ANNUAL REPORT

1997 - 1998

REGIONAL MEDICAL RESEARCH CENTRE
(INDIAN COUNCIL OF MEDICAL RESEARCH)
BHUBANESWAR - 751 023, ORISSA

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REGIONAL MEDICAL RESEARCH CENTRE
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CONTENTS

	DIVISION/ PROJECTS	Page No.
1.	**PARASITE IMMUNOLOGY**	
	1.1. Studies with purified antigens	1
	1.2. Antigenicity of filarial enzymes	4
	1.3. Studies on parasitic lipids	6
2.	**APPLIED IMMUNOLOGY**	
	2.1. E.C. Project on Immunology of filariasis	8
	2.2. Immune response in experimental filariasis	9
	2.3. Immuno biological studies in acute filariasis	10
	2.4. Studies on serum cytotoxic factors in malaria	13
	2.5. Development of laboratory animal model	14
	2.6. Studies on anti-disease response in malaria	15
	2.7. Studies on antibodies to DEC and filarial antigens	17
3.	**CLINICAL DIVISION**	
	3.1. Studies on Iodine deficiency disorders	19
4.	**MEDICAL ENTOMOLOGY AND PARASITOLOGY**	
	4.1. WHO/TDR project on *B.sphaericus*	22
	4.2. Production of *B.malayi* L_3	23
	4.3. Mosquito registry studies	24
	4.4. Studies on Persistence of malaria	25
	4.5. Insectary	25
	4.6. Studies on Aphid extracts and juvenoids	26
5.	**MICROBIOLOGY**	
	5.1. HIV/AIDS in Orissa	30
	5.2. Studies on diarrhoeal disorders	32

6. EPIDEMIOLOGY AND INFORMATICS

6.1. WHO/TDR project on community directed treatment of filariasis (ComDT) 36

6.2. WHO/TDR project on reporting system of filariasis 39

6.3. Computer services to various division/scientists 40

7. CLINICAL PATHOLOGY

7.1. Studies on haematalogical disorders 41

7.2. Studies on "G6PD Orissa" 42

7.3. Longitudinal studies on filariasis 43

7.4. Studies on primitives tribes 45

7.5. Molecular strain typing of *P. falciparum* 46

8. GENERAL INFORMATION

8.1. Publications 48

8.2. Conferences/seminars attended 50

8.3. Other assignments and recognitions 53

8.4. Scientific Advisory Committees 55

8.5. Budget and extramural funds 62

8.6. Annual Report Committee 64

1. PARASITE IMMUNOLOGY

1.1. IMMUNOLOGICAL INVESTIGATIONS IN HUMAN FILARIASIS USING PURIFIED ANTIGENS

Staff members	:	Dr.M.K.Das Dr.M.S.Bal Mr.N.N.Mandal Mr.H.S.Naik
Starting date	:	1993
Current status	:	Ongoing

1.1.1. Detergent soluble fraction of *Setaria digitata*.

Lymphatic filariasis caused by *Wuchereria bancrofti* represents a broad spectrum of clinical and parasitological symptoms which are mostly determined by the host immune response to the parasite. Attempts to correlate antibody levels with the intensity of infection have often yielded ambiguous results (except for IgG_4 subclass which is associated with the microfilaraemic state or circulating filarial antigen). It is likely that crude extract of parasites being an extra-ordinarily complex mixture of antigens is not able to resolve the finer aspects of immunoregulation operating in human filariasis. Cloned or biochemically purified antigens by stimulating different aspects of immune system may be able to detect differential immune responses among these groups that is often masked when whole parasite extract is used. We have reported isolation of an antigen ($Dssd_1$) which exhibited high antibody levels in amicrofilaraemic individuals compared to microfilaraemic ones.

Progress:

1. Rabbit Anti-$Dssd_1$ antiserum (1:16 fold dilution) showed binding to the sheaths of both *W.bancrofti* and *Setaria digitata* microfilariae (MF), as noted earlier by immuno peroxidase. Absorption with $Dssd_1$ resulted in marked reduction of antiserum staining. These experiments indicate the presence of $Dssd_1$ epitopes

on the surface of microfilariae.

2. $Dssd_1$ was determined to have a molecular mass of 156 KDa based on gel-filtration. SDS-polyacrylamide gel-electrophoresis of the antigen showed a band at 160 KDa in non-reducing condition. The antigen resolved into three bands (80 KDa, 67 KDa and 60 KDa) in a reducing gel, the 80 KDa band being predominant.

3. Analysis of IgG subclass response to $Dssd_1$ in pooled filarial sera was determined. IgG_3 is the predominant isotype in endemic normals (EN), IgG_1 in chronic filarial patients (CP) and IgG_4 in asymptomatic microfilaraemic carriers (AS). The prevalence of these subclasses (n=20 in each group) in filariasis was determined. Analyses of IgG subclasses in individuals of each group reveal interesting points. EN group was characterised by high IgG_3 prevalence (100%), CP group by IgG_1 (100%) and AS group by IgG_4 (80%). IgG_4 prevalence is low in CP (10%) whereas IgG_2 prevalence is relatively high in all groups. In EN, all are sero positive to IgG_3 and negative to IgG_4. Ten EN individuals (50%) are IgG_1 positive, which are also IgG_3 and IgG_2 positive. In CP, all are positive for IgG_1 and two (10%) are IgG_4 positive which are also positive for all other subclasses. Six sera which are positive for IgG_3 are also positive for IgG_1 and IgG_2. In AS group, sixteen sera (80%) are positive for IgG_4 and fifteen (75%) are IgG_2 positive. Among four IgG_4 negatives two are negative to all classes. Among six (25%) IgG_3 positives four are IgG_1 positive, all are IgG_4 positive and five are IgG_2 positive. Among seven (35%) IgG_1 positives, all are IgG_4 positives. It is interesting to note that among the sixty individuals studied in this endemic region only two individuals belonging to AS group did not respond to any subclass.

$Dssd_1$ represents an antigen preparation which generates anti-sheath antibodies and which shows sharply contrasting patterns of isotypes of human antibodies in different disease (filarial) states.

1.1.2. A FILARIAL ALLERGEN Sd30

Individuals with elephantiasis and hydrocele are the two major clinical groups in *W.bancrofti* endemic regions. While parasitology and epidemiologic differences exist between these two groups, immunological differences, if any, need to be ascertained. Filarial IgE response which is shown to be quite high in filariae-exposed subjects is determined in hydrocele patients.

1. Hydrocele patients can be differentiated into MF positive and MF negative.

2. Microfilaraemic persons (n=16) with hydrocele have lower (P<.01) IgE values to Sd30 than those in amicrofilaraemic men (n=27) with hydrocele.

3. Mean IgM levels to Sd30 were found to be lowest in persons with hydrocele. However, it does not differ between MF positive and MF negatives.

1.1.3. Carbohydrate epitopes of excretory-secretory (E-S) antigens.

1. The kinetics of carbohydrate (CHO) release in E-S antigens of adult *Setaria* was determined *in vitro* culture. The release of CHO was maximum at 24 hr and by 72 hr (3rd day) it has reached minimum. By 4th day CHO determinant was not detected chemically.

2. It was earlier reported that periodate oxidation of ES antigens leading to the loss in CHO determinants did not reduce antibody binding in AS sera (n=22 each group) but caused reduction in all other sera (P<0.01) compared to un-oxidised ES binding. This is further reflected in studying the inhibition of antibody binding with ES antigen, with oxidised ES and non-oxidised ES.

1.2. ANTIGENICITY OF FILARIAL ENZYMES IN ENDEMIC POPULATION

Staff members	:	Dr.M.K.Das Dr.M.S.Bal
Starting date	:	1993
Current status	:	Ongoing

1.2.1. Proteases:

1. A protease (Sdp1) was purified from adult *Setaria digitata* which revealed a single band (110 KDa) in gelatin-substrate gel analysis. Analysis with specific protease-class inhibitors indicated it to be a metalloprotease. For example, the protease activity was completely inhibited by EDTA but was unaffected by PMSF and E-64.

2. The effect of antibodies from filarial sera on the proteolytic activity of Sdp1 was determined. IgG from chronic filarial patients (with elephantiasis) exhibited maximum inhibition and least inhibition was exhibited by IgG from endemic normal sera. Microfilaraemics without clinical symptoms showed intermediate range of inhibition. Interestingly IgG from non-endemic normals (non-filarial region) did not inhibit Sdp1 activity. These results suggest that Sdp1 is antigenic in human exposed to *W.bancrofti* infection and inhibitory antibodies to the protease are generated during the course of disease.

3. Evaluation of IgG subclass response to the protease indicated the dominance of IgG_4 antibodies in asymptomatic carriers and IgG_1 in chronic filariasis. IgG_3 was found to be low. IgG_2 response though high did not differ among the filarial groups.

4. IgG and IgG_4 seropositivity rates were compared in 90 individuals (n=30, each group). About 95% of AS, 35% of both EN and CP were IgG_4 positive. But IgG positivity for the same sera was 100% in CP, 80% in AS and 25% in EN group. Thus all (100%) chronic patients reacted IgG positive but only 35% of such individuals were IgG_4 positive indicating that this proportion of CP group may carry active infection although all individuals were IgG positive. Sdp1-IgG_4 assay could differentiate past from present infection.

IgG_4 subclass serology using the protease antigen was assessed in children (n=110) living in the endemic region (Baniatangi village, Khurda district, Orissa). IgG_4 was detected in 38 (95%) out of 40 microfilaraemic children compared to 35 (50%) out of 70 amicrofilaraemic children. It is to be noted that none of 20 non-endemic normal sera reacted positive to IgG_4-Sdp1 assay. Two thirds (66.4 %) of children (73/110) were thus IgG_4 positive irrespective of microfilaraemic status.

5. Appreciable IgE levels to Sdp1 were detected in filarial subjects. IgE level was compared with IgG_4 in individual serum (n-30, each group) of different groups. There was positive correlation between these two isotypes especially in AS subjects ($r=0.85$, $p<0.001$). IgE and IgG_4 isotypes are proposed to be coordinately regulated in filariasis.

1.2.2. GLUTATHIONE-S-TRANSFERASE (GST)

1. It was earlier demonstrated that IgG antibodies to filarial GST were detected mostly (90%) in *W.bancrofti* infected individuals compared with endemic normals. Mean IgG level in EN (n=31) is significantly reduced ($p<0.01$) compared to either AS or CP sera. But IgE response in EN is considerable and even higher compared ($p<0.05$) to infected groups. However, negative correlation between IgE and IgG is not apparent at the individual level in EN group.

2. As noted earlier IgG response to GST is minimal in EN but IgM response is appreciable (about 50% of EN are IgM positive). IgE levels in children and adults of EN group differ, it is higher in adult individuals ($p<0.05$).

1.3. IMMUNE RESPONSE TO PARASITE LIPIDS IN HUMAN FILARIASIS

Staff members : Dr.M.K.Das
Dr.M.K.Beuria
Dr.A.K.Satapathy
Dr.M.S.Bal

Starting date : 1995

Current status : Ongoing

1. The role of carbohydrate epitopes in lipid antigens was assessed by periodate treatment. Periodate oxidation of lipids especially from microfilariae (MF) resulted in an overall decrease in antibody binding magnitude of which varied depending on antibody isotypes and filarial groups. Following periodate oxidation of MF lipids both IgG and IgM in AS sera exhibited decreased binding but only IgG binding in EN and CP sera was decreased. Thus IgM binding in microfilaraemic AS but not in amicrofilaraemic EN and CP groups was affected. IgG reactivities however in all groups were decreased. In case of adult lipids following periodate oxidation antibody reactivities did not exhibit reduction as noted in MF lipids. It may be suggested that filarial antibody recognition of carbohydrate epitopes in MF and adult stage lipids is different. Even in the same stage (MF lipids) the extent of antibody recognition to carbohydrate epitopes appears to be dissimilar in different clinical groups of filariasis.

2. As filarial sera contain appreciable antibody levels to parasite lipids; antibodies to major glycolipid antigens i.e. gangliosides and cerebrosides (from bovine brain) were measured in filarial sera. IgM levels to gangliosides did not differ among the filarial groups, whereas IgG levels were found to be slightly higher in chronic filarial sera (n=20), each group). IgG response to cerebrosides was negligible in these sera, but IgM response was appreciable and similar in these sera.

3. It was earlier reported that AS sera exhibited lowest levels of antibodies to parasitic lipid antigens compared to amicrofilaraemic EN and CP groups. The preparation of these antigens involves methods that remove protein antigens. "Surface lipids" are also isolated by the known method of rinsing live worms in chloroform/methanol solution. Antibody levels to surface lipids in filarial sera were also decreased in AS sera as noted earlier for previous lipid preparation. These results suggest that lipids isolated previously are similar to surface lipids in eliciting filarial antibodies. It also conforms well to the surface localization of lipid antigens in the sheath of *W.bancrofti* as noted earlier (Annual Report 1996)

2. APPLIED IMMUNOLOGY DIVISION

2.1. IMMUNOLOGY OF LYMPHATIC FILARIASIS MODULATION, VARIATIONS AND IMMUNITY

Staff members	:	Dr.B.Ravindran
		Mr.P.K.Sahoo
		Miss.M.C.Mohanty
Collaborator	:	Prof.Rick Maizels,
		University of Edinburgh, U.K.
Starting date	:	Aug. 1998
Current status	:	Ongoing

This project has an incubation period of two and half years from the preparation stage to the initiation stage of the project activity. The original project was prepared in July 1995 and SAC approved project was submitted to the Council for Health Ministry Screening Committee (HMSC) consideration in October 1995. The HMSC clearance and clearance of other Ministries were completed by August 1996 and the project reached Commission of the European Union (CEU) in the same month. Funds commitment was given by the CEU in May 1997 and transfer of funds could took place in early 1998.

This project funded by the European Commission is to be initiated in August 1998 after receipt of funds. The main objective 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 (Ravindran et al., Parasite Immunology 1994) 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 recognise clones from a c-DNA expression library of

W.bancrofti to identify and sequence genes for sheath associated antigens of *W.bancrofti* and then to type the strains by PCR technique.

2.2. STUDIES ON PROTECTIVE IMMUNE RESPONSE IN EXPERIMENTAL FILARIASIS

Staff members	:	Dr.B.Ravindran Miss. M.C.Mohanty Mr. P.K.Sahoo Dr.A.P.Dash.
Collaborators	:	Dr.Satyajit Rath and Dr.Vineeta Bal from National Institute of Immunology, New Delhi.
Current status	:	Submitted for funding

The origin of this project is the result of the ongoing interaction between the PI at RMRC, Bhubaneswar and CIs at NII and the time spent by one of the scholars of RMRC at NII in 1996 in connection with the project on antibodies to DEC (Vide Section No. 2.7.) and the observations made in RMRC on the susceptibility of XID mice to *B.malayi* infection (Vide Section 2.5.).

This project has been submitted to the Department of Biotechnology (DBT), New Delhi for funding. The primary objective of the project is to utilize XID mice to understand protective immunity in filariasis. XID mice were found to be susceptible by us for development of *B.malayi* (infective larvae develop into juvenile adult stage parasites) unlike immunocompetent mice that are completely resistant (Vide Section No.2.5.). Using this model system an attempt has been made to characterise the immune response to filarial antigens in XID mice (deficient in Brutans Tyrosine Kinase) and in normal controls-wild type (WT). Some of the salient observations of the study so far are as follows:

i) There was a significant Th1 bias in XID animals to both filarial and non-filarial antigens indicated by high levels of IFN-γ and low levels of IL-10 in immunized as well as infected mice.

ii) The immune response phenotype in XID mice could be changed to that of WT mice by adaptive transfer of peritoneal exudate cells (PECs) from WT to XID mice.

iii) The microfilaraemia profile could also be changed in XID mice by transfer of PECs from WT mice.

iv) Macrophages from XID mice were found to be significantly deficient in upregulation of inos as shown by production of nitrites on stimulation with LPS. The association between Th1 bias and inos deficiency and increased susceptibility of XID mice to filarial infection needs to be understood in the context of the biology of filarial parasites in mammalian hosts.

2.3. IMMUNOBIOLOGICAL STUDIES IN BANCROFTIAN FILARIASIS

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 1995
Current status	:	Ongoing

The factors that contribute to acute as well as chronic disease in filariasis are largely unknown. There has been convincing empirical evidence indicating that acquired immune response plays a significant role in disease manifestation. In more recent years experimental work in SCID mice and lymphosyntigraphic studies in humans have provided evidence for direct parasite mediated lymphatic pathology. One of the issues that we had addressed earlier was the role of TNF-*a*, an inflammatory cytokine in acute filariasis. High circulating TNF-*a* levels were associated with severity of acute filariasis based on which we had also proposed the possible use of TNF-*a* inhibitors for clinical management of the disease. While investigating further on the source of higher levels of TNF-*a* in filariasis we recognized the possible production of molecules biologically and serologically similar to mammalian TNF. The following is the summary of the findings so far.

Filarial parasite extracts or their *in vitro* culture products reacted with standard antibodies to mouse as well as to human TNF. All the developmental stages viz., L_3, adults and MF of *Setaria digitata* and *B.malayi* were found to have serologically detectable TNF-*a*. Recombinant TNF competitively inhibited the reactivity of anti-TNF to parasite extracts. The TNF-*a* like activity could be localized to the cuticle and surface of intrauterine eggs by immunohistochemical methods. The parasite products were found to possess biologically active TNF activity as shown by *in vitro* cytotoxicity to L-929 cells. The bioactivity could be inhibited by standard antibodies to mouse TNF-*a*. The presence of biologically active TNF in parasites could also be demonstrated in an *in vivo* assay viz., D-galactosamine primed mouse model. We could further demonstrate by northern blot a message for TNF-*a* in adult stage parasites of *Setaria digitata*. Based on these findings we propose a role for parasite TNF in the pathogenesis of filarial disease. These parasite molecules could be potential targets for development of anti-disease vaccines since immune response directed towards the large helminthic parasites often are associated with development of pathology.

Naturally occuring polyreactive autoantibodies have been demonstrated to play a role in innate immunity as well as in immunoregulation and immunedeviation. The status of such antibodies that react with a wide-variety of autoantigens such as actin, myosin, tubulin, DNA etc. were evaluated in human filariasis. Samples of sera collected from asymptomatic MF carriers were compared with those of elephantiasis cases. Significantly elevated levels of antibodies to actin/myosin/tubulin were demonstrable in microfilariae carriers (known to be immunologically hyporesponsive) in comparison to patients with chronic filarial disease. The precise role of elevated auto-antibodies in immunoregulation and immunedeviation in filariasis is currently not clear. Since, such polyreactive antibodies are known to be produced by B-1 type of B-cells ($CD5^+$B-cells) which have several immunoregulatory functions, we are currently monitoring the levels of circulating $CD5^+$ B-cells in MF carriers. Using a large panel of sera collected from patients with chronic filariasis and MF carriers, the reactivity of the antibodies to *B.malayi* and *Setaria digitata* were studied to evaluate cross-reacting antigens between the two parasites. There was a significant positive correlation between the two parasitic antigens in anti-filarial IgG when it was measured using adult worm extracts. However, such a relationship did not exist when the MF antigens of *B.malayi* and *Setaria digitata* were used indicating that microfilariae contain specific antigens for a given filarial parasite. This was further confirmed when antibodies to MF sheath was quantified by an immunoperoxidase assay using MF from three different filarial parasites viz. *W.bancrofti*, *B.malayi* and *Setaria digitata*. Since most of the anti-sheath antibodies have been known to recognise carbohydrate antigens of filarial parasites it appears that the species specific antigens could be sugars. This was substantiated by the observation that levels of IgG_4 filarial antibodies (that recognise only proteins) were very significantly correlated when tested against *B.malayi* and *Setaria digitata*.

2.4. STUDIES ON SERUM CYTOTOXIC FACTORS IN MALARIA

Staff members	:	Dr.B.Ravindran
		Mr.P.K.Sahoo
Starting date	:	July 1994
Status	:	Completed

Human malarial serum particularly those infected with *P.falciparum* have been reported to contain cytotoxic factors that induce 'crisis forms' of intraerythrocytic stage parasites. These have been considered to be non-immunoglobulins and presumably a mixture of TNF-α, IFN-γ and other products of lipid peroxidation. Unlike immunoglobulins which act on the extracellular parasites these cytotoxic molecules act on intra-erythrocytic stage parasites and mediate cytotoxicity. The current series of experiments were conducted to investigate if such cytotoxic factors produced by mammalian hosts during malaria could have an adverse effect on other blood borne parasites such as microfilariae. These studies are crucial from the point of view of concomitant parasitism in human communities.

It was observed that about 60% of sera collected from cerebral malaria cases and about 40% of sera of non-complicated cases of *P.falciparum* infection were capable of mediating *in vitro* cytotoxicity (at concentrations as low as 2.5%) to microfilariae of *Setaria digitata*, *B.malayi* and *W.bancrofti*. There was a good relationship between MF cytotoxicity and *P.falciparum* growth inhibition *in vitro*. Although chloroquine at physiologically unattainable concentrations mediate MF cytotoxicity *in vitro*, the observed malarial serum mediated MF cytotoxicity was not related to consumption of chloroquine. Similarly, serum TNF-α and IFN-γ levels did not correlate with MF cytotoxicity. The cytotoxic factor was dialysable and resistant to boiling and it was co-purified with immunoglobulins in an affinity column. Anti-filarial antibodies *per se* were not found to mediate MF cytotoxicity *in vitro* since sera collected from

human filariasis cases (acute or chronic disease or MF carriers) were not found to contain MF cytotoxic factor. The factor was found to get absorbed out very effectively by fumed silica indicating a clear possibility for lipid peroxidation products mediating MF cytotoxicity. Filarial parasites were found to be highly susceptible to various aldehydes although the parasites do produce enzymes such as glutathione -S- transferase that neutralize lipid peroxidation products. The results of the current studies indicate an interesting possibility of malarial infections affecting the viability of filarial parasites in mammalian host. Investigations are currently in progress in experimental models to test this hypothesis.

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

Staff members	:	Dr.B.Ravindran
		Ms.M.C.Mohanty
		Mr.P.K.Sahoo
Starting date	:	June 1993
Current status	:	Ongoing

There are no existing laboratory animal models for *W.bancrofti*, the filarial parasite responsible for causing nearly 90% of global lymphatic filariasis. This along with the absence of an *in vitro* system to grow the parasites has been largely responsible for the slow progress in our understanding of the immunobiology of the parasite. Several attempts to use various immunosuppressive drugs in jirds and other rodents to develop infective larvae into adult worms (of *W.bancrofti*) have been largely unsuccessful. It appears that a clear understanding of the factors that are responsible for inhibiting filarial parasite development in non-permissive hosts is a clear requirement for a rational approach towards development of animal models for *W.bancrofti*.

Brugia malayi, another human parasite has been adapted in jirds and *Mastomys coucha*. However, immunocompetent mice are non-permissive to *B.malayi* growth and development while nude and SCID mice are susceptible, indicating thus the role of T-lymphocytes in eliminating parasites from the host. We have observed that mice with X-linked immunodeficiency (XID mice) are susceptible and allow the growth and development of *B.malayi* L_3 upto juvenile adult stage parasites. XID mice have deficiency in Brutan's tyrosine kinase (Btk) and are known to be deficient in immune response to T-independent antigens. One other feature characterized by us was that macrophages of XID mice produce significantly less nitric oxide on stimulation with LPS.

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

Staff members	:	Dr.B.Ravindran Mr.P.K.Sahoo Ms.M.C.Mohanty Dr.B.K.Das S.C.B. Medical College, Cuttack
Starting date	:	June 1994
Current status	:	Ongoing

Development of acquired immunity to malaria in human communities takes several years and 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 a feature most commonly observed in holoendemic malarial areas. The other form of acquired immunity is anti-parasitic in nature and is associated with ability to clear circulating parasite. Most of studies of 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 on 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 in experimental models. We had earlier demonstrated a significant association between antibodies to phospholipids and serum TNF-α levels and consequently survival of patients in cerebral malaria. In particular higher levels of IgG_1 anti-phospholipid antibodies was significantly associated with better prognosis in cerebral malaria. Antibodies to α-linked galactose (anti-gal) is another autoantibody that was found to be significantly associated with malarial experience in human communities.

The presence of toxic malarial antigens that could induce TNF-α could be demonstrated in mice. A heat stable and protease resistant exo-antigen of the murine malarial parasite *P.berghei* was found to induce TNF-α as shown by mortality of mice primed with D-galactosamine. This effect was not associated with possible contamination of the preparation with LPS. Unlike LPS, the malarial exo-antigen was capable of inducing TNF and death in D-galactosamine primed C3H/HeJ mice, known to be non-responsive and resistant to LPS. The D-galactosamine-mice model system was utilised to demonstrate the ability of immunoglobulins purified from sera collected from areas hyperendemic for malaria to neutralize *in vivo* the toxic malarial antigens. Only purified Ig from high malarial endemic areas (and not from low or non malaria endemic areas) neutralised the TNF-α inducing toxic malarial antigens in the D-galactosamine primed mouse model system. These investigations reveal that antibodies in immune human sera neutralize toxic malarial antigens at least in experimental systems. Investigations are currently in progress to demonstrate that affinity purified autoantibodies in malarial sera are capable of neutralising toxic malarial exo-antigens.

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

Staff members	:	Dr.B.Ravindran
		Ms.M.C.Mohanty
		Mr.P.K.Sahoo
Starting date	:	June 1993
Current status	:	Ongoing

Several recombinant antigens of filarial parasites are being tested 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 and development 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 microfilariae. No potential MF surface specific antigens have been cloned with the exception of parasite chitinase.

Our approach in this direction has been different and novel. We had demonstrated that antibodies to the hapten, methyl piperazine carboxylic acid, a derivative of DEC when conjugated to carrier molecules could be made immunogenic and the resultant antibodies to DEC cross-react with a parasite component on microfilarial sheath. This filarial antigen was identified to be a glycoprotein and the antibodies were reacting to the carbohydrate moiety of the molecule. The carbohydrate Ag was found to be present on MF sheath of *W.bancrofti*, *B.malayi* and also *Setaria digitata*. Further this component designated as AgW by us was also found to be

expressed on infective larval (L_3) surface of *W.bancrofti* and *Setaria digitata* but not on the L_3 surface of the strain of *B.malayi* adapted in *Mastomys* or jirds. However the antigen, AgW was found to be expressed on the L_3 surface of *B.malayi* dissected out from *Mansonoides* mosquitoes trapped in the field. This indicates a possible change in antigen expression of the adapted strain of *B.malayi* in comparison to wild type strain.

The conserved carbohydrate determinant on filarial parasites recognized by monoclonal antibodies (mAbs) to DEC was also found to be expressed in some of the organs of the mosquito vector indicating an interesting possibility for its role in parasite transmission and development in mosquitoes.

The observation that mAbs to DEC recognize carbohydrate epitopes on AgW led to the development of neo-conjugates of the specific sugars coupled to protein carriers for raising antibodies in *Mastomys* that could react with microfilarial sheath. Animals thus immunized were found to effectively eliminate circulating MF when challenged with parasites. This approach has thus opened up possibilities for development of synthetic vaccines for filariasis using neo-conjugates of defined carbohydrates. An application is being filed to patent this methodology.

3. CLINICAL DIVISION

3.1. CLINICO-EPIDEMIOLOGICAL STUDY ON IODINE DEFICIENCY DISORDERS (IDD) IN A DISTRICT OF WESTERN ORISSA

Staff members	:	Dr.S.S.S.Mohapatra Dr.G.Bulliyya Dr.J.J.Babu Geddam Dr.A.S.Kerketta Mr.S.C.Rout Mr.T.Moharana Mr.K.Dhal
Starting date	:	September 1995
Duration	:	2 years

Introduction:

Micronutrient malnutrition has long been considered as a serious threat to the health of vulnerable groups in the population. Iodine deficiency disorders (IDD), causing most serious neurological and intellectual impairment, is only second to Vit.A and iron deficiency disorders in the world. This study is being conducted in Bargarh district and is ongoing.

Progress:

The study commenced with a target of covering 30 clusters. So far 13 clusters have been covered.

Results:

A total of 1390 primary school children were subjected to clinical examination, anthropometry and goitre examination by palpation. The clinical and biochemical parameters evaluated so far are as under.

Clinical evaluation:

Though the total goitre rate (TGR) was 11% in all the 13 clusters together, the block-wise analysis shows a very high TGR (24%) in Paikamal block and low TGR (4.5%) in Attabira block. Only 6.8% of children had Vit.B complex deficiency signs and 5.6% had Vit.A deficiency signs, as evidenced by the incidence of angular stomatitis and Bitot's spot, respectively.

Biochemical evaluation:

Anaemia: A total of 598 filter paper blood samples were collected and were subjected to Hb% estimation by cynomethaemoglobin method. Anaemia was classified as severe when Hb level is below 6 g/dl; moderate with Hb levels between 6.1 g/dl and 9 g/dl; mild with Hb levels between 9.1 g/dl and 11.9 g/dl. About 20.5% showed severe anaemia, 28% showed moderate anaemia and 39% had mild anaemia (WHO grading). Thus a staggering 88% of the children were found to be anaemic in different grades.

Urine samples: Out of 133 samples collected, urinary iodine concentration was estimated in 61 samples. The results show that 28% of the samples are below normal in different grades. However, no sample showed a severe deficiency of iodine.

TSH estimation: A total of 31 serum samples were collected and processed for estimation of TSH using test kits supplied by WHO. Fifteen of the samples from school children processed showed that all are normal. Of the 16 cord blood samples only one (6.2%) was found to be below normal.

T4 : So far 29 serum samples have been collected and are being processed.

Water samples:

So far, 45 drinking water samples are collected from different sources and are being processed for their iodine content.

KAP study:

A KAP study has been undertaken to know about people's perception of IDD by a pretested questionnaire. For this study, 257 people (male 182 and female 75) were covered. It is observed that only 14.3% (26/182) of males and 6.7% (5/75) of females knew about the goitre. None of the people had the knowledge as to how the goitre is caused. From the total 257 surveyed, 3% responded that the goitre is due to 'air', 8% attributed it to 'water', 5% to 'food' and 3% to 'cold'. A substantial proportion (81%) had absolutely 'no idea'. Only 16% used iodised salt and 9.3% used it only occasionally.

4. DEPARTMENT OF MEDICAL ENTOMOLOGY & PARASITOLOGY

4.1. FIELD EVALUATION OF *B.SPHAERICUS* AGAINST *CULEX QUINQUEFASCIATUS* IN ORISSA (WHO/TDR PROJECT)

Staff members	:	Dr.A.P.Dash
	:	Dr.N.Mahapatra
	:	Dr.R.K.Hazra
	:	Mr.H.K.Tripathy
Starting date	:	March, 1992
Completion date	:	Feb. 1998

The Orissa state has been an endemic home for lymphatic filariasis. Filariasis due to *W.bancrofti* accounts for 98% of the infection and is transmitted by the ubiquitous mosquito *Culex quinquefasciatus*. Vector control continues to be an important component in the prevention of the disease. In view of the high cost and adverse effects of insecticides, alternate methods like biocides are now increasingly tried against mosquitoes. *B.sphaericus* has been shown to be highly insecticidal to culex larvae. A particularly attractive features of *B.sphaericus* is its potential to persist and recycle under certain field conditions. Appropriate formulations have shown significant residual activity against *Cx.quinquefasciatus* in highly polluted breeding habitats. A large scale field evaluation of *B.sphaericus* against transmission of bancroftian filariasis was initiated in April 1992 with WHO/TDR support in Orissa. Two localities viz., Khurda (45000 population) and Pipili complex (35000 population) were taken up for the study. Khurda was selected as the experimental area and Pipili as the comparison area. Base line data on house holds, breeding places, species composition, vector density, infection and infectivity rates, biting habits of the vector, MF rate and MF density were collected in both the areas for one year.

Intervention started with *B.sphaericus* (5g/m²) application from April 1993 and continued at a frequency of two applications in a year. This was the final year of intervention. Double treatment strategy was followed as decided in Cameroun, West Africa in 1993. Mass treatment of breeding sites with biocide was done twice a year i.e., in May (pre - monsoon) and in October (post monsoon). The first application of the biocide in 1993 drastically reduced the larval and adult densities by 90% and the infectivity rate was reduced to 0%. Subsequently, however, the efficacy of the biocide decreased and densities (in 1997) are now maintained at 30 to 40% level of base line densities of 1993.

The larval density in Khurda (experimental area) varied between 16.8 and 37.8 per dip as compared to 21.5 and 48.3 in Pipili (comparison area), during 1997-98. The adult density in Khurda varied from 21.4 to 41.3 per man hour while the same varied from 27.3 to 55.3 per man hour in Pipili, during 1997-98.

The infectivity rate which was maintained at zero level till May 1996 in Khurda increased to 2.35 in November 1997 while it was 3.8% in Pipili. The impact of biocide on transmission indices like risk of infection index and annual transmission index were measured, which were 0.29 and 4092 respectively in Khurda as compared to 1.5 and 26003 in Pipili. The above indices are still very low (1/5 to 1/6) in experimental area as compared to comparison area during the year under report.

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

Staff members : Dr.A.P.Dash
Dr.N.Mahapatra
Mr.S.K.Parida

Starting date : October, 1991

Mastomys coucha infected with *Brugia malayi* were fed to black eyed *Aedes aegypti* (Liverpool strain) in successive batches (11 batches). Total of 3449 mosquitoes were fed and dissected after 14 days of incubation. A total of 613 infective larvae were procured, which were further used for reinfection of fresh *Mastomys.*

374 *Aedes aegypti* (black eyed liverpool strain) were also fed to *M.coucha* infected with *Setaria digitata.*

4.3. STUDIES ON MOSQUITOES OF ORISSA IN RELATION TO FILARIASIS AND MALARIA/MOSQUITO REGISTRY.

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

Starting date : June, 1992

Mosquitoes were collected from different areas of Puri, Khurda and Koraput districts. The areas are Pipili, Khurda (endemic for filariasis) and Baipariguda (endemic for malaria). The species composition reveals presence of 17 species belonging to five genera.

Feeding behaviour:

Blood meals of 110 mosquitoes belonging to eight species were analysed by gel diffusion technique. The anthropophilic indices of group I mosquitoes belonging to *Cx.quinquefasciatus, Mn.annulifera* and *Ma.uniformis* ranged from 60 to 90%. *Cx.quinquefasciatus, Ma.annulifera* and *Ma.uniformis* showed anthropophilic index of 90%, 70% and 62.3% respectively. The group II mosquitoes belonging to

An.subpictus, *An.vagus*, *Cx.gelidus*, *Cx.tritaeniorhynchus* and *Cx.vishnui* showed anthropophilic index 17.9%, 6.1%, 7.1%, 11.3% and 4.1% respectively which is less than 20%.

4.4. RISK FACTORS FOR PERSISTENCE MALARIA TRANSMISSION IN TWO GEOPHYSIOGRAPHICAL REGIONS OF ORISSA.

Staff members	:	Dr.A.P.Dash
		Dr.N.Mahapatra
		Mr.S.K.Parida
		Dr.R.K.Hazra
Starting date	:	July, 1995
Duration	:	3 years

The study carried out in Baipariguda (Koraput district)in May 1997 revealed no fever case as it was lean transmission period. Three species of *Anophelines* viz., *An. culicifacies, An.fluviatilis, An.vagus* were encountered in the survey. The man hour density were found to be 2.0, 1.25 and 1.25 respectively for *An.culicifacies, An. fluviatilis* and *An.vagus*.

4.5. Cyclic colonies in the insectary.

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

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

The eggs and larvae of above species were used for laboratory evaluation of different insect growth regulators (IGR), plant extracts, biocides etc. Laboratory bred mosquitoes were also used for developing filarial larvae through membrane feeding.

4.6. COMPARATIVE EFFICACY OF APHID EXTRACTS, SOME LARVICIDES AND INSECT GROWTH REGULATORS AGAINST DEVELOPMENT OF MOSQUITOES

Staff members	:	Dr.A.P.Dash
		Ms.R.Mohapatra
Starting date	:	February 1993
Completion date	:	March 1998

This study was carried out by the research scholar Ms.R.Mohapatra for the last 5 years under the guidance of Dr.A.P.Dash, DD. Some of the findings were given in part in the earlier Annual Reports. This project has been completed this year and comprehensive results are summarised below.

Susceptibility tests undertaken for different groups of compounds (JH, CSI, synthetic pyrethroids and O.P. compounds) show the EC_{50}/EC_{90} doses of TAEan, hexaflumuron, fenfluthrin, cyfluthrin and pyraclofos to be 0.023/1.12, $72 \times 10^{-7}/11 \times 10^{-4}$, $73 \times 10^{-5}/31 \times 10^{-3}$, $18 \times 10^{-5}/44 \times 10^{-4}$ and $14 \times 10^{-4}/55 \times 10^{-3}$ ppm respectively against *An. stephensi*, 0.013/1.44, $13 \times 10^{-6}/16 \times 10^{-4}$, $53 \times 10^{-6}/43 \times 10^{-4}$, $37 \times 10^{-7}/73 \times 10^{-5}$ and $32 \times 10^{-5}/21 \times 10^{-3}$ ppm respectively against *Ae.aegypti* and 0.014/1.76, $38 \times 10^{-7}/22 \times 10^{-4}$, $57 \times 10^{-6}/55 \times 10^{-4}$, $25 \times 10^{-6}/13 \times 10^{-4}$ and $1 \times 10^{-4}/1.19$ ppm respectively against *Cx.quinquefasciatus*. From the relative activity computation, hexaflumuron was found to be most effective against *An.stephensi* and *Cx.quinquefasciatus* while cyfluthrin against *Ae.aegypti*.

Comparative efficacy of sublethal (EC_{50}) and lethal (EC_{90}) doses of different insecticides on adult emergence, sex ratio, fecundity, fertility, biochemical parameters and histopathological changes were observed following treatment at the egg stage of the mosquitoes. Hexaflumuron, fenfluthrin, cyfluthrin (only at EC_{90} dose) and pyraclofos have shown ovicidal effect against *An. stephensi*, only cyfluthrin (at EC_{90}

dose) was found to be ovicidal against *Cx. quinquefasciatus* and EC_{90} dose of pyraclofos, hexaflumuron, fenfluthrin and cyfluthrin have shown ovicidal effects against *Ae. aegypti*.

All the test compounds induced various morphogenetic aberrations like short and stumpy larvae, larvae having extended cervix, larval - pupal intermediates, albino pupae, unsuccessful adults etc. However, hexaflumuron was the only test compound observed to induce adultoid pupae in all the three mosquito species. Hexaflumuron also produced maximum types and percentage of morphogenetic aberrations in mosquitoes.

The percentage of adult emergence inhibition was computed for different groups of test compounds. TAEan was found to have higher inhibiting potentiality against culicine mosquitoes, whereas the pyraclofos showed highest potentiality against *An. stephensi*.

The sex ratio and fecundity rates of mosquito species were affected differently by different test compounds. However, the fertility rates of all the three mosquito species were found to be significantly reduced by all groups of test compounds.

TAEan, hexaflumuron, fenfluthrin, cyfluthrin and pyraclofos have induced several histopathological changes in adult mosquitoes emerged from the sublethal treatment at larval stage. The atrophy of striated thoracic longitudinal muscle was found to be induced by all the test compounds. The malpighian tubules showed karyorrhexis in all treatments except the O.P. compound pyraclofos. Vacuolation in supra/sub oesophageal ganglion was observed to be induced by both the pyrethroids (fenfluthrin and cyfluthrin) and the O.P. compound (pyraclofos). The female mosquitoes treated with all the test compounds showed atrophy of ovaries, large number of oocysts with irregular shapes in the ovaries. The chitin synthesis inhibitor hexaflumuron was found to exhibit inhibitory activity on the cuticular system of both treated larvae and unsuccessful adults i.e., a reduction of cuticle excretion was detected.

The sublethal effects of different groups of insecticides on total protein, sugar, glycogen and lipid contents of the different developing stages of mosquitoes were measured. TAEan has reduced the total protein content of both immature and adult mosquitoes. Lipid contents of adult mosquitoes were increased after treatment with TAEan, hexaflumuron, fenfluthrin and cyfluthrin but the O.P. compound pyraclofos reduces the same in all mosquito species tested. TAEan has a positive influence on glycogen catabolism in different developmental stages of mosquitoes, while pyraclofos has similar effects only on immature stages of mosquitoes. The synthetic pyrethroids (fenfluthrin and cyfluthrin) were observed to have no significant effect on the total glycogen reserve of all the developmental stages of the mosquitoes. Effect of different test compounds on level of total sugar contents of mosquitoes were found to be opposite to the effect produced against glycogen reserve.

All the test compounds were found to be non lethal to non-target species like *C.mrigala, B.melanostictus* and a lower mammal *M.musculars.* Fish safety factor or Suitability index for *C.mrigala* and *B. melanostictus* against the three vector mosquitoes were computed. It showed maximum value for *C.mrigala* in case of hexaflumuron, which indicated its higher tolerance than *B.melanostictus.* It was also observed that when higher concentrations than LD_{50} dose of hexaflumuron was injected into the mice, it caused paralysis of the concerned leg.

Conclusions

Considering the lethal, morphogenetic, histopathological and biochemical effects of the test compounds the following conclusions are made:

As larvicides, hexaflumuron was found to be the most effective against *An. stephensi* and *Cx. quinquefasciatus* and cyfluthrin against *Ae. aegypti.* The test compounds are found to have adversely affected the adult emergence inhibition rate, morphogenetic and histopathological changes and reproductive potential of mosquitoes

which renders them as potential vector control agents. Hexaflumuron induced maximum types and numbers of morphogenetic aberrations, inhibition of cuticle synthesis along with other histopathological changes and also affected the hatchability and fertility rates of the mosquitoes even at sublethal levels. It has very low toxicity against the non target organisms.

5. MICROBIOLOGY DIVISION

5.1.1. STUDIES ON HIV/AIDS IN ORISSA.

Staff members : Dr.B.B.Pal
Mr.H.K.Khuntia
Mr.S.K.Mohanty, Project staff
Mr.S.Murmu, Project staff

Starting year : 1987 (ongoing)

This Centre was included for HIV Sero-surveillance from 1987 by the ICMR in initial years and by the National AIDS Control Organisation (NACO), New Delhi in recent years. Screening of referral cases from State Government health authorities, hospitals, jails and judicial authorities has been undertaken during the period under report. A total of 84 samples were screened during the year 1997-98. Out of these 70 samples were from drug addicts referred by Drug De-addiction and Counselling Centre and the remaining 14 were from other sources. Out of the 84 serum samples, 15 samples were found to be repeatedly ELISA positive and 14 were confirmed to be Western Blood (WB) positive for HIV antibodies by the National Referral Centre, National Institute of Cholera and Enteric Diseases (NICED), Calcutta.

Among the 14 positive samples, 7 were from drug abusers, 2 from blood donors, 3 from heterosexual males, one from a young female belonged to STD group and one from other category. This particular young female was the wife of a heterosexual male who was also found positive for HIV antibodies and they have a young child whose status is not known. This is the first report of a couple being both positive for HIV antibodies from this Centre.

Table-1. Year-wise seropositivity rate for HIV infection.

Year of examination	No. of positives/Total sera screened (Seropositivity per 1000 samples)	
	Indians	Foreigners
Upto 1993	7/6885 (1.01)	0/43 (0.00)
1994	13/7090 (1.83)	27/135 (200)
1995	13/7244 (1.79)	27/153 (176.47)
1996	16/7316 (2.18)	27/173 (156.07)
1997	30/7376 (4.07)	27/188 (144.62)

Parentheses show seropositivity rate/1000 samples screened.

This year the seropositivity rate for HIV infection for Indians has increased upto 4.1/1000 whereas it was 2.18/1000 in the previous year. But for foreigners, the seropositivity rate has decreased to 144.6/1000 sample screened. Though the seropositivity rate for Indian samples tested here is low in comparison to national level, precautionary measures should be taken immediately by strengthening the blood screening programme at all blood banks. Information, Education and Communication (IEC) activities should be intensified to cover different risk groups which are more prone to HIV infection. Sentinel surveillance in hospital setting may be carried out to monitor the trend of HIV infection from time to time.

5.1.2. SERO-SURVEILLANCE FOR HIV INFECTION AMONG THE DRUG ABUSERS.

On the request of the Drug De-addiction and counselling Centre, CYSD, Sahara (supported by Ministry of Welfare, Government of India), Saheed Nagar, Bhubaneswar, the blood samples under code were received and tested for HIV infection. The above

samples were collected from the indoor patients for a period of one year from June 1996 to July 1997. A total of 70 blood samples from different categories of drug addicts were tested for the presence of HIV antibodies. All the drug addicts were categorised as oral inhalation, intravenous drug use (IVDU) and mixed group. In general, it was found that 7 out of 70 (10%) drug addicts were positive for HIV infection, harbouring HIV-1 virus only. It was found that most of the drug addicts belonged to 21-30 years age group followed by 31-40 years age group. Again HIV infection was found highest among the IVDU group followed by oral drug users. The blood samples were collected with pre-test and post test counselling. The confidentiality was maintained during the study period. Such a high prevalence (10%) of HIV infection among the drug addicts is reported for first time from Orissa. Though this is a preliminary report, more detailed information can be obtained from this particular group. It is generally felt that population of Paradeep Port and temple cities of Puri and Bhubaneswar are more prone for drug abuse. High risk groups of these towns and cities may have greater risk of acquiring and spreading the HIV infection to the low risk groups. The seropositivity rate of HIV/AIDS infection is mounting steeply, though these patterns are seen in our referral centre which is expected to cater to suspected cases and high risk groups. Unless control measures for HIV infection are planned and executed the situation may go out of hand and the patterns recorded in the North Eastern states of our country, may be reproduced in the Eastern region also.

5.2. HOSPITAL BASED STUDY ON DIARRHOEAL DISORDERS

Staff members	:	Dr.B.B.Pal
		Dr.Ms.M.Anuradha
		Mr.H.K.Khuntia
Starting	:	August 1995
Completion	:	March 1998

Acute diarrhoeal disorders are one of the leading and major causes of mortality and morbidity, especially among the paediatric age groups. Characterisation of the diarrhoea causing pathogens is not only important from epidemiological point of view, but also to track the emergence of new serotypes among the gastroenteritis (GE)/ diarrhoea causing bacteria. In this study efforts were made to identify the bacterial pathogens causing acute G.E./diarrhoea among the children. Parasites and viruses were not included in this study.

This study was being conducted in two hospitals, viz. Capital Hospital, Bhubaneswar and S.V.B.P. Post Graduate Institute of Paediatrics, Cuttack. Rectal swabs were collected in the transport medium from the G.E./diarrhoea patients admitted to the hospitals. These swabs were sub-cultured on different selective media. Significant colonies were tested biochemically and finally antisera test was done for confirmation. A total of 134 samples were tested. These results are given in Table-1 and Table-2.

Table 1. Age group-wise distribution of patients.

Age group in years	Male	Female	Total (%)
0 - 1	64	20	84 (62.7)
1 - 4.9	20	21	41 (30.6)
5 - 13.9	6	2	8 (6.0)
≥ 14	0	1	1 (0.7)
Total	90	44	134

Table 1 showed that majority of samples were from infants of 0-1 year age group (62.7%) and 30.6 % were from preschool children aged 1-4.9 years.

Table 2. Percentage prevalence of bacterial pathogens.

Types of pathogens	P.G.I. of S.V.B.P., Cuttack	Capital Hospital, Bhubaneswar	Total (%)
E.coli	46	20	66 (49.3)
Shigella	12	5	17 (12.7)
Salmonella	5	0	5 (3.7)
V.cholerae	9	2	11 (8.2)
Total	72	27	99 (73.9)

The results show that, out of 134 rectal swabs processed during July 1997 to Dec'97, 99 samples (73.9%) were positive having single bacterial pathogen. During the year under report *E.coli* was added to the list of pathogens, unlike last year report. Out of 99 positive samples *E.coli* was seen in 66 samples constituting 49.3% of total (66/134). This was followed by *Shigella* (12.7%) and *Vibrio cholerae* (8.2%). All the *Vibrio cholerae* were *Vibrio cholerae* 01 Ogwa and *S.dysenterae* was the common pathogen. From this study it was evident that *E.coli* and *Shigella* were predominant pathogens causing G.E./diarrhoea among the paediatric age group.

6. EPIDEMIOLOGY AND INFORMATICS DIVISION

6.1. MULTI-CENTRE STUDY OF COMMUNITY DIRECTED TREATMENT (COMDT) OF LYMPHATIC FILARIASIS

Staff members	:	Dr. K. Satyanarayana Dr. A.P. Dash Dr. G.P. Chhotray Dr. B.V. Babu Dr. R.K. Hazra
Starting date	:	February 1998
Duration of the project	:	2 years.

Lymphatic filariasis is an important public health and socio-economic problem effecting over 120 million people world wide. The State of Orissa in India is an endemic home for lymphatic filariasis. Though there have been some significant successes in the control of the disease, the burden of lymphatic filariasis remains unaffected. However, the introduction in recent years of new drugs and single-dose treatment regimens with diethylcarbamazine (DEC) and/or ivermectin has been an important breakthrough for filariasis control. As a result, 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 with DEC (6 mg/kg body weight; once in a year; for several years). 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. Sustained drug delivery to all high risk communities is difficult to achieve by the government health services alone, either because they are overburdened with other responsibilities and short of resources, or because of lack of participation of the population with the official treatment programme. Recent research on drug delivery for another disease, onchocerciasis, in the African continent indicates

that greater involvement of the endemic communities in the delivery process may be a solution for sustained treatment compliance. The WHO/TDR has developed the concept of community-directed treatment (ComDT), in which communities themselves have the responsibility for the organisation and execution of the treatment of their members, once in a year for several years. Communities will be allowed to design their own strategy for drug delivery.

The WHO/TDR Task Force on Community-Directed Treatment of Lymphatic Filariasis and Onchocerciasis 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.

General 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, cost and potential sustainability of the two approaches.

Time frame:

This project was prepared in April 1997 and submitted to WHO/TDR as a letter of intent on their invitation. Approval of Scientific Advisory Committee (SAC) was obtained in October 1997 and Health Ministry Screening Committee (HMSC) approved the project in January 1998. Scientists from RMRC, Bhubaneswar participated in the development of project protocol in the New Delhi meeting (Dr.A.P.Dash and

Dr.B.V.Babu, July 1997) and Mukuno, Uganda meeting (Dr.B.V.Babu, November 1997) and contributed in the preparation of protocol including formats/research instruments and evaluation procedures. The WHO/TDR selected RMRC, Bhubaneswar as one of the sites for their multi-centric project and commitment for funding from WHO/TDR was received in January 1998. At this stage of the project Dr.A.P.Dash, DD and P.I. of the project was deputed to Institute of Life Sciences, Government of Orissa, Bhubaneswar, as its Director for one year period and Dr.K.Satyanarayana, Director of RMRC took over as the P.I. of the project.

The first phase of the project has started in March 1998 and this phase will be completed in June 1998. The second phase will start in September 1998 and intervention with DEC treatment will be done in November/December 1998 and the analysis will be completed by September 1999.

Study area:

Four block in Khurda district, namely, Khurda, Jatni, Tangi and Begunia are selected for the present study.

STUDY PHASE I: BASELINE SITUATION AND APPROACH TO THE COMMUNITY

The collection of basic data about the socio-economic situation in the study area, the presence and performance of health services, knowledge and awareness about filariasis among communities, etc. is being carried out. Further more information which are required for the design of the ComDT is being obtained.

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

Staff members : Dr. B.V. Babu
Mr. A.S. Acharya
Mr. P.K. Jangid

Duration of the project : 9 months

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 had shown that ComDT is feasible and effective. It had also pointed out the problems with reporting with community directed treatment as well as with health system directed treatment. Hence the present study is aimed to develop simple, practical and reliable method of reporting on ComDT by control programmes and by communities themselves, after understanding the existing mechanisms. With response to WHO/TDR's circular, this project was prepared and submitted to WHO/TDR in November 1997. The approval of Scientific Advisory Committee was obtained in February 1998 and was forwarded to ICMR for HMSC clearance. It was approved by HMSC recently.

Objectives:

1. To identify the type of recording system or type of information existing on filariasis at community level (including traditional methods of record keeping, role of traditional healers, etc.)

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 peripheral level health personnel and other personnel associated with community activities (including Anganwadi worker, traditional birth attendant, etc.) 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.

Study area and Methodology :

Two distinct areas are selected for the execution of the study. They are (1) Khurda district of Orissa State and (2) East Godavari district of Andhra Pradesh State. Both the areas, which are endemic for filariasis, are under mandatory study areas of the Centre. Various social science methods such as sample survey, in-depth interviews and focus group discussions will be used.

6.3. COMPUTER SERVICES TO VARIOUS DIVISIONS/SCIENTISTS

Staff member : Mr.A.S.Acharya

Services have been provided to the scientific staff in the preparation of project proposals, research papers and presentations. He also assisted in creation and handling of data bases, and in analysis of data. Apart from the above activities, active assistance was rendered in the preparation of various office documents by him.

7. CLINICAL PATHOLOGY

7.1. STUDIES ON HEREDITARY HAEMATOLOGICAL DISORDERS.

Staff members	:	Dr.G.P. Chhotray Dr.J.J. Babu Geddam Dr. M.R. Ranjit Mr. B.N. Sethi Mr.K.C.Dalai
Status	:	Ongoing diagnostics

During the period under report, a total of 46 cases (29 male, 17 female) were referred from various medical colleges and peripheral hospitals of Orissa State for diagnosis of various haematological disorders. A majority of patients (76.1%) presented with chief complaints of refractory anaemia and weakness and 17.4% of the cases had jaundice.

The age, sex and caste wise distribution of these cases revealed that 40 cases (26 male, 14 female) belonged to general castes and rest from Scheduled Tribes. Majority of the patients belonged to the coastal districts of Orissa and the rest from other parts of Orissa. There was a preponderance of males in the clinical study sample. It was observed that a majority of the patients were children followed by young adults. The median age being 18, 10, 29, 4.9, 4.27, 16 and 10 for Hb phenotypes Hb AA, Hb AA2, Hb AF, Hb FS,Hb AS and Hb SS respectivly. It was observed that 56.5%, 10.9%, 8.6%, 6.5%, 13.04% and 4.3% of cases belonged to Hb AA, Hb AA2, Hb AF, Hb FS, Hb AS and Hb SS phenotypes respectively.

Various clinical manifestations and peripheral blood picture in different groups of patients were studied. The clinical examination revealed that all Hb SS phenotype patients had splenomegaly and hepatomegaly. Patients having Hb AA2 have recorded high reticulocyte count. Jaundice was noticed in 66.6% of cases of Hb FS phenotype.

The peripheral blood smear examination revealed the presence of microcytic hypochromic blood picture in 28% of cases and normocytic, normochromic blood picture in 72% of cases.

7.2. A STUDY ON CLINICAL AND HAEMATOLOGICAL PROFILE,MORBIDITY PATTERN AND MOLECULAR CHARACTERIZATION OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE(G6PD) DEFICIENCY IN MALARIA ENDEMIC TRIBAL POPULATION OF INDIA WITH SPECIAL REFERENCE TO "G6PD ORISSA".

Staff members	:	Dr.G.P. Chhotray
		Dr.J.J. Babu Geddam
		Dr. M.R. Ranjit
		Mr. B.N. Sethi
		Mr. K.C.Dalai
Co-investigator	:	Dr. Dipika Mohanty
		Director,IIH, Mumbai

The Clinical Pathology Division of RMRC has been working on human hereditary enzyme disorders such as G6PD deficiency for the last 6 to 7 years. During the study, the major observations made were:

1) The frequency of G6PD deficiency was found to be varying from 3% to 15% in various tribal groups.
2) A new (previously unreported) G6PD variant "G6PD Orissa" (44 Ala → Gly) has been discovered and reported.
3) Amongst the 10 tribes so far studied, it has been shown that "G6PD Orissa" like G6PD Mediterranean is polymorphic within India.

The present project proposal has the following objectives.

1) To investigate and characterize the G6PD deficient variant and to identify the most frequent alleles responsible for the deficiency in Orissa and neighbouring states.

2) To screen and test the non tribal and tribal male population in Orissa and other States in India with reference to "G6PD Orissa" and to find out whether chronic haemolytic state exists in these cases or not.

3) to study the clinical profile,morbidity and mortality pattern in G6PD deficiency cases.

4) To study its relation with endemicity of malaria and which of the drugs that precipitate haemolysis if any, and whether any other tissues other than erythrocytes have any G6PD deficiency.

The project proposal has been circulated to the all SAC members and after getting their approval the project was submitted to Department of Biotechnology (DBT), Govt. of India for extramural funding.

7.3. A LONGITUDINAL STUDY ON LYMPHATIC FILARIASIS- A CLINICO - PATHOLOGICAL AND IMMUNOLOGICAL PERSPECTIVE IN ENDEMIC AREAS OF ORISSA.

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

Starting date : July 1998

A pilot study on clinico-pathological aspects of lymphatic filariasis was undertaken between 1993-96 by this Division in the two districts of Orissa (Puri and Khurda districts). A total 2187 cases (male/female 1155/1032) from Puri district and 1444 cases (male/female 789/655) from Khurda district were examined. The MF rate was found to be 9.2% and 13.5% and disease rate was observed to be 33.5% and 18.7% in both Puri and Khurda districts respectively. In Puri district, *W.bancrofti* was found to be 6.5%, *B.malayi* was found to be 2.5% and mixed infection was found to be 0.2%, where as only *W.bancrofti* infection was encountered in Khurda district.

OBJECTIVES

1) To undertake a longitudinal observation on the prevalence of various clinical manifestations of filarial disease in Puri and Khurda districts of Orissa.
2) To study the clinical manifestations and the progression of the disease with or without intervention by diethylcarbamazine (DEC).
3) To study the relevant immunological parameters to find out the age and sex related changes of the host response to filarial parasite, with particular reference to immunodiagnosis in areas of different endemicity.
4) To study the histopathological changes in selected cases to understand the pathogenesis of various stages of the disease.

The above project proposal was circulated to all the SAC members in 1998. After receiving their comments and approval, this project was initiated with intramural funds from July 1998.

7.4. 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.A.Mohapatra
Dr.J.J. Babu Geddam
Dr. M.R. Ranjit
Mr. B.N. Sethi
Mr. K.C.Dalai

The above mentioned project proposal was prepared and submitted for the World Bank assistance in response to a circular from the Council and Ministry of Health and Family Welfare, Govt of India with the following objectives.

Orissa occupies a unique place in the tribal map of India having the largest number of tribal communities(62) with a population of over 7 million constituting 22.43% of the State's population. There is a paucity of information of the health status and epidemiological profile of various diseases in different tribal groups of India and more so amongst the primitive tribes. Comprehensive research studies pertaining to health and nutritional status amongst different tribal groups including the primitive tribes in the State of Orissa are scanty and often completely lacking. Therefore the study plan has been envisaged.

OBJECTIVES:

1. A comprehensive assessment of health status and epidemiological profile amongst 13 identified primitive tribes of Orissa.
2. Various population growth and fertility parameters in context to the national scenario to explain the extinctive nature of the primitive tribes.

3. Demographic profile studies reflecting the vital events and their statistics such as various mortality pattern amongst the primitive tribes.
4. In depth study of various hereditary haematological disorders like haemoglobinopathies (sickle cell anaemia, thalassaemia, etc.), enzymopathy (G6PD deficiency), etc. amongst the primitive tribes to be undertaken.

This project was submitted to the Council for funding from the World Bank grant.

7.5. MOLECULAR STRAIN TYPING OF *P.FALCIPARUM*

Staff member	:	Dr. M.R. Ranjit
Supervisor	:	Prof. Y.D. Sharma Head, Dept. of Biotechnology AIIMS, New Delhi

Dr. M.R. Ranjit, RA was on study leave for one year (from 15th July 1997 to 14th July 1998), to undergo a specialised training on molecular biology as National Associate of Biotechnology under National Associateship Programme, of the Department of Biotechnology, Government of India.

The training programme took place in All India Institute of Medical Sciences (AIIMS), New Delhi, under the supervisor indicated above. During the training programme, the National Associate has learnt the basic techniques of molecular biology such as DNA/RNA isolation and purification, PCR technology, RFLP analysis, cloning, sequencing, gene expression in prokaryotic system, etc. and worked on a project entitled, "Molecular strain typing of *P.falciparum*." Summary of the project is given below.

The present study was designed to investigate the genetic diversity among *P.falciparum* isolates from Orissa, Madhya Pradesh and Rajasthan, employing five variable marker genes, i.e., CSP, MSA-1,MSA-2, KAHRP and TRAP. A total of 71

blood samples from persons who were positive for *P.falciparum* were collected and analysed by performing the PCR amplification of the repeat sequence of MSA-1, MSA-2 and CSP genes. All three genes showed several variant forms, where MSA - 2 has the maximum number of 10 variant forms (780bp to 1160bp), while MSA - 1 and CSP showed 8 (350bp to 510bp) and 6 (620bp to 800bp) variants respectively.

A large number of samples (27/71; 38%) showed presence of two or three variant alleles for one or more than one gene thereby indicating that there could be more than one *P.falciparum* parasite strain in the same infected individual. Amplification of the variable regions of KAHRP and TRAP genes showed three alleles for KAHRP gene (400bp, 340bp and 370bp) and seven RFLP patterns for TRAP gene, when digested with Taq I. Based on these markers 17 different isolates were identified.

The maximum variation was observed in cases from Orissa. Not only they showed the maximum number of variant forms for each gene, but also the maximum number of cases from Orissa were infected with distinctively different genotypes. The number of cases with mixed infection were also higher for Orissa.

The present study, therefore, not only records the variation in most popular vaccine candidate antigens among Indian isolates of *P.falciparum*, but also issues a warning for future malaria vaccine programmes. There is a probable association between malaria hyper-endemicity and the mixture of alleles present in the area. Therefore similar studies are recommended on a larger scale to cover the entire country, which can form a part of disease surveillance and molecular epidemiology of malaria in India.

8. GENERAL INFORMATION

8.1. PUBLICATIONS

PAPERS PUBLISHED IN JOURNALS/PROCEEDINGS:

1. Bal, M.S., Satapathy, A.K. and Das, M.K.- Increased antibody response to parasite lipids in amicrofilaraemic individuals from a region where *W.bancrofti* infection is endemic. Annals of Tropical Medicine and Parasitology, 92: 119-122 (1998).

2. Ravindran, B., Sahoo, P.K. and Dash, A.P.- Lymphatic filariasis and malaria: concomitant parasitism in Orissa, India. Trans. Roy. Soc. Trop. Med. & Hyg., 92: 21-23 (1998).

3. Mukhopadhyaya, S and Ravindran, B.- Antibodies to diethylcarbamazine potentiate the antifilarial activity of the drug. Parasite Immunol., 19: 191-195 (1997).

4. Mahapatra, N., Dash, A.P. and Hazra, R.K. - Application of Dyar's rule to the development of two species of *Culex* (Diptera, Culicidae). Trop Biomedicine, 13: 149-154 (1997).

5. Dash, A.P., Mahapatra, N. and Hazra, R.K.- Reduction of larval and adult densities of *Culex quinquefasciatus* by *Bacillus sphaericus*. Proc. 2nd Symp. on Vectors and Vector Borne Diseases: 247-252 (1997).

6. Mohapatra, R., Ranjit, M.R. and Dash, A.P.- Effect of Hexaflumuron on hatching and post - embryonic development of mosquitoes. Proc. 2nd. Symp. on Vectors and vector Borne Diseases : 212 - 221 (1997).

7. Dash, A.P., Mahapatra, N., Hazra, R.K. and Acharya, A.S.- Transmission dynamics of filariasis in Khurda district of Orissa, India. South East Asian J. Trop. Med. Public Health, 29 (1): 2025 (1998).

8. Babu, B.V.- Association of haptoglobin types with arterial blood pressure. Indian Journal of Physiology and Pharmacology, 41 (2): 185-186 (1997).

9. Nagaraj, K. and Babu, B.V.- Field trial of oral cholera vaccine in Vietnam (Correspondence). Lancet, 349: 1253-1254 (1997).

10. Parvatheesam, C., Babu, B.V. and Babu, M.C.- Genetic structure of Rajaka caste and affinities with other caste populations of Andhra Pradesh, India. Zeitschift fur Morphologie and Anthropologie, 81: 365-371 (1997).

11. Venkataramana, Y, Vindhya Poonappa, Kapoor, R.N. and Satyanarayana, K.- Energy intake, energy expenditure and physical activity pattern of selected sports persons. Journal of Rehabilitation (Medicine) In Asia, 1: 36-45 (1997).

12. Kumar, S, Wairagkar, N.S, Mahanta, J, Satyanarayana, K, Chetia, M, Phukan, R.K and Goswami, S.K.- Profile of Heroin Addicts in Nagaland, India. Southeast Asian J. Trop. Med. Public Health, 27 (4): 768-771 (1997).

PAPERS IN PRESS/COMMUNICATED:

1. Hazra, R.K. and Dash, A.P. - Distribution of *Mansonioides* in Orissa, India. Trop. Biomedicine (in press).

2. Pal, B.B., Acharya, A.S. and Satyanarayana, K.- Seroprevalence of HIV infection among jail inmates in Orissa. Ind. J. Med. Res. (communicated).

3. Babu, B.V. and Naidu, J.M. - Genetic variability of blood and salvia antigen, and serum proteins among sub tribes of Mali from Andhra Pradesh, India. Anthropologischer Anzeiger (in press).

4. Babu, B.V. and Parvatheesam, C.- Glucose-6-phosphate dehydrogenase deficiency in populations of Andhra Pradesh. The Indian Practitioner (in press).

5. Babu, B.V. - Demographic structure and its implications among two breeding isolates of Mali tribe from Andhra Pradesh, India. Journal of Biosocial Science (communicated).

6. Babu, B.V. - Association study of acid phosphatase locus 1 (ACP1) polymorphism and body mass variability in a lean Indian tribal population. Acta Medica Auxologica (communicated).

7. Pal, B.B. and Bhunya, S.P.- Genotoxic effect of an insecticide, carboxyl, in mouse *in vivo* test system. Perspectives in Cytology and Genetics (in press).

8.2. CONFERENCES/SEMINARS/SYMPOSIA/MEETINGS ATTENDED:

1. Dr.K.Satyanarayana, Director attended Annual Meeting of Nutritional Society of India held at the National Institute of Nutrition, Hyderabad, on 27th and 28th November 1997. He has co-chaired a scientific session, "Presentation of papers for award on community nutrition and experimental nutrition" on 28th November 1997.

2. Dr.M.K.Das, DD (Sr.G.) participated in "Interaction meeting on diagnostic tools on filariasis" organised at VCRC (ICMR) Pondichery, on 22nd April, 1997 and spoke on "Filarial diagnosis using parasite enzymes as antigens". He also gave a seminar on "Antibody responses to defined filarial antigens in people living in *W.bancrofti* endemic regions of Orissa, India" at VCRC (24th April 1997).

3. Dr.B.Ravindran, DD attended the Gordon Research Conference on Parasitism held at Salve Regina University at New Port, USA, during 6th-11th July 1997, while he was availing WHO Fellowship in USA.

4. Dr.B.Ravindran, DD participated in the 6th Annual Meeting of the Molecular Immunology during 12th-14th January 1998 at Sariska, Rajasthan and presented a paper entitled,"Synthesis of tumour necrosis factor like molecules by filarial parasites".

5. Dr.A.P.Dash, DD and Dr. B.V. Babu, SRO attended Protocol Development Meeting on Community-Directed Treatment of Lymphatic Filariasis organised by UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), held at NICD, New Delhi during 7th-11th July, 1997. They have participated in the above meeting as Temporary Advisers.

6. Dr.A.P.Dash, DD attended the IInd Global Meet on Parasitic Diseases at Hyderabad, during 18th-22nd August 1997 and chaired a scientific session on Ecology and Parasitic diseases.

7. Dr.A.P.Dash, DD was invited as an expert and attended the workshop on development of course curriculum on comprehensive vector control for South East Asia, at VCRC Pondicherry, during 22nd-25th February 1998.

8. Dr.A.P.Dash, DD, Dr.N.Mahapatra, SRO and Dr.R.K.Hazra, TO attended Symposium on 50 years of progress in animal sciences in Orissa: retrospect and prospect, at Utkal University, Bhubaneswar during 6th-7th December 1997.

9. Dr.N.Mahapatra, SRO, Dr.R.K.Hazra, TO and Dr.R.Mohapatra, SRF attended the IInd Global Meet on Parasitic Diseases at Hyderabad during 18th-22nd August 1997 and presented papers.

10. Dr.R.Mohapatra, SRF attended the 10th Anniversary Symposium on "Molecular Biology and Biotechnology for Development" at the International Centre for Genetic Engineering and Biotechnology, held in Trieste, Italy, during 25th-27th November 1997.

11. Dr. B.V. Babu, SRO attended National Seminar on Perspectives and Strategies for Sustainable Tribal Development Beyond 2000 AD, held at Andhra University, Visakhapatnam, during 29th-30th April, 1997. He presented a paper entitled "Sickle cell disease: A neglected public health problem among Scheduled Tribes".

12. Dr.B.V. Babu, SRO attended the Meeting on Training and Finalization of Research Instruments of ComDT Studies, organised by UNDP/World Bank/ WHO Special Programme for Research and Training in Tropical Diseases (TDR), held at Mukuno, Uganda during 17th-21st November, 1997. He participated in the above meeting as a Temporary Adviser.

13. Mr.A.S.Acharya, RA attended the Conference on "Decision making models and their applications" and presented a paper entitled, "Estimation of genotype and phenotype proportion for sequentially sampled data" at Utkal University, 20th-21st, December 1997.

14. Dr.B.B.Pal, RO attended National Symposium on Rapid Diagnosis of Infections in Immunocompromised Host, during 22nd-23rd November 1997 at AIIMS, New Delhi and presented a paper entitled, "Drug users-A new risk group for HIV infection in Orissa" by B.B.Pal, H.K.Khuntia and K.Satyanarayana

15. Y.V. Ramana, M.S. Rao, S.S. Rao and K. Satyanarayana. Childhood nutritional status (CNS), physical work capacity (PWC) and mechanical efficiency (ME)-

A rural Indian study. Abstract presented by Dr. Ramana at the 16th International Congress of Nutrition; 27th July-1st August 1997, Montreal, Canada.

TRAINING OBTAINED BY THE STAFF MEMBERS:

1. Dr.B.B.Pal, RO and H.K.Khuntia, LA attended training programme on diarrhoea at National Institute of Cholera and Enteric Diseases (NICED), Calcutta, in January 1998.

8.3 OTHER ASSIGNMENTS AND RECOGNITIONS:

1. Dr.K.Satyanarayana, Director attended a national level workshop as an expert on "Development of Nutritional Surveillance System" held at the National Institute of Nutrition, Hyderabad with the support of Department of Women and Child Development, Ministry of Human Resources Development, Government of India, during 15th-16th December 1997.

2. Dr.M.K.Das, DD (Sr.G.) was appointed as examiner for a Ph.D. thesis "Physiological and biochemical studies on toxin production by cyanobacteria" submitted to School of Biotechnology, Banaras Hindu University, Varanasi.

3. Dr.M.K.Das, DD (Sr.G.) was invited to participate in a symposium "Role of Zoology in sustainable development" at Dept. of Zoology, Utkal University, Bhubaneswar, during 18th-19th July 1997 and he delivered a lecture on "Protective immune responses in lymphatic filariasis".

4. Dr.M.K.Das, DD (Sr.G.) was invited to give three lectures on "Introduction to immunology" to M.Sc. students of Zoology Dept., Utkal University (March-April 1997).

5. Dr.B.Ravindran, DD availed WHO Fellowship and worked at the University of Connecticut, USA for 9 months from January - September 1997.

6. Dr.B.Ravindran, DD participated as an evaluation panel member (biological testing) of the NABL at Department of Science and Technology, New Delhi on 3rd March 1998.

7. Dr.A.P.Dash, DD acted as the Ph.D. examiner for University of Madras, Pondicherry Central University and Utkal University.

8. Dr.A.P.Dash, DD joined the Institute of Life Sciences, Bhubaneswar, Govt. of Orissa as its Director on 02.03.98 on deputation for a period of one year, after obtaining permission from the D.G., ICMR.

9. Dr.B.B.Pal, RO acted as resource person on Population Education for the college/university teachers on 25th October 1997, organised by Utkal University and Kamala Nehru Women's College, at Bhubaneswar. He talked on "Reproductive health, prevention and Control of STD and AIDS".

PH.D. PROGRAMME:

Dr.Rajashree Mohapatra was awarded the Ph.D. degree from the Utkal University in March, 1998 for her thesis " Comparative efficacy of aphid extracts, some larvicides and insect growth regulators against development of mosquitoes" under the supervision of Dr.A.P.Dash, DD.

COMPLETION OF SRF:

Dr.M.Anuradha completed her SRF and left the Division of Microbiology on 7th April 1998.

RELEASE OF PROCEEDINGS OF IInd INTERNATIONAL CONFERENCE OF NATIONAL ACADEMY OF VECTOR BORNE DISEASES (NAVBD)

The Proceedings of IInd International Conference of National Academy of Vector Borne Diseases (NAVBD), functioning from RMRC, Bhubaneswar was released on 5th December 1997. The Proceedings was released by Sri Bhupinder Singh, the Hon'ble Minister for Tourism and Culture, Government of Orissa. Dr.V.P.Sharma, Director, MRC, New Delhi and President of the National Academy of Vector Borne Diseases presided over the function. Dr.S.Pattanayak, WHO consultant was the chief speaker. Dr.A.P.Dash, DD, RMRC and Secretary General of the Academy invited the guests. Dr.K.Satyanarayana, Director, RMRC and Vice-President of the Academy gave welcome address and Dr.B.Ravindran, DD, RMRC and Executive Committee Member of the Academy proposed the vote of thanks.

8.4 SCIENTIFIC ADVISORY COMMITTEES OF THE CENTRE

Members of the 10th Scientific Advisory Committee:

1. Dr. D.S.Agarwal — Chairman
   Professor and Head
   Department of Microbiology
   University College of Medical Sciences
   and Guru Teg Bahadur Hospital
   Shahadara, Delhi 110 095

2. Dr.P.K.Das
   Director
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5. Dr.B.B.Tripathy
Retd. Prof. of Medicine
Saradiya Mission Road
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6. Dr.V.P.Sharma
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7. Directorate General of Health Services,
O/o. DGHS, Nirman Bhawan,
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9. Dr. L.N. Mohapatra
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10 Dr.R.S.Tiwary
Director
Regional Medical Research Centre
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Jabalpur 482 003

11. Dr. Sudha G. Gangal,
Director,
Bai Jerbai Wadia Hospital for
Children and Institute of Child
Health Research Society,
Acharya Donde Marg,
Parel, Bombay-400 012.

12. Dr. Manorama Bhargava
Professor and Head
Department of Haematology
A.I.I.M.S.
Ansari Nagar
New Delhi- 1100 029

13. Dr. Dipika Mohanty
Director
Institute of Immunohaematology (ICMR)
New Multistoried Building
13th floor, KEM Hospital Campus,
Parel,Bombay-400 012

14. Dr. R.K. Chatterjee
Scientist 'F'
Division of Parasitology
CDRI, Lucknow

15. The Addl. Secretary
Health Services
Orissa Secretariat
Govt. of Orissa
Bhubaneswar

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

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

18 The Principal
M.K.C.G. Medical College
Berhampur
Dist. Ganjam

or

The Principal
S.C.B. Medical College
Cuttack
Orissa

or

The Principal
V.S.S. Medical College
Burla
Dist. Sambalpur

or

The Principal
Medical College
Vishakapatnam

19. Dr.Kamala Krishnaswamy
Director
National Institute of Nutrition
Jamai Osmania
Hyderabad- 500 007

20. Dr.K.Satyanarayana (Member-Secretary)
Director
Regional Medical Research Centre
Chandrasekharpur
Bhubaneswar 751 016

The above Scientific Advisory Committee (SAC) which was constituted in June, 1996 met only once on 23rd July, 1996 and considered the Annual Report of 1995-96 and gave recommendations on the new projects. Among its members Dr.P.K.Das, Director, VCRC, Pondicherry replaced Late Dr.V.Dhanda, Ex-Director, VCRC, Pondicherry at Serial No.2. Dr.Kamala Krishnaswamy (Serial No.-19), Director, NIN, Hyderabad replaced Dr.M.Mohan Ram, Ex-Director, NIN, Hyderabad. Among the 4 medical colleges listed at Serial No.18, the Principal, VSS Medical College, Burla was the member for the period between 1996-98.

Several new projects for extramural funding [WHO/TDR; European Commission Union (ECU); DBT, Government of India] and intramural projects were circulated to the above SAC members and their comments and recommendations were obtained. Based on these recommendations, new projects were forwarded to the Council for necessary action and onward transmission to the funding agencies.

The 12th Scientific Advisory Committee was constituted during the month of October 1998 by the D.G., ICMR for considering 2 years Annual Reports of 1996-97 and 1997-98 (11th SAC and 12th SAC combined). Following is the list of 12th Scientific Advisory Committee.

Members of the 12th Scientific Advisory Committee:

1. Dr.D.S.Agarwal — **Chairman**
Professor and Head
Department of Microbiology
University College of Medical Sciences
and Guru Teg Bahadur Hospital
Shahadara, Delhi 110 095

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

3. Dr. R.K.Shinoy
Principal Investigator
Filariasis Chemotherapy Unit
T.D. Medical College
Alleppy-688011;

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

5. Professor B.C.Harinath
J.B. Tropical Disease Research Centre and
Department of Biochemistry
Mahatma Gandhi Institute of Medical Sciences
Sevagram-442102, Wardha

6. Dr.Harminder Singh
Former Professor of Microbiology
Post-Graduate Institute of Medical Sciences
Chandigarh
Corrsp. # 57, Sector 28-A; Chandigarh 160002.

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

8. Dr.V.P.Sharma
Emeritus Scientist
Malaria Research Centre
22, Madhuban, Delhi-110092

9. Dr.S.K.Bhattacharya
Director
National Institute of Cholera and Enteric Diseases
P-33, CIT Road Scheme XM
Beliaghata, Calcutta-700010

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

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

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

13. Prof. R.N.Rath
Ex-Professor of Medicine
Professor Para
Bajrakabati Road
Cuttack-753012

14. Dr.G.C.Mishra
Director
National Centre for Cell Sciences
NCCS Complex
Gaurhkhind, Pune-411007.

15. Dr.Lalit Kant
Sr.Dy.Director General
Indian Council of Medical Research
Ansari Nagar
P.B.No.4911, New Delhi-110029

16. Dr.K.Satyanarayana Member-Secretary
Regional Medical Research Centre (ICMR)
Chandrasekharpur, Bhubaneswar 751016, Orissa.

The above committee meeting was held on 24th and 25th November 1998 which is referred as 12th SAC meeting [since this committee considered the reports of 1996-97 (11th meeting) and 1997-98 (12th meeting)] and therefore referred to as 12th SAC meeting. This committee considered several new projects submitted by the scientists and gave its recommendations.

8.5 THE BUDGET ALLOCATION BY THE COUNCIL AND EXTRAMURAL FUNDS GENERATED:

The Council released Rs.117.39 lakhs for RMRC, Bhubaneswar during the year 1997-98. About Rs.90 lakhs was towards Pay and Allowances. The allocation for 'other charges' was about Rs.23 lakhs. The allocation for TA was Rs.2.5 lakhs.

There was no separate allocation for equipment and capital during the year from the Council for this Centre.

Two projects were approved by the SAC, Health Ministry Screening Committee and other Government Departments for extramural funding.

The multi centric **"Community directed treatment against filariasis (ComDT)"** project funded by WHO/TDR received about Rs.7 lakhs during March 1998 for phase-I of the project. Dr.A.P.Dash, DD was the Principal Investigator (PI) of this project upto March, 1998. Dr.K.Satyanarayana, Director was the PI from March, 1998 for this project, after Dr.A.P.Dash was deputed to the State Govt. of Orissa. This project is scheduled to receive Rs.10 lakhs during 1999 for the phase-II of the project.

The project on **"Immunology of lymphatic filariasis modulation, variations and immunity"** funded by the European Commission Union (ECU) was sanctioned about Rs.5.5 lakhs for the first year of its operation. This money is scheduled to receive during the middle of 1998. Dr.B.Ravindran, DD is the PI of this project and Prof. Rick Maizels, Univ. of Edinburgh, UK is the Principal Coordinator for this project operating from four Centres from four countries.

The WHO/TDR project on **"Field evaluation of *B.sphaericus* against *Cx.quinquefasciatus* in Orissa"** shown as Section 5.3 of 1996-97 Annual Report has been in operation from 1992. Dr.A.P.Dash, DD is the P.I. of multicentric project. A balance of Rs.3.4 lakhs was available in April 1996. During June 1996, a sum of Rs.2.6 lakhs was received from the funding agency. Out of the total Rs.6 lakhs available, a sum of Rs.4 lakhs was used during the year 1996-97, leaving a sum of Rs.2 lakhs for continuation of the project in 1997-98. This project was closed during February 1998 (Section 4.1 of 1997-98 Annual Report).

8.6. ANNUAL REPORT COMMITTEE

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