ANNUAL REPORT

1999-2000

REGIONAL MEDICAL RESEARCH CENTRE
(INDIAN COUNCIL OF MEDICAL RESEARCH)
BHUBANESWAR, ORISSA

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REGIONAL MEDICAL RESEARCH CENTRE
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Mr.R.S.Bahadur	Watchman
Mr.Sankar Bisoi	Cook-c-Guest House Attendant

CONTENTS

1. IMMUNOLOGY

1.1. IMMUNOLOGICAL INVESTIGATIONS IN HUMAN FILARIASIS USING PURIFIED ANTIGENS

Staff members	:	Dr M.K.Das Dr M.K.Beuria Dr M.S.Bal Mr N.N.Mandal
Starting date	:	1993
Current status	:	Ongoing
Closing date	:	January 2001 (proposed)

The objective of the project was to identify filarial antigens of interest for immunological studies, capable of detecting immunological changes in different clinical groups of lymphatic filariasis. In this context a high molecular wt. filarial surface antigen DSSd1 (Mw 160 kDa) was isolated which exhibits elevated antibody response, IgG3 and IgG1 sub-classes in microfilariae negative individuals compared to microfilaraemic subjects.

The relationship of DSSd1 antibody response with circulating filarial antigen (Og4C3) is being studied. Antigen assay was conducted in the sera of chronic filariasis (elephantiasis, hydrocele), asymptomatic microfilaraemics, asymptomatic amicrofilaraemics (endemic normals) and in non-endemic normals (from Agra & Delhi).

Antigen negative endemic sera exhibited high antibody level to DSSd1, and antigen positive sera (active infection) exhibited low antibody. This relationship was noticed irrespective of clinical symptoms/status. Antibody levels to DSSd1 correlate negatively with antigen titre.

Since one of the objectives was to conduct immunolongitudinal studies on endemic normal individuals, sera from these subjects (Olosingh village, Khurda district) were

collected at different periods. DSSd1 antibody responses are being assessed with parasitological and disease status of individuals. DSSd1 antigen is also found to be highly reactive with Og4C3 assay so that as low as 1ng of antigen could be detected by the assay. In other words, antigenic determinant recognised by Og4C3 (monoclonal) antibody is present in the DSSd1 antigen.

The microfilarial clearance potential of DSSd1 antigen from infected animals is under current investigation. This assumes importance considering the association of high antibody response to DSSd1 with the absence of microfilaraemia/active infection in filariasis.

It was earlier reported that microfilariae negative hydrocele individuals exhibited a higher extent of immediate type hypersensitivity (ITH) reaction measured as skin testing to a filarial allergen (Sd 30). IgE and the blocking IgG4 antibodies are determined in ITH positive and negative hydrocele individuals.

1.2. ANTIGENICITY OF FILARIAL ENZYMES IN ENDEMIC POPULATION

Staff members	:	Dr.M.K.Das
		Dr.M.S.Bal
		Mr.H.S.Naik
Starting date	:	1993
Current status	:	Ongoing
Closing date	:	January 2001 (proposed)

The objective of the project was to characterize and establish the immunogenicity of selective filarial enzymes namely proteases, glutathione S-transferase and superoxide dismutase in filarial infection. It was noted that elevated IgG levels to two enzymes, a protease (Sd P1) and glutathione S-transferase, were observed mostly in filariae-infected sera of microfilaraemics and chronic patients. The purified protease induced selectively IgG4 sub-class, otherwise known as a marker of active infection, in filariasis.

IgG4 antibodies to the protease is being evaluated in filarial sera to assess the potential of IgG4 determination with antigen (Og4C3) status. Only few filarial antigens are reported to induce IgG4 sub-class and use of purified antigen will enhance IgG4 determination. Preliminary results indicate that IgG4-SdP1 is higher in antigen positive sera. IgG levels however do not differ with antigen status.

Parasite proteases play various functions helpful to the growth and survival of parasites. One such function is facilitating host skin penetration by hydrolysing skin macromolecules. The ability of filarial proteases to degrade macromolecules (elastin, collagen, etc.) derived from skin is being studied. Proteases present in excretory-secretory, somatic, infective larval stage and the purified proteases are being investigated.

1.3. IMMUNE RESPONSE TO PARASITE LIPIDS IN HUMAN FILARIASIS

Staff members	:	Dr. M.K.Das
		Dr. M.K.Beuria
		Dr. M.S.Bal
		Mr. N.N.Mandal
Starting date	:	1995
Current status	:	Ongoing
Closing date	:	January 2001 (proposed)

The objective of the project is to describe immune response to lipid antigens of filarial parasite in human filariasis, for which limited data were available in contrast to protein antigens. We have isolated parasite lipids freed from protein antigens and demonstrated increased anti-lipid antibodies in microfilariae negative endemic individuals. Since the lipids isolated were crude mixtures, attempts are made to fractionate and purify the individual lipids [in collaboration with Dr.U.Sengupta, Dr.K.Venkateshan, JALMA (ICMR), Agra]. Six purified fractions were obtained from adult parasites through preparative thin-layer chromatography. The antigenicity of the fractions is being checked in filarial sera.

It was found that lipids of microfilariae and adult stage of *Setaria digitata* differ in their composition. Polar lipids are absent in microfilariae which contains only neutral lipids. This is in agreement with our earlier observation that antisera to microfilarial lipids cross react feebly with lipids from adult worms.

1.4. IMMUNOCHEMICAL CHARACTERIZATION OF FILARIAL ANTIGENS WITH POTENTIAL PROTECTIVE RESPONSE IN ENDEMIC POPULATION

Staff members	:	Dr.M.K.Das Dr.M.K.Beuria Dr.M.S.Bal Mr.N.N.Mandal
Starting date	:	2000
Duration	:	3 years

Although there are epidemiological studies to suggest the acquisition of immune resistance to filarial infection in endemic communities, the components of host immune system that participate in the induction of protective immunity are not understood. Immunological evaluation of antigens considered protective from animal studies often have yielded ambiguous results further confounding the problem. This Centre has detected two antigen preparations (DSSd1 and lipids) that were shown to have high antibody responses only in microfilarae negative individuals suggesting the association of specific antibody response with anti-microfilarial immunity.

Objectives:

1. Immunochemical characterization of DSSd1 and lipid antigens (antigen recognition pattern by western blotting).
2. Potential for microfilariae clearance from infected animals by the antigens.
3. Studies on cytokine profiles induced by the specific antigens in order to understand the immunoregulatory mechanisms.

The above project proposal was submitted to Department of Biotechnology, Govt. of India (1999) for extramural funding after getting the approval of the SAC (in 1997-98).

1.5. IMMUNOLOGY OF LYMPHATIC FILARIASIS : MODULATION, VARIATIONS AND IMMUNITY (E.C.U. FUNDED)

Staff members	:	Dr. B. Ravindran, Dr. A.K. Satapathy Dr. J.J. B. Geddam Mr. P.K. Sahoo Miss. M.C. Mohanty
Collaborator	:	Prof. Rick Maizels, University of Edinburgh, U.K.
Funding	:	European Countries Union (E.C.U.)
Starting date	:	August 1998
Completion date	:	August 2001

One of the objectives of the project is to develop molecular probes to identify and type different geographical 'strains' of *W.bancrofti*. The existence of polymorphic filarial antigens in *W.bancrofti* was demonstrated by us a few years ago by using serological methods indicating the possibility of typing isolates of *W.bancrofti* (microfilariae) purified from parasite carriers in different geographical areas. It is proposed to use affinity purified anti-sheath antibodies to recognize clones from a c-DNA expression library of *W.bancrofti* to identity and sequence genes for sheath associated antigens.

The other objective was to characterize anti-sheath antibodies – their induction, kinetics of appearance during natural course of infection and disease, since sheath antigens were demonstrated by us to be polymorphic. During the course of our investigations on protective immunity in human filariasis we observed that antibodies to MF sheath appear very early in the younger age groups much before onset of microfilaraemia and this prompted us to examine the relationship between anti-sheath antibodies and acquisition

of filarial infection in endemic areas. We hypothesized that as a consequence of appearance of anti-sheath antibodies the host remains amicrofilaraemic rather than elimination of circulating MF as a result of appearance of anti-sheath antibodies. We reasoned that studying the association between anti-sheath antibodies and circulating filarial antigen (CFA) in Bancroftian filariasis might be a useful indicator to address this issue.

There was a very significant inverse relationship between presence of CFA and absence of anti-sheath antibodies (ASAbs) in both symptomatic (Group-I) and asymptomatic (Group-II) cases of filariasis (Table-I). Group-I consisted of symptomatic patients with acute filarial disease (ADL) and those with chronic disease manifestations such as lymphoedema/elephantiasis and/or hydrocele. Group-II consisted of asymptomatic population, viz., a) asymptomatic individuals with circulating MF b) asymptomatic, amicrofilaraemic individuals testing positive for CFA and c) endemic normals, who are asymptomatic and amicrofilaraemic without CFA. The relationship was similar in both symptomatic and asymptomatic groups indicating that the observed association between the two parameters is not dependent on manifestation of filarial disease. About 80 % of individuals in both the groups were committed to have either CFA or anti-sheath antibodies. Fig. 1 shows the prevalence of MF, CFA and anti-sheath antibodies in 411 human sera grouped and stratified according to age. About 78% of children below the age of 10 years tested positive for antibodies to sheath. In this age group the prevalence of CFA and microfilaramia was only 22.7 % and 4.5% respectively. The high prevalence of anti-sheath antibodies seen in the younger age decreased with increasing age and increasing CFA positivity rate in the population. The prevalence of anti-sheath antibodies stabilized at about 55% after 30 years. The antigenemia rate on the other hand was 27.7% amongst children below 10 years, reaching a maximum of 42 % in the age group 30-40 years and marginally declining in higher age groups. These findings indicate that sheath specific antibodies appear very early in children during exposure to filarial infection in human filariasis. The significant inverse association between CFA and anti-sheath antibodies and the observation that anti-sheath antibodies are produced very early during exposure suggests that about 80% of the population in filariasis endemic areas are committed to only one of these parameters i.e. the individuals either display antibodies to MF sheath on being exposed to filarial infection or allow maturation of adult worms in their system resulting in CFA positivity.

The prevalence of CFA and/or anti-sheath antibodies in each of the six groups is shown in Table-II. About 75-80% cases were positive for either CFA or anti-sheath antibodies in all the groups. About 7.5% of the total cases were positive for both the parameters – however the frequency of double positive was significantly more in 'cryptic infection' cases than in other groups. Very broadly, the subjects in filarial endemic areas could be classified into three groups based on anti-sheath antibodies: endemic normals & patients with elephantiasis were high 'responders', patients with ADL and hydrocele were 'moderate responders' and microfilarial carriers and subjects with cryptic filarial infection were 'low responders'.

The inverse association observed between CFA and anti-sheath antibodies could mean that a) such antibodies mediate elimination of adult worms (an argument applied earlier for anti-microfilarial immunity) or b) the antibodies to sheath antigens inhibit growth and development of larvae into mature adult worms. We prefer the second explanation since chronologically the antibodies appear early during infection in childhood and currently we have no mechanistic explanation as to how antibodies to sheath could mediate adult worm killing *in vivo*. These findings reported here thus suggest a protective role for anti-sheath antibodies in a broader perspective of anti-filarial immunity rather than anti-microfilarial immunity.

Figure-1

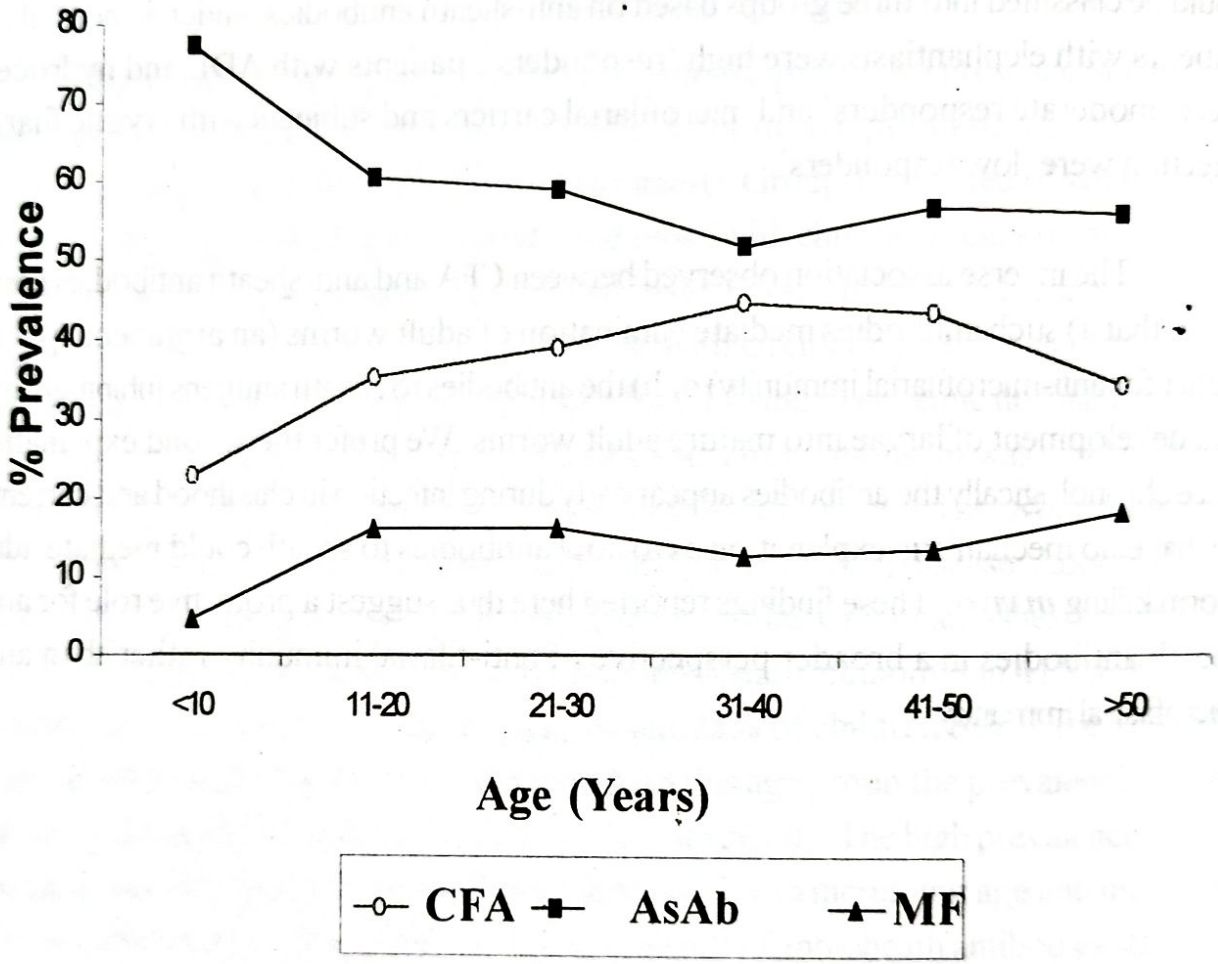


Fig.1 Prevalence of circulating filarial antigen (CFA), anti-sheath antibodies (AsAb) and MF in 411 age stratified cases of Bancroftian filariasis. Each group consists of samples from both symptomatic and asymptomatic subjects. N = 22 in <10 yrs, 100 in 11-20 yrs, 120 in 21-30 yrs, 73 in 31-40 yrs, 45 in 41-50yrs and 51 in >50yrs.

Table-1: Bancroftian filariasis: Correlation between anti-sheath (As) antibodies and circulating filarial antigen (CFA).

CFA	Symptomatic		Asymptomatic	
	No.	No. with As antibodies (%)	No.	No. with As antibodies (%)
Present	87	16 (18.4)	67	14 (20.9)
Absent	153	125 (81.7)	104	82 (78.8)

Table-II Prevalence of Anti-sheath antibodies in filarial disease spectrum

Category	No.(%)					
	MF+ve***	*CFA +ve ** AsAb -ve	CFA -ve AsAb +ve	CFA+ve AsAb +ve	CFA -ve AsAb -ve	Geometric mean units (CFA)
Endemic Normals (n=97)	0(0)	0(0)	79(81.44)	0(0)	18 (18.55)	0
Elephantiasis/ Lymphoedema(n=35)	0(0)	1 (2.85)	26 (74.28)	2 (5.71)	6 (17.14)	226.86
Acute filariasis						
ADL (n=161)	13(8.07)	51 (31.67)	79 (49.06)	15 (9.31)	16 (9.93)	1734.52
Hydrocele (n=44)	3 (6.81)	14 (31.81)	23 (52.27)	1 (2.27)	6(13.63)	2337.91
MF carriers(n=44)	44(100)	35(79.54)	1 (2.27)	5(11.36)	3(6.81)	3710.70
Cryptic infection (n=30)	0(0)	22(73.33)	0(0)	8 (26.66)	0(0)	1234.81

* CFA : Circulating Filarial Antigen

** AsAb : Anti-sheath antibodies

*** Geometric mean MF density per ml was 118.78, 547.72 and 382.28 in ADL, Hydrocele and MF carriers respectively.

1.6. STUDIES ON PROTECTIVE IMMUNE RESPONSE IN EXPERIMENTAL FILARIASIS

Staff members	:	Dr. B. Ravindran Ms. M.C. Mohanty Mr. P.K. Sahoo Dr. A.P. Dash
Collaborators	:	Dr. Satyajit Rath and Dr. Vineeta Bal National Institute of Immunology, New Delhi.
Starting date	:	March 1998
Completion date	:	August 2002

Extensive investigations conducted in human filariasis have failed to unequivocally establish existence of protective immunity against different developmental stages of filarial parasites. Several associations between *in vitro* immunological parameters and presence or absence of active filarial infections have been demonstrated – these studies however do not establish that the observed immune response phenotype were actually operational in eliminating parasites *in vivo*. Experimental models such as mice offer a system to monitor the fate of parasites *in vivo* and correlation with immunological parameters monitored *in vitro*. Immunocompetant mice are refractory to development of filarial parasites – however we had reported that XID-mice deficient in Brutan's tyrosine kinase are partially susceptible to *B.malayi* larval development. In XID mice which also display a deficiency for antibody response to T-independent antigens, the infective larvae of *B.malayi* develop up to juvenile adult stage and subsequently fail to survive, immunocompetent mice on the other hand rapidly eliminate the infective larvae. Further, XID mice sustain microfilariae in circulation for a long time and the magnitude of MF in circulation in them are many fold more than microfilaraemia observed in immunocompetent mice. We have taken advantage of the increased susceptibility of XID-mice to study protective immunity to filarial parasites.

T-cell response in XID-mice were found to be polarised towards Th1 phenotype to filarial as well as non-filarial antigens. This was demonstrated by significantly increased

IFN-γ response and higher IgG2a antibodies in comparison to wild type mice. The Th1 skewed immune response was found to be mediated by macrophages and not by B-cells of XID-mice. The macrophages of XID-mice produced increased levels of IL-12 in response to stimulation with LPS and this was found to be due to decreased upregulation of inducible nitric oxide synthase (inos) by XID macrophages. Enhanced IL-12 production and Th1 polarised immune response could be induced in normal wild type mice strains by exposure/ administration of inhibitors of inos. Administration of macrophages of wild type mice to XID mice could adaptively transfer filarial resistance and mediate MF clearance from circulation in XID mice. Similarly administration of inos inhibitors enhanced growth and development of infective larvae of *B.malayi*. The most crucial understanding from all these investigations is the interesting possibility that Th1 polarized immune responses could be beneficial for parasite growth and development. Immunological studies in human and experimental filariasis have shown that Th1 polarised response is associated with absence of active infection and this has been interpreted as protective immunity. In the light of observation reported in XID-mice the T-cell response phenotype *vis-à-vis* protective immunity in filariasis clearly needs to be reinterpreted.

1.7. IMMUNOBIOLOGICAL STUDIES IN BANCROFTIAN FILARIASIS

Staff members	:	Dr. B. Ravindran
		Dr. A.K. Satapathy
		Dr. J.J.B. Geddam
		Mr. P.K. Sahoo
		Miss. M.C. Mohanty
Collaborator	:	Dr. B.K. Das
		S.C.B. Medical College, Cuttack
Starting date	:	June 1995
Completion date	:	February 2001

Immunobiological studies in human filariasis require unambiguous delineation of 'putatively immune' endemic normals and identification of infected subjects who are otherwise asymptomatic and amicrofilaraemic. Identification of infected individuals can be currently attempted by detection of circulating filarial antigen (CFA) which are metabolic

products of the adult filarial worms in Bancroftian filariasis. This has facilitated precise identification of asymptomatic and amicrofilaraemic subjects into two categories i.e., these with cryptic infection, recognized by presence of CFA and 'putatively immune' endemic normals without CFA.

The present study was undertaken in coastal districts of Orissa to evaluate prevalence of clinical filariasis, microfilaraemia, filarial antigenemia and also endemic normals. Between the two chronic disease manifestations, the presence of CFA was significantly more in hydrocele cases (40%) than in patients with lymphoedema/ elephantiasis (17%). Only 43% of patients with current or history of episodes of acute filariasis were found to have current filarial infection.

Using the criteria of CFA and MF in circulation the asymptomatic population could be clearly divided into 3 categories i) endemic normals ii) cryptic infection and iii) MF carriers. The prevalence of cryptic infection was found to be 13-15% in the two areas and endemic normals were 34.8% and 27.7 % respectively in two areas. Infection rate as shown by CFA was not significantly different between males and females indicating that there is no gender bias for infectivity and development of filarial worms in human population. Antibodies to MF sheath and other filarial carbohydrate antigens were investigated in different spectra of human filariasis delineated using the following 3 criteria viz., microfilaraemia, CFA and clinical symptoms.

In human filariasis, microfilariae (MF) carriers characteristically produce higher antifilarial IgG4 than other subclasses of filarial specific IgG. Patients with chronic filariasis (elephantiasis and hydrocele) and subjects without demonstrable filarial infection (as shown by absence of circulating filarial antigen, CFA, a product of adult worms) on the other hand are found to possess lower levels of IgG4 filarial antibodies. For all the investigations on antibody responses in human filariasis only crude extracts of infective larvae, adult stage parasites and/or excretory-secretory antigens have been used so far. Curiously however, no attempt has been made so far to study the antibody responses to filarial carbohydrates in experimental or human filariasis.

The relative contents of carbohydrates and proteins in various developmental stages of *S.digitata* were quantified. The adult female and microfilarial extracts were found to be very rich in carbohydrates while the E-S antigens of adult female parasites contained relatively more carbohydrate than protein mass. The adult male worms on the other hand were found to be a protein dominant developmental stage of filarial parasites. The carbohydrate-protein ratio in males was about 8-10 fold less in comparison to adult female worms or microfilarial stages.

Filarial IgM and IgG2 antibodies reacted significantly more to Fil.Cho (filarial carbohydrates) than to Fil.Pro ($P<0.001$) while IgG4 antibodies displayed reactivity exclusively to Fil.Pro. There was a clear dichotomy in reactivity of IgG2 to Fil.Cho and that of IgG4 to Fil.Pro in the three categories of cases selected across the disease spectrum in human filariasis. Patients with chronic filarial disease and endemic normals were found to have significantly more IgG2 antibodies to Fil.Cho in comparison to microfilariae carriers (EN vs AS <0.01; CH vs AS < 0.05). On the other hand MF carriers produced significantly more IgG4 antibodies to Fil.Pro than endemic normals and patients with chronic filarial disease ($P<0.01$). This dichotomy in IgG2 and IgG4 reactivity to Fil.Cho and Fil.Pro respectively was not dependent on clinical manifestation since the pattern of reactivity was alike in endemic normals and chronic filariasis cases who are at the two extreme poles of the disease spectrum. The difference rather appeared to be dependent on the status of active filarial infection. When the sera samples were classified according to presence or absence of circulating filarial antigen (CFA, a more definite parameter of active filarial infection than microfilaraemia), individuals with CFA (with or without MF in circulation) were found to possess significantly more IgG4 antibodies to Fil.Pro than to Fil.Cho. Those who tested negative for CFA had significantly higher levels of IgG2 antibodies to Fil.Cho (Fig.2).

Anti-microfilarial immunity is characterized by presence of antibodies to microfilarial sheath (mostly IgM and IgG2) both in Brugian and Bancroftian filariasis and anti-sheath antibodies recognise mostly carbohydrate determinants on the microfilarial sheath. Similarly, anti-larval immunity in human filariasis is characterized by presence of antibodies to the surface of infective larvae. Such antibodies, mostly IgM and IgG2 but not IgG4 presumably recognize carbohydrate epitopes. Furthermore, production of antibodies reacting to the surface of infective larvae is a consistent feature in experimental

animals immunized with γ-irradiated infective larvae (a procedure that induces protective immunity) and attempts to implicate immune response to protective protein epitopes have not been successful. In this context, it is not surprising that the findings of the present study point towards a protective role for antibodies to carbohydrates in human bancroftian filariasis.

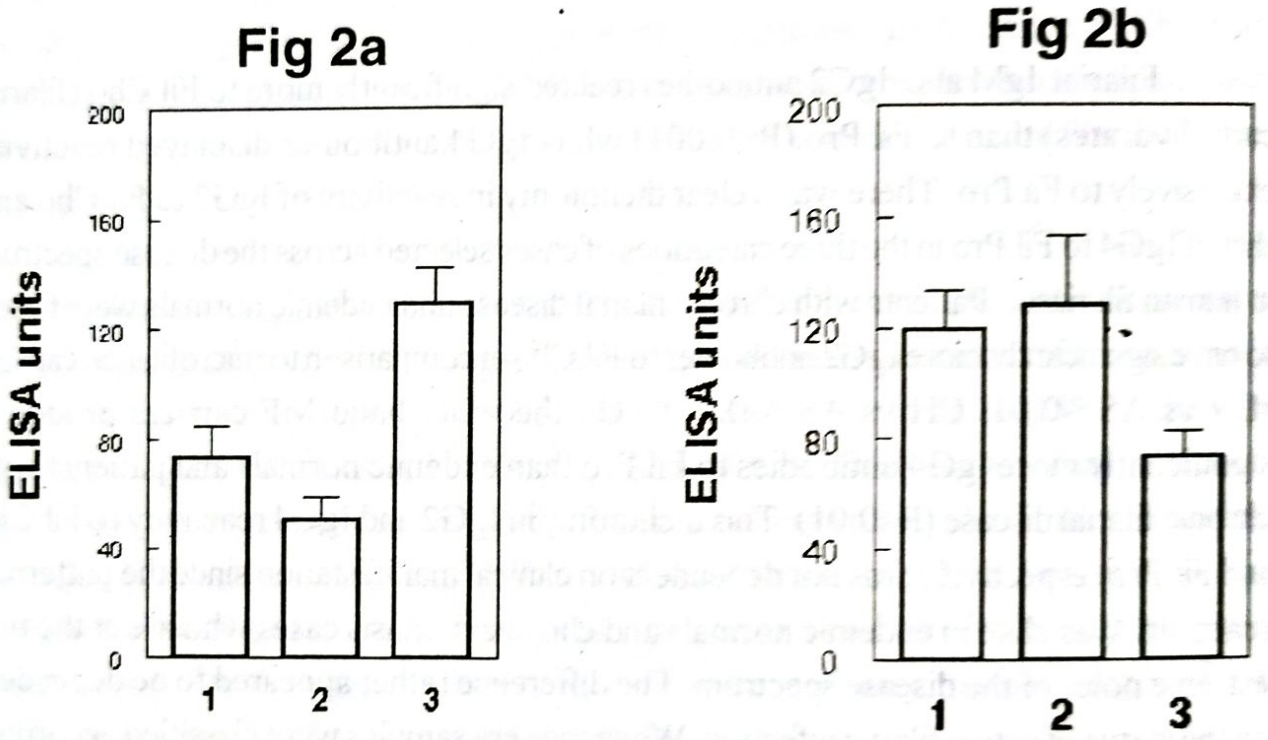


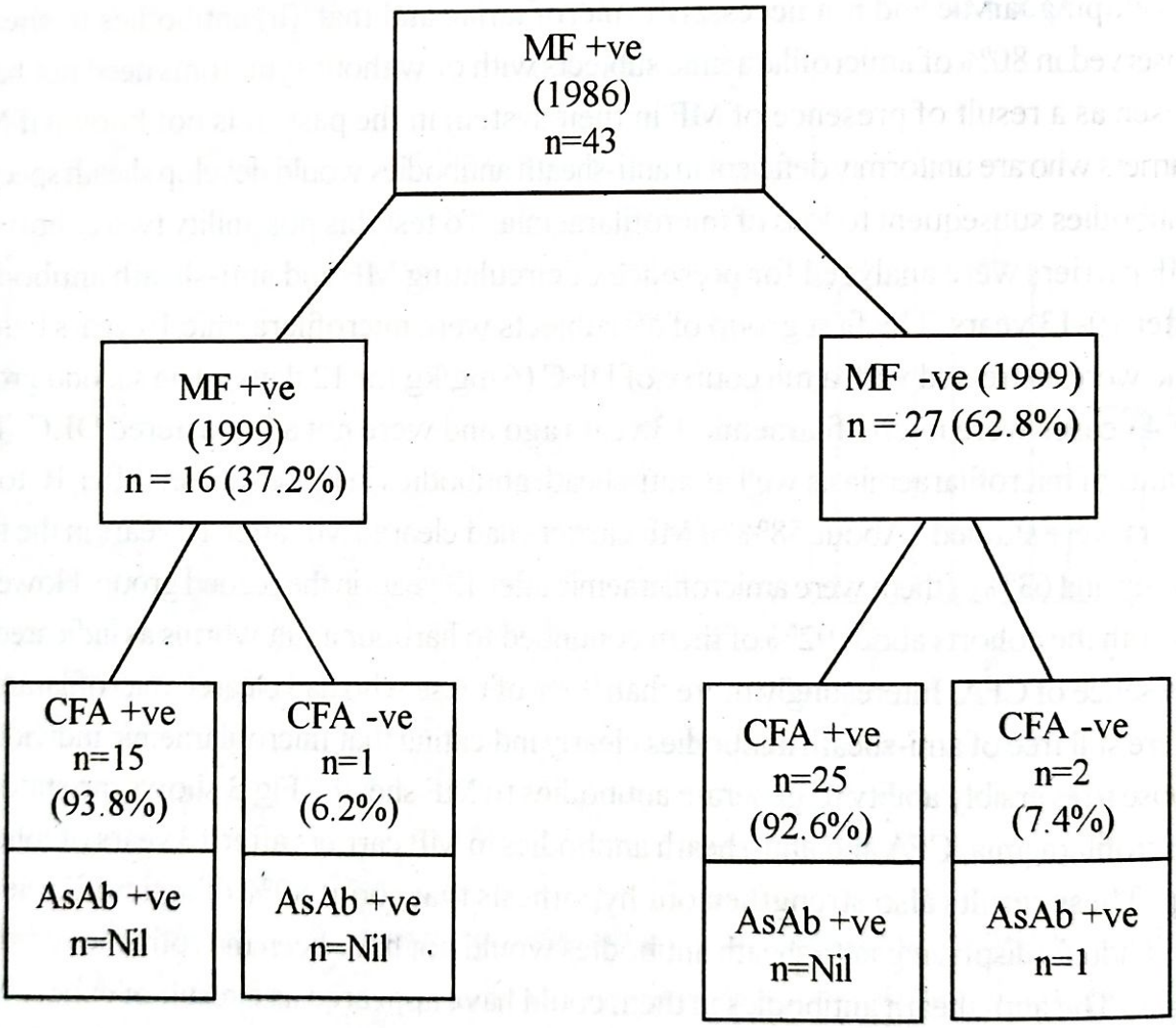
Fig.2

Antibodies to Fil. Cho and Fil.Pro and association with presence of circulating filarial antigen (CFA) and microfilaraemia in Bancroftian filariasis : Human filarial sera, positive for MF and CFA (n=21) or positive for CFA and negative for MF (n=13) or negative for both MF and CFA (n=38) were tested against Fil.Cho coated plates and probed with Anti-human IgG2 (2a); the same set of sera were tested against Fil.Pro and probed with Anti-human IgG4 (2b); Mean ELISA units ±SEM; 't' test : Fig 2a; 1 vs 3, $P<0.01$; 2 vs 3, $P<0.001$: Fig 2b; 1 vs 3, $P<0.01$; 2 vs 3, $P<0.05$ (1-MF +ve & CFA+ve; 2-MF -ve & CFA +ve, 3-MF -ve & CFA-ve).

Antibodies to MF sheath has been an interesting immunological parameter in human filariasis. We had demonstrated earlier an inverse relationship between anti-sheath antibodies and microfilaraemia. This was interpreted as a host immune mechanism for MF removal. However our recent observations (as reported in detail under project 2.1 above) of significant inverse association between anti-sheath antibodies and circulating filarial antigens implied thereby that anti-sheath antibodies are produced much before maturation of adult worms. These observations point towards the interesting possibility that (a) the source of antigenic stimulus for production of anti-sheath antibodies could be developing larvae and not necessarily microfilariae and that (b) antibodies to sheath observed in 80% of amicrofilaraemic subjects with or without symptoms need not have arisen as a result of presence of MF in their system in the past. It is not known if MF carriers who are uniformly deficient in anti-sheath antibodies would develop sheath specific antibodies subsequent to loss of microfilaraemia. To test this possibility two cohorts of MF carriers were analyzed for presence of circulating MF and anti-sheath antibodies after 10-13 years. The first group of 59 subjects were microfilaraemic 10 years before and were all treated with a full course of DEC (6 mg/kg for 12 days). The second group of 43 cases were micro-filaraemic 13 years ago and were not administered DEC. The status of microfilaraemia as well as anti-sheath antibodies in these subjects after 10 to 13 years were studied. About 58% of MF carriers had cleared MF after 10 years in the first group and 63% of them were amicrofilaraemic after 13 years in the second group. However in both the cohorts about 92% of them continued to harbour adult worms as indicated by presence of CFA. Interestingly more than 90% of these who had cleared microfilaraemia were still free of anti-sheath antibodies clearly indicating that microfilaraemic individuals loose irreversibly ability to generate antibodies to MF sheath. Fig.3 shows the status of microfilaraemia, CFA and anti-sheath antibodies in MF carriers after 13 years of follow-up. These results also strengthen our hypothesis that about 80% of amicrofilaraemic individuals displaying anti-sheath antibodies would not have been microfilaraemic in the past. The anti-sheath antibodies in them could have appeared as a result of exposure to L3. Anti-sheath antibodies could thus be used as an important window in understanding the natural history of filarial infection in human communities.

Fig. 3

Status of microfilaraemia, circulating filarial antigen (CFA) and anti-sheath antibodies (AsAb) in a cohort of MF carriers after 13 years



1.8. DEVELOPMENT OF A LABORATORY MODEL FOR *W.BANCROFTI*

Staff members : Dr. B.Ravindran
Dr.A.K.Satapathy
Dr. J.J. Babu Geddam
Ms. M.C. Mohanty
Mr. P.K. Sahoo
Mr. B.R. Sahoo (J.R.F.)

Starting date : June 1993

Completion date : February 2003

W.bancrofti, the human filarial parasite has not been adapted in experimental animals with the exception of leaf monkeys. The development of a laboratory model for *W.bancrofti* is required not only for large scale production of parasite material, but also for studying the biology of the parasite and for testing the efficacy of newer drugs and for vaccination studies. All efforts to develop a laboratory animal model for *W.bancrofti* by following most of the conventional protocol/ methods have been unsuccessful so far. It is clear that, like drug development, a rational approach is required for development of an animal model.

Although gerbils are the most susceptible animal models for a variety of human and animal parasites, the biological reason for their increased susceptibility are not however known – unlike gerbils, other commonly used rodents such as immunocompetent rats and mice are refractory to human filarial parasite development. However mice deficient in Bruton's tyrosine kinase (Btk), which also displays a functional deficiency in eliciting antibodies to T-independent antigens have been demonstrated by us to support growth and development of filarial parasites. These results were interpreted to indicate that immune responses to T- independent antigens could have been responsible for the refractoriness observed in immunocompetent mice and rats to filarial parasite development. In this study we have attempted to investigate the competency of gerbils to elicit antibodies to T-independent antigens with a view to understand their immune system and to gain insight into their increased susceptibility to a variety of parasitic infections.

The antibody response to a T-independent antigen, dextran was investigated in groups of BALB/c mice and gerbils by ELISA. Gerbils were found to be significantly deficient in eliciting antibodies to dextran when compared to immunocompetent mice ($P<0.001$). This was a consistent observation in two sets of experiments in which two different antigen dosages schedules were followed. While normal BALB/c mice readily responded by producing antibodies to dextran, the anti-dextran antibody levels in gerbils were significantly less and comparable to those observed in XID- mice, known to be deficient in eliciting antibodies to T- independent antigens. Gerbils were found to be very similar to XID- mice in responding to another T- independent antigen, Phosphorylcholine. An aqueous extract of filarial parasites known to be very rich in PC residues terminally attached to the carbohydrates of filarial glycoproteins was used for immunization of gerbils, BALB/c and XID mice. The response to PC was monitored by using PC-BSA in enzyme immunoassays in all the species of animals. The anti-PC levels in immunocompetent BALB/c mice were significantly elevated when compared with levels observed in gerbils or XID-mice. There was no significant difference in titres between XID mice and gerbils, both of which responded poorly to PC.

XID mice are known to be deficient in naturally occurring antibodies that recognize single stranded DNA (SS-DNA), phospholipids (PL) and bacterial lipopolysaccharides (LPS) since such antibodies are believed to be products of CD-5+ B-lymphocytes and XID mice are deficient in this population of lymphocytes. Normal sera collected from BALB/c mice, XID mice as well as gerbils were tested for antibodies to SS-DNA, LPS and PL to investigate if gerbils are similar to XID mice in this aspect. As expected antibody levels to all the three antigens were significantly high in BALB/c mice in comparison to XID mice. Gerbils were found to be as deficient as XID-mice in generating naturally occurring antibodies to SS-DNA, LPS and PL. The results of the present study indicate that the deficiency in eliciting antibodies to T-independent antigens could be one of the biological reasons for gerbils to readily support growth and development of a variety of parasites. This also implies that antibody response to T-independent antigens (mostly carbohydrates) could be crucial for development of protective immunity to these parasites and emphasizes the importance of studying structure-function relationship of carbohydrates in parasites that readily grow and develop in gerbils.

The series of investigations undertaken so far by us indicate three host factors crucial for development and maintenance of filarial parasites in mammalian hosts – a) decreased production of nitric oxide by macrophages as a result of deficiency in upregulation of inducible nitric oxide synthase (inos), b) deficiency in induction of antibodies to T-independent antigen and c) Th1 polarized immune response of the host to filarial antigens. The insights acquired from the above studies are being utilized currently to grow the infective larvae of *W.bancrofti* in laboratory rodents.

1.9. IMMUNOLOGICAL COMPONENTS OF ANTI-DISEASE RESPONSE IN HUMAN AND EXPERIMENTAL MALARIA

Staff members	:	Dr. B. Ravindran
		Dr. A.K. Satapathy
		Mr. P.K. Sahoo
		Miss. M.C. Mohanty
Collaborator	:	Dr. B.K. Das
		S.C.B. Medical College, Cuttack
Starting date	:	June 1994
Completion date	:	February 2001

Development of acquired immunity to malaria in human communities takes several years. As and when it develops, it manifests in two forms – one is a state of clinical immunity in which erythrocytic stage parasites continue to exist in circulation in the absence of clinical manifestations associated with malaria. This is a feature most commonly observed in holoendemic malarial areas (asymptomatic parasitemic). The other form of acquired immunity is anti-parasitic in nature and is associated with ability to clear circulating parasites. Most of the studies on vaccination with several synthetic peptides and/or recombinant fusion proteins have indicated the general failure of achieving an effective anti-parasite immunity in experimental malaria. This led to the proposal for a better understanding of anti-disease immunity which is considered more easily achievable for decreasing both mortality and morbidity associated with malaria. Some of the malarial antigens that induce TNF-α have been identified as potential parasite molecules that are responsible for the inflammatory response associated with clinical malaria. The active component was also identified to be a phospholipid (PL) in experimental models. We had demonstrated

enhanced antibody levels to PL in patients were inversely related to serum TNF-α titres levels. Similarly, raised levels of an autoantibody, anti-gal were associated with decreased TNF-α. The anti-gal autoantibody was demonstrated to be a polyreactive naturally occurring antibody indicating a role for such autoantibodies in human *P.falciparum* malaria.

Our studies in human cerebral malaria have been directed towards understanding the pathophysiological mechanisms and the factors that contributed to clinical complications associated with *P.falciparum* malaria such as cerebral manifestations, single and/or multiorgan failures found in a small but significant proportion of patients with *P.falciparum* malaria. While majority of infected individuals essentially present without the above clinical complications involving vital organs, it is not uncommon to encounter acute renal failure, pulmonary oedema, hypoglycemia, jaundice, convulsions etc., as clinical complications associated with *P.falciparum* malaria.

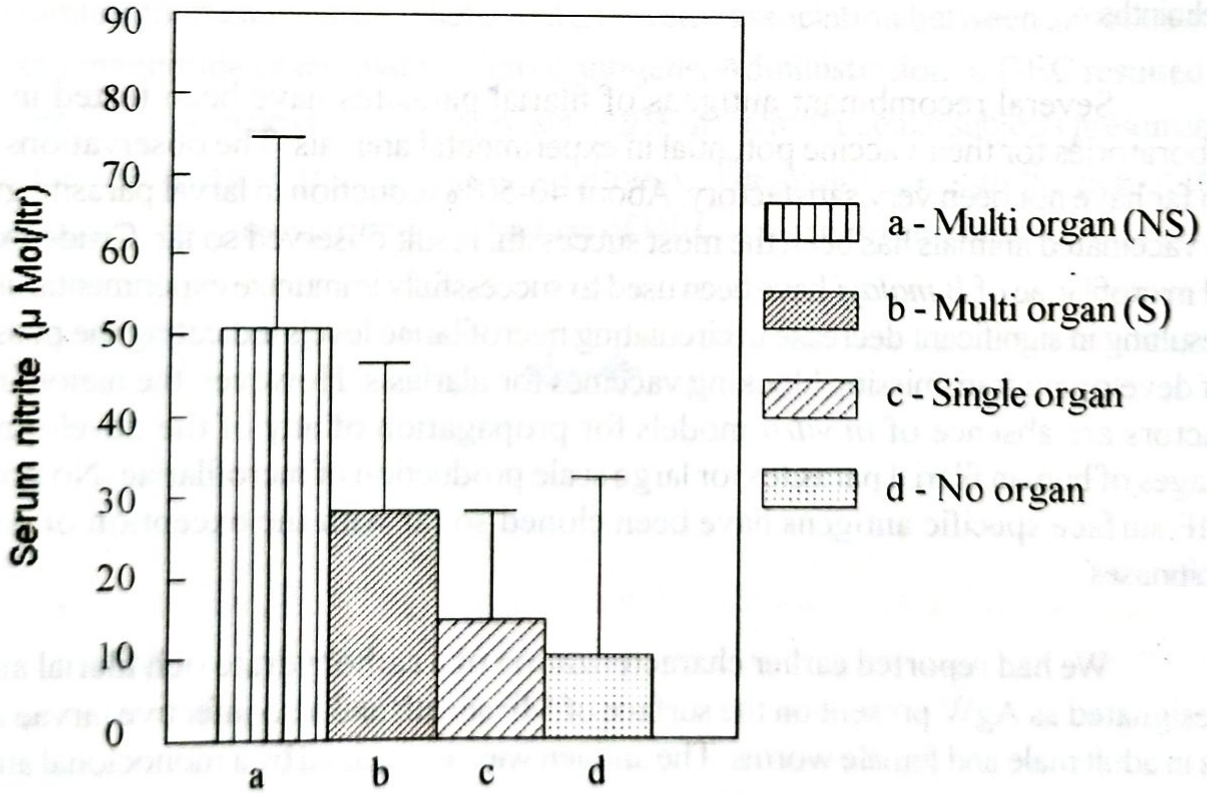
The biological basis of such complications are not clearly understood. The current investigations were undertaken in close collaboration with the Dept. of Medicine at SCB Medical College, Cuttack. Sera of *P.falciparum* cases with or without single/multi organ involvement collected for routine diagnostic investigations were transported to RMRC, Bhubaneswar and investigated for circulating levels of TNF-α and IFN-γ. The production of nitric oxide in the host were monitored by evaluating the serum nitrate levels in the following four groups of patients: a) Pf malaria with multiorgan involvement - Non-survivors (NS), b) Pf malaria with multi organ involvement– survivors (S), c) Pf malaria with single organ complication and d) complicated *P.falciparum* cases. Increased TNF-α levels, IFN-γ levels as well as nitrite levels were observed in the following hierarchy: Group a>b>c>d. Fig.4 shows nitric oxide production in the four categories of *P.falciparum* cases. There was a direct relationship between TNF-α and IFN-γ levels. TNF-α were consistently associated with increased IFN-γ production in all the four groups of patients. Similarly a direct relationship was observed between TNF-α and serum nitrite levels. These findings indicate that clinical complications in *P.falciparum* malaria are associated with enhanced production of inflammatory cytokines such as TNF-α and IFN-γ and molecules likes nitric oxide.

It is currently not known if this state of inflammation is a cause or effect of clinical complications observed in *P.falciparum* malaria. Investigations in experimental cerebral

malarial models have indicated a role for enhanced malarial specific Th1 response leading to pathology and that other parasitic infections which down-regulate Th1 responses would prevent pathological consequences associated with malaria. On this basis, our findings of enhanced clinical complications observed in *P.falciparum* malaria could be interpreted to be caused by inflammatory molecules such as TNF-α, IFN-γ and nitric oxide than as an effect of such complication. This opens up interesting possibilities for use of inhibitors of inflammatory cytokines or nitric oxide and the use of anti-inflammatory cytokines for clinical management of *P.falciparum* cases presenting with multi-organ complications which are the primary cause of mortality observed in *P.falciparum* malaria.

Fig. 4

Serum levels of nitrite in different categories of malarial patients



1.10. IMMUNOLOGICAL STUDIES ON ANTIBODIES TO DEC-AN APPROACH TO DEVELOPING AN IMMUNOPROPHYLACTIC AGENT AGAINST FILARIAL PARASITES

Staff members	:	Dr. B. Ravindran Dr. A.K. Satapathy Dr. J.J. Babu Geddam Miss. M.C. Mohanty Mr. P.K. Sahoo
Starting date	:	June 1993
Completion date	:	August 2001

Experimental vaccination against helminthic parasites have not been generally very encouraging. The complexity of the different developmental stages of the parasites, the ability of these extra-cellular parasites to survive in the infected hosts for several months/years and general lack of understanding of the pathogenesis of the disease processes have further complicated the approach towards development of vaccines against helminths.

Several recombinant antigens of filarial parasites have been tested in other laboratories for their vaccine potential in experimental animals. The observations made so far have not been very satisfactory. About 40-50% reduction in larval parasite growth in vaccinated animals has been the most successful result observed so far. Crude extracts of microfilariae of *B.malayi* have been used to successfully immunize experimental animals resulting in significant decrease in circulating microfilariae levels indicating the possibility of developing transmission blocking vaccines for filariasis. However, the major limiting factors are absence of *in vitro* models for propagation of any of the developmental stages of human filarial parasites for large scale production of mcrofilariae. No potential MF surface specific antigens have been cloned so far with the exception of parasite chitinases.

We had reported earlier characterization of a carbohydrate rich filarial antigen, designated as AgW present on the surface of MF sheath and also infective larvae as well as in adult male and female worms. The antigen was recognized by a monoclonal antibody P1E3 that was found to react with a carbohydrate epitope of AgW as well as to methyl piperazine carboxylic acid, an acid hydrolysis product of DEC, the antifilarial drug. The monoclonal antibody (Mab) was found to recognise residues of N-Acetyl D-glucosamine on AgW since reactivity of the MAb to AgW and to MF surface could be completely

inhibited by pre- incubation with the monosaccharide. The MAb on passive administration to microfilaraemic XID-mice and/or *Mastomys coucha* significantly decreased circulating microfilariae. Further, active immunization of *M.coucha* with a synthetic conjugate of N-Acetyl D-glucosamine coupled to BSA resulted in elicitation of antibodies reacting to the monosaccharide residue as well as to MF surface and other developmental stages of filarial parasites. The immunized animals on challenge with microfilariae (by intraperitoneal or intravenous routes) very rapidly eliminated MF in circulation in comparison to control animals immunized only with the carrier molecule viz., BSA. This approach has thus offered an immunization protocol/procedure to elicit anti-filarial antibodies by using a synthetic carbohydrate carrier protein conjugate. A patent has been filed for this experimental vaccination protocol. The efficacy of this approach in eliminating circulating MF needs to be established in primate models.

Antibodies to this protective carbohydrate epitopes are detectable in human filarial sera. In general the levels were found to be significantly less in microfilaraemic subjects than in amicrofilaraemic cases. There was an inverse association between antibodies to AgW and magnitude of circulating filarial antigens. Administration of DEC resulted in significant decrease in detectable levels of anti-AgW in microfilaraemic subjects presumably due to the reactivity of the drug to this antibody. The biological significance of this observation in the context of mode of action of DEC is currently not clear.

2. MEDICAL ENTOMOLOGY AND PARASITOLOGY

2.1. LONGITUDINAL STUDY OF *B. MALAYI* FILARISIS IN ORISSA

Staff members	:	Dr.N.Mahapatra
		Dr.R.K.Hazra
		Dr.S.K.Parida
		Mr.R.K.Das
		Mr.D.P.Hansda
		Mr. H.K.Tripathy
Starting date	:	January 1999
Completion date	:	January 2001

Filariasis due to *Wuchereria bancrofti* and *Brugia malayi* are the two common infections prevalent in Orissa. Though the former is wide spread the latter is restricted to a few areas like Sakhigopal area of Puri district and Chudamani area of Balasore distrtict. An extensive survey was made in these areas a decade ago. Again a followup study was initiated to study the natural history of brugian filariasis

The entomological and parasitological resurvey carried out in the Sakhigopal area of Puri district (endemic pocket of *B. malayi*) revealed *Ma. annulifera* to be the dominant species and the infection and infectivity rates were 0.2 % and 0.1% respectively.

During the survey in 1989 about 399 individuals from 143 families were covered and it was observed that 16.5% had microfilaraemia, 26.3% had acute disease and 8.3% had chronic disease (Table-III). From these 143 families, 101 families with 302 members were surveyed again in 1999 and it was observed that the prevalence of micorfilaraemia was 7.3%, acute disease was 14.9% and chronic disease was 7.6%. Thus, there is substantial reduction in the prevalence of microfilaraemia and acute disease in the current round, though the prevalence of chronic disease remained the same. While following up the previously surveyed families, 106 new families were surveyed and the

results are shown in Table-III. The prevalence of microfilaraemia was 4.4%, acute disease was 16.5% and chronic disease was 2.5%. These results indicate that prevalence of various indicators of filariasis are on the decline, either in the old follow up families or in the newly registered families.

Table-III : Parasitological and Epidemiological survey of Sakhigopal area in 1989 and 1999.

Variables / Survey	Old survey 1989	Follow up 1999	New 1999
No. of families surveyed	143	101	106
No. of persons surveyed	399	302	520
Male	209	157	238
Female	190	145	282
No. of positive for Bm	66 (16.5%)	22 (7.3%)	23 (4.4%)
Male	41	16	19
Female	25	6	4
Acute disease	105 (26.3%)	45 (14.9%)	86 (16.5%)
Chronic disease	33 (8.3%)	23 (7.6%)	13 (2.5%)
No. of persons diseased	138 (34.6%)	68 (22.5%)	99 (19%)

Among the families that were followed up, the following observations were made. In these families 28.4% of earlier (1989 surveyed) endemic normal population developed disease and 63.7% of MF carriers became negative and 42.8% of acute cases became negative. This pattern is similar to observations made by the Immunology Division and Microbiology and Pathology Division in the follow-up studies carried out by those Divisions.

2.2. EFFECT OF ANNUAL SINGLE DOSE OF DEC ON TRANSMISSION DYNAMICS OF FILARISIS

Staff members	:	Dr.N.Mahapatra
		Dr.R.K.Hazra
		Dr.S.K.Parida
		Mr.R.K.Das
		Mr.D.P.Hansda
		Mr.H.K.Tripathy
Starting date	:	January 1999
Completion date	:	January 2001

Lymphatic filariasis is a major public health problem in India. Orissa State is highly endemic for the disease. Recent studies have shown that annual mass chemotherapy with DEC can reduce the MF rate and more particularly MF density and MF load in the community. During November 1997, Khurda and Puri district of Orissa were covered by annual dose of DEC to majority of population in the district. Therefore, a study has been initiated to find its impact on transmission dynamics and MF rate in the community.

The MF prevalence did not show any decline in the current survey and the prevalence was 8.2% in 1999-2000 survey on 499 persons as against 9.6% in earlier surveys. However, the coverage rates on National Filaria Day (NFD) for DEC tablet consumption are not known with certainty in this area for the NFD round of November 1997. Infectivity rate was found to be 3.6% in *Cx.quinquefasciatus* as against 5.1% in the earlier surveys in this area. The filariasis control programme, which was carried out only once during November 1997 and that too with limited success, did not show any beneficial impact on the transmission indices of filariasis in these villages. The design of DEC mass drug distribution to eliminate filariasis and to prevent occurrence of new cases needs 75-80% participation of the eligible population for DEC consumption, over 5-6 years. The study area could operationalise DEC distribution only once and that too with limited success. Operation of NFD on one occasion with limited outreach, two years back was not sufficient to record beneficial results on transmission parameters.

2.3. STUDY ON SIBLING SPECIES OF MALARIA VECTORS IN ORISSA

Staff members : Dr. N.Mahapatra
Dr. S.K.Parida
Dr. R.K.Hazra

Starting date : January 1999

Completion date : January 2002

Sibling Anopheles species although morphologically indistinguishable may differ in biological features such as larval habitat, host feeding preference and other traits that have an important bearing on their vectorial competence and amenability to control strategies. Studies on the above parameters in different areas in the country have clearly shown distinct variation among sibling species. Though the Orissa State has only about 3.7% of India's population, it contributes 19.5% of total malaria cases, 43% of *P.falciparum* and more than 50% of malaria deaths in the country. Therefore a study was carried out on the sibling species (*An.culicifacies* and *An.fluviatilis*) prevalence, their relationship to the malaria incidence in two different geographical regions of Orissa

This Project has just been initiated. *An. fluviatilis* and *An. culicifacies*, the major vectors of malaria have been identified as a complex of 3 and 5 sibling species respectively in other parts of the country. Our study revealed the presence of *An. culicifacies* B and C in the two areas surveyed (Keonjhar and Gania). Details are given in Table-IV.

Table-IV Details of *An.culicificies* sibiling species composition

Species	% of complex	Anthropophilic index	SPR	SfR
		Keonjhar		
An.culicifacies				
(B)	55	22 %	14.9	13.8
(C)	45	41%		
		Gania		
An.culicifacies				
(B)	67	18 %	13.2	11.3
(C)	33	43 %		

2.4. Studies of mosquitoes of Orissa in relation to filariasis and malaria (Mosquito registry)

Staff members : Dr. N. Mahapatra
Dr.S.K.Parida
Dr.R.K.Hazra
Mr.H.K.Tripathy

Mosquitoes were collected from different areas of Puri, Khurdha (endemic for filariasis) Keonjhar and Gania (endemic for malaria). The species composition reveals presence of 19 species belonging to five genera. Precipitin test conducted for the identification of the blood meals reveals high anthropophilic indices of *Cx.quinquefasciatus* (89%), *Ma. annulifera* (63%) from filaria endemic area, where as *Cx. quinquefasciatus* collected from malaria endemic area showed 58% anthropophilic index and *An.fluviatilis* showed an index of 76%.

2.5. DEVELOPMENT OF FILARIAL PARASITES IN *AEDES AEGYPTI* LIVERPOOL STRAIN

Staff member : Dr.N.Mahapatra
Dr.R.K.Hazra
Dr.S.K.Parida
Starting date : October, 1991
Nature of activity : Service facility

Mastomys coucha were fed to black eyed *Aedes aegypti* (Liverpool strain) in successive batches. Total 744 mosquitoes were fed and 315 mosquitoes were dissected. A total of 100 infective larvae were procured which were further used for reinfection of fresh mastomys.

2.6 CYCLIC COLONIES IN THE INSECTARY

Nature of activity : Service facility

Cyclic colonies of different mosquitoes were maintained for conducting different experiments, such as development of different strains and species of filarial worms which will help in the selection of proper animal model, conducting bio-assays of different insecticides, biocides and insecticidal properties of plant products, etc.

Cyclic colony of the following mosquito species are being maintained in our insectary

1. *Aedes aegypti* (black eyed Liverpool strain)
2. *Anopheles stephensi*
3. *Culex quinquefasciatus*

2.7. SURVEYS CARRIED OUT ON MOSQUITOGENIC CONDITIONS FOR POSSIBLE OUTBREAK OF VECTOR BORNE DISEASES IN SUPER CYCLONE AFFECTED AREAS OF ORISSA

The recent unprecedented super cyclone in Orissa in October '99 has devastating effect in 10 districts of Orissa covering nearly 1.5 crores populations. The areas were totally water logged for more than 15 days and paddy fields and lower lands were under water for more than a month. Taking all these factors in view, investigation on epidemiological and entomological aspects of malaria and other vector borne diseases was undertaken in the cyclone hit districts of Orissa.

From preliminary investigation it was observed that anopheline densities in several places have increased. *An.culicifacies* density increased to 16 per man hour densities (PMHD) in some areas. A total 17 species of mosquitoes belonging to 5 genera were collected in these districts. Though these areas were not endemic for malaria earlier, a lot of malariogenic conditions have been created after the cyclone. Malaria cases were registered in Bhadrak district and the situation was kept under control using various methods of mosquito control. Details were given in the 6th section of this Annual Report.

Cx. vishnui (group) was the dominant species(64 PMHD) in some waterlogged areas. From the preliminary study it was surmised that a sudden decline in cattle population in some of these areas approaching zero, increses the possibility of man vector contact to be high. In some areas pigs and water birds were also present. Therefore possibility of Japanese encephalitis (JE) epidemic could not be ruled out.

Considering the above situation and changes in the ecological conditions, immediate monitoring on the species diversity of the mosquitoes and on possibilities of outbreak of vector borne diseases was carried out. There was no out break of JE in the cyclone affected districts. However, Korai block of Jajpur district experienced undefined disease with mortality which was later diagnosed as leptospirosis infection. These details were given in the 6th section of this Annual Report.

3. MICROBIOLOGY AND PATHOLOGY

3.1. LONGITUDINAL STUDY OF LYMPHATIC FILARIASIS IN AN ENDEMIC AREA OF ORISSA.

Staff members	:	Dr. G.P. Chhotray Dr. M.R Ranjit Mr. B.N. Sethi Mr. H.K.Khuntia Mr. K.C. Dalai
Starting date	:	January 1999
Duration	:	3 years

A pilot study was conducted in 21 villages of Satyabadi, Puri Sadar and Jatani blocks of undivided Puri district of Orissa, which are endemic for lymphatic filariasis during the period 1989 to 1993. A door to door, clinical and parasitological survey was undertaken and a clinico-epidemiological and pathological profile was documented. The total population available for the study was 3331 (M:F 1844/1487), which is 11.7% of the total population of the area. The MF rate was found to be 10.6% and the disease rate was observed to be 27.5%. A longitudinal study had been taken up in these villages, from January 1999.

During the period between January 1999 and March 2000 a total of 1379 (M/F:870/509) individuals from 6 villages of Satyabadi block were followed up- out of 2187 cases (M/F:1155/1032) of the studied population. The follow up study revealed a considerable reduction of MF rate from 9.2 % to 4.1% and the disease rate from 33.5 to 19.7%. Further, the number of cases of asymptomatic microfilaraemia carrier (AMC), acute filarial disease (AFD) and chronic filarial disease(CFD) in the follow up study was found to be 57 (38/19), 161 (117/44), 110(86/24) respectively as compared to 201 (113/88), 539 (306/113), 194 (117/77) in the initial round of the study. Amongst the 57 AMC followed up cases in the present study 48 were found to be positive for *W.bancrofti* and 9 for *B.malayi* - on parasitological examination of the night blood smear-as compared to 143 and 55 respectively in the earlier study. Amongst 1253 endemic

normals, 822 cases were examined both clinically and parasitologically and 8(1.0%) were found to be MF positive. Out of 201 cases from AMC group 127 were followed up and it was observed that 33.1% of them became MF negative with no symptoms, while 26% people have progressed to acute manifestations having no MF in the blood smear and 1.5% to chronic manifestations. Of the 286 followed up cases in the AFD category, 53.1% had become symptomless, 43.7% had still acute disease manifestations and 2.5% of the cases had developed chronic manifestations.

Except 2.1% of the cases developing bilateral hydrocele in the follow up study, all of them had unilateral hydrocele with a moderate increase in size and 13.9% of them undergone surgery. Around 20% of the cases have progressed to grade II and grade III lymphoedema from grade I and 66% of cases to the grade III from grade II lymphoedema, while all the grade III lymphoedema cases have remained static. As advised by the 12th SAC, the detection of filarial Ag and Ab was carried out by using FILA TEST kit in various clinical categories of filariasis patients and the results were compared with that of Og_4C_3 kit. The exact sensitivity and specificity is yet to be compiled since the study is in progress.

In the longitudinal follow up study area of Puri Tehsil, the single dose administration of DEC (6mg/kg body weight) was conducted as part of the National Filaria Day (NFD) during Nov. 1997. While carrying out the longitudinal study on filariasis during 1999, the DEC distribution, receipt of tablets and consumption of tablets under NFD carried out in Nov. 1997, was also assessed in these villages. To assess the impact of the programme in the community 10-15% of the representative samples were covered and information was collected through questionnaire method. It was observed that 68% of the population received DEC tablets, 54% of the population consumed medicine while 21% of them reported side reactions.

3.2. STUDIES ON HEREDITARY HAEMATOLOGICAL DISORDERS (DIAGNOSTIC SERVICES RENDERED FOR REFERRAL CASES)

Staff members : Dr. G.P. Chhotray
Dr. M.R Ranjit
Mr. B.N. Sethi
Mr. K.C. Dalai

During this period under report, a total number of 100 cases (M:F/41:59) were referred from various medical colleges and peripheral hospitals of Orissa State for investigation and establishing the various haematological disorders .The majority of the cases presented with chief complains of refractory anaemia and fatigue.

A detailed clinical and laboratory investigation was carried out for all the referred cases. Fifty cases (50%) were found to be electrophoretically normal, whereas 22%, 3%, 17%, 3% and 5% were diagnosed to be cases of heterozygous sickle cell disease (Hb AS), homozygous sickle cell disease (Hb SS) , sickle ß thalassaemia (Hb S-ß thal), ß thalassaemia (ß thal.) and Hb E- ß thalassaemia. The DNA extracted from 25 cases was sent for further molecular characterization to IIH, Mumbai. The results are awaited.

3.3. BACTERIOLOGICAL AND MOLECULAR CHARACTERIZATION OF ENTEROPATHOGENS ISOLATED FROM THE DIARRHOEAL STOOL SAMPLES OF THE CYCLONE AFFECTED AREAS OF ORISSA

Staff members : Dr. G.P. Chhotray
Dr. B.B.Pal
Mr. H.K.Khuntia

The super cyclone struck 9 districts of coastal saline tract of Orissa from 29th Oct 99 to 31st Oct 1999, along with high tidal wave and caused a havoc/disaster with huge loss of life and property. This is one of the worst disasters of the century, which has ruined the coastal districts of Orissa. Following the cyclone there was a sudden outbreak of gastroenteritis/ diarrhoea in the cyclone affected areas.

A total number of 107 stool samples were collected from different hospitals/ PHCs/ CHCs of the cyclone affected areas. Rectal swabs were collected from all fresh cases before any antibiotic was administered. Bacteriological analysis was performed in all 107 stool samples collected from 6.11. 1999 to 6.12.1999, after being transported to Microbiology & Pathology laboratory of RMRC in Cary- Blair medium using standard techniques. The first set of 44 samples were collected and tested by 11th November 1999. Out of these 44 stool samples 22 samples were found to be positive for *V.cholerae*

and these results were communicated to local health authorities through the Control Room. Details of survey work and cholera epidemic control efforts are outlined in the 6th section. Out of total 107 samples, 83 (77.6%) were found to be culture positive and 24 (22.4%) were culture negative. Of the 83 culture positive samples, 66 (79.5%) were *V. cholerae*, 16 (19.3%) were *E. coli* and 1 (1.2%) was *Shigella flexneri*. Of the 66 *V. cholerae* isolated, bacteriological analysis revealed 60 of them to be *V.cholerae* 01 Ogawa and 6 to be *V.cholerae* 0139. Clustering of cases of *V.cholerae* occurred in worst affected districts of Cuttack and Jagatsinghpur (Erasama, Balikuda, Kujanga, Manijanga) and Astaranga and Kakatpur area of Puri district.

The antibiotic sensitivity was also performed and all were found to be sensitive to tetracycline, ciprofloxacin, furazolidine, streptomycin, cotrimoxazole, norfloxacin, gentamicin but resistant to nalidixic acid. The sensitivity results on the first set of 22 positive samples were available on 12th November 1999 and these results were communicated to health authorities to initiate public health measures. These details on the response of various institutions, Central and State Governments and Army units are given in Section 6. The death rate due to diarrhoeal disorders came down after 15th November 1999. A total 75 water samples were collected from tube wells, dug wells, open wells and other sources from the cyclone affected areas during the same period, of which 3 (4%) were positive for *V. cholerae*.

A total number of 60 *V.cholerae* 01 Ogawa and 6 *V. cholerae* 0139 isolates were further analysed at the molecular level with the help of NICED, Calcutta. Multiple PCR assay was done using primer specific for ctxA, tcp A gene for the detection of cholera toxin and toxin co-regulated pilli gene (Classical and ElTor). It was observed that 59 out of 60 *V. cholerae* isolates belong to *V. cholerae* 01 serogroup and ElTor biotype and were positive for ctxA gene. Of the 6 *V. cholerae* 0139 strains 5 harboured ctxA gene.

Besides the antibiogram, the strains were randomly selected from different areas for molecular epidemiological study using ribotyping, RAPD analysis of the isolates. For ribotyping, Bgl 1 digested chromosomal DNA was probed for 16S and 23S rRNA. Almost all the strains exhibited ribotype R3 pattern, as it has been reported from different parts of the country after the emergence of 0139 strains of *V. cholerae*. The primer

1281 and 1283 were used for RAPD to detect their clonality if any. Like ribotyping results, the *V.cholerae* 01 strains exhibited similarity with Calcutta strains i.e. *V.cholerae* 01 that appeared after the *V. cholerae* 0139 epidemic. *V.cholerae* 0139 strains isolated in Orissa exhibited similarity with SG24, the strains isolated during 1994 *V. cholerae* epidemic in Calcutta.

The early detection and identification of the organisms specifically *V. cholerae* from stool and water samples of the cyclone affected areas and timely reporting of the results to Govt. of Orissa, resulted in the immediate institution of public health measures and could prevent a much larger outbreak of cholera epidemic in cyclone affected areas of Orissa. The epidemiological analysis is presented in the 6th section dealing with post cyclone health problems.

3.4. SERO-SURVEILLANCE OF HIV /AIDS AT RMRC, BHUBANESWAR

- Staff members : Dr. G.P. Chhotray
  Dr. B.B.Pal
  Mr. H.K.Khuntia

This centre has been identified as one of the sero-surveillance centres in the state of Orissa by the National AIDS Control Organisation (NACO), New Delhi and ICMR since 1987. The seropositive rate for HIV infection was 0.0% in the year 1991, which steadily increased to 5.19 per 1000 samples (cumulative figures) during the year 1999 - 2000.

A total of 143 samples were screened for HIV infection during the study period. Out of the 143 samples 137 belonged to high risk group i.e. 96 patients from STD clinic, 41 haemophilic patients who were regularly taking blood transfusion and 6 from other categories. Of the 143 samples tested from the Indian nationals, three were found to be ELISA and Western blot positive. Of the three, one was from STD clinic, one was heterosexual male and the other was a general female patient. None of the haemophiliac cases were positive for HIV infection.

3.5. MAINTENANCE OF VARIOUS BACTERIAL STRAINS OF ENTERO-PATHOGENS ISOLATED DURING EARLIER STUDIES

The microbiology section is undertaking studies on diarrhoeal disorders in the State since 1996. About 66 strains of various enteropathogenic bacteria such as *V.cholerae*. *Salmonella*, *Shigella*, etc. have been isolated and maintained in the laboratory. This requires frequent changing of media and further isolation and characterisation which will enable further studies at molecular level.

3.6 NEW PROJECTS

3.6.1. INTERVENTION PROGRAMME FOR NUTRITIONAL ANAEMIA & HAEMOGLOBINOPATHIES AMONGST SOME PRIMITIVE TRIBALS OF INDIA

This multicentric National Task Force (NTF) project on intervention programme has been implemented at RMRC, Bhubaneswar in two primitive tribes of Malkangiri district namely Bonda and Didayi. Dr G.P. Chhotray, DD is the CI of this Project and coordinates the work of this project for RMRC, Bhubaneswar. This multicentric project is coordinated by Dr.Dipika Mohanty, Director, IIH, Mumbai as its PI. Staff members have been recruited and vehicle was procured .The preparatory phase of the project has been started.

Starting date : October 1999
Duration : 4 years

Objectives:

(i) To find out the prevalence and aetiology of nutritional anaemia.
(ii) Clinical evaluation, management and monitoring of detected cases of anaemia and haemoglobinopathies.
(iii) To provide necessary supplementary intervention programme for formulating the future strategies of education and training to the doctors of the PHC level.

3.6.2. INTERVENTION PROGRAMME FOR CHOLERA, INTESTINAL PARASITISM, VIT-A DEFICIENCY AND SCABIES AMONGST SOME PRIMITIVE TRIBAL POPULATION OF ORISSA- A PILOT STUDY

Staff members : Dr.G.P. Chhotray
Dr.S.S.S. Mohapatra
Dr.B.B. Pal

Duration : 5 years

Starting date : March 2000

This extramural research project has been approved by the Ministry of Health, Govt. of India to be undertaken in some primitive tribal population of Orissa.

Objectives:

(i) For comprehensive assessment of the health status and epidemiological profile in respect of the above infectious / non- infectious disease.

(ii) To execute various intervention programmes amongst the beneficiaries with a view to augment the existing health care delivery system.

(iii) To assess awareness of health, health culture and related behaviour and develop a module for educating and training medical and paramedical workers of PHC level for timely detection and management of these cases.

Four investigating teams will be formed under the leadership of four medical officers. The teams will be equipped with essential field kits and medicines. The teams will monitor demographic patterns, morbidity, mortality and health care delivery system of primitive tribes in four different geographical regions of the State. Each zone will have one team which will be based at the respective zonal field station.

3.6.3. A COMPREHENSIVE STUDY ON DELIVERY OF HEALTH CARE RESEARCH FOR CAPACITY BUILDING AMONGST THE PRIMITIVE TRIBES OF ORISSA

Staff members	:	Dr.G.P.Chhotray Mr.Amarendra Mohapatra
Duration	:	3 years
Starting date	:	December 1999

During the first year of the project, the study will be initiated in two primitive tribes namely, Bonda and Didayi of Koraput district having a population of 5050 and 5990 respectively as per 1991 census. During the 2nd and 3rd year, the study will be extended to other primitive tribes like Kutia Kondha, Dangoria Kondha, Langia Saura and Paudi Bhuyan, etc. which are distributed in other geographical zones of the State other than Koraput district. Studies on various health parameters including nutritional anthropometry will be carried out in the selected households.

3.7. COMPLETED PROJECT

3.7.1. Studies on iodine deficiency disorders (IDDs)

Staff members	:	Dr.S.S.S. Mohapatra Dr.G.Bulliyya Dr.A.S.Kerketta

The clinico-epidemiological aspects of iodine deficiency disorders (IDD) were studied in a district of western Orissa. The PPS cluster sampling method was used and 3088 primary school children were examined, distributed in 30 clusters. The total goitre rate (TGR) varied from 0.7% to 29.6%. The severity of IDD varied from mild to moderate degree as per TGR. Similar observations were found by considering the urine, serum TSH and serum T4 estimation values. However, the drinking water sample analysis revealed severe grade of IDD in addition to mild and moderate grades. A KAP study by a pre-tested questionnaire revealed that 14.3% of males and 6.7% of females know about goitre, none had the knowledge as to how it is caused and only 16% used iodized salt regularly. This grim picture of the awareness and attitude of the people towards IDD in the face of the global challenge for eliminating IDD by 2000 AD stands out as a great set back in the present context.

4. HUMAN GENETICS

4.1. HAEMOLYTIC GENETIC DISORDERS AMONG THE SIX MAJOR POPULATIONS OF ORISSA

Staff members		Dr.R.S.Balgir
		Dr.B.P.Dash
		Mr.B.Murmu
		Dr.A.S. Kerketta
		Mr.T.Moharana
		Mr.R.N.Nayak
Starting date	:	July 1999
Duration	:	2 years

A total of 634 samples of three major tribals, namely, Saura (177) from Ganjam and Gajapati districts, Kondh (254) from Phulbani district and Gond (203) from Kalahandi district were screened for sickle cell haemoglobinopathy, beta-thalassemia, G-6-PD deficiency and blood group serology. Sickle cell gene was found to be very high in Gond (22.3%) in comparison to Saura (7.3%) and Kondh (3.1%) tribals. The frequency of beta-thalassemia was higher in Kondh (6.3%) and Saura (6.2%), whereas, it was very low in Gond (0.5%). The G-6-PD deficiency was found almost equally distributed in all the three tribes, Saura (7.9%), Kondh (7.5%) and Gond (5.9%). The blood group serology showed low prevalence (0.5%) of Rhesus negativity among the tribals of Orissa.

The clinical signs and symptoms of vitamin deficiencies, anaemia and skin infections were commonly observed among the Saura, Gond and Kondh tribals of Orissa. A total of 457 students were clinically examined. About 46% of the children showed visible pallor, splenomegaly (13.6%), hepatomegaly (0.6%) and hepato-splenomegaly (3.5%). History of recurrent fever, joint pain, and blood transfusion were observed 4.8%, 2.2% and 0.9%, respectively. No case of leg ulcer and priapism has been detected so far.

Haemoglobin level grading were done which showed about 65-85% mild to moderate anaemia in Gond, Kondh and Saura tribal groups of Orissa. Among the other

clinical findings, vitamin A deficiency (9.8%), i.e. Bitot's spot (2.1%), conjunctival xerosis (6.6%), etc.; vitamin B deficiency, i.e. angular stomatitis (8.3%), glossitis (5.7%), cheilosis (0.4%), etc.; dental caries (21.4%); scabies (18.0%) and Iodine deficiency (9.8%), i.e. both palpable and visible goitre, were also observed.

4.2. ASSESSMENT OF HEALTH AND NUTRITIONAL PROFILE AMONG THE ELDERLY POPULATION OF ORISSA PRIMITIVE TRIBES

Staff members	:	Dr.G.Bulliyya Dr. S.S.S. Mohapatra Dr. A.S. Kerketta Mr.R.N.Nayak
Funding	:	Extra-mural Funding (ICMR)
Starting date	:	January 2000
Duration	:	2 years

Objectives :

i) To study morbidity pattern of the elderly among three primitive tribal groups.

ii) To screen the malnutrition, dietary habits and food intake patterns.

iii) To compare the findings with data of the other states.

iv) To find out the possible causes and to suggest remedial measures.

A large proportion of elderly population is predicted to be malnourished and no baseline data are available on the health and nutritional status for the state of Orissa, more so on the primitive tribes. This study will help to provide baseline data for the planners and policy makers to understand the nutritional problems of the elderly for the well being of primitive tribes.

This study was initiated in the month of January 2000, and field work was carried out on elderly primitive tribes namely, Paudi Bhunya in Lohunipara block of Sundargarh

district and Desia Khond in Muniguda block of Rayagada districts of Orissa. A total of 280 elderly individuals were covered so far.

A total of 150 subjects (51 males and 99 females) over the age of 60 years were surveyed for their health and nutritional status of Bhunya tribe from Sundargarh district. Data on diet survey (24 hours recall method), anthropometry (body weight, height, arm span, mid-arm circumference and skinfolds at biceps and triceps), finger prick blood for haemoglobin and clinical assessment were carried out by using standard procedures.

The results of the first survey on 150 elderly subjects show that mean body weight, height, arm span and mid-arm circumference measurements are 38.6 kg, 146.3cm, 153.9cm and 20.3cm respectively. Males dominated over females for these variables. However, the values of biceps, triceps skinfold measurements, body-mass index (BMI) and body mass index for arm span (BMA) are more in females than males.

Clinical examination in elderly populations of Paudi Bhuyan showed that 62.7% were having visible pallor. Low back ache (30.0%) and joint pain (20.7%) and chronic cough (8.0%) were reported. Other known cases of chronic diseases like pulmonary tuberculosis and bronchial asthma were found in 2.0%, leprosy in 1.3% and arthritis in 6.0% were reported in this study.

The nutritional status of the elderly is assessed by using BMI (kg/m^2). About 68% of the study population are suffering from chronic energy deficiency (CED:BMI$\leq$ 18.5), while only 10% are normal (BMI=<20.0) and 22% are below normal (BMI=18.6-20.0). The prevalence of CED grades in the form of mild (BMI=17.1-18.5), moderate (BMI=16.1-17.0) and severe (BMI=$\leq$ 16.0) are 20%, 26% and 22% respectively. The proportion of males suffering from mild category of CED is lower than the females. More than 85% of the elderly are with different grades of anaemia and over 50% of them are moderate grade of anaemia and the prevalence is more in females (89.9%) than in males (76.5%). By using the definition of hypertension (systolic blood pressure >140 mm Hg and diastolic pressure >90 mm Hg), 23% and 5% are hypertensive for systolic and diastolic blood pressures respectively.

The overall nutritional status of the elderly Bhunya primitive tribe of Sundergarh district is inferior than the rural elderly of the State Orissa and other states of India reported by NNMB rural surveys. More recently, another field survey was done at Muniguda block of Rayagada district on 180 elderly subjects belonging to Khond tribe and the data are being analysed.

4.3. INTERVENTION FOR HEREDITARY COMMON HAEMOLYTIC DISODERS AMONG THE MAJOR TRIBALS OF SUNDARGARH DISTRICT OF ORISSA

Staff members	:	Dr. R.S. Balgir Dr. B.P. Dash Dr. A.S. Kerketta Mr. B. Murmu Dr. G. Bulliyya
Starting date	:	February 2000
Duration	:	5 years

Objectives:

Epidemiology of haemoglobinopathies and G-6-PD deficiency in major tribes of Sundargarh district of Orissa and to develop a suitable intervention package for prevention and control of these hereditary anomalies.

This is an extra-mural project from the Ministry of Health and Family Welfare, Govt. of India, funded through the Council. Funds for this project were received in February 2000. One Laboratory Technician and one Driver have been recruited and a vehicle has been procured to initiate the field work in Sundargarh district of Orissa.

5. EPIDEMIOLOGY AND INFORMATICS

5.1. MULTI-CENTRE STUDY OF COMMUNITY DIRECTED TREATMENT (COMDT) OF LYMPHATIC FILARIASIS (WHO/TDR PROJECT)

Staff members	:	Dr. K. Satyanarayana Dr. B.V. Babu Dr. G.P. Chhottray (Microbiology & Pathology) Dr. R.K. Hazra (Medical Entomology & Parasitology) and Project Staff
Starting date	:	March 1997
Completion date	:	September 2000

Lymphatic filariasis is an important public health and socio-economic problem affecting over 120 million people world-wide. The States of Orissa and Andhra Pradesh, in this region, are endemic for lymphatic filariasis. Though, there have been some significant successes in the control of the disease, the burden of lymphatic filariasis remains unaffected. The introduction, in recent years, of new drugs and single-dose treatment regimens with DEC has been an important breakthrough for filariasis control. Consequently, the global control strategy for lymphatic filariasis has been redefined, and the principal control strategy is now based on annual, single-dose treatment of all eligible members of high-risk communities. Thus, the principal challenge for filariasis control is to deliver single-dose treatment to the populations of high-risk communities and to sustain annual delivery for a sufficiently long period to bring about the control of the disease. Recent research on drug delivery for another disease, onchocerciasis, indicates that greater involvement of the endemic communities in the delivery process may be a solution. WHO/TDR has developed the concept of community-directed treatment (ComDT), in which community itself has the responsibility for the organisation and execution of the treatment of its members.

The WHO/TDR Task Force on Community-Directed Treatment of Lymphatic Filariasis and Onchocerciasis (presently, the Task Force for Filariasis Intervention Research) has selected RMRC, Bhubaneswar to participate in a multi-country study to develop effective and sustainable large scale treatment methods for lymphatic filariasis that are directed by the endemic communities themselves. Dr. K. Satyanarayana, PI from Phase-II and Dr. B.V. Babu, CI of the project attended several WHO/TDR workshops for implementation of the project by this Centre.

Objectives:

1. To assess the process and effectiveness of a delivery strategy of mass treatment by the regular health care system and to identify possible improvements.
2. To develop, implement and assess the process and effectiveness of a system of Community directed treatment (ComDT) of filariasis, which incorporates the health services at the level of implementation.
3. To compare the feasibility, effectiveness and potential sustainability of the two approaches.

Progress:

As the Government of Orissa did not undertake the mass drug distribution for filariasis control in 1998 and 1999, an alternative site was selected in Andhra Pradesh for the implementation of ComDT, where the State Government is willing to undertake mass DEC administration in 1999. The approval of SAC of this Centre and the approval of Health Ministry Screening Committee (HMSC) and the concurrence of the funding agency (WHO/TDR) were taken before changing the site of operation. The researchers of this project have undertaken this study in East Godavari district of Andhra Pradesh, as the Government of Andhra Pradesh has shown willingness to implement the programme in two districts, selected by Govt. of India. Four blocks (PHCs) of East Godavari district were selected for operation of this project in consultation with the local health authorities and district administrators.

Processes of drug distribution and implementation of ComDT:

Sensitisation of State government authorities:

The PI and CI of the project were involved in the sensitisation of State level health authorities. They met Secretary (Ministry of Health), Director and Deputy Director (Entomology) of Health Services, Government of Andhra Pradesh, and stressed the need to undertake DEC mass treatment. The Secretary (Health) sent a GO letter agreeing, in principle, to DHS, District Collectors, DM & HOs and Director, RMRC in August 1999.

Sensitisation of district authorities:

The District Collector was the key to this type of public health programmes. He received the letter from Health Secretary to implement Filaria Day. On the very first visit of researchers along with Medical Officer of Filariasis Research and Training Centre (FRTC), the date for filaria day was fixed. The District Collector decided to intersperse the National Filaria Day (NFD) between two pulse polio doses (on 15th November 1999). Also, the researchers sensitised all district level officials, including District Medical and Health Officer (DM&HO) and Medical Officer, FRTC. The District Collector and other officers were briefed about filariasis problem and control in the district, the need of single dose of DEC treatment and aims of the ComDT project. The authorities accepted to implement ComDT in 2 blocks.

Sensitisation of medical officers and other administrative staff in the district:

The filariasis control programme was added on to the operation of pulse polio programme (PPP) between the two PPP rounds. The district authorities of East Godavari district convened a meeting for medical officers and senior staff of 62 PHCs of the district to cover both the programmes. The researchers were also involved actively in this meeting. This meeting was attended by the District Collector, DM&HO and Deputy Director (Entomology), Directorate of Health Services. Various resource persons from RMRC, Bhubaneswar and local medical college, attended and delivered talks on various issues of filariasis control and IEC materials were used. Before this meeting at the same venue, all the Mandal Revenue Officers, Mandal Development Officers, Nodal Officers,

Municipal Commissioners and Municipal Health Officers of the District have been invited for a meeting addressed by the District Collector and in the same meeting they were fully explained about filariasis and the need to control the disease.

Sensitisation of ComDT medical officers:

The medical officers of two PHCs selected for implementing ComDT were contacted many times by researchers and explained about recent developments in filariasis control, single dose treatment, importance of community involvement for higher coverage, etc. They were also briefed about the concept of ComDT (genesis and experiences in African Onchocerciasis control) and the protocol of ComDT. Phase I results were presented for understanding the situation and communities and plan of action for ComDT was prepared in consultation of medical officers and along with the Medical Officer of local FRTC, Kakinada.

Sensitisation of peripheral staff of ComDT PHCs:

The medical officers of ComDT blocks convened a sensitisation meeting at PHCs for their peripheral health workers. The contents of the training meeting included extent of problem of filariasis, filariasis control / single dose, meaning of ComDT and how to involve the community, phase 1 results, need to sensitise communities, community structure and caste dynamics and implications in the programme, etc. The health workers have actively participated in the form of discussions on various issues like need of ComDT, dosage, side effects, management of cases, etc.

Sensitisation of communities to take up ComDT:

In ComDT areas, these activities were undertaken by peripheral health staff of health sub-centres in their concerned villages. Researchers advised health staff on this issue with the results of phase-I. The health workers initially met the village leaders and panchayat leader, but later on they also sensitised active groups like DWACRA (self help women groups), youth clubs, etc. to undertake the drug distribution (in addition to panchayats). Health workers explained these groups about the plan of implementation of ComDT at village/community level.

Sensitisation of communities in ComDT with researchers arm (4 villages):

In these four villages also peripheral health workers were involved extensively in the sensitisation of villagers as in other villagers. However, researchers also visited these villages during sensitisation and interacted with community leaders.

Distribution of drugs by health authorities (HST):

A total number of 2,17,05,000 tablets of DEC (50 mg.) have been distributed well in advance to all PHCs and municipalities in the district, from there to the village/ ward level. To combat side effects that may arise due to administration of DEC, precautions were taken by supplying 4,00,000 Paracetamol tablets, 50,000 Avil (25mg) tablets and 5000 Dexamethasone (0.5mg) tablets to the PHCs / municipalities, well in advance. The State Government of Andhra Pradesh had sanctioned money for management of side effect and IEC material. The East Godavari district was allotted a sum of 4.5 lakhs for the entire gamut of NFD activities excluding the DEC tablets. The DEC tablets were supplied by the. Government of India, free of cost, to State Governments. Necessary instructions were issued to all medical officers of PHCs, Government Dispensaries, and in charges of Government Hospitals in the District to be available to attend any emergencies. No reports of serious emergencies were received under National Filaria Day implementation due to administration of DEC tablets on 15th Nov. 1999 (NFD day). Minor side effects were taken care by health workers by using the medicines supplied.

Selection of ComDT procedures/period, etc.:

The communities (through panchayats/ DWACRA groups) planned the process of drug distribution in consultation of PHC/SC health staff. They decided to implement distribution of DEC tablets during November and December 1999 through local volunteers. Initially they thought to give tablets by visiting door-to-door.

Selection of community drug distributors (CDDs):

For undertaking drug distribution, community leaders (Panchayat president, members, etc.) identified various members from their village to distribute drugs. Mostly

they selected drug distributors from youth groups, DWACRA (self-help women groups), etc. and most of the villages, ensured to cover all communities/groups by selecting these community drug distributors (CDDs) from respective groups. Basically CDDs were nearly of the same category in ComDT blocks as well as HST blocks.

Training of CDDs:

The training of community drug distributors was undertaken by health workers with the help of IEC material supplied by the RMRC. They have undertaken this activity village wise. In this training the health workers gave brief information on the programme, dosage as per age, exclusion criteria, appropriate timings for giving drugs, side effects and their management and reporting (filling enumeration books and reporting coverage, which were decided by the health staff).

IEC material:

The IEC materials were prepared by FRTC, Kakinada and researchers of RMRC, Bhubaneswar. These materials were prepared and pretested in the field. Contents from the pamphlets and baners prepared earlier by the FRTC, Kakinada were used in the final material. The RMRC, Bhubaneswar prepared and supplied IEC material for two ComDT PHCs. For remaining PHCs of the district, the IEC materials were provided by district health authorities. The researchers have given the pretested samples to district authorities for their use. IEC material developed by the FRTC, Kakinada and RMRC, Bhubaneswar formed the backbone for IEC material in HST blocks.

Evaluation of study :

The study has been evaluated through various qualitative and quantitative methods. The qualitative methods are key-informant interviews, focus group discussions (FGDs) with community members including members of vulnerable groups, semi-structured (SS) interviews with health personnel and drug distributors. The qualitative data focussed on the extent of involvement of communities in drug distribution, process of drug distribution in ComDT and HST arms and the factors that influence the coverage.

For coverage survey, structured coverage survey questionnaire was used and data have been collected from 42 villages (20 HST, 20 ComDT, and 2 ComDT with researcher) (Table-V). In each of the 42 villages, 20 households were randomly selected from four random points (one of these to start in minority/vulnerable group). At each random start, five households were covered in random directions. While qualitative data were collected in 12 (6 ComDT and 6 HST) villages. The details of various surveys were given below (Table-V).

Results of evaluation survey :

The data obtained in coverage survey was entered in MS Excel and analysed in SPSS. The results indicate that the regular process of government health services (HST) achieved slightly higher coverage (80.5%) of DEC distribution compared to 74.1% of coverage in the community directed treatment. However, the ComDT undertaken with the involvement of researchers achieved the coverage of 89.5%. Regarding the actual consumption of tablets, these three approaches achieved 68.3%, 60.0% and 73.6% respectively. It is to be noted that the communities achieved nearer to that of government health system. Unlike in the case of African studies community directed approach alone could not achieve much greater coverage exceeding the HST coverages. The approach of community directed treatment seems to be feasible if it is implemented with more involvement of the health services. In other words, the approach of drug distribution by the health services will achieve higher coverages of drug distribution and drug treatment, if there is more involvement of communities.

Table-V Details of research tools administered

	Survey/instrument	Per village* (to be done)	Per block (to be done)	Total done per district
1.	Household coverage survey	20	200 (HST) 220 (ComDT)	984 (5520 persons)
2.	In-depth interviews with key informants	2	6	25
3.	SS interview with drug distributors	2	6	24
4	FGDs (main village)	-	1	11
5.	FGDs (sub-groups)	1	3	16
6.	SS Interview with health worker	1	3	14
7.	SS Int. with MO of PHC		1 or more	5
8.	SS Int. with MO, FRTC		--	1
9.	SS Int. with DM & HO		--	1
10.	Village level information sheet	1	10 (HST) 11(ComDT)	42

* Total villages : 42 for household coverage survey and 12 for qualitative surveys in 4 blocks

The survey disclosed the reasons for non-reception and non-consumption of DEC. The main reasons for non-reception of tablets are 'distributor not visited the household', 'respondents not available', 'not aware of the programme', etc., where as the reasons for non-consumption (after receiving tablets) are fear of side effects, forgot/ missed, perceived unnecessary, etc. Higher coverage and treatment rates can be achieved by taking these factors in to consideration in IEC activities. The problem of side effects seems to effect the compliance. Around 12 percent of people who consumed tablets experienced different type of side effects and the most frequent side effects are gastric irritation, fever, giddiness, etc. Though there are minor problems like side effects form people's point of view, a great majority of people showed willingness to take drugs in the next round. The qualitative data collected from different health system personnel, drug

distributors, community members, etc. addressed various issues related to feasibility of ComDT, problems in undertaking mass drug distribution and factors influencing the coverage and compliance. The data computerization is completed and analysis is being undertaken to examine the relationships between variables and to help the filariasis control programme to improve coverages.

5.2. AN EXPLORATORY STUDY ON RECORDING AND REPORTING SYSTEM OF LYMPHATIC FILARIASIS AT THE COMMUNITY LEVEL (WHO/TDR PROJECT)

Staff members	:	Dr. B.V. Babu Mr. A.S. Acharya Mr. P.K. Jangid Mrs. G. Mallick Mr.K. Dhal And Project Staff
Starting date	:	August 1999
Completion date	:	August 2000

Lymphatic filariasis is a serious public health and socio-economic problem in India. Recent studies have shown that annual single dose treatment with DEC is a promising tool for filariasis control. However, the sustainable method of delivery of this single dose treatment is a challenging task. The concept of community directed treatment (ComDT) has been developed and a multi-country study is ongoing to test its feasibility and effectiveness. A similar study on Onchocerciasis in Africa which showed that ComDT is feasible and effective, also pointed out the problems with reporting on mass drug distribution. Hence, the present study aimed to develop simple, practical and reliable method of reporting on drug delivery system by control programmes and by communities.

Objectives:

1. To identify the type of recording system or type of information existing on filariasis at community level.

2. To report the present method of recording and reporting system of filariasis adopted by health system.
3. To identify the type of information needed for the effective execution of community directed treatment of filariasis.
4. To identify the type of information to be reported by the communities to develop feasible method of recording and reporting by communities.
5. To develop feasible method of recording and reporting by the health system, including involvement of periphery level health personnel and other personnel associated with community activities in the recording and reporting process. And ultimately, to develop methods for bi-directional reporting to ensure more reliable reporting and strengthening the sustainability of community directed treatment.

Progress:

This project was undertaken in two districts namely, (1) Khurda district of Orissa State and (2) East Godavari district of Andhra Pradesh State, and from each district 4 blocks were selected. Various social science methods such as sample survey, in-depth interviews and focus group discussions were used in order to know the general reporting system in the community. An attempt was made to know how the people were reporting/informing their problems, particularly health related, and to whom they are reporting. A total of 749 and 400 respondents from, 12 villages each of, Orissa and Andhra Pradesh were interviewed regarding way of giving information for their health problems, by household sample survey. For general problems they approach village/ community leaders, but they inform and approach local doctors for their health problems. It is noticed that almost all villagers approach the local doctor (either government doctor or private physician) and this contact plays important role in the transmission of health related information. In both the sites, the health staff recorded the vital events like births and deaths. To probe the role of peripheral health workers in recording and reporting process of various health issues, in-depth interviews were undertaken for 30 health workers (17 from Khurda district + 13 from East Godavari district). Also information was collected from vital statistics clerks of PHCs in Khurda district. It is noticed that all the information collected at village level by the health workers was reported to PHC once a month and the same information was forwarded to the higher authorities at district and state levels. Similarly, to elucidate the role of local bodies (panchayats), an in-depth study has been

conducted by interviewing panchayat personnel in both the districts. These institutions played an important role in issuing birth/death certificates.

In order to record the process of recording and reporting of various issues related to drug distribution in both community directed drug treatment and health system operated drug distribution, in-depth studies have been carried out with key informants in the village, drug distributors and health workers. Various documents and records relevant to these issues were examined. Computerisation of these qualitative data is completed and analysis will be completed shortly.

5.3. A STUDY ON SOCIO-ECONOMIC BURDEN OF LYMPHATIC FILARIASIS IN COASTAL ORISSA

Staff members	:	Dr. B. V. Babu Mr.A.S. Acharya Mr.A.N.Nayak (J.R.F.) Mrs. G. Mallick Mr. P.K. Jangid Mr.K. Dhal Mr. S.C. Rout
Starting date	:	January 1999
Completion date	:	February 2001

Lymphatic filariasis is an important public health and socio-economic problem and around 120 million individuals world-wide are estimated to suffer from lymphatic filariasis. Among 120 million people estimated to be infected with lymphatic filariasis in the world, 48 million are living in India alone. It is estimated that in India, 389.47 millions of people are estimated to be exposed to the risk of filariasis. Out of this, 25.05 million (6.4%) belong to Orissa. The disability and the social and economic burden caused by lymphatic filariasis is poorly understood and remain unquantified. The adverse effects caused by the disease are not well documented, because they have serious socio-economic impact on the society by significantly lowering the productivity and causing economic loss as a result of its chronicity. There is inadequate understanding of the social stigma and psychological effects resulting from chronic disease, but more severely affected people

are probably socially restricted as well as physically burdened. Indirect economical losses result from social and physical confinement of people with chronic conditions and from loss of working days when they go for treatment/surgery. The costs incurred by individuals as well as by the health system are also substantial. As filariasis is a severe problem in coastal Orissa, the current project was aimed to estimate the socio-economic burden of lymphatic filariasis from this part of Orissa. The public health significance of the disease will be quantified, including loss of income due to acute attacks and chronic manifestations as well as direct and indirect costs of medical care to individuals and health system.

Objectives:

1. To study the importance of filariasis to individuals and the community in relation to other problems and to study the societal reaction to the individual affected with chronic disease.
2. To study the degree of physical impairments of individuals with various forms of the disease and its influence on the social activities.
3. To analyse the extent of dependence and burden of the affected individuals on the family members.
4. To study the direct costs to individuals and households for treatment and other medical care for different forms of filariasis outside the government control programme.
5. To study the impact of the disease on the activities, productivity and economic situation of affected individuals and their families.

Progress:

For this study, twelve villages from Khurda district were selected and a survey for various forms of lymphatic filariasis was undertaken in these villages. In these twelve villages all households (around 6000 individuals) were covered and people with various filarial manifestations (cases) were identified. It revealed that the prevalence of elephantiasis among males and females was 2.6% and 3.4% respectively, where as the prevalence of hydrocele among men was 4.2%. The details of age specific prevalences are to be analysed. Also, 5.2% of individuals had suffered from acute fever during last 3 months.

During these investigations arm elephantiasis as well as breast swelling were recorded in 0.18% of total respondents and 0.15% of women respectively.

Case-control study on KAP, risk factors and economic loss due to chronic conditions

First follow-up (July – October 1999):

From the above cases, 63 cases with chronic conditions (38 elephatiasis [18 men + 20 women], 21 hydrocele and 4 with both) were selected and followed for further studies. For each case, an age, sex and occupation matched control was selected. The means and corresponding standard deviations for age of cases and controls are 46.2±16.6 years and 45.6±16.6 years respectively, and the mean annual income levels are Rs. 8301±9769 and Rs. 7696±11302 respectively among cases and controls. The survey tools used in this follow-up are: (1) a questionnaire on social aspects of the cases (only for cases) (2) a questionnaire on treatment seeking behaviour and economic loss (common for both cases and controls) (3) a checklist on daily work activities (for both cases and controls) and (4) a questionnaire on KAP (common for both cases and controls). Data were computerised and preliminary analysis was done.

The results of first follow-up indicated that most of the elephantiasis cases were suffering form longer period (37% cases are from 11-20 years and 29% cases are from 21-30 years), where as majority of hydrocele cases (52%) are suffering from last 5 years. Around 95% elephantiasis cases and 33% of hydrocele cases sought relief from different sources such as nearest government or private hospitals. Mostly they go for modern medicines. Around 50% of elephantiasis cases and 30% of hydrocele cases adopt some home remedies like massaging with coconut oil, castor oil, etc. and anointing different herbals like turmeric, etc. Regarding the effect on mobility, in 49% of elephantiasis cases and 90% of hydrocele cases, the condition kept them from going out freely. They (54% of elephantiasis cases and 48% of hydrocele cases) felt that their daily work has been affected due to their condition, as they can not work like normal persons. Regarding effect on caring themselves (eating, washing, toilet, etc.), 56% of elephantiasis cases and 48% of hydrocele cases felt that their condition has affected the self-care. The psychological

feelings regarding their condition were also probed from the respondents. About 85% of elephantiasis cases and 71% of hydrocele cases feel bad about their condition. Ninety-Five percent of elephantiasis cases and 76% of hydrocele cases had worry or fear about their condition. Also, 56% of elephantiasis cases and 23% of hydrocele cases felt that they feel like burden on other family members due to this condition. It is mainly due to affect on work and lower income. The results also showed that 49 % of elephantiasis cases and 24% of hydrocele cases usually stay away from functions like weddings, festivals, etc. It is due to disfiguring of their condition and some times due to pain. Also, 54% of elephantiasis cases and 42% of hydrocele cases feel that people make fun of them because of their condition. Hence, 34% of elephantiasis cases and 71% of hydrocele cases try to conceal/hide their condition by way of dressing or some other way. Regarding the effect on marriagiability / marital life, a few unmarried respondents said they are not getting alliances for marriage due to this condition. A majority of respondents (59%) felt the difficulty in getting marriage alliances for their family members due to presence of this condition in their family. A considerable proportion of respondents (33% of hydrocele cases and 15% of elephantiasis cases) said that they had problem during sexual intercourse, particularly due to pain in the affected parts. They said that it effected the relations with their spouse. The results of case control study of KAP revealed that there were no significant differences between cases and control in family type, housing type and other household level characteristics. Similarly, there were no significant differences in knowledge levels on filariasis, between cases and controls. The data on direct costs are being analysed.

Second follow-up (November 1999 – February 2000):

Sixty cases and their corresponding controls from the above selected samples were followed for second time during winter period. Similar methods and tools were used in this follow-up. The computerisation of the data has been completed and analysis has to be done.

Third follow-up (March 1999 – June 2000):

The third follow-up of the chronic cases was initiated. It will be completed by June 2000.

Studies on acute filarial cases (fortnightly surveillance):

These investigations were initiated in March 2000 and will be continued till February 2001. For this, two villages were selected (census of these villages was carried out earlier) and acute clinical manifestations characterised by the presence of local signs and symptoms such as pain, tenderness, local swelling and warmth in the groin, with or without associated constitutional symptoms such as fever, nausea or vomiting were monitored in these two villages on every fortnight. During every fortnightly visit, the incidence of acute cases will be recorded for a period of one year. For the individuals identified as affected with acute attacks during the fortnight, the clinical symptoms and their duration will be recorded. The direct costs and indirect costs for all ADL cases will be estimated. The direct costs include expenditures on consultation, medicines, travel and escort (patients' companion) and also on self-medication. The indirect costs will be estimated for all ADL cases and neighbourhood control matched by sex, age and occupation, but without the history of acute or chronic disease. The details on loss of work/productivity will be collected. The data on treatment seeking behaviour and KAP will also be collected.

6. INVESTIGATIONS ON POST CYCLONE HEALTH PROBLEMS

Surveillance and diagnostic support for the cyclone related health problems to the Govt. of Orissa:

The State of Orissa has a large coast line beginning from West Bengal to Andhra Pradesh. Unfortunately the super cyclone struck 8 districts of coastal tract from 29th October to 31st October 1999. The velocity of the wind super imposed with the high tidal wave entering the main land from sea, caused a havoc and disaster and huge loss of life and property.

The RMRC, Bhubaneswar along with staff from NICED, Calcutta carried out field studies on diarrhoeal disorders. Molecular characterisation of the causative enteropathogens was carried out at NICED, Calcutta by the scientists of both the institutions. The staff of RMRC, Bhubaneswar, MRC Field Station, Rourkela; RMRC, Dibrugarh and NIV, Pune carried out entomological surveys, surveillance and diagnostic work related to malaria and dengue fever. Apart from these ICMR Institutions, staff from NICD, New Delhi and Regional Office for Health & Family Welfare, Bhubaneswar also participated in these surveillance duties. The staff of RMRC, Bhubaneswar and RMRC, Port Blair carried out epidemiological work related to leptospirosis. Serological studies for leptospirosis were mostly conducted at RMRC, Port Blair.

6.1. DIARRHOEAL DISORDERS

Since Orissa has a past history of good number of attacks and deaths due to diarrhoeal disorders in previous years and over 60% of disease burden of Orissa is due to water borne diseases, an epidemic outbreak of gastroenteritis disorders was forecast and investigations were undertaken.

The RMRC, Bhubaneswar initiated studies on diarrhoeal disorders on 7th November and the team from NICED, Calcutta joined the studies by 9th November 1999. The scientists and technical staff of various divisions of RMRC, Bhubaneswar

were constituted as two teams with 7 members each and were placed under the coordination of Dr.G.P.Chhotray, DD. The teams started survey work and rectal swabs were collected from untreated cases of diarrhoeal disorders from 8th onwards.

Close contact was kept with Dr.Shiv Lal, Director, NMEP who was coordinating the Central Control Room on behalf of Government of India. Dr.K.Satyanarayana, Director and Dr.G.P.Chhotray, DD joined the central teams (3 teams) and participated in the testing of water samples for chlorination and organisation of studies on diarrhoeal disorders from 8th November onwards. The Director of Health Services, Government of Orissa selected the list of hospitals to be screened for studies on *Vibrio cholerae* and other pathogens on 7th November. The NICED team consisting of Dr.Sengupta and Dr.Niyogi, AD arrived on the 9th evening to join the RMRC, Bhubaneswar scientists to carry out the investigations.

By 11th November 1999 the results of 1st set of 44 stool samples and 6 water samples became available. It was observed that 22 of the 44 rectal swabs tested were positive (50%) for *V.cholerae*. Out of 6 water samples tested, one sample from a tube well was found to be positive for *V.cholerae*. The results were immediately conveyed to the Central Control Room for immediate action.

The Hon'ble Health Minister, Government of India arrived on 11th November 1999 to review the post cyclone scenario. The Central Control Room officials briefed the Hon'ble Minister about the findings of various studies.

By 12th November 1999 the sensitivity pattern of *V.cholerae* to various antibiotics was found out by the scientists of ICMR. These results were handed over personally by Dr.G.P.Chhotray, DD and Dr.K.Satyanarayana, Director to the DHS, Government of Orissa under the supervision of DGHS, Government of India. The scientists of ICMR accompanied the Hon'ble Minister to the affected areas. The Government of Orissa has initiated action on war footing for distributing relevant antibiotics in all the out patient departments (OPDs) held by health officials of State Government, Army officials and other NGOs. The rural water department, Government of Orissa took steps to block those wells which were positive for *V.cholerae* on 12th & 13th November 1999. There after serious efforts were made to chlorinate all drinking water sources in the affected districts.

The Health Secretary, Government of Orissa informed the press that *V.cholerae* was detected in about 50% of stool samples from the affected hospitals. She had also outlined the contribution made by National Institute of Communicable Diseases (NICD), New Delhi and other Government of India institutions. The press statements of Health Secretary, Government of Orissa and subsequent coverage in the local news papers on 15th and 16th about the out break of cholera, made people aware of the need for hygiene, to avoid the spread of the disease. Several teams were pressed into the service by the Central and State Government authorities to chlorinate water sources and to test water samples for available chlorine with simple procedures. At this stage Dr.Rashmi Arora, DDG and Dr. Deepali Mukherji, DDG from ECD division of ICMR headquarters have visited Bhubaneswar and participated in the efforts of ICMR Institutions to provide technical guidance to the local health authorities.

Scientists from Rourkela Field Station, MRC, New Delhi; RMRC, Dibrugarh; NIV, Pune and RMRC, Port Blair joined the efforts to provide surveillance support to the local health authorities by working with Central Control Room. Dr.B. Ravindran, DD had assisted in the standardisation of reporting formats by the state health authorities to the Central Control Room and Dr.S.S.S. Mohapatra, AD continued this task by sharing duties of the Central Control Room. Practically all the scientists and technical staff of RMRC, Bhubaneswar were on surveillance duties during second half of November and December 1999. All these details are described to outline the magnitude of the emergency and the nature of response of ICMR Centres / Institutes to help the health administrators to detect and contain health problems.

There were 32,000 OPD cases of diarrhoeal disorders and 55 deaths due to diarrhoeal disorders up to 15th November 1999. Up to this period during the first two weeks of post cyclone, the death rate due to diarrhoeal disorders was varying from 1.3 to 2.1 per 1000 OPD cases (Fig.5 & 6). Each week claimed 23 to 32 deaths due to diarrhoeal disorders in the 1st two weeks. The situation could be reversed by the 3rd week after applying the results of research studies by the local health authorities with the help of Army and Central Government institutions. The 5 day period from 16th to 20th transformed the entire picture of mortality (Fig.5 & 6). Even though about 30,000 cases were reported during those 5 days there were only 10 deaths. The death rate due to diarrhoeal disorders came down steeply to 0.33 per 1000 cases. Prompt public health intervention strategies based on diagnostic services provided by the ICMR and NICD,

New Delhi had helped to slash the death rate to a low level. Thereafter the death rate per 1000 remained at low level despite of opening of inaccessible areas by the Army from time to time.

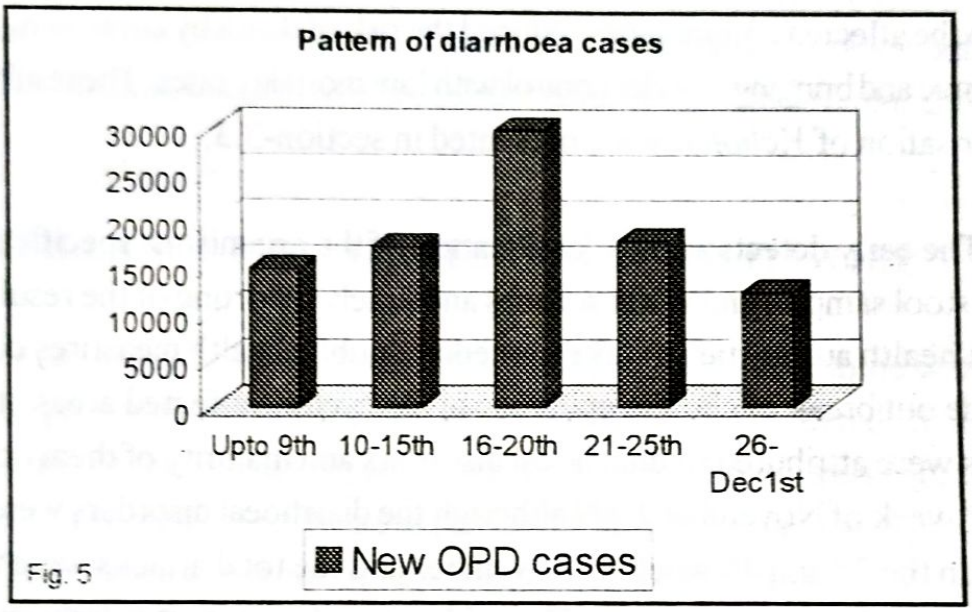


Fig. 5

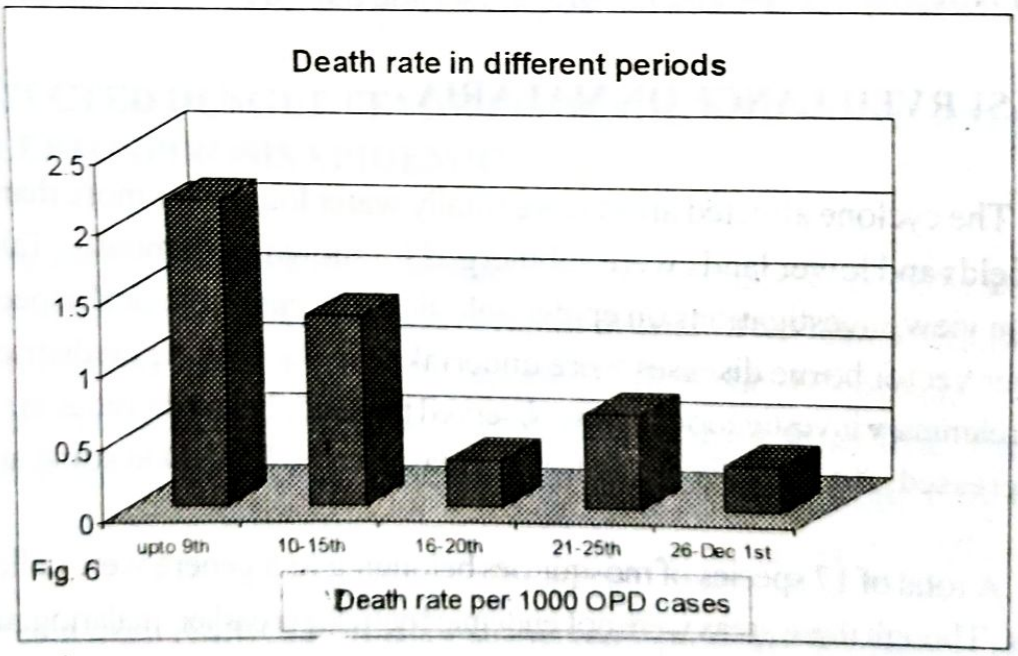


Fig. 6

The changes in death rates could be perceived by the experienced epidemiologists in the 3rd and 4th week of November, but actual figures could be calculated only by the

end of November, 1999, when all the data could be analysed, with epidemiological perspective. By 4th week of November 1999 all the health managers heaved a sigh of relief and emergency duties were changed to surveillance duties. The results would appear to indicate that while the epidemic was increasing in its intensity, application of research results to the affected communities reduced the risk of death by controlling the severity of the epidemic and bringing it under control with low mortality rates. The results on molecular characterisation of *V.cholerae* are presented in section-3.3.

The early detection and identification of the organisms, specifically *V.cholerae* from the stool samples and water sources and timely reporting of the results to the Govt. of Orissa health authorities to take immediate public health measures could prevent a large scale out break of cholera epidemic in the cyclone affected areas of Orissa. Only 81 deaths were attributed to diarrhoeal disorders and majority of them occurred during 1st and 2nd week of November 1999 although the diarrhoeal disorders were continuously reported in the 3rd and 4th week of November and the total attacks were 91,242 during entire period of November month. The epidemic and more particularly severe morbidity and deaths due to diarrhoeal disorders were brought under control during 3rd and 4th week of November 1999.

6.2 SURVEILLANCE ON MALARIA

The cyclone affected areas were totally water logged for more than 15 days and paddy fields and lower lands were submerged for more than a month. Taking all these factors in view, investigations on epidemiological and entomological aspects of malaria and other vector borne diseases were undertaken in the cyclone hit districts of Orissa. From preliminary investigations it was observed that anopheline densities in several places have increased. *An.culicifacies* density increased to 16 PMHD in some areas.

A total of 17 species of mosquitoes belonging to 5 genera were collected in these districts. Though these areas were not endemic for malaria earlier, malariogenic conditions have been created by the unprecedented cyclone and floods, during the post-cyclone period. Only Bhadrak district reported 366 cases of malaria by 20th November 1999. Other districts reported stray cases of malaria and the total number of cases of malaria remained stationary around 500 in the last week of November 1999. Therefore large

scale occurrence of malaria cases was not seen in the cyclone affected districts. Only exception was the Bhadrak district and even in this district, the total number of malaria cases reported were less than 400 for the entire month of November 1999. Thus the cyclone affected area did not experience malaria as serious health problem and limited cases recorded in Bhadrak district were kept under control through different containment procedures.

6.3. SURVEILLANCE FOR JAPANESE ENCEPHALITIS (JE)

Cx.vishnui (group) was the dominant species (64 PMHD) in some waterlogged areas. From the preliminary study it was surmised that due to sudden decline in cattle population in some of these areas approaching zero, possibility of man vector contact would have been very high. In some areas pigs and water birds were also present. The possibility of JE epidemic could not be ruled out during post cyclone period. Rourkela town had reported earlier, JE cases from time to time in Orissa. Therefore careful watch has been maintained to pick up any cases of JE in coastal Orissa after the cyclone. However JE cases were not reported during the post cyclone period in these districts.

6.4. SUSPECTED DENGUE FEVER EPIDEMIC AND CONFIRMATION OF LEPTOSPIROSIS EPIDEMIC

During the second week of November there were reports of deaths and cases resembling dengue fever from Korai block of Jajpur district. Two teams with members from ICMR institutions visited the area and reported to the Central Coordination Room. Entomological team did not find *Aedes aegypti* mosquitoes in the study area. The results of sera tested at NICD, New Delhi indicated that samples were negative for dengue fever.

The team from RMRC, Port Blair suspected leptospirosis infection from the case histories conducted earlier. The blood samples obtained on 16th November by the RMRC, Bhubaneswar were analysed at RMRC, Port Blair in the 1st week of December 1999. The results indicated leptospirosis infection in some of the samples. In effect what was suspected as dengue fever epidemic turned out to be a possible leptospirosis epidemic. Joint investigations with RMRC, Port Blair and RMRC, Bhubaneswar confirmed

leptospirosis infection in 15.5% of 142 persons investigated in the month of December 1999 and January 2000. This study indicated that leptospirosis is a potential health hazard after calamity like cyclone and floods and may cause large scale out breaks. In the post-cyclone period in Orissa large scale utilisation of tetracycline to control the health problems associated with cyclone helped to reduce the severity of the leptospirosis out break and acted like a chemoprophylactic agent.

Active participation of ICMR Institutions in the surveillance and diagnostic aspects of various health problems during post-cyclone period helped the Govt. of Orissa to tackle epidemics that were building up and to reduce the severity of morbidity and the magnitude of mortality with timely and specific intervention measures. The impact of epidemiological research was mostly noticed in bringing down the component of severe morbidity and mortality from diarrhoeal disorders to very low levels by the 4th week of November 1999. It is noteworthy to point out that timely results on the sensitivity of *Vibrio cholerae* organisms and distribution of relevant antibiotics through the peripheral health centres and military hospitals resulted in a substantial decrease of morbidity and mortality from diarrhoeal disorders, though diarrhoeal disorder attacks were continuously reported in 3rd and 4th weeks. There were about 3000 diarrhoeal disorder attack cases and 62 admissions on 25th November, 1999, though deaths due to diarrhoeal disorders were practically 'Nil' during that period.

Large scale administration of tetracycline to reduce morbidity due to various illnesses has helped to bring down the impact of leptospirosis epidemic which was confirmed from Korai block of Jajpur district. Sharing of information on the nature of disease agents, vector densities, vector susceptibility and the sensitivity of pathogens to various antibiotics with the local health authorities on day to day basis helped to contain the epidemics that were building up and helped to lower the peaks of severe morbidity forms and contributed in tapering off of the epidemics very quickly.

7. GENERAL INFORMATION

7.1. PAPERS PUBLISHED IN JOURNALS :

1. B.V. Babu, G.P. Chhotray, R.K. Hazra and K. Satyanarayana, 2000 – Perceptions and interactions of vulnerable groups with the government health services. *The Indian Journal of Social Work,* 61, 1: 54-65.

2. B.V. Babu and J.M. Naidu, 1999 - Genetic variability of blood and saliva antigens, and serum proteins among sub tribes of Mali from Andhra Pradesh, India. *Anthropologischer Anzeiger* (Germany), 57 (2): 105-110.

3. B.V. Babu and J.M. Naidu, 1999 – Sickle cell disease: a neglected public health problem among scheduled tribes. In: H.C. Upadhyay (Ed.), *Current Status of Scheduled Tribes in India,* Anmol Publications, New Delhi.

4. B.V. Babu, Y.S.Kusuma and J.M. Naidu, 1999 - Jatapu tribe of Andhra Pradesh: an ethnographic profile. In: *Contemporary Society: Tribal Studies (Vol. 4; Social Realities)*. D.K. Behera and G. Pfeffer (eds.), Concept Publishing Company, New Delhi, pp. 216-224.

5. M. Bal and M.K. Das, 1999 - Antigenicity of a filarial protease from *Setaria digitata* in *Wuchereria bancrofti* infection. *Annals of Tropical Medicine & Parasitology,* 93: 279-288.

6. M. Bal and M.K. Das, 1999 - Antibody response to a filarial antigen fraction in individuals exposed to *Wuchereria bancrofti* infection in India. *Acta Tropica,* 72: 259-274.

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11. M.K.Beuria, K.K.Mohanty, K.Katoch and U.Sengupta 1999 – Determination of circulating IgG subclasses against lipoarabisomannon in the leprosy spectrum and reactions. *Int. J. Leprosy,* 67:422-428.

12. G. Bulliyya, 1999 - Digital formulae of the Vannekula Kshatriya of Andhra Pradesh. *South Asian Anthropologist,* 20(2): 89-93.

13. G. Bulliyya, 1999 - Differences in some haemostatic variables between the fish-eating and non fish-eating populations. *Asia Pacific Journal of Clinical Nutrition,* 8 (4): 263-267.

14. G. Bulliyya, 2000 - A study on the mode of some behavioural characters of Vannekula Kshatriyas in Andhra Pradesh, India. *The Anthropologist,* 2 (1): 61-62.

15. G.P.Chhotray, M.R.Ranjit and H.K.Khuntia, 1999 - Effect of anthelmintic/ antiprotozoal treatment on the nutritional status of school children in a sub urban area of Orissa, India. *J.Human Ecology,* 10 (5-6): 363-366.

16. G.P. Chhotray. S.K. Kar, S.S.S. Mohapatra and A. Kumar, 1999 - Out break of meningitis in Koraput district of Orissa. *Man in Society,* 12: 48-57.

17. B.P. Dash, A. Mitra and B.C. Kar, 1999 - Osmotic fragility of normal and sickle haemoglobin containing red blood cells. *Indian Journal of Physiology & Pharmacology*, 43 (2): 267-269.

18. N. Mahapatra, R.K. Hazra, S. Rup, A.S. Acharya and A.P. Dash 1999 - *Bacillus sphaericus* interferes with the development of *Brugia malayi* in *Aedes aegypti*. *Journal of Helminthology*, 73: 279-280.

19. P.P. Majumder, B. Roy, R.S. Balgir and B.P. Dash, 1998 - Polymorphisms in the beta-globin gene cluster in some ethnic populations of India and their implications on disease. In: *Molecular Intervention in Disease*. Gupta, Sushma and Sood (eds.). Ranbaxy Science Foundation, New Delhi, pp. 75-83.

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27. U.Sengupta, M.K.Beuria, K.K.Mohanty and K.Katoch, 1999 – Serological diagnosis of leprosy using full thickness skin cultures in vitro: a preliminary study. In: "10th International Congress of Immunology", Eds. G.P.Talwar, Indira Nath, N.K.Ganguly and K.V.S. Rao (eds.), pp.793-796.

28. G. Sudhakar, B.V. Babu and V. Padma, 1999 - Distribution of ABO and Rh (D) blood groups among Koppala Velama caste of Andhra Pradesh. *Journal of Human Ecology*, 10 (4): 319.

29. S. Tripathy and A.N. Nayak, 1999 – Birsa Munda: An Apostle of Social Justice. In: *Contemporary Society: Tribal Studies (Vol. 4; Social Realities)*. D.K. Behera and G. Pfeffer (eds.), Concept Publishing Company, New Delhi, pp. 165-172.

30. G.R. Varma, B.V. Babu and A. Rohini, 1999 – A study on fertility and its socio-demographic determinants among rural population of West Godavari district, Andhra Pradesh. *Journal of Human Ecology*, 10 (3): 179-182.

7.2. MEETINGS / SEMINARS ATTENDED:

1. Dr. K. Satyanarayana, Director and Dr.B.V. Babu, SRO attended Protocol Development and Data Management Training Workshop on Development of Communication Materials for Advocacy in Lymphatic Filariasis Control, organised by UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), as Temporary Advisers, in Pune during 7 – 12 June, 1999.

2. Dr.K.Satyanarayana, Director attended the ICMR-VCRC meeting on "utilisation of research results towards filariasis elimination" held on 30 July 1999 at VCRC, Pondicherry and took part in the discussion.

3. Dr.B.Ravindran, DD attended as invited speaker, the International Meeting on "Parasitic Helminths: From Genomes to Vaccines" organized at Edinburgh, UK during 8-11 July 1999 and presented a paper on "Immunogenicity of carbohydrate antigens in experimental and human filariasis".

4. Dr.K.Satyanarayana, Director attended a National Workshop on "Tribal health and nutrition" held during 26 - 27 August 1999 at NIN, Hyderabad and presented a paper on "Health and nutritional status of tribal population in Orissa".

5. Dr G.P. Chhotray, DD and Dr. B.B. Pal, RO attended 27th Annual Conference of Indian Association of Pathologists & Microbiologists (Orissa chapter) held at Port Trust Hospital, Paradeep on 11 September 1999 and Dr.G.P. Chhotray presented the paper on: Emergence of *V. Cholerae* 0139 in Orissa.

6. Dr.K.Satyanarayana, Director attended a National Workshop on "Research management" organized at TRC, Chennai during 14 – 16 September 1999 and took part in the discussion.

7. Dr.B.P.Dash, RA attended the 42nd Annual Meet of the Zoological Society of Orissa held during 21-22 October 1999 at Khurda and presented a paper entitled, "A study of some genetic markers of blood in tribals of Orissa" (R.S, Balgir, B.P. Dash and B. Murmu).

8. Mr.A.N.Nayak, JRF attended National Seminar on Culture, Ecology & Sustainable Development in the 21st Century, organized by Ethnographic and Folk Culture Society, Lucknow during 30-31 October, 1999 and presented a paper entitled, "Drought, deforestation and changing tribal economy: a study among the Gonds of Kalahandi, Orissa".

9. Dr. K. Satyanarayana, Director and Dr.B.V.Babu, SRO attended Data Analysis and Report Writing Meeting for ComDT Filariasis, organised by UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), as Temporary Advisers, in Vector Control Research Centre, Pondicherry during 1 – 5 November, 1999.

10. Dr. B.Ravindran, DD attended as an invited speaker, the Annual Conference of Indian Association of Medical Microbiologists at PGI, Chandigarh during 19-21 November 1999 and presented a paper on "Immunology of filariasis: lessons from XID mice".

11. Dr.G.Bulliyya, RO attended 32nd Annual Conference of the Nutrition Society of India held during 25-26 November 1999 at Coimbatore and presented a paper entitled, "Iodine deficiency disorders in Bargarh district of Western Orissa" (S.S.S. Mohapatra, G. Bulliyya, A.S. Kerketta, N.S. Marai and A.S. Acharya).

12. Dr.B.V.Babu, SRO attended the IEC Training Workshop on Biomedical Sciences, organised by ICMR, held at National Institute of Nutrition, Hyderabad during 20-24 December, 1999.

13. Dr.R.S. Balgir, DD attended 87th Indian Science Congress held during 3-7 January 2000 at Pune and presented a paper entitled " Do the academic curricula of anthropology in the universities need overhauling at least in the 21st Century in India?" Dr. Balgir was presented a memento for his paper.

14. Mr.B.Murmu, RA attended the 25th Annual Conference of Indian Society of Human Genetics and 2nd Conference of South Asia Pacific Society of Human Genetics, during 9-10 January 2000 at Nagpur and presented a paper entitled, "Hereditary hemolytic disorders among the ten tribal populations of Orissa, India" (R.S. Balgir, B.Murmu and B.P. Dash).

15. Dr. B.Ravindran, DD attended as an invited speaker in the Annual Conference of Indian Immunology Society at CRI, Bombay during 13-15 January 2000 and presented a paper on "Development of anti-filarial vaccines: time to change gears towards carbohydrates".

16. Dr.B.B.Pal, RO attended the National Conference of Laboratory Medicine and workshop on gene amplification techniques in disease diagnosis from 21-25 January 2000 at AIIMS, New Delhi and presented a paper entitled, "Emergence and re-emergence of *V.cholerae* 0139 in Orissa" (G.P.Chhotray, B.B.Pal and H.K.Khuntia)

17. Mr. A.N. Nayak, JRF attended National Seminar on Sociology for the 21st Century at Sambalpur University, Burla during 11-12 February, 2000 and presented a paper "Tribal health problems: an anthropo-sociological appraisal" (A.N. Nayak and B.V.Babu).

18. Dr.M.R.Ranjit, SRO attended 5th International Symposium on Vectors and Vector Borne Diseases held at Department of Zoology, Punjabi University, Patiala from 16th-18th February 2000 and presented a paper, "Super cyclone in Orissa has created mosquitogenic conditions for possible out break of vector borne diseases". (N.Mohapatra, R.K.Hazra, S.K.Parida, H.K.Tripathy, A.P.Dash and M.R.Ranjit).

19. Dr.N.Mohapatra, SRO, Dr. B. V. Babu, SRO, Dr.R.K.Hazra, TO and Mr. A. S. Acharya, RA attended as observers in the "Informal Consultation Meeting on Lymphatic Filariasis in SEA Region", held in Bhubaneswar during 23-25 February, 2000.

20. Dr.B.Ravindran, DD attended the 8th Annual Meeting of the Molecular Immunology Forum at the Indian Institute of Science, Bangalore from 4-6 March 2000 and participated in a panel discussion on 'Host parasite interactions'.

21. Dr G.P. Chhotray, DD attended the seminar on Pulse Polio Immunisation programme organised by PIB, Ministry of Information & Broadcasting, Govt. of India at Bhubaneswar on 16th March 2000, as guest of honour (speaker).

7.3. OTHER ACTIVITIES:

1. Dr. K. Satyanarayana, Director and Dr. R.S. Balgir, DD were appointed as examiners for Ph.D. viva-voce by the Andhra University, Visakhapatnam.

2. Dr. K. Satyanarayana, Director was nominated on to the Advisory Board of *Annals of Human Biology* published by the Society for the Study of Human Biology, UK for two years from 1999.

3. Dr. K. Satyanarayana , Director was nominated into the Advisory Board of *Journal of Human Ecology* published by Kamla Raj Enterprises, Delhi. He was also nominated as Member of the Editorial Board of Journal "*The Anthropologist*" published by the Kamla Raj Enterprises, Delhi.

4. Dr.K.Satyanarayana, Director has been appointed as the member of the Board of Studies in Life Sciences, Utkal University, Vani Vihar, Bhubaneswar for the academic year 1999-2000.

5. Dr.R.S.Balgir, Deputy Director was awarded the International Gold Medal Award-1999 for his research contributions by the All India Medicos Society.

Training to the staff of RMRC:

1. Dr.R.K.Hazra, TO and Mr.H.K.Tripathy, RA participated in the training course in 'Malaria Entomology' held at the Malaria Research Centre, 22, Shamnath Marg, Delhi-110054 from January 10 to February 18, 2000.

2. Dr.S.K.Parida, TO was awarded Ph.D. degree by the Utkal University, Bhubaneswar. Dr. A.P. Dash, DD was his guide.

3. Dr.B.Sahoo, Sr.Lib.Inf.Asst. was awarded Ph.D. degree by the Utkal University, Bhubaneswar. Dr. Sahoo worked under an external guide (Dr. B.B.Shukla, Reader, S.B. Govt. Women's College, Cuttack) for his doctoral work.

7.4. MEETINGS ORGANISED BY RMRC, BHUBANESWAR:

7.4.1. District level health education workshop on filariasis control:

District level workshop for medical officers and senior staff of 62 PHCs has been organised on 12th October 1999 at Kakinada, East Godavari district, Andhra Pradesh as part of ongoing ComDT project. This meeting is aimed to sensitise and train the medical officers and other senior staff of PHCs to undertake mass drug distribution of

DEC under National Filariasis Control Programme. This meeting was organised in co-ordination with district authorities of State Govt. of Andhra Pradesh and was attended by Mr. Satish Chandra, IAS, District Collector, Dr. M. C. Reddy, District Medical & Health Officer, Dr. M. V. Subba Rao, Medical Officer, Filariasis Research and Training Centre (FRTC), Kakinada and other district level officers. Dr. K. Satyanarayana, Director, Dr. G. P. Chhotray, Deputy Director, Dr. B. V. Babu, Senior Research Officer of RMRC, Bhubaneswar attended and organised the meeting. Dr.G.Sudhakar, Plastic Surgeon from local Rangaraya Medical College, Kakinada and Dr.Gopal Singh, DD from DHS office, Hyderabad have participated as facilitators. Various topics on the control of filariasis, including recent strategies for filariasis control, management of various forms of disease, action plan to be followed at district level, community participation, etc. were covered by various speakers in this meeting.

7.4.2. PHC level training workshop on filariasis control:

PHC level training workshops for peripheral health staff were organised at Karapa and Vetlapalem PHCs of East Godavari district, Andhra Pradesh on 25th September 1999. These training meetings were intended to provide training to staff of primary health centres including peripheral health workers to undertake mass drug distribution of DEC for filariasis control. Various aspects of filariasis control and action plan for mass drug distribution including way of distribution of tablets and management of side reactions were covered during this training. Dr. K. Satyanarayana, Director, Dr. B. V. Babu, Senior Research Officer of this Centre, Dr. K. Subba Rao, Medical Officer, Filariasis Research and Training Centre (FRTC), Kakinada attended and organised these meetings.

7.5. SCIENTIFIC ADVISORY COMMITTEE:

The Scientific Advisory Committee was constituted by the D.G., ICMR during 1999 and some more members were added during January and February 2000 for the 13th SAC meeting that was held on 25th & 26th February 2000. The following is the list of the Scientific Advisory Committee of RMRC, Bhubaneswar.

Members of the 14th Scientific Advisory Committee:

Chairman

1. Dr.D.S.Agarwal
Ex- Professor and Head
Department of Microbiology
University College of Medical Sciences
and Guru Teg Bahadur Hospital, Delhi
Corresp. B-24, Swasthya Vihar
Vikash Marg, Delhi, 110 092

2. Dr. L.N. Mohapatra
Ex-Director, RMRC
GM-10, V.S.S. Nagar
Vani Vihar, Bhubaneswar-751 004

3. Dr.R.C. Mahajan
Emeritus Medical Scientist &
Advisor (Parasitology)
Postgraduate Institute of
Medical Education and Research
Chandigarh-160 012

4. Dr.R.K.Shinoy
Principal Investigator
Filariasis Chemotherapy Unit
T.D. Medical College
Alleppy-688 011

5. Dr.Abraham Joseph
Professor of Community Medicine
Christian Medical College
Vellore

6. Professor B.C.Harinath
JB Tropical Disease Research Centre and
Department of Biochemistry
Mahatma Gandhi Institute of Medical Sciences
Sevagram-442 102, Wardha

7. Dr.Harminder Singh
Former Professor of Microbiology
Post-Graduate Institute of Medical Sciences
Chandigarh
Corrsp. # 57, Sector 28-A; Chandigarh 160 002

8. Dr. Dipika Mohanty
Director
Institute of Immunohaelmatology
New Multi Storeyed Building
13 Floor, KEM Hospital Campus
Parel, Mumbai-400 012

9. Dr.Kamala Krishnaswamy
Director
National Institute of Nutrition (NIN)
Jamai-Osmania
Hyderabad-500 007 (A.P.)

10. Dr.V.P.Sharma
Emeritus Scientist
Malaria Research Centre
22, Madhuban, Delhi-110 092

11. Dr.S.K.Bhattacharya
Director
National Institute of Cholera and Enteric Diseases
P-33, CIT Road Scheme XM
Beliaghata, Calcutta-700 010

12. The Director
Health Services
Heads of Dept. Building
Govt. of Orissa
Bhubaneswar

13. Director
Medical Education & Training
Heads of Dept. Building
Govt. of Orissa
Bhubaneswar

14. Dr.P.K.Das
Director
Vector Control Research Centre
Medical Complex, Indira Nagar
Pondicherry 605 006

15. Prof.R.N.Rath
Ex-Professor of Medicine
Professor Pada
Bajrakabati Road
Cuttack-753 012

16. Dr.G.C.Mishra
Director
National Centre for Cell Sciences
NCCS Complex
Gaurhkhind, Pune-411 007

17. Dr.Lalit Kant
Sr.Dy.Director General
Indian Council of Medical Research
Ansari Nagar
P.B.No.4911, New Delhi-110 029

18. Dr.K.Satyanarayana **Member Secretary**
Director
Regional Medical Research Centre (ICMR)
Chandrasekharpur, Bhubaneswar 751 023, Orissa

7.6. BUDGET ALLOCATION AND EXTRAMURAL GRANTS

The Council released Rs.213.5 lakhs for RMRC, Bhubaneswar during the year 1999-2000 as against Rs.158.8 lakhs during 1998-99. A sum of Rs.108.64 lakhs was towards Pay and Allowances and Pension. The allocation for "Other charges" was Rs.33.71 lakhs and there was no separate release for library journals during 1999-2000. The allocation for TA was Rs.3.30 lakhs. An amount of Rs.35.0 lakhs was released by the Council for equipments, registering a substantial increase during the current year. An amount of Rs.32.87lakhs was released for capital works including initiation of Animal House construction and Quarters construction.

EXTRAMURAL GRANTS

Nine projects received funds from different sources during the year under report :

1. The Project on **"Community directed treatment against lymphatic filariasis"** was funded by WHO/TDR, Geneva with Dr.K. Satyanarayana, Director as PI of the project for the 2nd phase. A sum of Rs.8 lakhs was available under this project in April 2000 during the 3rd year of the project.

2. The project on **"Immunology of lymphatic filariasis, modulation variation and immunity"** was funded by European Countries Union (ECU) with Dr.B.Ravindran, DD as the PI of this project. Prof.Rick Maizles, University of Edinburgh, UK is the Principal Co-ordinator of the project, operating from four centres from 4 countries including India. A sum of Rs.3.7 lakhs was the balance available under this project which is in its 3rd year.

3. The project on **"An exploratory study on recording and reporting system of lymphatic filariasis at the community level"** was funded by WHO/TDR Geneva with Dr.B.V. Babu, SRO as the PI of the project. A sum of Rs.1.30 lakhs was released under this project.

4. The project on **"Comprehensive study on delivery of health care research for capacity building among the primitive tribes of Orissa"** was sanctioned by the Council as extramural project with Dr.G.P. Chhotray, DD as the PI of the project. A sum of Rs.3.38 lakhs was released as the 1st year grant for this project.

5. The project on **"Studies on elderly population of primitive tribes of Orissa"** was funded by the Council as Extramural project with Dr.G. Bulliyya, RO as the PI of the project. A sum of Rs.44,000/- was available under this project during May 2000 and 2nd instalment is expected for the 2nd year of the project.

6. The project on **"Intervention programme of nutritional anaemia and hemoglobinopathies among some primitive tribal population of India"** was funded by Ministry of Health and Family Welfare with Dr.Dipika Mohanty, Director, IIH, Mumbai as the Principal Co-ordinator for this project. Dr.G.P. Chhotray, DD is the Co-Investigator for this project from RMRC, Bhubaneswar. A sum of Rs.1.26 lakhs was released during 1999-2000 under this project along with a vehicle and other equipments. Second instalment of this project is under release.

7. The project on **"Intervention programme for cholera, intestinal parasitism, vitamin-A deficiency disorder and scabies amongst some primitive tribal population of Orissa"** was sanctioned by the Ministry of Health and Family Welfare with Dr.G.P. Chhotray, DD as PI of the project. This project was released a budget of Rs.25 lakhs in March 2000 for the initial phase of operation. This is a 5 years project.

8. The project on **"Intervention for hereditary haemolytic disorders among the major tribes of Sundergarh district of Orissa"** was sanctioned by the

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Ministry of Health & Family Welfare through the Council with Dr.R.S. Balgir, DD as the PI A sum of Rs.6.0 lakhs was released during 1999-2000 as the 1st instalment, including a vehicle.

9. The project on **"Surveillance Centre on HIV Infection"** was sanctioned by National AIDS Control Organisation (NACO), New Delhi through the Council. A sum of Rs.34,762/- is available as balance in April 2000 under this project. Dr.G.P. Chhotray, DD is the PI of the project. The NACO had released a grant of Rs.1.31 lakhs for the year 2000-2001 under this project.

7.7. ANNUAL REPORT COMMITTEE

Dr. K. Satyanarayana, Director	Chairman
Dr. B. Ravindran, D.D.	Vice-Chairman
Dr. B. Veerraju Babu, S.R.O.	Secretary
Dr. S.K. Parida, T.O.	Member
Mr. A.S. Acharya, R.A.	Member
Mr. P.C. Nayak, P.A.	Convenor