed project in the format of the ICMR *ad-hoc* projects within a period of not more than 6 months and submit to the Council online. The system has been developed by ICMR in technical collaboration with C-DAC, NOIDA. The system has started functioning w.e.f. January 2012 and stands “First” in introducing a complete online system of its “Extramural Project Processing” among any of the Funding bodies in the field of Science & Technology in India.

On an average-140 pre-proposals are received every month. The system encompasses the complete life-cycle of a proposal funding beginning with the submission of project proposals to it’s processing, sanction, funding till it’s completion through web-based system only.



Percentage share of Preproposals for different Technical Divisions

During the year under report (April 2013-January 2014), 1603 preproposals were received on the web portal of ICMR. These proposals were reviewed and of these, 760 pre-proposal were shortlisted for submission of detailed proposals.



Subject wise short listed preproposals

During the year under report, a total of 876 full proposals were received and marked to respective technical divisions for processing. A fully operational on line system has brought about transparency and differential access to the system provided to the concerned technical heads and the Director General.

There has been an increase in the number of proposals received by ICMR using this system. One of the reasons to the increase can be attributed to the ease of proposal submission process in e-PPS.

An initial analysis of the data culled out from the system for 'ad-hoc' proposals being submitted from the different parts of India, have clearly indicated change of productive institutions, subject areas being covered by investigators and the pattern of Cities and the 'Major Discipline' being chosen by investigators. Some of the remote cities, which have entered in the ICMR Extramural Project Scheme, are East Khasi Hills, Ri-Bhoi, West Garo Hills, Aizawl, Bhadrak, Dhenkanal, Ganjam, Mayurbhanj, Karaikal, East Sikkim, Dharmapuri, Dindigul, Erode, Midnapore and Nadia.

Dissemination of ICMR activities: ICMR participated in Mega S&T Exhibition Organized as part of 101st session of Indian Science Congress at Jammu University, Jammu during February 3-7, 2014 and displayed scientific achievements, contribution and activities of ICMR for public. Scientists from ICMR Headquarters, NIN, Hyderabad, NIOH, Ahmedabad and NIMR, New Delhi answered queries of visiting delegates and public.

ICMR also participated in S&T Exhibition Organized at Jammu during June, 2013, at Srinagar during July 2013, at Kolkata during June, 2013 and at Goa during September 2013.

Apart from these a two page advertorial feature was published in flight magazine of Air India "Shubh Yatra" in February 2014 highlighting important activities, achievements of ICMR and DHR.

Other activities by Various Divisions of ICMR Headquarters

Bio-informatics

Bioinformatics Centre (BIC) was established as **Integrated Research Information System (IRIS)** in 1983 under the Division of Publication & Information (P&I) at ICMR with a mandate to computerize activities of ICMR. It was renamed as Bioinformatics Centre in 1999. During the reporting period the BIC was primarily involved managing Task-Force project 'Biomedical Informatics Centres of ICMR, Management of Research in the area of Bioinformatics & Medical Informatics and providing services to ICMR.

DHR Website: BIC has developed website for Department of Health Research (DHR) <http://www.dhr.gov.in>. The site, maintained and updated regularly by BIC, highlights department's organizational structure, staff, activities and schemes initiated by the department. Announcements related to workshops, call for proposals, employment opportunities are flashed on the Website for wider publicity.

Final Report Uploading System: BIC has developed an online system for uploading final reports of projects. This system allows uploading final report, Display of Abstract, Conclusion and the Report as whole. The system also allows search by Project No, Division File No, String search on Title, based on Project Investigator-wise and Program Officer.

ICMR Network and Management: Servers maintained by BIC are ICMR Blade Server which includes icmrhqnd.in for domain logs, AV server is antivirus server, icmrntserver is a local

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host for OPA File Tracking System and intranet, bmi.icmr.org.in for BIC Website, TMG Proxy Server, STS / MACE Server, TMG Server & Remote Server, FIN SERVER, ICMR Exchange server for email logins of all employees of ICMR headquarters and its institutes. Management of ISP links for providing Internet and Videoconferencing are (NKN, NIC, Ernet). Troubleshooting of servers and Centralized Antivirus Solutions, e-mail and other support is provided by BIC to ICMR headquarters and institutes.

ICMR Website: BIC has developed and maintains ICMR web site <http://www.icmr.nic.in> with highlights about activities of ICMR headquarters and its institutes. It is regularly updated with information related to workshops, call for proposals, employment news, grant schemes, annual reports, IJMR etc.

The site is linked to other ICMR resources including web-based email access, searchable general circulars, pay-slip generation, Gastrointestinal Tract Pathogens Repository (GTPR), National Culture Collection of Pathogenic Fungi (NCCPF), Health Account Scheme, Vector Borne Diseases Science Forum, Medicinal Plant Unit, Biomedical Informatics Centres of ICMR, Indo-German Science Centre for Infectious Diseases, National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT), Management of Acute Coronary Event (MACE) Registry, International Symposium on Accelerating Research on Multipurpose Prevention Technologies for Reproductive Health and Extramural and Intramural information system. Updation of databases related to Publications, Projects, Scientists profile, Seminars/Symposia, general circulars etc is done regularly. Excerpt from Web Analysis software developed by NIC is as follows (April 1, 2013 – November 24, 2013)

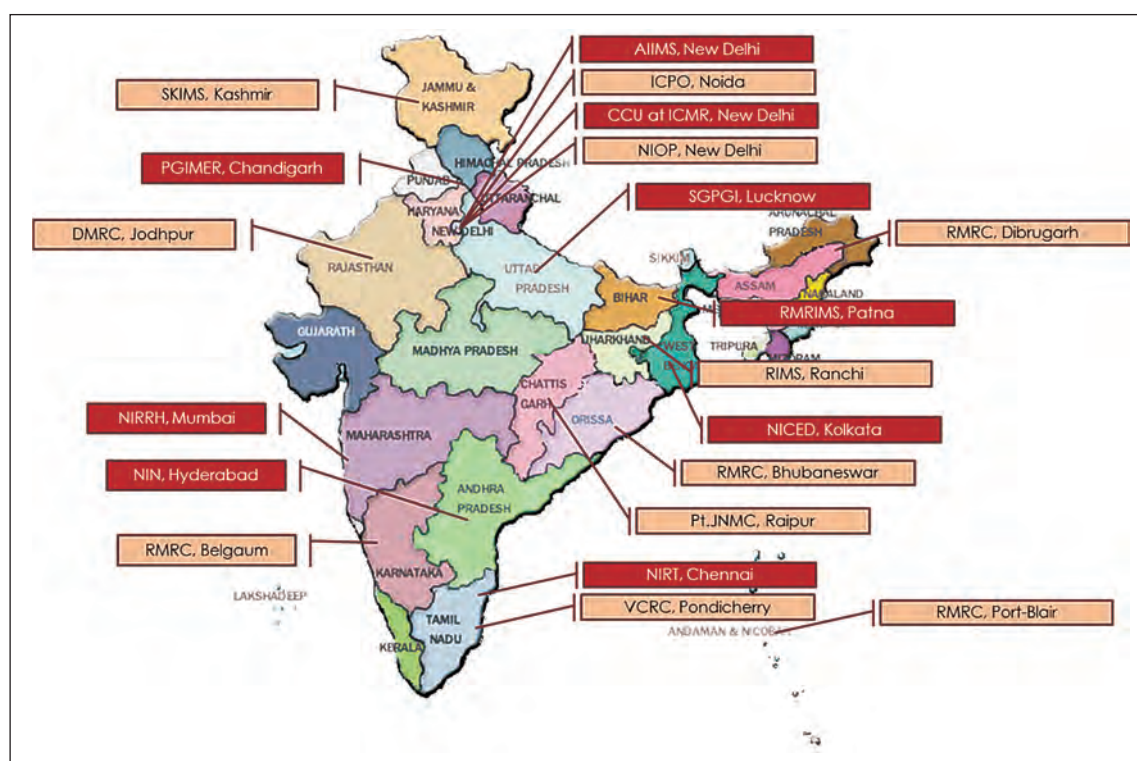
Visit Summary	
Visits	2,209,893
Average per Day	9,285
Average Visit Duration	00:12:09
Median Visit Duration	00:02:03
International Visits	37.20%
Visits of Unknown Origin	1.20%
Visits from Your Country: India (IN)	61.60%

Intramural, Extramural and IJMR Databases: BIC is maintaining databases and information systems on i-series AS400 server they pertain to both extramural and intramural research. The information covers Projects Detail, Publications, Scientists Profile, Seminars/Symposia/Conferences. Information generated through this system is used to answer time bound parliament questions, queries from the ministry as well as from the DG, ICMR. Data related to IJMR contents is also maintained on the same server.

Legal Cell Management Information System (LCMIS): BIC has developed ICMR Legal Cell Management Information System (ILCMIS) which provide the information about ICMR's court cases in various Hon'ble courts. It will provide the information about the subject of the case, Name, location & state of the court the case is currently running and details about the petitioner & respondent and their lawyer, case status (next Hearing date) and affidavit details.

Online Recruitment System: BIC has developed a two stage e-recruitment portal for ICMR. Portal allows online registration and submission of applications by the applicants providing details on Educational Qualification, Religion, Category, Nationality, Marital Status, etc. Employment details, Photo and signature upload, payment of requisite fee applicable to

Task-Force Project: Under the task-force project (Biomedical Informatics Centres of ICMR), it established 20 Biomedical Informatics Centres at premier medical research institutes like AIIMS, PGIMER Chandigarh, SGPGI Lucknow *etc.* besides several Research Institutes/Centers of ICMR & medical colleges across India (Fig.). The mandate of these Centres is to nucleate and promote informatics in medical research through increasing awareness, providing services and initiating collaborative research projects. The project has been initiated from April 1, 2013.



Biomedical Informatics Centres of ICMR

Human Resources Development

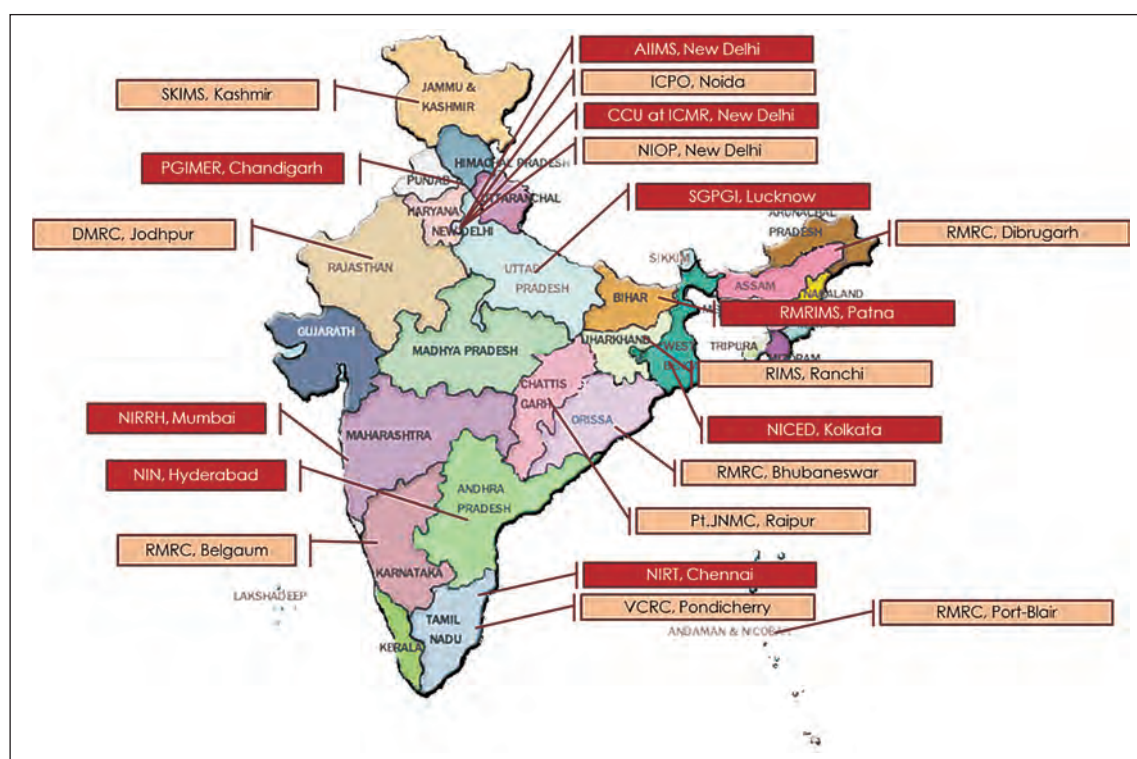
Financial assistance to MD/MS/DM/MCH thesis in priority areas of Biomedical Research.
(50/Yr)

Financial assistance of Rs.25, 000/- is provided (50/year) to MD/MS/DM/MCH students who are in the 2nd year of MD/MS course. The Selection Committee recommended financial assistance to a total of 442 **MD/MS/DM/MCH thesis** out of 1374 proposals received so far. Out of 314 -thesis protocols 76 protocols/candidates awarded financial assistance during reporting period. (Fig.).

the post *etc.* are also included. The portal allows online reviewing and evaluations of applications.

Research Management: BIC is managing nearly 30 ad-hoc projects and 70 fellowships in the area of Bioinformatics and medical informatics. BIC is taking initiatives to promote projects on medical informatics and projects involving use of primary patient data with objective to promote informatics in medical research.

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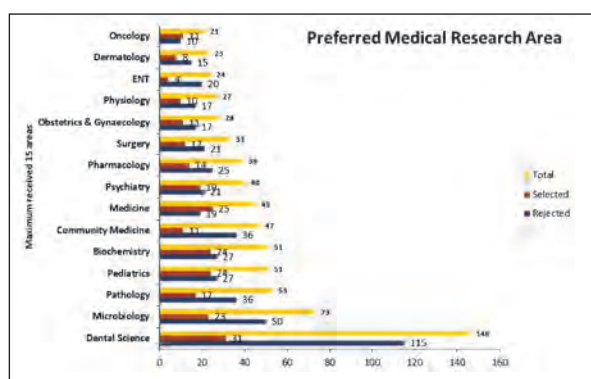


Biomedical Informatics Centres of ICMR

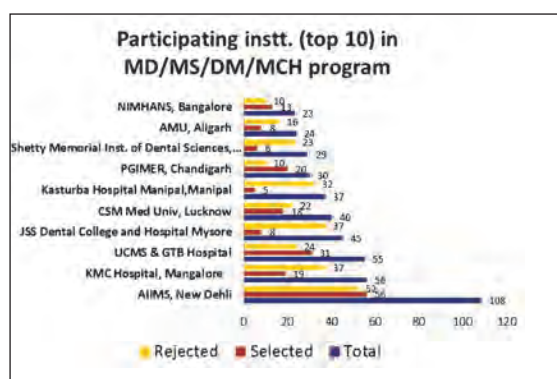
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Preferred Medical Research Area (Top 15)



Participating institutes (Top 10)

Grant-in-aid for Organising Seminars/Symposia/Workshops

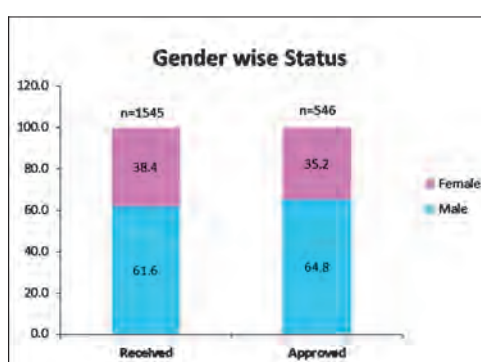
To update knowledge, transfer from lab to land at national and international level in the concerned area, Conference/CME/programmes/Workshops etc. scheme is ongoing and out of total 701 applications, 388 were approved during January to December 2013.

ICMR Awards

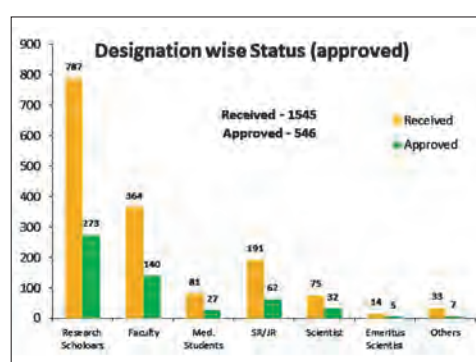
A total of 220 applications were processed for evaluation through different committees for selection. 50 scientists were awarded (for the year 2009-2010). Process has already started for processing ICMR awards and Prizes for applications (2011 & 2012).

International Conference/Training/Workshops to Non ICMR Scientist Support Scheme

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 Conference/Training programmes/ Workshops etc. Out of total 1545 applications 546 (35.33 %) applicants were supported during January-December 2013. Out of the total 546 approved applications 261 participants were availed till November 2013. Out of total 1545 applications 383 (25%) were more than 35 years & 1162 (75%) were below 35 years of age group. An analysis of the approved 546 applications shows that, 64.8 % i.e. 354 were male & 35.2% i.e. 192 were female. (Fig.).

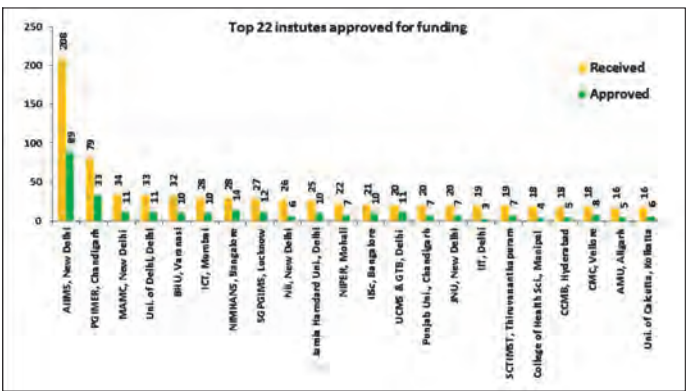


Gender wise analysis



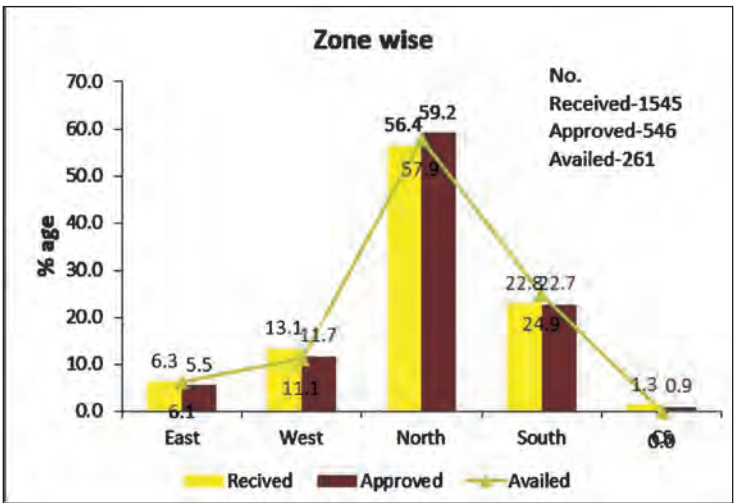
Designation wise analysis

Designation wise analysis of the applications that were approved (546), reveals that maximum number of Research Fellows (JRF-SRF) i.e. out of 787 applications received 273 were benefitted from this scheme followed by Faculty (Medical & Basic-out of 364 approved 140), Senior Residents /Junior Residents(62 out of 191), Medical Students (MBBS & MD-27 out of 81), Scientist (32 out of 75), Emeritus Scientist (5 out of 14) & Others (7 out of 33) applications. (Fig.).



Institution wise analysis

AIIMS, New Delhi emerges as the top most institute (208 out of 89), followed by PGIMER, Chandigarh (33 out of 79), MAMC, New Delhi (11 out of 34), Delhi University (11 out of 33) etc. details given in (Fig.).



Zone wise analysis

A zone-wise analysis indicates that North Zone is most active with most number of applications received, approved and availed from North Zone only (Fig.).

Junior Research Fellowship

During the period under report, the Council conducted 13th 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 appeared in the year 2013-14 was approx.11,000. The examination was conducted at **10 centers** (Bhopal, Bhubaneswar, Chandigarh, Chennai, Delhi, Guwahati, Kolkata, Mumbai, Hyderabad and Varanasi). A total of 560 JRFs is on-going (2009-2013) at various national level institutions. The value of fellowships is at present Rs.16, 000/- p.m. The annual contingency grant is up to Rs.20, 000/- p.a. + HRA.

MD, Ph. D. Programme 25 slots/year

This 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 candidate

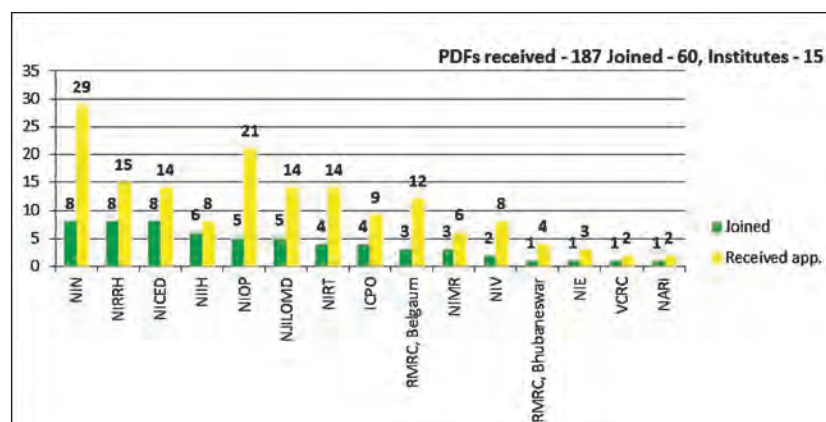
who passes all MBBS examinations in the first attempt with 60% or more aggregate marks is eligible for the examination. Under this programme selected medical graduates are provided financial assistance for 4 to 5 years. The eligible candidates were selected through national level examination.

Programme is on-going at three universities i.e. King George University, Lucknow, NIMHANS, Bangalore & Sri Ramachandra Medical College, Chennai. During 2013-14 out of 15 allotted slots 12 were selected. So far 47 candidates have joined the MD/PhD programme. five candidates have submitted their thesis.

Post Doctorate Fellowship Programme(50/year)

To identify and support young Ph.Ds. for the conduct of research using ICMR Institutes working on priority areas of Health Research. 47 applications were short listed for personal discussion and 9 were selected. (Fifteen (15)-ICMR's Institutes shown their interest viz: NIN, Hyderabad-7, NICED, Kolkata-5, NIRRH, Mumbai-5, NIOP, New Delhi-5, NIRT, Chennai-4, RMRC, Belgaum-2, NIILOMD, Agra-2, NIMR, New Delhi-2, NIIH, Mumbai-1, DMRC, Jodhpur-1, RMRC, Bhubaneswar-1, NIE, Chennai-1, RMRIMS, Patna-1, ICPO Noida-1, NIV, Pune-1, Others-8 (not received from ICMR Institutes.)

Programme is on-going at ICMR Institutes so far 48 candidates have joined, 26 PDFs completed the 2 years duration. A total 22 PDFs were Ongoing (Fig.).



Details of PDF's

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 being used in other institutes in India. The tenure is three months.

Intellectual Property Rights (IPR)/Translational Research

Translational research unit was established to identify leads that could be translated into products, processes and technologies for improving the health care delivery services. The mandate of IPR Unit is to provide technical, legal and other support on IPR-related issues to all ICMR supported research (intramural/ and extramural) and facilitate technology transfer,

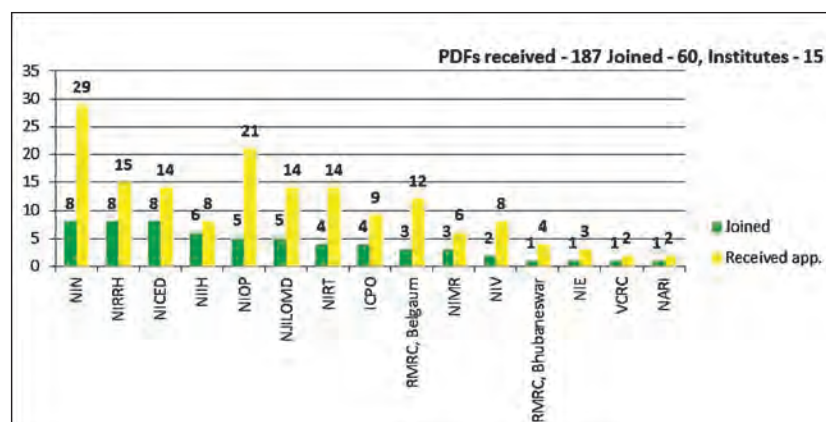
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Intellectual Property Rights (IPR)/Translational Research

Translational research unit was established to identify leads that could be translated into products, processes and technologies for improving the health care delivery services. The mandate of IPR Unit is to provide technical, legal and other support on IPR-related issues to all ICMR supported research (intramural/ and extramural) and facilitate technology transfer,

licensing and commercialization under IPR policies which needs regular monitoring from time to time. During the period under review, further translation work on the 30 available leads was continued.

Release of technologies: Thirty indigenous affordable technologies for public health are targeted to be ready by 2014.

The following four technologies were also released by Shri Ghulam Nabi Azad, Union Health Minister for use in public health.

- (1) The first indigenously developed Japanese Encephalitis vaccine (JENVAC) under Public Private Partnership was launched on 4th October, 2013 by the Hon'ble Health Minister. The indigenous virus strain was isolated and characterized by the ICMR's National Institute of Virology at Pune and the strains were transferred to Bharat Biotech for further vaccine development.



Launch of Indigenous Affordable Technologies by the Hon'ble Union Minister for Health Detection of Diabetes

- (2) RDB Kit (NIIH, Mumbai). RDB Kit for the detection of the common Beta-thalassemia mutations and abnormal hemoglobin developed by NIIH, Mumbai was launched on 17 December, 2013, New Delhi.
- (3) AV Magnivisualizer (ICPO, Noida). A device for screening of cervical cancer lesions named AV Magnivisualizer developed by ICPO, Noida was launched on 23 December, 2013 at New Delhi.
- (4) Diabetes testing kit (BITS, Hyderabad). A low cost point of care device for the detection of blood glucose levels developed by BITS, Hyderabad by ICMR support was launched on 13 January, 2014.
- (5) During the year, a total of 12 patents were filed – eight from intramural research and four from extramural research.
- (6) Three patents granted during this period belonged to VCRC, Pondicherry and NIOP, Delhi.
- (7) Two PCT has been filed, one from extramural research done at PGIMER, Chandigarh and other from intramural research done at NIRT, Chennai.

Two National phase PCT applications were filed in China and Brazil from intramural research done at ERC, Mumbai. Besides patent filing, some technologies were upscaled through technology transfer like Fertility Assessment Kit (NIRRH, Mumbai), Monoclonal Antibody for detection of *Chlamydia trachomatis* (NIOP, New Delhi).

Steps have been initiated towards a transparent process seeking collaboration by private/public sector companies through newspaper and website advertisement. The criteria for selecting the collaborators have been finalized. To manage the IP portfolio from time to time, amendment has been done with regard to IP policy. The revised policy aims to reduce the extra expenditure done on the patented technology that does not have commercial potential.

To promote indigenous technologies in vector control, standard operating system and protocol have been revised to provide robust and transparent system for introduction of public health related products like biopesticides, biolarvicides, insect growth regulators (IGRs), chemical insecticides, long lasting insecticidal nets (LLINs) etc. which are ultimately used by NVBDCP for public health programmes.

To promote awareness among the scientists about the criticality of IP and technology transfer, the IPR Unit organized workshops on “IPR in Medical Research” at NIRT, Chennai and NICED, Kolkata on 10-11 September, 2013 and 18-19 September, 2013. The IPR Unit continued its training of women scientists under the Women Scientists’ scheme of TIFAC/DST. The IPR Unit displayed the ICMR’s patented and non-patented technologies at various exhibitions which were considered relevant for industrial partnering like Bio Bangalore 2013, Bangalore; Pharmacy India 2013, Hyderabad. The research efforts of ICMR were very well appreciated by scientists and the ICMR stall won India Bio-2013 “Best Communication and Information” Award.

Medicinal Plants

Adhoc Project

Herb-drug Interaction Studies of Selected Herbs and Allopathic Drugs used in Treatment of Type 2 Diabetes, Rheumatoid Arthritis and Epilepsy

The project envisages evaluation of herbal drug interaction in 3 disease conditions requiring chronic medication viz., Diabetes type 2, Epilepsy and Rheumatoid Arthritis with one prototype drug used in each condition and selected herbs used in Traditional system of medicine.

Development of a Website Exclusively Dealing with Medicinal Plants

A website has been developed exclusively on the units activities and hyperlinked with the ICMR’s main website. It is regularly being updated.

Quality Standards of Indian Medicinal Plants

During the year the Quality Standards on 35 medicinal plants were developed, monographs prepared, finalized, technically reviewed and published as Vol. 11 as part of series on “Quality Standards on Indian Medicinal Plants”.

Earlier 10 volumes have been brought out containing quality standards of a total of 344 plants. Monographs on another 35 plants are being finalized for 12th volume.

Generation of Phytochemical Reference Standards and Development of Repository of Reference Phytoconstituents of Important Indian Medicinal Plants:

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



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these plant remedies with focus on pharmacological, toxicology, clinical, phytochemical, pharmacognostic, on the other.

The monograph on Perspectives of Indian Medicinal Plants in the management of diabetes mellitus is in different stages of review.

Task Force Projects

Review Monographs on Indian Medicinal Plants

During the year three Volumes 11-13 (with botanical names F-K) covering monographs on about 1100 medicinal plants species carrying multidisciplinary information were published.



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”.

Each monograph includes regional names of the medicinal plant, its Sanskrit synonyms as well as the Ayurvedic description (wherever available), ethno-botanical 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 complete references and bibliography on each aspect of the information cited, besides the colour photographs of important medicinal plants.

Health Systems Research

The Health Systems Research (HSR) Division is engaged in fostering health systems research in the country through supporting ad-hoc research projects on various issues of HSR, developing and implementing multi-centric research project on issues of national importance.

Ad-hoc Projects

Issues Related to Adolescent Health

Studies on health problems on adolescents that are in progress in the states of Andhra Pradesh, Karnataka and Orissa document the implementation and impact of government adolescent health programmes. In Andhra Pradesh, it was found that the overall prevalence of stunting is 37% and of anaemia is 40% among adolescent girls. A great proportion of adolescent girls (86%) have low serum ferritin levels. Of these adolescent girls only 3% are of government adolescent programme. In tribal districts of Odisha, the prevalence of

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stunting is as high as 45% and about 70% of adolescents are suffering from different grades of anaemia. Less than 2% of adolescents are aware of the ARSH programme. The Odisha study is developing an advocacy based intervention to improve the utilization of government programmes, particularly the ARSH services. Studies from Chandigarh addressed the impact of mentoring relationship on adolescents. About 70% students thought mentors could help them in overcoming adolescent related problems and about 52% of adolescents felt the need of sex education. The study provides strong basis for incorporating mentoring at school/college level. Another study from Pune, studied the problems of physically-challenged adolescents. Adolescents (25%) and their parents (30%) faced stigma due to their disability. Under a study from NIMHANS, Bangalore, training manuals on adolescence sexuality, gender discrimination and reproductive health to capacitate social work trainees have been developed. A study from Karnataka qualitatively focused on adolescent health issues pertained to males, which are neglected in many studies.

Issues Related Gender Perspectives

A study from Rajasthan focused on developing competency framework for mainstreaming gender-responsive health services. In a study from Maharashtra, the outcome is the TB-specific quality of care framework with gender perspective for the use in RNTCP. In Jammu & Kashmir state, health system's perspectives of gender in the context of conflict were studied. It revealed that conflict aggravated and intensified the women's problems in Jammu & Kashmir during last two decades.

Issues Related to Health Care Delivery and Access

Currently two studies on health insurance are progressing in Andhra Pradesh and Karnataka states aimed to collect information of awareness and prevalence of health insurance and other issues pertained to acceptance of health insurance by the community. About 60% of tribal population in Andhra Pradesh are not aware of the concept of insurance. Among those who aware of it, most (88%) were aware of life insurance and only 18% were aware of health insurance. However, about 70% of tribal households are keen to take health insurance for themselves and their families. However, in rural community of Karnataka, about 72% of people are aware of health insurance. Mostly they got information and availed the health insurance through women self help groups. Of those not having health insurance, only 30% have shown their willingness to pay.

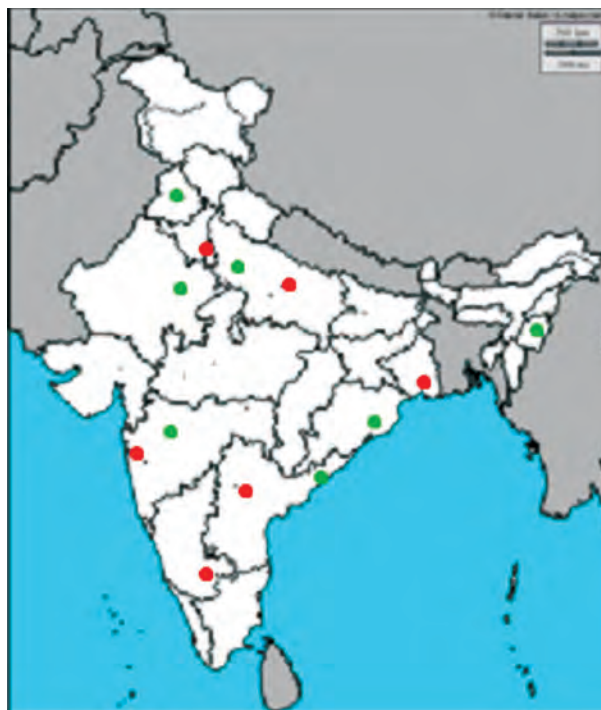
Other Issues

The project funded to Surat Medical College studied critically the negative studies published in various Indian biomedical journals. It provided some guidelines for publication of negative studies.

Two Multicentric Task Force Studies on Migrants' Health Care

Interventions to improve the health care access among migrants living in 13 cities of India. The intervention is planned and implemented with the principles of advocacy, partnership and community mobilization. The findings of formative research on migrants' access to government health care facilities and health system's responsiveness are used during advocacy efforts. Policy briefs were prepared and widely used. Partnership with state/municipal health officials, non-governmental organization and industries was developed to address the problems related to low health care access. The supply-side issues were addressed by these partners. Community mobilization activities were undertaken at community level

to improve the demand for health care. Health services have undertaken the community mobilization activities in collaboration with local non-governmental organizations and community-based welfare and religious organizations. Strategies have been implemented to address both supply and demand-side issues. The impact evaluation is being carried out. The preliminary observations reveal that both health system's responsiveness and migrants' access have improved. It was observed that the coverage of geographical areas and the quality of services in the existing areas where migrants are living also showed some improvement. The utilization of health care services from government facilities also increased during the intervention period.



Cities of National Taskforce projects of HSR Division on migrants' health care (red dots are major/metro cities and green dots are smaller cities)

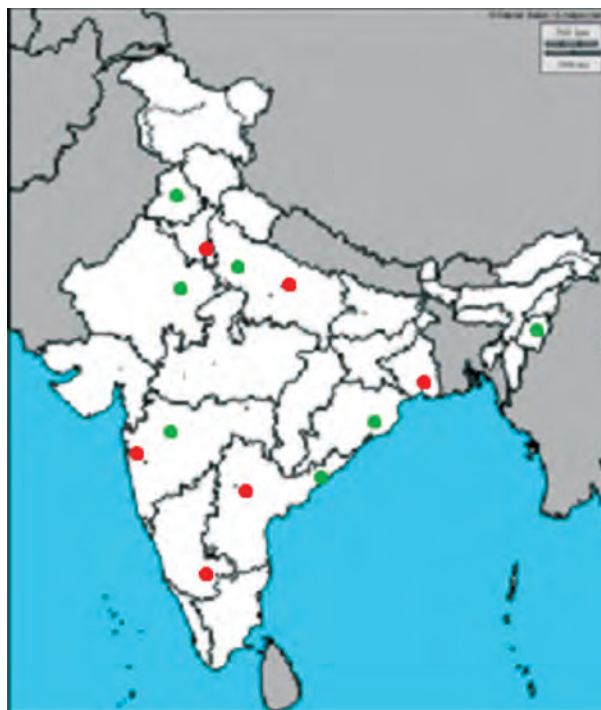
Social & Behavioural Research

A Rapid Appraisal of Total Sanitation Campaign in the four Selected Districts of Madhya Pradesh

The Total Sanitation Campaign (TSC) of the Rajiv Gandhi National Drinking Water Mission (RGNDWM), Govt. of India (GOI) was launched to cover all households with water and sanitation facilities and promote hygienic behaviour for overall improvement of health of the rural population belonging to BPL category. Aim of the study was therefore to assess whether the principles and quality of the NGP are maintained during the scale up of the TSC.

Most people used public hand pumps for drinking & using water but took resort to far off rivers & wells when main source got defunct. Though 100 percent households have access to individual, community or shared toilets, only around 81.56 percent are using it as toilet. Lack of resources combined with neglect by the Sarpanch/ Panchayat members has emerged as the single largest combination factor reported to be responsible for not constructing an individual household latrine. Non functionality of toilets in school was due to absence of overhead tank, tap and water and the toilets too were not clean. The disposal of solid waste

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was either in the form of dumping and indiscriminate throwing.

Acceptability and Effectiveness of Three Community Based Health Insurance Schemes in Karnataka

This study was carried out in Dakshin Kannada and Udupi districts of Karnataka where three community based insurance schemes namely Rastriya Swasthya Bima Yojna (RSBY), Manipal Arogya Suraksha, and Sampuran Suraksha schemes were functioning. A total of 3439 households – 2641 insured families and 798 non-insured families were studied through a cross-sectional survey of in the community in these two districts.

The study found that the female headed households, below graduation educated with non-professional occupations, having some family member with chronic illness, and relatively larger family size were more likely to be acceptors of such community based health insurance schemes which offer differing benefits and flexibilities in terms of payment of premium, coverage of hospitals and providing other benefits. The study reported all three schemes functioning effectively in these districts. Some of the reasons for non-enrollment were apprehensions leading to indifference, financial constraints, lack of information and non-affordability.

Behavioral Addiction in the Community

The present cross sectional study adopting a house survey methodology study explored the pattern of behavioral addiction in an Indian context with a sample of 1392 males and 1363 female participants of 18 years and above from an urban locality in East Bangalore. The survey questionnaire incorporated demographic schedule, the Lie-Bet Tool, Face book intensity Scale, Exercise addiction Inventory, questions for other behavioral addictions, General Health Questionnaire and Modified Mental Health Screening Questionnaire.

Behavioral Addictions have been observed with 1.3% for Internet (2% males & 0.6% females); Shopping (4%) (male-3.2% & female-4.8%); cell phone (4.1%-5% males & 3.1% females); Eating (1.6%); Television (2.9%; 3.3% male, 2.4% female); work (9.7%; 10.5% males & 8.9% females); Sex (0.2%) (0.3% males & 0.1% females); Exercise (5.85%) (7.5% males & 3.8% females); 1.2% of the sample had Gambling Addiction. 1051 participants reported that they were using face book as a social network media with a mean of 20.48 Physical distress was found as a co morbidity with eating addiction (1.6%); mobile phone addiction (6.8%); and television addiction (5.3%). 18.8% of subjects with eating addiction were having gambling addiction and 13.5% of television addicts had problematic gambling. 9.3% of people reported that they want to change their alcohol related behaviors. 5% wanted to change cell phone use, 4.8% people reported that they wanted to change their TV use and also internet activities (3.3%). 4.2% of the participants wanted to change their monthly expenses for cell phone use, 3.8% reported modification was needed in their shopping expenses and 2.9% wanted to reduce their smoking expenses. There is absence of treatment seeking behavior for behavioral addictions. Focus group discussion revealed presence of unemployment, lack of awareness, cultural differences; easy availability, acceptance of these behaviors and easy availability were associated with addictions.

Do our Medical Colleges Inculcate Health Promoting Life Style among Medical Students?

The study was carried out among 3250 students drawn from one Government Medical College and four Private Medical Colleges selected out of 41 medical colleges in Karnataka. It was observed that number of smokers among medical students had increased by 2.7 times ($p < 0.001$), males (2.4 times) and females (4.2 times). Students consuming alcohol had increased

2.1 times ($p < 0.001$), males (2.2 times) and females (2.0 times). Students abusing drugs had increased by 2.4 times ($p < 0.001$), males (3.1 times) and females (9.5 times). Students doing regular physical activity had decreased by 1.7 times ($p < 0.001$), males (1.6 times) and females (1.7 times). There was not much increase in junk food consumption after joining medical college as 95.7% were already taking junk foods. 229(7%), 634(19.3%), 290(8.8%), 112(3.4%) and 1356(41.2%) did not believe that tobacco use, alcohol consumption, drug abuse, physical inactivity and junk food consumption can be health hazards respectively.

There is an urgent need to develop support strategies to put an organized effort to inculcate health promoting lifestyles among those entering as well, already in the profession.

Hypertensive Patients' Perception of the Disease and Pattern of Utilisation of Services in Kamshet area of Maharashtra

The main objective of the study was to determine the socio-economic characteristics of hypertensive patients. 311 hypertensive patients were recruited from outpatient clinics in Kamshet for the survey. 26 in depth interviews were conducted to get detailed insight into their views regarding their illness. Information about health providers approach towards management of hypertension was collected. The study showed that patients perceived hypertension as a chronic illness and that they have very less control over their illness. Adherence to medication was not associated with perception of illness and adopting healthy lifestyle habits. Patients take their medication regularly because of fear of reappearing the sign and symptoms of the hypertension. The threatening views about the illness affected the quality of life negatively in terms of perceived health status and psychosocial wellbeing of the hypertensive patient.

Identification of Social and Behavioral Determinants affecting Delivery and Utilization of Zinc and ORS for Treatment of Childhood Diarrhea in Tribal area of Vadodara District, Gujarat

Despite the evidence of beneficial effect of zinc in severity and duration of childhood diarrhea, its widespread introduction and utilization is missing. The objective was to study the utilization of zinc and ORS as primary treatment of diarrhea among under-five children, as affected by perceptions, beliefs and behaviors of tribal community and health service providers.

A cross-sectional exploratory study was undertaken in four tribal blocks of Vadodara, Gujarat, utilizing a mix of quantitative and qualitative research methods. Majority (80%) of the study children were taken for treatment of which 73.5% were treated at private health facilities. Treatment seeking behaviors of caregivers were not significantly associated with any of the socio-demographic factors. ($p < 0.05$) Knowledge and practices of caregivers regarding use of ORS were good, although it was received by only 40.7% children. Zinc was not received by any child. Qualitative assessments revealed a lack of awareness/Knowledge about zinc therapy among communities as well as healthcare providers, further complicated by erratic supplies and lack of clear guidelines.

Utilization of Emergency Contraception Pill among Rural and Urban Women in Rajasthan: A Study of Psychosocial Determinants

The study aimed to assess the level of knowledge of the women about emergency contraceptive pill (ECP) viz-a-viz other contraceptives and to know its utilization pattern among rural and urban women of Rajasthan. A total of 978 married and 228 unmarried women were interviewed for the study.

Almost all the unmarried woman respondents were aware of some or the other FP method; however, about 15 percent were aware of all FP methods. Around 87 percent were aware of ECP which is almost double of the proportion of married respondents' knowledge. For

almost all respondents (96%), TV was the primary source of information about ECP, for more than half of the respondent (58%), friends were the source of information. About half of the respondents were aware of use of ECP within a time limit of 72 hours. Half of the respondents were aware of probable side effects of ECP. More than half of unmarried respondents were having boyfriends or male partners and 16 percent of them were sexually involved. All of the sexually involved women reported contraceptive use, majority (84%) reported for using ECP. Around 63 percent were using ECP as regular method of contraception. Major reasons for using ECP were 'it does not hinder pleasure' and 'contact was unplanned'. About 69 percent of respondents admitted that availability of ECP had benefitted women. About 71 percent women suggested for creating awareness of the side effects of ECP to curb its irrational use.

BE/ RE (2013-14) and Actual Expenditure upto 31.3.2014 under Plan & Non-Plan and BE (2014-15) under Plan and Non-Plan for Department of Health Research										Annexure-I
(Rupees in Crores)										
S.No.	Scheme/Programme	Budget Head	2013-14			2013-14			2014-15	
			PLAN			NON PLAN			PLAN	NON-PLAN
			BE	RE	Actual expr. upto 31.3.2014	BE 2013-14 Non- Plan	RE-2013-14 Non-Plan	Non-Plan Actual expenditure 2013-14 (31.3.2014)	BE-2014-15	BE -2014-15
1	2	3	4	5	6	7	8	9	10	11
1	Secretariat-Social Services	Secretariat-Social Services	5.00	1.65	0.14	10.00	6.31	5.21	5.00	10.00
2	Human Resource Development for Health Research	Advanced Training in research in medicine and health	41.00	4.00	1.51	0.00	0.00	0.00	17.00	0.00
		International cooperation in medical and health research	5.00	0.50	0.17	0.00	0.00	0.00	2.00	0.00
3	Grant-in-aid Scheme for inter-sectoral convergence & promotion and guidance on research governance issues	Inter-sectoral coordination in medical, biomedical and health research	13.50	5.35	2.60	0.00	0.00	0.00	26.00	0.00
		Promotion & guidance on research governance issues.	2.70	0.00	0.00	0.00	0.00	0.00	3.00	0.00
		Matters relating to scientific societies and associations, charitable and religious endowments in medicine and health research.	9.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
		Coordination with Governments/ organizations	10.80	0.00	2.35	0.00	0.00	0.00	1.00	0.00

4	Managing epidemics and national calamities	Matters relating to epidemics, natural calamities and development of tools to prevent outbreaks	40.00	30.00	34.00	0.00	0.00	0.00	31.00	0.00
5	Development of infrastructure for promotion of health research	Promotion, coordination and development of basic, applied and clinical research	49.00	44	48.65	0.00	0.00	0.00	72.00	0.00
		Establishment of Model Rural Health Research Units.							18.00	0.00
6	ICMR	ICMR	477.40	432.00	480.20 (including NER)	272.00	299.25	299.25	477.40	281.67
7		Provisions for projects/Schemes of North East areas.	72.60	57.50	0.00	0.00	0.00	0.00	72.60	0.00
Total			726.00	575.00	569.62	282.00	305.56	304.46	726.00	291.67

<p style="text-align: right;">Annexure-II</p> <p style="text-align: center;">LATEST STATUS OF AUDIT PARA IN RESPECT OF ICMR AS ON 13-05-2014 Statement indicating pending C&AG para - Autonomous body-ICMR</p>				
Sl. No.	Report No.	Para No.	Subject	Status
1	5 of 2000	2.1.9(D)	Regional Medical Research Centre for Tribal,(RMRCT), Jabalpur (D-12012/43/2000-Audit) OPA No. 7655	Draft ATN sent to Audit for vetting on 22-11-2013. Reminded on 13-12-2013 and 30-4-2014 to expedite the vetting.
2	5 of 2005	9.1	Wasteful expenditure and blocking of funds due to improper planning(ICPO) (D-12012/03/2005-Audit) OPA No. 2781	Draft ATN sent to Audit for vetting on 30-4-2014.
3	5 of 2007	Chapter 2 (performance) 2.6.1	National Institute of Malaria Research (D-12012/56/2006-Audit) OPA No. 12176	Draft ATN sent to Audit for vetting on 13-10-2013. Reminded on 13-12-2013 and 24-3-2014 to expedite the vetting.
4	16 of 2011-12	10.1	Work Management of ICMR. (D-12012/35/2011-Audit) OPA No. 14632	Draft ATN was received from ICMR on 14-02-2014. After examination, certain modifications / corrections were made in the ATN and returned to ICMR for providing four copies of the fair ATN vide letter dated 24-3-2014. There is no response.
5	16 of 2011-12	8.5	Delay in commissioning of equipment, NIOH, Ahmedabad (D-12012/43/2009-Audit) OPA No. 7337	Draft ATN has been sent to PDA, Scientific Departments, Mumbai on 17-4-2013 for vetting. Reminders were sent to them on 11-6-2013 and dated 9-7-2013 to expedite the vetting. Reminded to expedite the vetting on 13-12-2013 and 24-3-2014.

Annexure-III

Activities in the North Eastern States

The following three schemes of the Department of Health Research (DHR), approved and rolled out during 2013-14, were implemented in the North Eastern Region as mentioned below:

(1) Establishment of Multidisciplinary Research Units (MRUs) in Govt. Medical Colleges

1. Assam: Silcher Medical College and Hospital, Silcher
2. Manipur: Regional Institute of Medical Sciences, Imphal
3. Tripura: Agartala Govt. Medical College, Agartala

(Each medical college has been released first installment of Rs.1.25 crore during the year 2013-14)

(2) Establishment of Model Rural Health Research Units (MRHRUs) In The States

S.No.	State	Location of MRHRU	Funds released during 2013-14
1	Assam	PHC Chabua	Rs.1.50 crores
5.	Tripura	Kherengbar Hospital Khumulwng	Rs.1.50 crores

Regional Lab

Regional Medical Research Centre (RMRC), ICMR, Dibrugarh (Grant of Rs. 7.47 Crores. released during 2013-14)

State level Lab

North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences (NEIGRIHMS) Shillong, (Meghalaya) (Grant of Rs.2.97 Crores released during 2013-14)

Grievances Redressal

DHR has grievances redressal mechanism in place with Ms Sunita Sharma (Deputy Secretary) as the Nodal Officer for the purpose. During the year 2013-14, a total number of 98 grievances were received at DHR. All were addressed and disposed off online.