REGIONAL MEDICAL RESEARCH CENTRE

BHUBANESWAR

ANNUAL REPORT
1990

REGIONAL MEDICAL RESEARCH CENTRE

(INDIAN COUNCIL OF MEDICAL RESEARCH)

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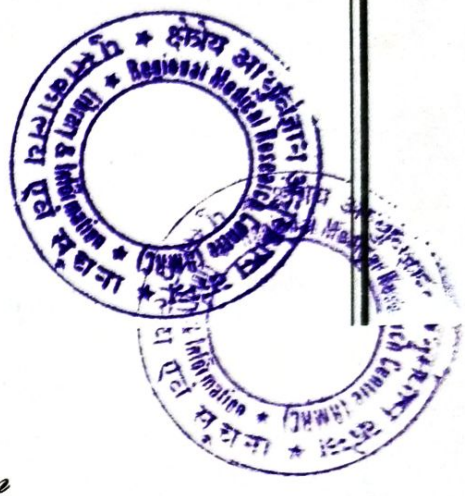

With compliments from

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ACKNOWLEDGMENT

The Director expresses his gratitude to all members of this Centre for the work carried out during the year and for their excellent cooperation offered.

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Preface

Research is a continuous process like time while annual report is a periodic account of activities of an organization. Present activities are always based on the past and therefore in presenting annual report I mention in brief what this young institute has achieved in the short period of its existence. Of course, in doing this I would highlight only some major events which contributed to its present glory.By mere accident I have been closely associated with this institute as the Officer-in-charge in a stop-gap-arrangement. This being the fact I have merely attempted to introduce such changes which I felt absolutely necessary. Starting with cleaning the wild growth in the campus and elsewhere, the dark campus has been enlighted with bright tube lights all round. A sense of accountability and discipline can be seen among workers in contrast to what we observe in our daily life today.

This centre was born in 1981 to undertake original research work on diseases prevalent in this region, hence the name Regional Medical Research Centre. The institute is equipped to conduct advanced researches in Filariasis, Malaria, intestinal parasites, Haemoglobinopathies and now in Leprosy. It also functions as a centre for surveillance of AIDS. In epidemics it assumes additional task of assisting local medical authorities in their efforts to combat diseases. The institute has well qualified scientists in medicine, biochemistry, physiology, pathology, microbiology, immunology, entomology and biostatistics. The institute also takes active part in training and guiding research students for Ph.D. degrees of Utkal University and Sambalpur University. Presently ten students are working for Ph.D. and two have obtained Doctorate degree in the past. It is a pleasure to state that two Senior Research Officers, Dr. A.P. Dash and Dr. B. Ravindran have been promoted to the rank of Asst. Directors with effect from July 1990.

Lab work on Filariasis has already developed immuno diagnostic assay methods for detection of filarial infection in asymptomatic microfilaria carriers and characterization of antibodies to microfilarial sheath. The observation of antigenic mimicry between Diethylcarbamazine and microfilariae has opened newer avenues for possible development of a vaccine against Filariasis. In clinical studies of filaria effects of a new drug named Ivermectin has been found to be very effective in reducing circulating microfilaria by a single dose. It appears to have a promising future. The project is financed by a WHO grant. In the field of experimental and human malaria for the first time a very specific immunodiagnostic spot assay has been developed in this centre to diagnose cases of cerebral malaria. Further, antimalarial property of a plant named *Streblus asper* has been demonstrated in lethal murine malaria (Results under publication). Genetic studies have indicated a weak association between (G-6-PD) deficiency and malaria in tribal population. In entomology biological vector control using *B.sphericus* and other larvicides like aphid extracts have been initiated with encouraging results. Work on micobacterial genetics has yielded a large number of auxotrophic mutants that can be used for gene

transfer experiments in micobacteria. Recently an electrophysiological laboratory with modern equipments is being established to undertake neurological studies in leprosy and allied neuropathies in conscious human subjects using tungsten microelectrodes and conventional methods. The Biostatistics section has acquired a modern computer to undertake advanced work.

Recently Dr. J.L. Patra, R.O. (Clinical) with special training in Epidemiology has joined the institute while Dr. N.M. Pattnaik, SRO, left on transfer to VCRC, Pondicherry. I take the opportunity to welcome Dr. Patra, Sri S.C. Rout, R.A., Biostatistics and Insect Collectors Sri R.K. Patra, B.Pradhan, C.S. Tripathy and S.S. Beuria as new members. Some major events of the year 1990 need to be mentioned. These are taking over of the new laboratory-cum-administrative building, shifting of laboratories, convening of SAC meetings in two sittings, development of parks and lawns, electrification of the campus, building approach road, maintenance of the inside roads, construction of the garages, scooter sheds and cycle stands.

The institute has played a special role in assisting local medical authorities in tackling cholera epidemic in July 1990 and arranging seminars on different aspects of leprosy at Dist. H.Qrs. The institute also investigated the cause of selective male deaths in mysterious circumstances in a remote tribal village in response to a call from the Parliament. Under the advice of the Scientific Advisory Committee a field unit of RMRC is being started at a remote tribal village in Phulbani to study the impact of malaria.

Brig. M.S. DASH (Retd).

Ongoing Projects

1. FILARIASIS :

F.1. Immunological studies on Filariasis

Scientist	:	**Dr. Manoj K. Das**
Technical Staff	:	**Mr. M.K. Beuria**
Starting date	:	**July 1985**

Objective :

Since infective larval (L_3) stage initiates the filarial infection and is the first to encounter with the host immune system, the logical target of immunological investigations should be the L_3 stage. Such an approach will be useful in determining exposure to infection, in immunological changes associated with the progress of the disease and in characterizing the protective immunity, if any, in the endemic population.

Progress :

1.1. Prevalence of *W.bancrofti* L_3-specific IgE antibodies

Earlier reports from this centre (Annual report 1989) demonstrated appreciable levels of specific IgE antibodies in filariae endemic population but not in people living in non-endemic regions (e.g., Keonjhar district of Orissa).

IgE positivity by ELISA was calculated in comparison with a panel of non-tropical sera (European & American). The results obtained are as follows for people in Puri district of Orissa.

Table-1

Group	n	L_3/IgE positivity (%)
Chronic filarial patients	25	96.00
T P E	20	100
Asymptomatic carriers	21	71.40
Endemic normals	60	80
Normal individuals from non-coastal regions (Angul & Keonjhar)	60	13.30

The acquisition of IgE positivity was determined in two different age groups (children and adult) of endemic normals, and the data suggest that it is age - related (Table-2). Infective-larvae specific IgE levels vary considerably with age.

Table-2

Group (n)	IgE positivity (%)
Children (23) (3-8 yrs) mean 6.0 ± 1.70 yrs	17.40
Adult (30) (23-40 yrs) mean 31.40 ± 6.10 yrs	80.0

ITH (skin-sensitivity) reaction to L_3 antigens was also studied in infected people. ITH response was observed in 28% of endemic normals (n=42), and about 13% each in chronic and mf carrier patients (n=15). ELISA results demonstrated that clinical patients exhibiting negligible ITH reactions have high IgG antibodies in addition to IgE. The high IgG levels could act as "blocking antibody" to ITH reactions. Because of the scarcity in obtaining *W.bancrofti* L_3s in large numbers, antigens were fractionated from cattle filarial parasite *S.digitata* and their cross-reactivity was checked with L_3 antigens. Thus an antigenic fraction was purified, which is of low molecular wt. (LMW) glycoprotein and found to possess negligible phosphorylcholine determinants. It's IgE profile in filarial sera is shown below (Table-3).

Table-3

Group	n	LMW/IgE positivity (%)
Chronic filarial patients	25	100
Asymptomatic carriers	20	90
Endemic normals	47	89.4
Normal individual from non-coastal regions	40	25

Immunological involvement of carbohydrate residues in filariasis is also ascertained.

1.2. IgG4 Serology in Filarial Patients :

IgG4 antibodies to L_3 antigens were found to be preferentially expressed in asymptomatic microfilaraemic patients. Results obtained are as follows :

Group	n	IgG4 positivity (%)
Endemic normals	25	16.0
Asymptomatic carriers	20	75.0
Chronic	20	25.0

More number of sera is being checked.

1.3. Studies are in progress to quantitate the levels of L_3 antigens, phosphorylcholine and of infective-larvae conjugated carbohydrate moieties in the sera of filarial infected population.

F.2. Studies on antibodies with reactivity to Diethylcarbamazine.

Scientists : **Dr. B. Ravindran**
Dr. N.M. Pattnaik

Technical staff : **Ms. T. Hussain**
Mr. A.K. Satapathy
Mr. P.K. Sahoo

Starting date : **July '85**

Antibodies reacting with DEC were produced by us four years ago by using a hapten, methyl piperazine carboxylic acid (MPCA), an acid hydrolysis product of DEC. Interestingly anti-DEC antibodies were found to cross-react with microfilariae of *W.bancrofti* indicating

thereby a possible antigenic mimicry between the parasite surface and the drug. Further it was demonstrated that anti-filarial antibodies in human filarial sera would cross-react with DEC. Studies were continued further to characterize the antigenic determinants reacting with anti-DEC antibodies and to analyse other closely related haptens and carrier systems for elicitation of anti-DEC antibodies in rabbits. The following were the observations :

a. Two derivatives of piperazine namely piperidine carboxylic acid (PCA) and piperidine propionic acid (PPA) were used along with MPCA as haptens. Tetanus toxoid was used as a carrier molecule instead of bovine serum albumin to raise anti-DEC antibodies in rabbits. The resultant antisera were tested by inhibition ELISA for DEC specificity. MPCA and PPA elicited comparable titres of anti-DEC while PCA was relatively inferior in this respect.

b. Anti-PPA, anti-MPCA and anti-PCA antibodies reacted with microfilarial surface of *W.bancrofti* as shown by indirect immunofluorescence assay. The reactivity could be effectively inhibited by preincubation of the antisera with free haptens, viz., MPCA, PPA, PCA and also with DEC.

c. Attempts were made to characterize the molecular specificity of the cross-reacting filarial antigen. Treatment of microfilaria of *W.bancrofti* with proteolytic enzymes, sodium periodate, chitinase, lipase and a variety of other enymes indicated that the anti-DEC could recognize carbohydrate moieties on microfilarial sheath. Wheat germ agglutinin (WGA) which has a specificity for N-Acetyl glucosamine (Gluc NAc) residues and thus to the microfilarial sheath was found to competetively inhibit the binding of anti-DEC antibodies to microfilariae. Since chitin (poly Gluc NAc) has been shown to be a component of microfilarial sheath, the possibility of using chitin binding lectin for development of idiotype vaccine for polysaccharide antigens has been proposed in Immunology Today (see under publication).

F.3. Immunological studies on antibodies to Diethyl Carbamazine - an approach for developing an immunoprophylactic agent against filarial parasites

Scientist	:	**Dr. B. Ravindran**
Technical staff	:	**Ms. T. Hussain** **Mr. A.K. Satapathy** **Mr. P.K. Sahoo**
Starting date	:	**September, 1990.**

Circulating microfilariae are responsible for transmission of the disease in human communities and antibodies reacting with microfilarial surface have been shown to be responsible for elimination of microfilariae. Since antibodies to DEC were demonstrated by us to react

with microfilarial surface of *W.bancrofti*, it was logically expected to extend this observation to *in vivo* studies involving circulating microfilariae in experimental animals. The following are some of the observations made :

a. Attempts have been made to raise anti-DEC using carrier molecules other than BSA. Tetanus toxoid (TT) and keyhole limpet haemocyanin (KLH) have been used to couple MPCA and antibodies to DEC were raised in rabbits. Anti-DEC and anti-microfilariae (*W.bancrofti)* titres were monitored. Tetanus toxoid was found to elicit very good titres while KLH was far less effective.

b. Apart from Freund's complete adjuvant (CFA), other adjuvants such as Alum hydroxide and Freund's incomplete adjuvant were also used alongwith plain antigen for raising anti-DEC in rabbits. Anti-DEC and anti-parasite titres were compared. The results indicated that CFA is superior to others in eliciting anti-microfilariae titres - however plain antigen (TT-MPCA) in the absence of adjuvant elicited good anti-parasite antibody titres in rabbits.

c. Since *W.bancrofti* has not been adapted in small laboratory animals, *in vivo* studies can be performed only with *Brugia sp.* which are adaptable in Jirds and Mastomys. Initial studies have indicated the cross-reactivity of anti-DEC to microfilarial (mf sheath and somatic antigen) and adult antigens of *Brugia pahangi* indicating thereby that *Brugia* sp. can be used for undertaking *in vivo* studies using anti-DEC. Attempts are underway to procure *Brugia malayi* infected jirds/mastomys for maintenance and use in RMRC, Bhubaneswar.

F.4. Detection and characterization of anti-sheath antibodies in Bancroftian filariasis.

Scientist : **Dr. B. Ravindran**

Technical staff : **Mr. A.K. Satapathy**
Ms. T. Hussain
Mr. P.K. Sahoo

Starting date : **March 1986**

Antibodies to microfilaria sheath play a central role in elimination of circulating microfilariae in human lymphatic filariasis. Our studies in the past had shown the relevance and the immunoglobulin isotypes with anti-sheath activity in various clinical spectrum of Bancroftian filariasis. We had also reported preliminary characterization of the sheath determinants recognized by anti-sheath antibodies. The following is the summary of investigations undertaken this year :

a. Species specificity of anti-sheath antibodies was investigated with a panel of Bancroftian filariasis sera-sheathed microfilariae of *W.bancrofti, Brugia pahangi* and *Setaria digitata* were used to detect antisheath antibodies in the sera. The results indicated the absence of correlation in their reactivity to homologous and heterologous parasites. The study was extended to ten Brugian filariasis sera (obtained from WHO filariasis serum bank) and tested against homologous and heterologous parasites. The results confirmed the species specificity of anti-sheath antibodies. This is in contrast to the general observation that filarial antibodies are highly cross-reactive with somatic antigens of various filarial parasites.

b. Antibodies to N-Acetyl glucosamine (Gluc NAc) in filarial sera were affinity purified through a column of Sepharose-Gluc NAc and the carbohydrate specific antibodies were found to be reactive to microfilarial sheath of *W.bancrofti.* Atleast some of the anti-sheath antibodies in Bancroftian filariasis appear to recognize carbohydrate moieties in the sheath. Further studies are in progress to analyse the sheath components since understanding the immune response to them in infected people will be critical for developing future methods for the control of filariasis in human communities.

F.5. Characterisation of plant (Shakhotak, Streblus asper) Microfilaricidals.

Scientists	:	**Dr. Manoj K. Das (effective from Nov.1990)** ***Dr. N.M. Pattnaik**
Technical staff	:	**Mr. Dasarathi Das**
Starting date	:	**February 1987**

Progress :

It was earlier shown that Shakhotaka (*Streblus asper*) aquous extract possess microfilaricidal activity (RMRC Annual Report 1989) *in vitro.*

Recent works suggest that the aqueous extract even after dialysis retains the microfilariae (*W.bancrofti)* toxic activity indicating that the active components are of high mol. wt. Similar result was also obtained on Sephadex gel chromatography where a high mol. wt. fraction is isolated. This fraction is capable of killing effectively microfilariae *in vitro*. The characterization and the killing mechanism of mf-toxic fraction is being pursued.

* Associated till Oct. 1990.

Justification for continuation :

Detection and characterization of mf-toxic substances in plant products will provide :

(1) a relatively simple way of isolating these substances;

(2) in trying to understand the mechanism of killing microfilaria;

(3) possibly, the *in vivo* application in reducing microfilaraemia.

F.6. Role of Insect hemolymph in the development of *Wuchereria bancrofti* microfilariae in culture.

Scientists : **Dr. M.K. Das (effective from Nov. 1990)**
***Dr. N.M. Pattnaik**

Technical staff : **Mr. Pramod K. Rana (S.R.F.)**

Starting date : **July 1987**

Progress :

In our earlier investigations we had observed the distribution of microfilaricidal (and rbc lytic activity) in hemolymph of adult tussar moth *Antheraea paphia* (RMRC Annual Report 1989).

The major activity for *mf* killing *in vitro* was found to be associated with a lipoprotein fraction of the hemolymph. Killing activity in the protein fraction is being investigated.

Hemolymph	Vol.	Time of killing
Larvae	100 ul	36 h
Larvae (protein)	100 ul	36 h
Adult	10 ul	1 h
Adult (protein)	100 ul	36 h
Adult (lipid)	10 ul	1 h

However, this mf-cidal activity was negligible in the hemolymph of the larvae. On the other hand, a predominant hemagglutinating activity was found here. The comparative rbc agglutinating titer is shown below :

* Associated till October,1990.

Erythrocytes	Titer
Human O^+	0
A^+	0
B^+	0
Rabbit	256
Goat	0
Sheep	0
Mouse	2

The agglutinating activity is found to be specific only for melibiose (Gal 1 6 Glu), since other sugars such as D-glucose, Galactose, Mannose, Lactose are ineffective. The binding of the lectin with mf of *Wuchereria bancrofti* and *Setaria digitata* will be ascertained.

F.7. Characterization of filarial antigens in bancroftian filariasis :

Scientists : **Dr. V.R. Subramanyam**
Dr. B. Ravindran
***Dr. N.M. Pattnaik**
Ms. Keshar K. Mohanty (SRF, CSIR)

Technical staff : **Nil**

Started : **October '88**

1.2.1 DEC-like determinants in bancroftian filariasis sera :

Progress :

Studies in this Centre had shown that antibodies to DEC react with the surface of *W.bancrofti* microfilariae. This finding encouraged us to look for possible antigens of parasite origin in filariasis sera, that resembled DEC (antigenically).

i. An ELISA system has been standardized for this. The assay uses a coating of rabbit anti *Brugia pahangi* IgG to trap the antigens of parasite origin in bancroftian filariasis sera and rabbit anti DEC IgG coupled to alkaline phosphatase as the probe.

* Associated till October,1990

ii. In this system, 30.4% of endemic normals (n=46), 39.1% of asymptomatic carrier (n=64), 22.2% of acute (n=54) and 28.5% of chronic (n=35) bancroftian filariasis sera were positive for the presence of DEC-like determinants.

iii. Preliminary experiments indicate that the reactivity is associated with a large (nondialysable) molecule.

1.2.2. Immunology of lipids of filarial parasites :

Progress :

An ELISA has been optimised to quantitate antibodies in bancroftian filariasis sera that react with lipids extracted from *Setaria digitata*. Briefly the findings are :

i. Both IgG and IgM class of antibodies were detected with reactivity to *Setaria* lipids, though titers of IgM were higher.

ii. There was a positive correlation between the titres of IgM antibodies reactive to parasite lipid and those reactive to phospholipid (commercially obtained) in endemic normal, asymptomatic carrier and acute bancroftian filariasis sera. This correlation was not seen in chronic filariasis sera.

iii. Reactivity of the filarial sera with *Setaria* lipids could be inhibited by phospholipid, except in the case of serum from chronic filariasis.

F.8. Evaluation of cardiopulmonary involvement in Tropical Pulmonary Eosinophilia and response to DEC.

Scientist	:	**Dr. S.K. Kar**
Technical staff	:	**Ms. J. Mania** **Mr. K. Dhal** **Mr. T. Moharana** **Mr. R.N. Nayak**
Starting date	:	**June 1988**

Progress :

Sixty-eight new cases have been screened during 1989-90 and given DEC treatment in

the OPD at Unit-III dispensary as per the study protocol. They have been (total 120 cases) followed up periodically as per the schedule.

Investigations :

The detailed clinical, haematological (DC, TLC, AEC) examination, ECG & immunological tests (filaria specific IgG, IgE, antigen and circulating immune complex) of the cases were carried out at pre and post-drug period. They were followed up at the time of intake, 3rd, 6th & 12th month post drug period.

Results :

Table 4: Haematological test results of TPE patients at intake

No. of patients studied (1989-90)	Mean age (yrs)	Mean E%	Mean AEC	Mean TLC
40 M : 27 F : 13	30	47.9	10624	16846

There was a significant reduction in average percentage eosinophil count, absolute eosinophil count, total leucocyte count with significant clinical improvements of symptoms, signs and lung functions after DEC administration. A significant reduction in antibody status was observed alongwith a simultaneous significant rise in circulating immune complex level.

Justification for continuation :

This prospective study will highlight the immunological and clinical alterations at different dosage schedule of DEC.

F.9. Studies on Ivermectin in the treatment of Bancroftian filariasis in Orissa, India.

Scientist : **Dr. S.K. Kar**

Technical staff : **Ms. Jayanti Mania**
Mr. T. Moharana
Mr. R.N. Nayak
Mr. K. Dhal

Starting date : **June '89**

Aim :

The study on Ivermectin in the treatment of Bancroftian filariasis in Orissa aimed to determine the optimal dosage of Ivermectin effective for clearing *W.bancrofti* with few associated side reactions.

Study Subjects :

60 males microfilaraemic subjects between age ranging from 18 to 50 years were screened and selected from 9 endemic villages of Puri district. The subjects were screened according to the criteria for eligibility as outlined in the protocol.

Evaluation & Drug Administration :

The selected subjects were admitted to the Unit-IX dispensary, Bhubaneswar, where the hospital based trial was undertaken. The following evaluations were carried out :

i. Clinical examination.

ii. Parasitological tests - mf (MFT).

iii. Haematological tests : DC, TLC, AEC, Hb %, PCV & PTT.

iv. Blood biochemistry : SGPT, SGOT, Alkaline phosphatase, Bilirubin & Creatinine.

v. Routine stool & urine examination

vi. X-ray chest (PA) view, Dry-spirometry & electrocardiogram.

vii. Four different doses of Ivermectin (20,50,100 & 200 ug/kg) were administered as per the patients body wt. in double blind fashion to 4 groups of patients.

viii. Its effect on microfilarial clearance and side reactions if any were closely monitored during hospitalisation period as per protocol.

ix. The above subjects were followed up for 6 months after getting discharged from hospital on day 14, 30, 90 & 180 and the results noted.

Results :

Table 5 : The microfilaricidal effect of different doses of Ivermectin

Drug allocated (Ivermectin single dose in ug/kg)	No. of patients	Mean age (years)	Sex	Microfilarial count % of pre-RX value	
				Day 14	Day 180
20	15	23	M	0.3	74.1
50	15	23	M	0.005	48.4
100	15	25	M	0.05	61.0
200	15	26	M	0.04	26.2

Self limiting minor side reactions like fever, headache, lethargy, dizziness, myalgia & arthralgia were noted for very short period. These were possibly due to allergic response to the dying parasites which could be easily managed by oral administration of analgesics.

2. MALARIA :

M.1. Studies on naturally occurring antibodies with galactosyl activity in *P.falciparum* malaria.

Scientists	:	**Dr. B. Ravindran** **Dr. M.K. Das**
Technical Staff	:	**Mr. A.K. Satapathy** **Mr. P.K. Sahoo**
Starting date	:	**March 1986**

Autoantibodies with specificity to α-linked galactose (anti-gal) have been implicated in elimination of senescent erythrocytes. We had demonstrated earlier that anti-gal increases appreciably in *P.falciparum* infected individuals. We had implicated a role for anti-gal in malarial immunology since (α - galactose) determinants have been demonstrated in malarial parasites. Studies were continued this year to purify and analyse circulating anti-gal in human malaria.

Anti-gal were affinity purified by passing through a column where a trisacharide, Gal (1-3) Gal (1-4) Glu Nac - was bound to diatemecious earth. The affinity purified anti-gal was found to be reactive to phospholipids, single stranded and double stranded DNA and keyhole limpet haemocyanin. Antibodies with polyreactivity have been studied in other diseases - our investigations with anti-gal have revealed the importance of such antibodies in human *P.falciparum* malaria. Since polyreactive antibodies have been known to be products of CD5+ B-lymphocyte population it is proposed to undertake studies on the activation of CD5+ B-cells in *P.falciparum* malaria.

The possible presence of anti-gal in cerebrospinal fluid was also studied in confirmed cerebral malaria (CM) cases and were compared with CSF of normal controls. High titres of anti-gal were detected in more than 80% of CSF samples of cerebral malaria. Further, anti-malarial antibodies were also detected in 88% of cases of CM cases. The possible development of an immunodiagnostic kit for diagnosis of cerebral malaria is being seriously studied currently.

M.2. Role of carbohydrate determinants in the interaction between *P.berghei* infected erythrocytes and macrophages in BALB/c mice.

Scientists : **Dr. B. Ravindran**
Dr. M.K. Das

Technical Staff : **Mr. A.K. Satapathy**

Starting date : **March 1986**

Studies were initiated originally to investigate the factors that contribute to interaction between parasites/parasitized erythrocytes and host macrophages in experimental malaria. The presence of autoantibodies with sppecificity to N-Acetyl neuraminic acid (sialic acid) residues present on erythrocytes were detected and characterized by us (vide RMRC annual reports 1989 and 1990). The following were the new observations made in this direction.

a. The naturally occuring sialic acid specific antibodies that increase during acute *P.berghei* infections were affinity purified using a column of fetuin agarose. The eluted antibodies were demonstrated to react with the surface of normal as well as parasitized erythrocyte monolayers by ELISA.

b. The affinity purified antibodies were found to be polyreactive - they cross reacted with phospholipids, single and double stranded DNA. The relative affinity of the antibodies to the various ligands were studied by analysing the dissociation constant in the presence of sodium thiocyanate. The purified antibody was found to have high affinity to erythrocyte surface (i.e. sialic acid determinants) moderate affinity to phospholipids and single stranded DNA and low affinity to double stranded DNA. Since poly reactive natural antibodies have been shown to be products of CD5+ B-lymphocytes it is proposed to enumerate such lymphocyte population in various lymphoid organs of experimentally infected animals.

M.3. Induction of cell-mediated immunity in malaria by immunomodulators.

Scientists : **Dr. M.K. Das**
Dr. B. Ravindran

Technical Staff : **Mr. M.K. Beuria**

Starting date : **June 1986**

Objective :

Mononuclear phagocytic system is known to play important roles in protection against malaria. Activated macrophages are a source of soluble mediators in reducing parasitaemia.

Studies using immunomodulators will have both theoretical and practical implications in human vaccination.

Progress :

Earlier it was demonstrated by us that immunological adjuvant could stimulate CMI, which is otherwise depressed, in malarial infection. Non-toxic adjuvants like alum, liposomes and saponin were used to stimulate DTH and MIF production in *P.berghei* infected Balc/c mice, a lethal model (Ind.J.Biochem.Biophys. in press). In order to understand the mechanism of CMI stimulation, the effect of adjuvants on the function of macrophage is studied.

1. It is observed that lysosomal enzymic activity (as measured by acid hydrolase assay) of peritoneal macrophages from infected mice diminished around 13 day of infection. Pretreatment with adjuvant (i.p) stimulated the enzyme activity by 5-fold.

The effect of liposome on the course of *P.berghei* infection is studied.

3. CLINICAL PATHOLOGY :

3.1. Study of Erythrocytic Glucose-6-Phosphate dehydrogenase (G6PD) deficiency and it's variants in tribal population of Orissa.

Scientist	:	**Dr. G.P. Chhotray**
Technical Staff	:	**Mr. M.R. Ranjit** **Mr. H.K. Khuntia** **Mr. B.N. Sethi**
Starting date	:	**April, 1986**

Screening for G6PD deficiency was further continued amongst the tribal population of Keonjhar district. Apart from the detailed clinical examination, their place of origin, ethnic group, language of parents etc. were noted as per protocol.

10-20 ml of venous blood was collected from 27 persons having severe G6PD deficiency and 8 nondeficient persons of the same area (to serve as control) and was transported to RMRC laboratory in ACD antocoagulant at 4°C within 12 hrs of collection.

a. The haemolysate was prepared and G6PD enzyme assay was carried out. The enzyme activity varied from 1.02 - 2.34 IU/g Hb in deficient samples as compared to 7.4 - 9.69 IU/g Hb in control cases.

b. The Km for G6PD was calculated which ranged from 38 - 51 uM in deficient cases as against 55 - 66 uM in nondeficient cases.

c. Electrophoretic characterization of G6PD enzyme was done by submerged agarose gel electrophoresis (TBE buffer pH 8.6).

From all these data collected so far it appears that the most common deficient samples have similar properties with G6PD activity of about 10-20% of normal and B like electrophoretic mobility. DNA extraction was carried out and the purity of the DNA extracted was established by running in a gel with control (in Prof. Luzzatto's laboratory, UK). 23 DNA samples have already been sent to Prof. Luzzatto for further analysis at molecular level since these facilities are not available here.

Justification for continuation :

This project has been approved by the Health Ministry and ICMR Screening Committee

held on 23.3.88 for Indo-UK collaboration (Ref 50/6/88 ECD-II dt. 30.9.88). A reply is awaited from ICMR headquarters regarding the further development. The scientific advisory committee of 1988, 1989 of this centre had also recommended earlier for a collaborative study. The SAC of 1990 1st half emphasised the need of extending the work and recommended that it should be carried out in all the tribal population of Orissa. This is particularly important because a lot of preliminary ground work has already been done on this project (Ref IJMR (B) 92, Dec.1990 pp.443-446). The 5th SAC meeting (2nd half) 1990 recommended that the project should be referred to Dr. S.K.Sood for opinion and suggestion. Accordingly the protocol has already been submitted to Director for needful. In the meantime we have extracted 12 more DNA samples (9 deficient and 3 non-deficient) for further analysis.

3.2. Immunologic status of the patients with sickle cell anaemia.

Scientists : **Dr. G.P. Chhotray**
Dr. G.S. Bhattacharya
Dr. B. Ravindran

Technical staff : **Mr. M.R. Ranjit**
Mr. H.K. Khuntia
Mr. B.N. Sethi

Starting date : **April 1990**

The above mentioned project has already been approved by ICMR expert committee and ICMR has already agreed to sanction additional funds required for this project. The project has also been cleared by the ethical committee of this centre and the work has already been started.

Trends in immunoglobulins (IgA, IgG, IgM) by single radial immunodiffusion method (using tripartigen plates) supplied by Hoechst India Ltd. has been measured in 20 cases SCD (Hb SS) steady state, 16 cases of SCD (Hb SS) in Vaso-occlusive crisis, 10 cases of SCD (Hb SS) in haemolytic crisis, 10 cases of sickle cell trait and 16 control cases.

Other immunological tests like complement level estimation etc. are yet to be performed due to the non-availability of the plates and reagents.

3.3. A chronological study of the histopathology of malayan filariasis in cats of Orissa.

Scientists : **Dr. G.P. Chhotray**
Dr. A.P. Dash

Technical staff	:	**Mr. M.R. Ranjit** **Mr. H.K. Khuntia** **Mr. R.K. Hazra** **Mr. B.N. Sethi**
Starting date	:	**November 1990**

The above research proposal was approved by the 5th SAC (1st half) and 2nd half of 1990 and the work has just been started in September 1990. Keeping in view the aims and objectives of the study, so far about 100 domestic cats *(Felis catus)* from different villages endemic for lymphatic filariasis of Sakhigopal and Puri area have been screened for the presence of mf (microfilaria) in their peripheral blood at different intervals of time. The study is in progress.

3.4. Effect of drug treatment on the prevalence of intestinal parasites amongst school children in a suburban community.

Scientist	:	**Dr. G.P. Chhotray**
Technical staff	:	**Mr. M.R. Ranjit** **Mr. H.K. Khuntia** **Mr. B.N. Sethi**

This project was completed (vide Annual Report 1987-88 page 54-55) and the results were published (ref IJMR(A) 91, July 1990. p.266-269). After reviewing the results the 5th SAC (2nd half) held on 19th & 20th September 1990 suggested to continue the above work as a long term comprehensive project to be applied in the field and results monitored and evaluated in the community. As per the recommendation of the SAC the work is yet to be started again.

3.5. Asymptomatic microscopic haematuria in a filarial endemic area of Orissa.

Scientist	:	**Dr. G.P. Chhotray**
Technical staff	:	**Mr. M.R. Ranjit** **Mr. H.K. Khuntia** **Mr. B.N. Sethi**

Although this project was completed (vide Annual Report 1988-89, page 36, 37) and the findings have already been sent for publication, the 5th SAC (2nd half) held on 19th & 20th September, 1990 suggested that the above work should be continued after defining a clear objective. As per the recommendation of the SAC further work is yet to be started again.

4. ENTOMOLOGY :

4.1.1 Present status of *Mansonioides* and *B.malayi* in Orissa.

Scientist : **Dr. A.P. Dash**

Technical staff : **Mr. R.K. Hazra**
Mr. H.K. Tripathy
Mr. G.D. Mansingh

Starting date : **September, 1989**

4.1.1.1 Monthwise densities of *Mansonioides* mosquitoes :

The per man hour densities of *Mansonia annulifera* and *Ma. uniformis* during 1990 (upto November) in Puri district were as follows :

Month	Per man hour density of	
	Ma.annulifera	*Ma.uniformis*
January	2.5	2.0
February	3.8	5.0
March	5.3	0.5
April	13.0	17.0
May	17.5	14.5
June	5.0	4.0
July	50.7	67.5
August	10.6	47.6
September	12.0	45.0
October	38.5	28.5
November	19.8	22.0

4.1.1.2 Prevalence of *B.malayi* in Puri district :

Till November, 90, *B.malayi* was detected in 5 villages of Puri district viz., Kadua, Bhatapur, Biraramchandrapur, Biragovindapur and Banapur, out of 14 surveyed. The slides were reconfirmed by Dr. J.W. Mak, Head, Malaria & Filaria Division, Institute for Medical Research, Malaysia. It is confirmed that both *B.malayi* and *W.bancrofti* are present in the area. The prevalence is summarised below :

Total number of slides collected and examined	:	1076	
Total number of positive	:	106	
Total number of *B.malayi*	:	37	(3.43%)
Total number of *W.bancrofti*	:	64	(5.94%)
Mixed infection	:	5	(0.46%)

4.1.1.3 Infestation of water mites on *Mansonia* mosquitoes.

The water mites represent an extremely successful lineage of the order Acariformis, sub class Acari that secondarily adapted to an aquatic existance. More than 300 genera in 45 families and seven superfamilies contain over 3000 species of water mites are distributed worldwide. The water mites are small rounded usually red or orange in colour, larvalformsof which are parasitic to fish, carb or aquatic insects.

Mosquitoes are also parasitised by larval water mites which are attached to abdomen or thoracic region. They oftenly found attached to cervical region of newly emerged adults. Though a number of reports exists on mosquitoes parasitized by larval mites in different parts of India such studies are lacking in Orissa, which is rich in mosquito fauna. During our studies onMansonioides in Puri district of Orissa, larval mites were found parasitizing Mansonia mosquitoes throughout the year. Mean intensity, prevalence, abundance of larval mites on mosquitoes are reported here.

Parasitic mites (*Arrenurus* sp.) were observed on the head, thorax and abdomen of mosquitoes. They were found infesting mostly on abdomen (90%). The mites were found infesting the mosquitoes throughout the year except in December and January with a peak in July and August (Table 6). *M.annulifera* is more parasitized by *Arrenurus* sp. than *M.uniformis*. An average of 10.33 and 9.41 mites were collected from *M.annulifera* and *M.uniformis*. The prevalence rate varies from 0 to 33% in *M.annulifera* and 0 to 25% in *M.uniformis* and abundance was (0 to 0.66) and (0 to 0.55) respectively in both the species (Table 7). Out of 73 parasitized Mansonia mosquitoes dissected (21 *M.annulifera* and 52 *M.uniformis*); 14 (8 and 6) were with one dilatation, the rest being nulliparous. From this study it may be concluded that though mite infestation cannot be taken as a marker of nulliparity, the mite infestation might decrease the parous rate and number of dilatation in *Mansonioides*.

The progress of work is slow due to non-availability of staff and transport (for budget cut in diesel, etc.). Recently few insect collectors appointed will be utilized soon after training.

4.1.1.4 Egg laying of Mansonia mosquitoes.

Both the species of *Mansonioides* are found to lay eggs under the leaves of Pistia plants. Three types of water plants are found in the Mansonia breeding sites viz., *Pistia stratiotes*,

Table 6. Infestation of *Arrenurus* sp. on *Ma.annulifera* and *Ma.uniformis* in different Months

Sl. No.	Months	No. of mites collected on *Ma.annulifera* H	T	A	Total No.	Total %	*Ma.uniformis* H	T	A	Total No.	Total %	Total H	T	A	Total No.	Total %
1.	January	-	-	-	-	0	-	-	-	-	0	-	-	-	-	0
2.	February	-	-	-	-	0	-	-	1	1	0.88	-	-	1	1	0.42
3.	March	1	2	13	16	12.9	1	3	14	18	15.92	2	5	27	34	14.34
4.	April	-	-	10	10	8.06	-	-	14	14	12.38	-	-	24	24	10.12
5.	May	-	1	5	6	4.83	-	-	2	2	1.76	-	1	7	8	3.3
6.	June	-	-	3	3	2.41	-	1	10	11	9.73	-	1	13	14	5.9
7.	July	-	1	24	25	20.16	4	2	32	38	33.62	4	3	56	63	26.58
8.	August	1	1	41	43	34.67	-	-	4	4	3.53	1	1	45	47	19.83
9.	September	-	-	18	18	14.51	-	-	14	14	12.38	-	-	32	32	13.5
10.	October	-	-	3	3	2.41	-	-	7	7	6.19	-	-	10	10	4.21
11.	November	-	-	-	-	0	-	1	3	4	3.53	-	1	3	4	1.68
12.	December	-	-	-	-	0	-	-	-	-	0	-	-	-	-	0
	Total	2	5	114	124		5	7	101	113		7	12	218	237	
	Mean	0.16	0.41	9.75	10.33		0.41	0.58	8.41	9.41		0.58	1	18.16	19.75	
	SD ±	±0.38	±0.66	±12.62	±13.23		±1.16	±0.99	±9.24	±10.48		±1.24	±1.53	±18.7	±20.5	

H - Head T - Thorax A - Abdomen T - Total

Table 7. Mean Intensity, Prevalence and Abundance of *Arrenurus* sp. on *Mansonia annulifera* and *Mansonia uniformis*

Months	*Ma.annulifera*			*Ma.uniformis*		
	Mean intensity	Prevalence	Abundance	Mean intensity	Prevalence	Abundance
January	-	-	-	-	-	-
February	-	-	-	1.0	0.2	0.2
March	2.66	0.17	0.47	2.25	0.15	0.33
April	5.0	0.02	0.12	3.5	0.04	0.15
May	2.0	0.33	0.66	1.0	0.07	0.15
June	3.0	0.02	0.08	2.2	0.25	0.55
July	4.16	0.05	0.21	2.23	0.07	0.16
August	2.68	0.09	0.26	1.33	0.03	0.04
September	1.5	0.11	0.16	3.5	0.04	0.16
October	1.5	0.06	0.09	2.3	0.18	0.43
November	-	-	-	2.0	0.18	0.36
December	-	-	-	-	-	-

Eichornia crassipes and *Marsilea quadrifoliate.* A survey of 500 plants revealed eggs only under the Pistia plants. The results are as follows :

Plant	No. of plant checked	No. with eggs	% of plants with eggs
Pistia	300	205	68.33
Eichornia	125	0	0
Marsilea	75	0	0

4.2 Influence of Aphid extracts and Juvenoids on the development of mosquitoes

Scientists : **Dr. A.P. Dash**
Dr. G.P. Chhotray

Technical staff : **Mr. M.R. Ranjit**

Starting date : **January, 1987**

4.2.1 Histopathological effects of aphid extracts and some juvenoids during the development of mosquitoes.

This is in continuation to the previous reports. The project will be completed in early 1991. The histopathological observations of developing mosquitoes (larval stage) after application of EC_{50} and EC_{90} doses of aphid extract (extracts of *Aphid craccivora* and *A.gossypii*) and juvenoids (Methoprene, Neporex, OMS 3007, OMS 3019 and DPE 28) are as follows :

a) Muscle tissue : The cephalic, thoracic and abdominal muscles are degenerated due to the effect of both the doses of all the compounds tested.

b) Malpighian tubule : It has been observed that necrosis (karyorrhexis) of the cells of malpighian tubules occurs invariably in both the doses of all compounds used.

c) Nervous system : Only OMS 3007 and OMS 3019 affect the histomorphology of the nervous system. The neuropile of the supra-oesophageal, sub-oesophageal and thoracic ganglions are vacuolated. Other compounds have no effect on the nervous system.

4.3 Laboratory Biology and colonization of Mosquitoes. (It is a cyclic process)

Cyclic colonies of the following mosquito species have been established in the laboratory since long :

i) *Aedes aegypti*
ii) *Culex quinquefasciatus*
iii) *Culex tritaeniorhynchus*
iv) *Mansonia uniformis*

Colonies of the following three species have been established in the current year :

i) *Anopheles stephensi*
ii) *Aedes vittatus*
iii) *Aedes aegypti* (black eyed Liverpool strain)

Laboratory bred mosquitoes (both larvae and adults) are supplied to different research workers including Utkal University and Calcutta University.

Sometimes mosquitoes are used for developing filarial larvae through membrane feeding.

4.4 Studies on mosquito of Orissa.

After repeated recommendation of the previous SACs, this project has just started after recruitment of few staff, in May/June 90, already sanctioned since long. In a very recent preliminary study, the following species have been identified in Puri district :

Aedes aegypti, Ae.alobopictus, Ae.vittatus.
Anopheles aconitus, An.annularis, An.barbirostris, An.culicifacies, An.'hyrcanus group, *An.karwari, An.pallidus, An.subpictus, An. tesselatus, An.vagus* and *An.varuna.*

Armegeres theobaldi, Arm.obturbans, Arm.kuchingensis. Culex epidesmus, Cx.gelidus, Cx.quinquefasciatus, Cx.'Vishnui' group *Cx.whitmorei.*

Mansonia annulifera, Ma.indiana, Ma.uniformis and *Coquillettidia crassipes.*

5. MYCOBACTERIAL GENETICS :

Scientist : **Dr. V.R. Subramanyam**

Technical staff : **Mr. B.B. Pal**

Starting date : **January 1985**

Progress :

The purine and pyrimidine requiring mutants were tested for their ability to grow in basal medium supplemented with various nucleobases, nucleosides or nucleotides. The growth response of the mutants is given in Table 8 & 9.

Table 8 : Growth of Purine auxotrophs on various supplements.

Supplement	Growth of mutant				
	SM19	SM21	SM38	SM3	SM24
Adenine	+	+	+	+	+
Adenosine	+	+	+	+	+
2'deoxyadenosine	+	+	+	+	+
AMP	(+)	–	–	–	–
2'deoxy AMP	+	+	(+)	+	+
Guanine	+	+	+	+	+
2'deoxyguanosine	+	+	+	+	+
GMP	±	–	(±)	(+)	(+)
Xanthine	–	–	–	–	–
Hypoxanthine	+	+	+	+	+
Inosine	+	+	+	+	+
2'deoxyinosine	+	+	+	+	+
IMP	(+)	–	(+)	(+)	(+)

Table 9 : Growth of pyrimidine auxotrophs on various supplements.

Supplement	Growth of mutant	
	SM33	SM69
Cytosine	+	+
Cytidine	+	+
CMP	–	(+)
Thymine	–	–
Thymidine	–	–
Uracil	+	+
Uridine	+	+
2'deoxyuridine	+	+
UMP	–	(+)

Further characterisation of these and the other (amino acid requiring) mutants would be undertaken when radioactive facility becomes available.

6. BIOSTATISTICS :

6.1. An assessment of the levels and trends of mortality and morbidity in Orissa - district level analysis.

Scientist : **Mr. Anil Kumar**

Starting date : **August, 1989**

The project was started to assess the mortality and morbidity levels at district level in Orissa, since existing levels of mortality and morbidity mainly reflect on health situation in a population. The continuous monitoring of health trend, in terms of mortality and morbidity is necessary and helps to improve the public health situation. Initially, attempts have been made for the tribals dominated districts, viz., Sundargarh, Koraput, Mayurbhanj and Keonjhar. The preliminary results are presented. Mortality estimates are indirect estimates from census data and refer to *circa* 1980-81. There is possibility that estimates may reflect under reporting.

6.1.1. Estimates of childhood mortality (Rural) :

District	% Tribals	Mortality rate per 1000 before age			Ratio q(5) : q(2)
		q(2)	q(3)	q(5)	
Sundargarh	65	126	146	160	1.27
Koraput	60	148	160	128	1.16
Mayurbhanj	60	103	116	128	1.25
Keonjhar	47	148	156	164	1.11
ORISSA (R)		154	150	184	1.19

Among the four tribal districts, the child mortality at age 2(q2) is highest in Koraput and Keonjhar and lowest in Mayurbhanj. However the state level estimate is 154. One point is clear that the tribal concentration alone has weak association with mortality levels. However, the increase in mortality level, from age 2 to 5 is highest in Sundargarh (27%) followed by Mayurbhanj (25%), Koraput (16%) and Keonjhar (11%).

Age-specific survival probability clearly indicate that even though Sundargarh has lower mortality rate in early ages it increase very substantially after age 20 and by age 75, only 1/6th population survive. The trend in Keonjhar is much better followed by Koraput and Mayurbhanj.

However, these estimates are preliminary and much more extensive analysis is needed to understand differentials in the levels of mortality.

6.1.2. Principal disease and causes of death.

There are six major diseases in the tribal districts of Sundargarh, Koraput, Mayurbhanj and Keonjhar. These are Dysentry, Avitaminosis, Upper Respiratory tract Infection, Scabies, Malaria and Anaemia accounting for above 40% of the cases registered. However, the potential killer (high case fatality) diseases are Tetanus, Meningitis (Non meningoccol and meningoccal), Encephalitis acute infection, Heart diseases and disease of vascular lesion, though their reported occurrance is low. Tuberculosis as such takes the highest toll.

Data by age/sex at district level need to be collected for an indepth analysis.

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7. SICKLE CELL RESEARCH CENTRE AT VSS MEDICAL COLLEGE, BURLA.

7.1. Study of natural history of sickle cell disease.

Sickle cell disease patients are being followed up with clinical and hematological examinations in the sickle cell clinic and new cases are being added. 173 new cases have been added from 01.01.90 to 31.12.90 thus making a total of 923 cases in the series under observation. The attendance in the sickle cell clinic has been 2129 during the year. Relevant scientific data will be analysed after a long term study, for 10-15 years. The study is being continued.

7.2. Study of glucose metabolism in Hb S containing RBCs.

The study had to be discontinued due to want of microcentrifuge which has been sent for repair since last 6-8 months and a suction apparatus, requisition for which has been sent since March '90 and has not yet been received.

Projects completed

1. **Chemotherapy of Filariasis : Comparative study on efficacy of DEC in different dosage schedule.**

Scientist : **Dr. S.K. Kar**

Technical staff : **Ms. J. Mania**
Mr. K. Dhal
Mr. R.N. Nayak
Mr. S.C. Rout

Starting date : **January 1988**

Aim :

The study was initiated in a bancroftian endemic village of Orissa to evaluate the efficacy of long term DEC regimen and conservative therapy in reversing the persistent filarial lymphoedema and hydrocele of various grades.

Study Design :

The subjects presenting with Grade II & III filarial lymphoedema and/or hydrocele were selected (146 cases) for the study. They were stratified according to age, sex and were divided into two groups by random allocation. The subjects in the first group served as controls (n=21), were given DEC regimen in standard dosage (6 mg/kg wt/day) and others as cases, (n=125) received DEC in higher dosage (10 mg/kg wt/day). Both the groups were given the above DEC course for 3 weeks every month for 1 year. It was ensured that all the subjects had consumed the total course of DEC through continuous surveillance by village volunteers. Further, the cases with grade II & III lymphoedema in both cases and controls were subdivided into two subgroups in each category, the 1st being given conservative therapy and the other did not. Conservative physiotherapy included massage, limb elevation and elastic pressure bandaging with exercises. Besides, fungal and bacterial infections were also treated with individual cases.

Pre drug and subsequent periodic follow up examinations included detail clinical examination, history of lymphangitic attacks, blood microfilariae, biochemical tests (SGOT, SGPT, Alkaline phosphatase, Serum cholesterol) and immunological tests (Filaria specific IgG, IgM, antigen and circulating immune complex. Tissue compressability was measured by a tissue tonometre, limb circumference by a measuring tape and the scrotal skin (upper and lower) and the testes (vertical and horizontal diameter) by a slide callipers.

Results :

The dropout rate was (13%, n=19) which was insignificant. Seven cases who were positive for mf at intake were found to be amicrofilaraemic after the first course of DEC.

Significant reduction of acute lymphangitic attack rate/yr in both the cases and control were observed after 1 year of chemotherapy.

Considerable proportion of cases of Grade II oedema and mild hydrocele had shown complete reversal of lymphoedematous state after the chemotherapy. But similar conversion was neither observed in Grade III oedema or elephantoid hydroceles. After the initial course of chemotherapy, the limb became soft, the patients had relief of pain and heaviness of limb. This reduction was first observed in upper part of the affected lower limb, upper part of the scortal skin and vertical diameter of testes in patients with hydrocele. Although significant subjects in control group did not show the reduction, there was no further increase in limb size. Further the subjects with conservative physiotherapy had shown significant reduction of limb circumference and increased tissue compressability as compared to those cases who had high dosage DEC alone.

No significant clinical or biochemical adverse reactions were observed in cases with higher DEC dosage. However, the symptoms like headache, malaise, fever and arthralgia were observed in few following initial course of DEC which were short lasting and within tolerable limits.

Significant progressive fall of mean filarial-specific anti-bodies of IgG class was observed during 1 yr post drug and then it was significantly raised (24 months). Reversal of this pattern was observed in the mean circulating immune complex level of these patients. There was an initial increase in the percentage of subjects with filarial specific antigen which later was reduced significantly (1 yr post drug).

The above study has shown that high dose of DEC have beneficial effect in reducing lymphoedema and size of hydrocele. This reduction was more marked when conservative physiotherapy was supplemented alongwith the high dosage DEC particularly in grade II oedema. The reduced response as observed in Grade III oedema was possibly due to the recurrent bacterial and fungal infections of the unhealthy skin of lower limb. DEC in above dosage might have helped to evaccuate the stagnant lymph of lower limb by reducing inflammation in and around the lymphatics, thus releasing the block at higher level. Besides, the evidence of adulticidal effect of high dose DEC might have beneficial effect in clearing infection, since there was significant reduction of lymphangitic attacks and reduction in circulating antigen in these cases. However, these cases need to be followed up for 1 more year to observe any recurrence of symptoms and sign.

2. Long term follow up of asymptomatic microfilaraemics in an endemic area with reference to their peripheral eosinophils and antibody level.

Scientist : **Dr. S.K. Kar**

Technical staff : **Ms. J. Mania**
Mr. P.K. Kar
Mr. T. Moharana
Mr. S.C. Rout

Starting date : **November 1985**

Date of completion : **November 1990**

Aim :

A follow up study on asymptomatic microfilaraemics was carried out with an aim to evaluate any conversion of microfilaraemic to amicrofilaraemic state with or without any clinical signs or symptoms over period of time and any related host immune alterations.

Evaluation :

The study was carried out in an endemic village of Puri district, where the carriers were detected after detailed clinical & parasitological examination. The carriers of all ages and both sexes thus obtained (n=163) were followed up periodically.

Results :

Conversion of asymptomatic microfilaria carriers on 5th follow up was presented in the Table-1.

Table-1 : Conversion of Asymptomatic Microfilaria Carriers on 5th follow up

AMC population covered at 5th follow up	AMC	Total microfila-raemics	Converted to			
			Disease			No disease
			mf+ve	mf-ve	Total	mf-ve
	A	A + B	B	C		D
115 (70.6%)	50	89	39	12	51	14

The carrier state was more prevalent in younger age group. Conversion to disease was more in this age group but this rate was progressively lower in higher age groups. Conversion to disease in males was more than that of females ($P < 0.05$).

Clinical symptoms :

Episodic filarial fever was a common occurrence as most (94%) of the subjects manifesting clinical disease suffered from one or more attacks of fever. Adenolymphangitic attack pertaining to limbs alone was observed in 17 subjects. Orchitis, funiculitis and/or epididymitis was seen in the rest subjects manifesting the disease. Twentythree cases developed lymphatic nodules and five filarial abscesses. Arthralgia pertaining to limbs and malaise were the commonest symptoms among the carriers.

Humoral Immune Response :

Circulating filarial antigen was not detectable in significant proportion of subjects in Group C & D sera. In Group B significant percentage of subjects had detectable antigen in their blood.

The mean filaria-specific antibody of IgG class was significantly increased in subjects of group C ($P < 0.05$) & D ($P < 0.001$) whereas in others no significant alteration was observed.

Reports on studies on course of AMC are scanty. This prospective study shows the course of the carrier state, the conversion of this stage to others in course of events with their concomitant alterations of immune response, which may add to the knowledge in pathogenesis of the disease.

3. Analysis of lipids of *Setaria digitata*, a bovine filarial parasite.

Scientists : **Dr. V.R. Subramanyam**
Dr. N.M. Pattnaik
Ms. Keshar K. Mohanty

Starting date : **April 1989**

Total lipids were extracted from adult *Setaria digitata*, by Bligh and Dyer method. The lipids were analysed on TLC in conjuction with standard (known) lipids. TLC showed the presence of phosphatidyl choline, sphingomyetin and some lysophosphatidyl choline in *Setaria*.

Sickle Cell Research Centre, Burla

4. G-6-PD deficiency and sickle cell disease - a correlation

Mutations for both sickle haemoglobin and G-6-PD deficiency are supposed to have arisen as a protective mechanism against falciparum malaria. Both being potentially hemolytic processes are likely to influence the morbidity of each other.

In this study 100 patients of SCD, 100 persons with S.C.trait and 100 persons with normal haemoglobin pattern were screened for G-6-PD deficiency by DCIP method, while Hb phenotype was determined by both Acids and Alkaline electrophoresis. The findings were as follows :

Type of persons	No. tested	G-6-PD abnormality
Sickle Cell Disease	M - 68	def. 19 + partial def. 3 = 22 (32%)
	F - 32	partial def. 11 (34%)
Sickle Cell trait	M - 82	def. 21 + partial def. 1 = 22 (26.8%)
	F - 18	partial def. 1 (5.5%)
Normal Hb	M - 82	def. 20 + partial def. 5 = 25 (30.5%)
	F - 18	partial def. 3 (16.66%)

Some casts with high S-gene frequently tend to have higher frequency of G-6-PD def. while the latter is prevalent in all casts and communities.

Regarding influence of G-6-PD deficiency on SCD, steady state haemoglobin was found to be less (7.71 $\pm$ 2.16 G% and 8.69 $\pm$ 2.05 G%) in enzyme deficient patients than persons without enzyme deficiency. Similarly mean spleen size was found to be bigger (3.23 $\pm$ 2.73 cm) in enzyme deficient individuals, than in patients (2.71 $\pm$ 2.28 cm) with normal quantity of the enzyme. Transfusion requirement was also higher (0.73 $\pm$ 1.44 units per pt.) in the former than the latter (0.52 $\pm$ 1.42 units per pt.) group.

5. Foetal Hb levels in SS patients in Western Orissa and its significance :

Foetal haemoglobin levels in Indian patients of sickle cell disease are reported to be high though it's real significance is largely unknown. This work was undertaken to get an insight into the cause of such high levels.

Foetal haemoglobin was estimated by Betke's method in 100 consecutive SS cases, 195 persons with sickle cell trait and 96 persons with normal haemoglobin. All were above 1 yr. of age ruling out of normal high foetal haemoglobin encountered in infancy.

In 96 normal persons 94.5% were having haemoglobin F below 1.5% and 78% were having below 1%. Thus in our laboratory set up in the population of the area the highest apparent sex variation, though slightly larger no. of females (28%) had values between 1 and 1.5%, as against 11% of male in this range.

In the sickle cell trait cases 56.7% only were having Hb F below 1.5% (within accepted normal range), while 43.3% of the trait cases had high values. In 12% of cases the values were above 3%. No sex discrimination was notable in sickle cell trait cases.

Amongst the 100 homozygous sickle cell anaemia (SS cases) the values were, = 5% in 1%, 5-10% in 8%, 10-15% in 20%, 15-20% in 28%, 20-25% in 25%, 25-30% in 16% and above 30% in 2% cases respectively. A large no. of females (45%) had values between 20-25% much higher than males (15.94%).

The results indicate that the high F levels are probably linked to 'S' leading to higher Hb F production in heterozygous cases with single S-gene than normals and very high levels of F with homozygous gene defects. Data on study of parents, sibling, children and relations will be analysed to bring out more details about genetic significance of F and S-gene linkage.

New Projects Proposed for 1991

1. **Immune responses of patients with clinically defined filariasis :**

Scientist : **Dr. Shantanu K. Kar**

Collaborator : **Dr. D.A. Denham**
LSG & TM London, UK

Indo-UK collaboration project - awaits clearance.

2. **Role of sex hormones in Filariasis.**

Scientists : **Prof. Indira Chakravarty**
Head, Dept. of Biochemistry
AIIPH, Calcutta

Dr. Shantanu K. Kar

Various epidemiological experimental studies have shown the sex predilection in human lymphatic filariasis. The males appear to be more susceptible to filarial infection and severity than females (in their reproductive age). It is presumed that sex hormones might have protective role in females against this infection during their reproductive age. So the relationship of sex hormones with the filarial disease pattern needs to be evaluated.

3. ***W.bancrofti*** **: Development of L_3 larvae to L_4 stages in plexiglass chambers by implantation in laboratory animals.**

Scientists : **Dr. B. Ravindran**
Dr. A.P. Dash

The antigens expressed on the surface of infective larvae (L_3) have been the topic of great interest to understand the immune response of infected individuals in endemic areas. However, it has been demonstrated in recent years that the determinants expressed on the L_3 stages get shed during the moulting process of transformation to L_4 stages. The process of shedding L_3 surface antigens takes only 10-20 days after the entry of infective larvae in the mammalian host. The L_4 larvae however continue to exist for 6 months or longer before becoming juvenile adult. Thus the

surface antigens of L_4 are critical determinants since they are exposed to the immune system for a long time in the vertebrate host - the immune response of the host to these antigens could determine the course of the disease. L_4 stages, however, cannot be obtained for studies since no convenient experimental animal model exists for *W.bancrofti*. However, in recent years L_4 stages have been harvested by intraperitoneal implantation of infective larvae (L_3) of *Brugia malayi* in plexiglass chambers. It is proposed to translate this approach for development of L_4 stages of *W.bancrofti*.

4. Development of experimental microfilaraemia of *W.bancrofti* in different strains of mice.

Scientist : Dr. B. Ravindran

W.bancrofti has not been adapted in any small laboratory animal. There exists a possibility of developing an *in vivo* model of microfilaraemia in mice by intravenous inoculation of microfilariae purified from infected human blood. Initial attempts in our laboratory and elsewhere had indicated that microfilariae of *W.bancrofti* get cleared from circulation of BALB/c mice very rapidly. However, it has been reported that *B.malayi* microfilaraemia can be maintained in CBA/N mice for a long time since this strain of mice is partially deficient in T-independent responses to polysaccharides. It is proposed to develop a model of microfilariaemia for *W.bancrofti* by using the above approach. Such a model would be useful for undertaking *in vivo* immunological studies and can also be applied for drug design and chemotherapeutic studies.

5. Studies on cerebral malaria and development of immunodiagnostic tests for cerebral malaria.

Scientists : Dr. B. Ravindran
Dr. G.P. Chhotray
Dr. T.K. Bose

A bigger project is being prepared and protocol will be submitted.

6. Antigenicity of some selected enzymes of filarial parasites in endemic population.

Scientist : Dr. Manoj K. Das

Generally all works examining the immunological parameters of filarial patients have used crude extracts of parasite material containing hundreds of proteins and glycoproteins. The

particular antigenic determinants in these extracts responsible for triggering the immune response *in vitro* or *in vivo* are unknown. Thus until defined antigen preparations are available, the nature of immunological reactions in filariasis will remain ill-defined and non-specific. A potentially interesting approach is to identify and isolate certain biologically important enzymes from the filarial parasites. The enzymes belonging to this category are proteinases, glutathione-S-transferase and superoxide dismutase. Recently it has been shown that these enzymes possess antigenic activity in humans infected with helminths. They have been used as immunodiagnostic marker and even as protective antigen(s). Similar studies which is lacking in human filariasis may yield useful information. This project will be an attempt in that direction. Cattle filarial parasite *S.digitata* and *W.bancrofti* L_3 will serve as the source of parasite materials.

7. Cellular immune responses to Infective larvae of *W.bancrofti* in people living in filariae-endemic regions.

Scientists : Dr. M.K. Das
Dr. A.P. Dash

The presence of large proportion of normal individuals in endemic regions suggest that these people inspite of continuous exposure to mosquito bits have developed an effective immune mediated resistance, yet uncharacterized. It is probable that T-lymphocytes play a major role in human resistance to lymphatic filariasis. Although few studies on cellular immune reactions (as measured by lymphocyte proliferation) has been carried out in filarial patients; reaction against L_3 antigen has not been evaluated. The present project will attempt to identify the type of cellular responses in people living in endemic regions.

It is imperative that a major emphasis needs to be devoted in trying to raise large number of L_3s as antigen source.

8. Health survey of Aluminium company workers in Orissa with special reference to fluoride exposure.

Scientist : Dr. G.P. Chhotray

Technical staff : Mr. M.R. Ranjit
Mr. H.K. Khuntia
Mr. B.N. Sethi

As recommended by the 5th SAC (2nd half) held on 19th-20th September 90, a detailed project protocol has already been submitted through proper channel to Deptt. of Science & Technology, Govt. of Orissa for financial grant. The work shall be commenced once the grant from DST becomes available.

9. Epidemiological studies on human lymphatic filariasis in Orissa & development of mathematical model.

Scientists : Dr. G.P. Chhotray
Mr. Anil Kumar
Dr. A.P. Dash

As per the recommendation of the 5th SAC held on 19-20th September 90, a detailed and comprehensive project protocol has already been prepared and forwarded to Dr. P.K.Rajagopalan for comments.

10. Field evaluation of *B.sphaericus* against *Cx.quinquefasciatus*.

Scientist : Dr. A.P. Dash

This project has been strongly recommended several times by the SAC to be started as a TDR project. The last SAC held in September '90 again approved this project and endorsed that previous recommendations stand.

The project proposal has been forwarded to the ICMR headquarter for onward transmission to the WHO for necessary action.

The project will be started as soon as the TDR support is received.

11. Leprosy : Peripheral Nerves
Scientist : Brig. M.S. Dash (Retd).

To work on neural involvement in leprosy and allied neuropathies an updated Neurophysiological laboratory is being established. Equipments for this purpose have been indented. On receipt of the same studies on altered structure and function of the receptors and peripheral nerves in affected limbs would be undertaken using both conventional methods and tungsten microelectrodes. Special attention would be laid on small medullated and unmedullated fibres in peripheral nerves, thermoreceptors and autonomic involvement. At an appropriate stage in collaboration with JALMA skin grafting over anaesthetic areas would be undertaken and objective estimation of sensory recovery, if any, would be studied.

12. An assessment of availability, utilization and impact of health services in Rural Orissa.

Scientist : Mr. Anil Kumar

A revised protocol has been sent to Dr. M.V.V.L. Narasimham as advised by the SAC.

13. Health survey of the elderly in Orissa with special reference to food habits.

Scientist : Dr. J. Prabhakar Patro

This study is part of International multi-centre study on "Food Habits and Health in Later Life : A cross cultural study". International Union of Nutritional Sciences (I.U.N.S.) in conjunction with the W.H.O. global programme for the elderly has started this programme to test key hypothesis in relation to food habits and health status in the elderly in developed and developing countries. The study has already started in Australia, China, Greece, Sweeden and England.

14. Sickle Cell Research Centre, Burla.

a) Continuation of ongoing project no. 1

Study of natural history of sickle cell disease.

b) Study of Glucose Metabolism in Hbs containing RBCs - to be resumed when equipments are rceived.

c) Study of Iron Metabolism in SCD in Western Orissa.

Though it is well known that there is no significant iron deficiency is SCD, yet with given nutritional standard of the patients in India, some degree of iron deficiency is likely even in SCD patients, as in persons with normal Hb pattern. It is also observed that with short course iron therapy the patients show some rise in Hb level. A more scientific study involving serum transferin, total iron binding capacity and serum iron levels will be determined in a small number of cases (as the test are very costly) and effect of one month's iron therapy on pre-treatment values, and on clinical/haematological parameters will be studied.

d) Study on alteration of foetal haemoglobin levels in SCD patients during their clinical course :

It is not known whether there is any fluctuation in HbF levels during the life of patients after infancy and/or in relation to the crisis, or other haematological changes. Repeated estimation of HbF level in a group of patients in steady state, during crisis and after crisis may reveal such fluctuations if any.

Publications

A. Papers :

1. Development of lectin based idiotype vaccine for polysaccharide antigens.
B. Ravindran (1990)
Immunology Today 11(11); 388.

2. Antibodies to microfilarial sheath in Bancroftian filariasis - prevalence and characterization.
B. Ravindran, A.K. Satapathy, M.K. Das, N.M. Pattnaik and V.R. Subramanyam (1990).
Annals of Tropical Medicine and Parasitology 84(6); 607-613.

3. Anti-malarial property of an extract of the plant Streblus asper in murine malaria.
M.K. Das & M.K. Beuria.
Transactions of the Royal Society of Tropical Medicine and Hygiene (in press).

4. Stimulation by adjuvants of cell mediated immune response to Plasmodium berghei infected mice.
M.K. Beuria, B. Ravindran & M.K. Das.
Indian Journal of Biochemistry and Biophysics (in press).

5. Dextran sulfate induced suppression of Plasmodium berghei parasitaemia.
M.K. Beuria & M.K. Das.
Indian Journal of Experimental Biology (in press).

6. Production of antibodies to Dextran using liposome as adjuvant.
A.K. Sarkar & M.K. Das.
Immunological Investigations (in press).

7. Health situation in tribals dominated districts of Orissa.
Anil Kumar & A.S. Acharya.
Forthcoming in "Tribals Demography" (eds) R.N. Pati, Population Research Centre, Utkal University, Bhubaneswar.

8. Effect of drug treatment on the prevalence of Intestinal parasites amongst school children in a suburban community.
G.P. Chhotray & M.R. Ranjit.
IJMR (A) 91, July 1990 pp.266-269.

9. Prevalence of G6PD deficiency in a malaria endemic tribal area of Orissa (India).
G.P. Chhotray & M.R. Ranjit.
IJMR (B) 92, December 1990 pp. 443-446.

10. Comparative efficacy of three larvicides against mosquitoes in a filaria endemic area of Orissa.
A.P. Dash & R.K. Hazra.
Proc.Symp. on Entomology for Defence Services, pp. 107-112.

11. Effect of aphid extracts and juvenoids on the development of *Cx.quinquefasciatus*. Ibid, pp. 135-140.
M.R. Ranjit, A.P. Dash & G.P. Chhotray (1990).

12. Infestation of water mites on *Mansonia* mosquitoes in Orissa. Ibid, pp. 129-134.
R.K. Hazra & A.P. Dash (1990).

13. Homoeopathic treatment of filariasis : experience in an Indian rural setting.
V.R. Subramanyam, N. Mishra, Y. Rai, G. Rakshit & N.M. Pattnaik.
British Homoeopathic Journal 79 : 157-160 (1990).

14. Absence of Human Immunodeficiency Virus (HIV) antibody reactivity in filariasis and malaria sera.
V.R. Subramanyam
World Journal of Microbiology & Biotechnology (in press).

15. Sickle haemoglobin G-6-PD deficiency and Malaria in Western Orissa.
B.C. Kar, *et al.*
J.Assoc.Phys.Ind. 1990, 38 : 555-558 (based on work with an ICMR grant).

16. Sickle cell disease in India.
B.C. Kar.
J.Assoc.Phys.Ind. (accepted for publication).

Abstracts :

1. Immune response to diethylcarbamazine citrate therapy in tropical pulmonary eosinophilia (TPE).
   S.K. Kar, J. Mania & P.K. Kar.
   Souvenir joint annual conference of Association of Physicians of India (1990) JAPI Vol.38(1) p.29.

2. Immune responses of microfilaraemics in natural course.
   S.K. Kar, J. Mania & P.K. Kar.
   Souvenir of 59th annual meeting of society of biological chemists (India), page 32.

3. Malaria morbidity and mortality in Orissa. Abstract in Proc. Indian Asson. Study Popln., 1990.
   Anil Kumar.

4. Studies on purine and pyrimidine auxotrophs of Mycobacterium (Abstract).
   V.R. Subramanyam.
   Proceedings of IUMS Congress : Bacteriology & Mycology, Osaka 1990.

Papers submitted for publication :

1. "Study on ecological factors influencing the nutritional status of pre-school children (1-5 yrs) of low socio-economic status". Submitted for participation in preparation of the publication on "Studies on growth & development of Indian children and infants" to be brought out by Institute for Research in Medical Statistics, New Delhi for publication.
   S.K. Kar, *et al.*

2. Human natural antibodies to *Culex quinquefasciatus* : Age dependent occurrence - submitted to J.Amer.Mosq.Control Asson.
   M.K. Das, A. Mishra, M.K. Beuria & A.P. Dash.

3. Evaluation of reversed mutation frequency of *Mycobacterium* auxotrophs using a multiple tube most probable number method.
   V.R. Subramanyam.

4. Characterisation of *Bacillus* species isolated from mosquito larvae in a filariasis endemic area.
V.R. Subramanyam, K. Ramaswamy & A.P. Dash.

5. T-cell derived proteins from normal human sera and their relationship to T-cell antigen binding molecules - Clinical Immunology and Immunopathology.
M. Debrino, B. Ravindran & R.E. Cone.

6. Human cerebral malaria : characterisation of malarial antibodies in cerebrospinal fluid - Clinical and Experimental Immunology.
S. Mitra, B. Ravindran, *et al.*

7. Prevalence of asymptomatic haematuria in a filarial endemic area of Orissa - Indian Journal of Medical Research.
G.P. Chhotray, M.R. Ranjit & Anil Kumar.

SCIENTIFIC CONFERENCES/WORKSHOPS/SEMINARS ATTENDED

Name of the Scientist/ Participant	Scientific Conferences/Workshops/Seminars attended with dates or Name of the Institute where lectures delivered	Papers presented/lecture delivered
Brig. M.S. Dash	Sixth Annual Conference of the Association of Physiologists of Orissa, dated 10 November 1990, University of Berhampur	Mind, memory and recall
	Workshop on "Sodium transport across animal membrane". Department of Physiology, MKCG Medical College, on 9 & 10 November 1990.	Sodium transport across animal membrane
	Workshop on Hansen's disease, 16 November 1990, Bhubaneswar.	Anaesthetic Hand and rehabitation in leprosy.
Dr. M.K. Das	Future research needs in lymphatic filariasis, 8-10 October 1990, at VCRC, Pondicherry	Participated in immunology of filariasis
Dr. S.K. Kar	International conference of Parasitology & Ivermectin lymphatic filariasis, 23-25 August 1990, at Paris	–
	Seminar on Future Research Needs in lymphatic filariasis, 8-10 October 1990, at VCRC, Pondicherry	Participated in chemotherapy of filariasis
Dr. A.P. Dash	Symposium on Entomology for Defence Services, 12-14 September, 1990 at Gwalior	Comparative efficacy of three larvicides against mosquitoes in a filaria endemic area of Orissa
	Seminar on Future Research Needs in lymphatic filariasis, 8-10 October 1990, at VCRC, Pondicherry	Participated in Transmission dynamics of filariasis

Name of the Scientist/ Participant	Scientific Conferences/Workshops/Seminars attended with dates or Name of the Institute where lectures delivered	Papers presented/lecture delivered
Dr. V.R. Subramanyam	Seminar at Astra Research Centre, March, 1990 at Bangalore	Importance of mutants in mycobacterial genetics
	Third All India People's Science Congress, 8-11 March,1990, at Bangalore	–
	Workshop on self sufficiency. All India Peoples Science Network, 8-11 June, 1990 at Delhi	–
	Annual Congress of Indian Academy of Science, November 1990 at Bhubaneswar	–
Dr. B. Ravindran	First National Brain Storming Session on Neuro-immunology, 19-21 February, 1990 at National Institute of Immunology, Delhi	Immunology of human cerebral malaria
Dr. G.P. Chhotray	National Seminar on Health for Tribal People, 21-26 May, 1990 at Bangalore	G6PD deficiency in a malaria endemic tribal population of Orissa
	18th Annual Conference of IAPM Orissa Chapter, 10 November, 1990 at Cuttack	Histopathological study of genital lesion in lymphatic filariasis
	39th Annual Conference of IAPM, 17-20 December, 1990 at Chandigarh	-do-
Mr. Anil Kumar	VIII Annual Conference of Indian Society of Medical Statistics, 31 October-2nd November, 1990 at CMC, Vellore	Health information system : A biostatisticians view

Name of the Scientist/ Participant	Scientific Conferences/Workshops/Seminars attended with dates or Name of the Institute where lectures delivered	Papers presented/lecture delivered
	National Seminar on Health for Tribal People, May, 1990 at Mysore	Health status and major health problems of tribals in Orissa
	Indian Association for the study of population, 27-29 December, 1990 at Udaipur	Malaria Morbidity and Mortality
Mr. M.K. Beuria	59th Annual General Body Meeting of SBC(I), 27-29 December, 1990 at Udaipur	Antimalarial property of *Streblus asper*
Mr. P.K. Kar	-do-	Immune responses in microfilaraemics in natural course ***(Got Best Poster Award)***
Mr. B.B. Pal	7th All India Congress of Cytology & Genetics, December,1990 at Kalyani University	Mutagenecity testing of Blitox (Copper Oxychloride) *in vivo* mouse system
Mr. M.R. Ranjit	Symposium on Entomology for Defence Services, 12-14 September, 1990 at Gwalior	Effect of aphid extracts & some juvenoids on development of *Cx.quinquefasciatus*
Mr. R.K. Hazra	-do-	Infestation of water mites on Mansonia mosquitoes in Orissa
Mr. B.P. Dash	Annual Conference of Indian Society of Haematology and Blood Transfusion, 1990	Studies on inheritance pattern of sickle cell disease
Ms. T. Hussain	59th Annual General Meeting of SBC(I), 27-29 December, 1990 at Udaipur	Antigenic mimicry between Piperazine derivatives and *W.bancrofti* microfilariae

CONFERENCES/SYMPOSIA/WORKSHOP ARRANGED

Dr. G.P. Chhotray	XVII Annual Conference of Indian Association of Pathologist & Microbiologist - Orissa Chapter, 11 November, 1989.
Dr. A.P. Dash & Dr. G.P. Chhotray	Environmental Priorities of Orissa at the Regional Science Centre, 7th July, 1990.

Ph.D. PROGRAMME

The Centre has been affiliated to the Utkal University for Ph.D. degree. As many as 13 candidates are working at the Centre for Ph.D. degree. One Ms. Namita Tripathy has submitted her thesis, whose viva-voce is scheduled in early '91.

SCIENTIFIC ADVISORY COMMITTEE

LIST OF MEMBERS

1. **Prof. A.S. Paintal**
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VSS Medical College
Burla
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15. **Dr. B.B. Purohit**
Director of Health Services
Govt. of Orissa
Bhubaneswar

16. **Dr. N.C. Panda**
Addl. Secretary
Health & F.W.
Govt. of Orissa
Bhubaneswar

17. **Brig. M.S. Dash** (Retd.)
Officer-in-charge
Regional Medical Research Centre
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ETHICAL COMMITTEE

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   Charu Bhavan
   Cuttack 753 003

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   State Social Welfare Board
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3. **Dr. K.N. Ojha**
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   Saradiya Mission Road
   Cuttack 753 001

5. **Brig. M.S. Dash**
   Director
   Regional Medical Research Centre
   Bhubaneswar 751 016

VISITORS

26th & 27.4.1990	**Dr. E.A. Ottesen**, M.D. Head, Clinical Parasitology NIH, Bethesda, U.S.A.
	Dr. Collin Ginger, M.D. Onchocerciasis Control Programme W.H.O., Geneva.
	Dr. C.P. Ramachandran, Ph.D. Secretary, Steering Committee Filariasis Control Programme W.H.O.
	Prof. V. Vijayasekharan Professor of Clinical Pharmacology Madras Medical College Madras 600 003
	Dr. V. Kumarswami Asst. Director TRC, Madras
27.11.1990	**Prof. V. Ramalingaswamy**, FRS Ex-Director General, ICMR
03.01.1991	**Dr. B.B. Samal**, Ph.D. Senior Scientist Exploratory Research Programme Amgan, USA
23rd & 24.01.1991	**Dr. D.A.P. Bundy** Director, Parasite Epidemiology Research Programme Imperial College of Science, Technology & Medicine London

Dr. J. Remme
Epidemiology Division
TDR, WHO Headquarters
Geneva

Dr. T.W. Lim
WHO Representative
at Delhi

Dr. C.P. Ramachandran
Secretary, Steering Committee
Filariasis Control Programme
W.H.O.

SCIENTIFIC STAFF

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	Asst. Director	Dr. B. Ravindran, M.Sc., Ph.D.
Clinical	Asst. Director	Dr. Shantanu K. Kar, M.D., D.E.
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	R.O.	Dr. J.P. Patra, M.B.B.S., M.D.
Entomology	Asst. Director	Dr. A.P. Dash, M.Sc., Ph.D., F.Z.S.I., F.I.S.C.D.
Biochemistry	S.R.O.	Dr. N.M. Pattnaik, M.Sc., Ph.D.
Microbiology	S.R.O.	Dr. V.R. Subramanyam, M.Sc., Ph.D.
Pathology	S.R.O.	Dr. G.P. Chhotray, M.D.
Statistics	S.R.O.	Mr. Anil Kumar, M.Sc., M.Phil., D.C.P.

Research Assistants

Mr. Mihir K. Beuria, M.Sc.
Mr. Dasarathi Das, M.Sc.
Mr. A.K. Satapathy, M.Sc.
Mr. Bibhuti Bhusan Pal, M.Sc.
Ms. Jayanti Mania, M.Sc., B.Ed.
Mr. Manoranjan Ranjit, M.Sc.
Mr. A.S. Acharya, M.Sc., M.Phil.

Mr. B. Sahoo - Asst. Librarian

Research Fellows

Ms. K.K. Mohanty, M.Sc.
Ms. Tahziba Hussain, M.Sc.
Mr. Prasanta K. Kar, M.Sc.
Mr. Pramod K. Rana, M.Sc.

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Mr. H.K. Tripathy
Mr. B.N. Sethi

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Mr. P.K. Sahoo
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Mr. H.K. Khuntia

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Mr. R.N. Nayak

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Mr. G.D. Mansingh
Mr. R.K. Patra
Mr. B. Pradhan
Mr. C.S. Tripathy
Mr. S.S. Beuria

Laboratory Attendants

Mr. B.K. Kanhar
Mr. C.R. Samantray
Mr. K.C. Parichha
Mr. N.N. Pattnaik

Field Attendants

Mr. G. Simhachalam
Mr. H.K. Jena
Mr. R.K. Hembram

Animal House Attendants

Mr. S.K. Dash
Mr. A. Senapati
Mr. S.K. Mallick
Mr. S.C. Das

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Mr. B. Sutar	Assistant
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Mr. A.K. Nayak	Jr. Steno
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Mr. A.R. Khan	Driver
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Mr. R.C. Dash	Attendant
Mr. Jaladhar Naik	Sweeper-cum-Attendant
Mr. B. Nayak	Sweeper
Mr. K.G. Samal	Sweeper
Mr. Sankar P. Sharma	Watchman
Mr. M.B. Thappa	Watchman
Mr. R.S. Rai	Watchman
Mr. T. Bahadur	Watchman
Mr. Som Pr. Sharma	Watchman
Mr. R.S. Bahadur	Watchman
Mr. B. Sahoo	Gardener
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