

# Preface

On behalf of the staff of the Vector Control Research Centre (VCRC), I have the privilege to present the 29<sup>th</sup> Annual Report of VCRC highlighting the activities and achievements of 2004. The year ending has been traumatic and challenging for all of us as TSUNAMI hit the eastern coast of Indian Ocean on 26<sup>th</sup> December. I am grateful to all the staff that rose to the occasion and participated in rescue, relief and rehabilitation activities. They set up a surveillance system to monitor risk of water and vector borne diseases throughout the eastern coast, including the Andaman and Nicobar Islands. This was preceded by an initial assessment and monitoring carried out in four sectors, viz., Nagapattinam, Cuddalore, Mamallapuram and Pulicat, along with Andaman & Nicobar Islands. I have mentioned in an earlier report that VCRC has prepared itself to respond to any challenges and opportunity that arise due to globalization, urbanization, climate change, armed conflicts and natural disasters. We respond to these challenges by research, HRD, consultancy, networking and partnership. Here we highlight how VCRC had gone about building upon its strengths and minimizing weaknesses.

## Staff position & structure

This year has seen us growing in stature as more and more scientists get involved in national and international programmes. The total staff strength of 242 consists of 25 scientists, 129 technical and 88 administrative, accounts and other supportive staff. The work ethics and temperament of the

staff have always been of a high standard, as has been the VCRC culture for years. Apart from research, the staff devote considerable amount of time in imparting knowledge to personnel from educational institutions, health departments as well as training & maintaining facilities such as insectarium, animal house, local area network (LAN) of computers (68 nodes and 4 servers), designing, launching and updating of websites, and producing quality presentation materials. A centralized database has been created on different aspects of filariasis (7,65,507 records), malaria (2,59,766 records) and miscellaneous records on Filariasis (3,45,136 records), which is being constantly updated. Our commitment to provide quality services and consultancy to local, national and international organizations has been widely accepted and acclaimed by all. Contribution of our scientists in research, human resource development and consultancy services has won us national and international acclaim. The VCRC has evolved as a center of excellence in not only in Comprehensive Vector Control (CVC), control/elimination of Vector Borne Diseases (VBD), particularly Lymphatic Filariasis (LF) but also in newer fields such as Molecular biology, Genomics, Bioinformatics, Geographic Information Systems, Drug development and Clinical Trials, Health economics, Operational research, Health system research and Systematic reviews in the control of vector borne diseases. This has been possible without diluting the existing strength in classical fields of Vector biology and control, Microbiology, Chemistry, Epidemiology and Population sciences.

## Human Resource Development (HRD)

Our HRD activities were focused on two main areas, namely the formal training courses (Ph. D. programmes, etc.) and informal (Short-term) training courses. In the first category, a total of eight candidates registered for Ph.D. (one in Geography and seven in Microbiology). During this year, three candidates obtained their Ph.D. (one in Mathematical/Statistical Modelling of Filariasis at Erasmus University, Netherlands and the other two in Microbiology at Pondicherry University). Eight candidates of Post-Graduate students were trained on various topics. In the category of informal training, six public health personnel from Sri Lanka (2), Nepal (3) and India were trained under the international Comprehensive Vector Control training programme with networking through the WHO/ SEARO. Two WHO fellows from Maldives and two students from St. Olaf College, USA visited VCRC for informal training programmes. Medical students and nurses from France were also trained on tropical diseases with special reference to VBD in their own areas of specialization. During the year, four of our staff underwent training on new research areas in their disciplines at different national (3) and international (1) laboratories. The VCRC takes great pride of the fact that a great number of students from various educational institutes visited our Centre in search of knowledge (10 public health personnel from four health departments of different Southeast Asian countries and 967 students from 26 educational institutions took part in the training programmes).

## Finance and infrastructure

Total cash inflow during the year was Rs. 5.87 crores of which the ICMR (the VCRC's parent body) provided Rs. 5.15 crores. An additional Rs. 0.72 crores was generated by the VCRC from other sources such as research, training and technical service activities. The decline in funds generated from outside sources was mainly due to the policy decision of the Centre

to discourage contract research because of ethical and legal complexities and lack of policy direction in this regard. The funds received from ICMR were mostly utilized for staff salaries and establishment, leaving behind a small amount of Rs. 0.34 crore (6.7%) for consumable in support of research activities. As a policy, intramural funds are allocated for exploratory research and to support research related to vector biology and ecology, which is a low priority area for external funding agencies.

## Highlights of Research Activities of VCRC during the year 2004

Vector Control Research Centre (VCRC) continues to focus its activities on research, human resource development, dissemination of scientific information, building effective linkages and partnerships and providing consultancy services towards control/elimination of Vector Borne Diseases (VBD). Lymphatic filariasis, malaria, dengue and Japanese encephalitis (JE) continue to be the focus of this Centre. The five major scientific divisions of the VCRC, namely Vector Biology and Control; Product Development, Clinical Epidemiology and Chemotherapy; Applied Field Research, and Population Science, Epidemiology and Modelling and Bio-informatics are engaged in research with a theme and team approach. There is now increasing attention to the development of networking with other institutions/organizations within and outside the country.

VCRC, as a Global leader in lymphatic filariasis, continues to play an important role in the national and international arena for malaria, dengue & JE epidemiology and control. Altogether, a total 53 research projects were undertaken during the reporting period out of which five got completed. Five new projects were initiated, 36 continued as ongoing projects and seven projects approved by the Scientific Advisory Committee await funding.

During the year, research projects addressed the issues related to development of drugs; diagnosis

of lymphatic filariasis; epidemiology of vector-borne diseases - heterogeneity exposure; biodiversity of vectors and parasites; evaluation of interventions; community based drug trials; disease burden estimation; surveillance and rapid response. Some of the important areas addressed during the year, which have immediate relevance are listed below.

- A RT-PCR assay for detecting infective stage larvae of *Wuchereria bancrofti* was developed and evaluated for its specificity and sensitivity. The assay was found to be highly specific, detecting only infective stage larvae of *W. bancrofti* among different stages of the parasite in mosquitoes.
- An outbreak of suspected dengue occurred between October 2003 and February 2004. This was investigated in a passive survey utilizing serological and molecular. Ninety-two cases were found to be positive for anti-dengue antibodies and viral RNA RT-PCR assay. Molecular investigations revealed that the etiologic agent was dengue virus 3.
- The mosquitocidal factors of a potent bacterial isolate, VCRC B474 were characterized and found to be four proteins of molecular weight 27, 67, 125 and 134 kDa.
- Larvae and adults of *Culex quinquefasciatus*, pre-exposed to sub-lethal doses of *Bacillus sphaericus* and *B. thuringiensis*, had higher level of N-acetylglucosamine (GlcNAc)-specific and GlcNAc non-specific lectins. These observations suggest that these lectins have a role in the regulation of *Wuchereria bancrofti* development.
- Immunoblot analysis of haemolymph proteins of *Cx. quinquefasciatus* adults exposed to mf of *W. bancrofti* indicated the presence of two new proteins of molecular weight 40 & 70 kDa. These were of mosquito origin and were not found in uninfected mosquitoes. These proteins immobilized the microfilariae *in vitro*.
- Out of 20 substituted 1-N-Methyl-4 (substituted benzoyl) piperazides synthesized, six showed potential anti-macrofilarial effect as these resulted in 100% inhibition in the mobility of *Setaria digitata* adult worms at 10 mg/ml.
- Structure-activity relationship studies showed that the macrofilaricidal potential of the lead molecule, 5-hydroxy-2-methyl-1,4-naphthoquinone, was enhanced with dimethylamino, butylamino, propylamino and isopropylamino groups in C-3 atom of the dione ring and reduced by 3-dimethyl amino-1-propyl amino, 3-diethyl amino-1-propyl amino and 3-butylamino-1-propyl amino groups.
- A MOU was signed between VCRC, Pondicherry and CDRI, Lucknow to test the macrofilaricidal activity of the lead molecule, 5-hydroxy-2-methyl-1,4-naphthoquinone against adult human filarial parasite in suitable animal models.
- A three dimensional structural model of Glutathione-S-transferase (GST) of the lymphatic filarial parasite *W. bancrofti* (*wb*) was constructed by homology modelling.
- DNA sequences were constructed for 56 individual anopheline mosquitoes, which belonged to 47 haplotypes, corresponding to 47 identified species, belonging to 15 genera. The sequences which form the "Barcodes" for those species have been deposited with the Gene Bank.
- The sequences of the D3 domain of the 28S gene and the Internal Transcribed Spacer 2 region (ITS2) of the ribosomal DNA of morphologically identified samples of *Anopheles fluviatilis* and *An. minimus* species indicated that these populations are present in Kheonjhar district of Orissa. These belong to the sibling species, S and A of *An. fluviatilis* and *An. minimus* respectively.

- A mosquito museum has been established at the VCRC which currently holds 181 species of 19 genera and 37 subgenera. This facility serves as a taxonomic reference centre for mosquito systematics and identification.
- The reappearance of *Anopheles minimus* in Singbhum hills, East central India, has been recorded. This species was not detected for nearly 45 years since the launching of malaria control programme in this region.
- Impact of Rain Water Harvesting System (RWHS) towards proliferation of mosquito vectors was assessed in Cuddalore district of Tamilnadu State and mosquito breeding was observed in 16.1% of the RWHS.
- Vector control products such as Neem Azal, Novaluron, Diflubenzuron and Lambda-cyhalothrin CS were evaluated for effectiveness against different mosquito vector species.
- Factors related to acceptance and use of long lasting treated mosquito nets (LLTN) along with washing practices and willingness to buy LLTN in a rural society were determined in two districts of Orissa which are endemic for malaria.
- Co-administration of DEC and Albendazole is operationally as feasible as the administration of DEC alone. It is safe for community consumption. However, addition of Albendazole did not improve consumption.
- Co-administration of Albendazole with DEC resulted in higher reduction in both mf and antigen prevalence than DEC alone. However, evidence of persistent transmission suggests that three rounds of Mass Drug Administration (MDA) are not adequate to interrupt transmission and prevent new infections.
- Co-administration of Albendazole results in significant reduction in geo-helminth prevalence compared to DEC alone.
- Evaluation of the impact of MDA with DEC or Ivermectin, or co-administration of DEC with Ivermectin or with Albendazole on the transmission of bancroftian filariasis, carried out in 20 villages of Tamilnadu, indicated that the drug consumption rates given in supervised manner range between 53 per cent and 75 per cent and it is difficult to reach higher consumption rate.
- Highest reduction in microfilaraemia prevalence and intensity as well as in transmission parameters was recorded in DEC arm. mf prevalence, its intensity as well as vector infection and infectivity continued to show a marked declining trend in the DEC arm.
- The epidemiological and entomological incidences generally showed a declining trend over the first 4 to 6 rounds of MDA. However, these parameters remained more or less at a stable level for the past three to four years indicating the existence of persistent foci of infection and transmission.
- A risk mapping tool for Lymphatic Filariasis transmission has been generated, based on geo-environmental risk model (GERM) on GIS platform. The 'risk map' identifies the areas where transmission is likely to occur thus facilitating a geographically targeted approach for intervention.
- The level of agreement between environmental variables and the risk of transmission is fairly good as the vector breeding potential at the micro level has been mainly due to man-made features and environmental factors act as confounders.

- The demarcation of the areas in terms of filariasis transmission risk index, as being at 'risk' or at 'no-risk' derived from geo-environmental variables is a one-time exercise and is highly advantageous. This approach could be employed for delimitation purpose for any vast geographical area due to its rapidity, reliability and cost-effectiveness.

### Publications

- Sixteen (16) articles were published in scientific journals, among which twelve were in international and four in national journals. The average impact factor is 1.551, which shows an increasing trend.

### Consultancy and Linkages

The Centre has been providing consultancy to the Directorate of Public Health, Govt. of Pondicherry and state public health departments in Tamilnadu, Orissa and Karnataka. It also has linkages with several national (NVBDC, DST, National Task Force on filariasis and malaria, NRDC) and international (WHO/SEARO, New Delhi, WHO/TDR, Geneva, GAELF (Global Alliance for Elimination of Lymphatic Filariasis)) organizations and plays a significant role in influencing policy and strategy in vector borne disease control, nationally as well as globally.

Jai Hind

Dr. P.K. Das  
Director

Eliminate Filariasis, Alleviate Poverty