

Preface

The year 2005 dawned for India and many other South-East Asian countries face to face with the devastation, shock in the aftermath of one of the greatest human tragedies in history due to Tsunami of 26th December 2004. The immediate response of the VCRC and its staff was to become a partner to all governmental, non-governmental as well as public efforts in serving the affected communities by providing all assistance and help in restoring their life towards fulfilling their immediate need: food, water, shelter, safety, sanitation and healthy environment. By the end of 1st week after the tsunami, VCRC had gathered itself and got organized to facilitate the central and state governments as well as other ICMR institutions and academic institutions in providing healthcare and prevention of diseases outbreak. For next few days it worked closely with other organizations in orienting all health officials / administration and public at large on the special surveillance efforts during the post-disaster situation, giving importance to early warning and rapid communication mechanism using community volunteers and others. The VCRC received direct messages from volunteers of several affected villages about occurrence of fever / gastroenteritis and measles. The messages were passed to the appropriate authorities, which acted promptly and responded adequately so that actual larger outbreak or epidemic situation was averted.

After the tsunami, the VCRC found itself facing the real challenge that the center deserved to face and work for a solution. The question was direct, what is the risk of vector borne diseases outbreak in the changed and changing eco-environmental conditions in and around the affected communities as well as new human settlements that were established during post tsunami period and how to mitigate such risk. The VCRC staff formed several teams and carried out meticulous periodic investigations on different eco-environmental parameters and vector breeding status. This investigation was carried

out in seven areas covering the entire stretch of tsunami hit coastal areas in Tamil Nadu, Andhra Pradesh, Pondicherry, and Andaman Nicobar islands. The important lesson learnt from this experience was that continued vector and vector borne disease surveillance in dynamically changing eco-environmental condition (whether natural or man made) is very important not only for giving early warning, prevention of disease outbreaks but also to prepare the public health system as well as the community for a rapid and appropriate response in the case of a challenge. These activities were possible without taking any external assistance but reorganizing and reallocating staff and other resources already at VCRC.

Some of the research and other activities had to be re-prioritized due to the redeployment of staff and other resources. In spite of this, the VCRC continued to play its important role in the Global and National programmes towards Elimination of Lymphatic Filariasis and to respond to the challenges due to urbanization, climate change, natural resources, etc. by research, HRD, consultancy, networking and partnership.

Staff position & facilities

The total staff strength is 246 (25 belonged to research and 110 to technical cadre, 81 support/administrative staff, 1 Library Information Officer). As time passes by, the hierarchal pattern of staff, particularly the scientific and technical has become an inverted pyramid with no provision for lateral entry. This has not only hampered research output, but also made science administration extremely difficult. The ageing research & technical staff maintain a high standard of work ethics and are prepared to adapt to the changing demands. Apart from research, the staff devote considerable amount of time in human resource development activities involving training & imparting knowledge to

personnel from local, State, National & International educational institutions & health departments. The staff are also engaged in maintaining several facilities such as insectariums, mosquito museum, clinic, animal house, local area network (LAN) of computers (68 nodes and 4 servers); designing, launching and updating of websites, and producing quality presentation materials. Several of the senior research staff is also providing consultancy to ICMR head quarters, other ICMR institutions; and local, State, National & International organizations, which is widely accepted and acclaimed by all.

The VCRC library maintains a centralized database with 4.8 lakhs searchable records and approximately 10,000 full text articles (in pdf format) on vector borne diseases. All the VCRC publications (papers published in journals, miscellaneous publications / reports) have been digitalized; which are being constantly updated. Our center has evolved as a center of excellence in the fields of Vector-borne diseases, Genetics and Bio-informatics.

The center continues to be a WHO Collaborating Centre for Research and training in Lymphatic Filariasis & Integrated Methods of Vector control.

Human Resource Development (HRD)

The VCRC has been recognized as a Center of Excellence for HRD activities on vector borne diseases by the Ministry of Health & Family welfare, Govt. of India. Main areas of HRD activity include Ph.D. programme, Short term training courses, Capacity building (Scientists & Administrative Staff of VCRC), Organizing Meetings and Workshops.

- Eight candidates have registered and are working for Ph.D. (one each in Geography and Zoology, and six in Microbiology).
- 103 UG & PG students from different parts of the country were trained on various topics related to diagnosis and treatment of lymphatic filariasis, parasitological and immunological techniques, mosquito larvae rearing

techniques, molecular biological techniques, bioinformatics, vector control techniques, bioinformatics, bioprocess engineering & mosquito biodiversity.

- Three students from St. Olaf College, USA visited VCRC for a short term training on vector borne diseases and their control.
- Under the WHO/Country Budget programme, 50 Public Health personnel (Sri Lanka-44, Myanmar-3, and Nepal-3) were trained on Entomology and Malaria control.
- Three Medical and four Nursing students from France and Belgium were trained on tropical diseases with special reference to Vector Borne Disease and their control.
- Seven of our Scientists underwent training on various fields (Data Analysis in Social Sciences, Research Methodology for Rural Development Professionals, Bioinformatics and Functional Genomics Applied to Insect Vectors of Human Diseases, Biology of Disease Vectors, and GCP Course) in different Laboratories at National (TATA Institute of Social Sciences, Mumbai; National Institute of Rural Development, Hyderabad) and International institutions (Mahidol University; Thammasat University, Thailand) level.
- Twenty five Administrative staff of our centre were trained on SC/ST/OBC/Roster Maintenance at VCRC.
- 3 National level meetings, 2 Workshops (including International Cochrane collaboration), and 2 Continuous Medical Education (CME) programmes for Scientists & Students were organised.
- Six hundred and sixty six students from 16 Educational Institutions from different parts of the country visited the VCRC Laboratories, as part of their curricula.

Finance and infrastructure

Total cash inflow during the year was Rs.7.04 crores, of which the ICMR (the VCRC's parent body) provided Rs. 6.50 crores. An additional Rs. 0.54 core was generated by the VCRC from other sources for research, training and technical service activities. The Centre has generated 8% of its total fund from outside sources. This proportion is less than the previous year, and was due to the Centre not taking up sponsored projects during the year, as the need was for deploying all available staff for post-tsunami surveillance and related studies. The Centre's research activities continued to address national needs, and was almost entirely supported by the ICMR itself. Moreover, Centre's policy to discourage donor driven research is another reason.

Highlights of Research Activities of VCRC during 2005

This year has been significant for research in many aspects. The centre contributed to the national cause by undertaking research on environmental and vector borne disease risk assessment following the Tsunami. The VCRC continues to be a global leader in Filariasis research as well as in National and International arena for Malaria, Dengue & JE Epidemiology and control. All together a total 65 Research projects were undertaken during the report period out of which 11 were completed. Fourteen new projects have been initiated, 34 were ongoing, and 6 SAC approved projects are awaiting extramural funds. The following are the highlights of the year 2005:

Post Tsunami disaster: the burden, water quality and assessment of risk of vector borne diseases

- Initially, the VCRC provided technical help to the National & State Governments to detect high-risk population and forecast epidemic-prone diseases in these populations and to guide relief, prevention, and control efforts.
- Impact of tsunami on productivity loss and years of life lost were estimated to be Rs.411.03 Million and 722,264 respectively.
- Principal vectors of malaria *An. stephensi* and

An. culicifacies, and the secondary malaria vector, *An. vagus* were found breeding in different kinds of tsunami water inundated habitats in the eastern coastal areas of mainland.

- The breeding of *An. stephensi* in the tsunami water inundated habitats was a new finding.
- Japanese Encephalitis vector, *Cx. tritaeniorhynchus* and *Cx. vishnui*, dengue vector *Ae. aegypti*, and filariasis vector, *Cx. quinquefasciatus* were also recorded in many breeding habitats.
- The geo-spatial structure of most part of the islands got changed and the fresh water habitats including the paddy fields became saline with tsunami water, and thereby acting an ideal breeding ground for saline loving *An. sundaicus*, the major malaria vector in Andamans. Subsequently, malaria became rampant, as has been predicted.
- The water quality was assessed for the purposes of drinking, agriculture, etc. in the coastal areas of mainland as well as Andaman Islands.
- The 'coliforms' was detected in drinking waters, and hence suggested water treatment ('chlorination') before supply.
- The record of cyanobacteria in shoreline water and its economic exploitation was brought to light.
- Temporary shelters contributed to a very high fly population. They were found to belong seven different species. The abundance was high for nearly one month following tsunami and the local health authorities were alerted for fly control measures. In the subsequent months, the fly population declined.

Microbiology and Immunology

- Two new highly mosquitocidal bacteria (VCRC B469 and VCRC B471) were identified as *Bacillus subtilis* strains.
- A new strain of *Bacillus thuringiensis* was isolated which shared the serological identity

with *B. thuringiensis israelensis* as well as *tochigiensis*, although it had larvicidal toxins similar to the former with the presence of Cry toxins and Cyt toxins.

- Host-parasite interaction studies showed that a new humoral immune protein, Transferrin, was found to be specifically expressed in *Culex quinquefasciatus* upon infection with *Wuchereria bancrofti*.

Chemistry

- Six new 1-N-Methyl-4 (substituted benzoyl) piperazines were synthesized, and were screened for macrofilaricidal activity against adult worms of *Setaria digitata*.
- While DSTD-15 showed the highest inhibition of Methylene tetrahydrofolate reductase (MTHFR), DSTD-24 showed the highest inhibition of Serine trans hydroxymethyltransferase (SHMT).
- Structural analogues of the macrofilaricidal lead molecules, P-19, P-21 evaluated in vitro against adult worms of *Brugia malayi* and found to be effective.

Molecular Biology and Bioinformatics

- A RT-PCR assay useful for xenomonitoring of infective larvae (L3) of *W. bancrofti* in *Culex quinquefasciatus* has been developed and the assay was found to have 98% sensitivity and 100% specificity.
- Genetic loci in the Arachidonic acid pathway have been found to be genetic determinants for variation in response to antifilarial drug, DEC and are non-synonymous SNPs in Prostaglandin I₂ Synthase (PGI₂S), Lipoxygenase A4 Hydrolase (LTA₄H) and Lipoxygenase C4 Synthase (LTC₄S).
- PGI₂S was found to contain maximum number (8) of nSNPs, of which 2 nSNPs were found to be located in the β -sheet when mapped on to its tertiary structure and hence may result in mis-folding and affect its function, thereby causing varied response to DEC among treated individuals.
- Structural characterization of the repeat sub unit of the gene coding for gp15/400

polyprotein, a lipid binding allergen, among 45 isolates of *W. bancrofti* showed that it is highly conserved with only two synonymous nucleotide changes at nucleotide positions 369 (A-G) and 375 (C-T).

- The allergen cloned and expressed and immunological characterization showed that it is associated with elevation of specific IgE antibody levels leading to Th₂ type of immune response. Due to its multifarious roles in the survival and pathogenesis of the parasite, it has good potential as a target for drug, immuno-modulation tools and development immunotherapy.
- Anti-dengue antibodies tested in 318 individuals residing in and around houses of dengue cases detected earlier (year 2003) in Pondicherry showed that 1.9% (n=6) of were positive for IgM, 70% (n=223) for IgG and 17% for both IgM and IgG (n=55), indicating the presence of activity of and exposure of individuals to Dengue virus in these areas.
- Genotyping for HPA-1 alleles among dengue cases showed that Dengue fever (DF) cases were homozygous (a/a) for the locus, while Dengue Shock Syndrome (DSS) cases were heterozygous (a/b).

Vector Biology and Control

- During the reporting period, DNA barcodes for 62 species of mosquitoes belonging to 15 Genera prevalent in the country have been constructed.
- Mosquito biodiversity recorded in the forested ecotype of the eastern hill ranges of India accounted to 63 species in 16 subgenera and 10 genera.
- *An. minimus*, one of the malaria vectors in the Jeypore and Singhbhum hills of Orissa State, India during the pre DDT era believed to have disappeared, reappeared in Singhbhum hills. A high proportion of this species was recorded and PCR assays showed that 91% were species A and 9% were species C out of the 22 specimens processed.

- The catalogued collection in the museum contains more than 16,000 adult mosquitoes, 1,500 male and female genitalia preparations and 1,600 larval and pupal exuviae. Mosquitoes of 20 genera, 39 subgenera and 213 species are housed in the museum, representing about 65% of the known species from India. The collection includes representative specimens from 16 States and Union territories of the country.
- The acceptability of long lasting treated nets (LLTN) for malaria prevention amongst a rural community was assessed in malaria endemic districts of Orissa State. About 60% of the people perceived that sleeping inside LLTN could reduce the occurrence of malaria. Between 70%-90% of the LLTN distributed were found hanging inside the house and more than 90% of the respondents perceived the benefit of reduced mosquito bites.
- Underlying mechanisms of DDT resistance in the field populations of malaria vectors viz., *An. culicifacies*, *An. fluviatilis* and *An. annularis* has been investigated. While *An. fluviatilis* is susceptible to DDT, *An. culicifacies* and *An. annularis* are resistant to DDT. All the three vector species are susceptible to synthetic pyrethroids. The GST activity in *An. culicifacies* was found highly elevated when compared to that in *An. fluviatilis* and such elevation might be responsible for conferring resistance in *An. culicifacies* to DDT.
- Diflubenzuron formulations (2% WG and 25% WP) were effective against *Cx. quinquefasciatus* at 50-100 g/ha for about 2 weeks. The DT formulation was effective only at the higher dosage of 100 g/ha.
- Spinosad (metabolites of the soil actinomycete *Saccharopolyspora spinosa*) formulations were found effective against *Cx. quinquefasciatus* immatures at the application rate of 150mg/m² at fortnightly intervals in cesspits and drains and at 50mg/m² monthly applications in disused wells.

Clinical Epidemiology & Chemotherapy

- Comparison of operational feasibility and

impact of co-administration of albendazole and DEC with DEC alone showed that it was Feasible to distribute the drug to the target population. The change in microfilaria prevalence and density was comparable but the co-administration appeared to have an edge over DEC alone in reducing antigenemia prevalence.

Health Economics & Disease Burden Estimation

- Effective coverage of DEC salt distribution to eliminate persistent foci of transmission of Lymphatic filariasis could be sustained with the delivery through salt vendors. One year of DEC salt distribution / consumption could reduce mf prevalence below 1% and no children born after the intervention was positive for filarial antigen, indicating total interruption of transmission.
- Disability weight of health states of filarial disease, essential to develop rehabilitation package and disease burden was derived. Community rating was higher than the providers' rating, indicating the perceived need of the morbidity management measures.

Environmental Sciences

- A conceptual framework for JE Transmission model was developed and key risk factors associated with the transmission were identified. Model based analysis showed two main patterns of JE, one determined by human activity i.e. 'endemic' and the other by climatic / natural causes, i.e. 'epidemic'.
- Endemic JE is influenced by perennial irrigation, year round agriculture activities and animal husbandry practices.
- Epidemic JE is mainly due to vagaries of climate/meteorological variables (flood following a prolonged drought), bird sanctuaries (ardeid birds' migration) etc. in the region.
- Based on this observation, country has been stratified into endemic and epidemic JE prone areas.

Operational Research & Surveillance

- Development of LYMFASIM model variants for use in planning and evaluation of LF programmes.
- Heterogeneities in exposure to mosquito biting and eliciting immune response are the key factors describing the patterns of transmission, infection and immunity.
- Models with appropriate estimates for the parameters of exposure and immune heterogeneities have been developed to explain the regional differences in epidemiological patterns.
- Application of the model to predict the impact of MDA with DEC or ivermectin indicated that elimination cannot be reached with 9 rounds of MDA for an average drug consumption rate of 65%. Further, the prevalence would revert back to the pre-MDA situation (14%) in about 15 years.

Formulating a frame work for Dengue surveillance and forecasting:

- *Aedes aegypti* and *Ae. albopictus*, relatively high PMD was recorded during monsoon season, indoors and outdoors.
- Anti-adult measures need to be focused both indoors and outdoors, as resting mosquitoes were collected there in equal proportion.

Impact of evaluation of Mass Drug Administration (MDA) with single dose DEC or Ivermectin or both in village scale.

- The results imply that (a) low levels of microfilaraemia continues to persist even after several rounds of MDA (b) the role of low density microfilaraemia needs to be understood in the resurgence of transmission (c) progress from excellent control to elimination appears to be a long process.

Publications/Patents

The number of publications in this year was 33 (22 in international journals), which has doubled compared to the last year number of 17. There has also been a rise in the average impact factor to 2.48 as compared 1.55 in last year. This year two patents have been filed.

Consultancy and Linkages

Vector Control Research Centre (VCRC) continues to forge ahead in achieving its mission and vision by focusing its activities on research, human resource development, and dissemination of scientific information, building effective linkages and partnerships and providing consultancy services towards control / elimination of Vector Borne Diseases. Lymphatic filariasis, malaria, dengue and JE continue to be the focus of this center. The research with a theme and team approach followed at the center has been highly productive. There is now increasing attention on partnership approach for fruitful collaboration and networking with other organizations within and outside ICMR as well as other International agencies.

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Dr.P.K.Das
Director

Eliminate Filariasis, Alleviate Poverty