



VECTOR BIOLOGY & CONTROL

Vector Biology & Control Project

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**Assessment of Malaria, Bancroftian Filariasis
and Onchocerciasis Research in Tanzania**

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by

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and

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I. Introduction

Statement of Objectives

1. To brief USAID/Dar es Salaam regarding the objectives, travel plans, outcomes and possible follow-up after the assignment.
2. To evaluate the status of facilities and to review current research and priorities of the National Institute for Medical Research.
3. To work with Dr. Kilama (Director General of the NIMR) and his staff to prepare a list of research priorities and needs for technology transfer and training.
4. To prepare a draft implementation plan for future VBC/JHU assistance to the NIMR.
5. To debrief USAID and VBC.
6. To submit a trip report.

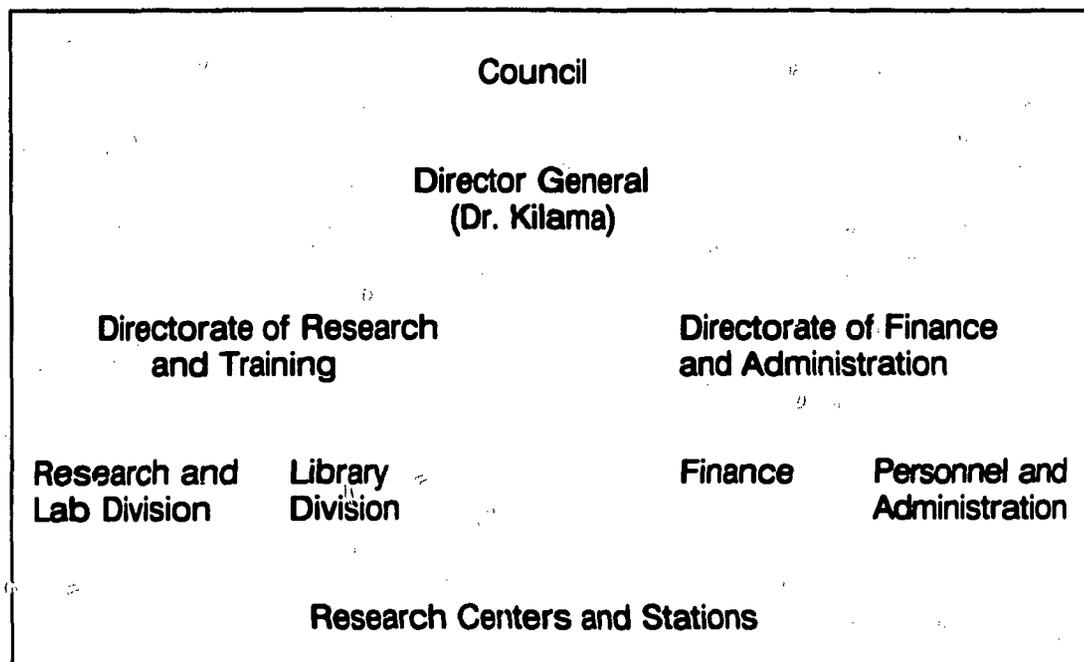
The National Institute for Medical Research

The National Institute for Medical Research (NIMR) is a parastatal organization that controls, coordinates and promotes medical research in Tanzania. The NIMR staff consists of 28 investigators, 18 technical personnel and 10 high-level administrative personnel. The Institute was established by an Act of Parliament in 1979 and was empowered to control and manage all former East African Medical Research Council institutions in Tanzania.

Modern medical research in Tanzania was initiated by the Germans at the end of the 19th century. The British succeeded the Germans after World War I and continued to control research activities in Tanzania into the 1970s.

Institution-based medical research was initiated in the 1940s, when the East African Medical Survey was launched at Malya and the Filariasis Research Unit was formed in Mwanza. These two entities were merged in 1954 to form the East African Institute for Medical Research. The Malarial Unit that was established in 1949 in Muheza was moved to Amani in 1953 and later became known as the East African Institute of Malaria and Vector-Borne Diseases. The Onchocerciasis Control Project and the Helminthiasis Research Unit were started in the early 1970s in Tukuyu and Tanga, respectively. Both of these units are now part of the NIMR.

The organization of the NIMR is outlined below:



The NIMR governing policies and general research agenda are formulated by the NIMR Council, which is composed of members appointed by the Minister for Health and Social Welfare. Council members are selected from specified institutions relevant to health research. The Council Chairman and the Director General are appointed by the President of the United Republic of Tanzania. The Council meets four times per year. Research projects that fall outside the areas approved by the Council must be approved by the Council before studies can be initiated. The present research program for the NIMR, covering the years 1986-1991, is included in the annex.

NIMR headquarters is located in Dar es Salaam and acts as a link between the various centers and stations, the Ministry of Health and Social Welfare, the NIMR Council and the scientific community. NIMR headquarters develops long-range plans and strategies, sets standards and controls finances, staff recruitment and development of the research centers and stations.

The following is a list of the different research centers and stations of the NIMR and a brief outline of the areas of research that are ongoing or planned for each unit:

Amani Medical Research Center
S.G.M. Irare, MD, M.Sc, Ph.D., Director

The center is very active in malarial research and has the facilities to do research on onchocerciasis, Bancroftian filariasis and plague. The facilities at Amani include laboratories, an insectary, a library and a rest house.

Information on Personnel and Facilities can be found on pages 6-9.

Ubwari Field Station

The station is located about 35 kilometers from the Amani Center (which operates the Ubwari Field Station) on the outskirts of Muheza town. Research here focuses on the mosquito vectors of malaria and Bancroftian filariasis. Facilities include laboratories and an insectary.

Tanga Field Station

The Tanga Field Station, which is also controlled by the Amani Center, is located along the coast in Tanga within Bombo Hospital. This station undertakes research on the vectors of Bancroftian filariasis.

Mwanza Medical Research Center
J.B. Rugemalila, M.D., Ph.D., D.P.H., Director

The center undertakes research on schistosomiasis, diarrheal diseases, intestinal helminths, STDs and AIDS.

Tabora Medical Research Station

The station coordinates research on trypanosomiasis throughout Tanzania.

Tukuyu Medical Research Station

Located in southwest Tanzania, the station carries out research on vectors of onchocerciasis.

Muhimbili Medical Research Station

This station focuses its efforts on tuberculosis.

II. Personnel and Facilities at the Amani Medical Research Center

The Amani Medical Research Center is a well-staffed facility that is carrying out a number of research projects, most of which concentrate on malarial control. The NIMR is in the process of implementing a program to bring the staffs of the other centers and stations to full capacity. The following is an outline of the scientific and technical staff of the Amani Center.

Department of Malaria

a) Scientific Staff:

S.G.M. Irare, M.D., Ph.D. M.Sc.

Training: Medical Parasitology

Interest: Malaria chemotherapy

T.K. Mutabingwe, M.D., M.Sc.

Training: Clinical Tropical Medicine

Interest: Malaria epidemiology

A.E.V. Kilimali, Ph.D., M.Sc.

Training: Biochemistry

Interest: Biochemistry of malaria parasites

Miss M.M. Lemnge, B.Sc.

Training: Biochemistry

Interest: Malaria cultures

Mr. A.E.P. Mnzava, B.Sc.

Training: Medical Entomology

(In training at Swiss Tropical Institute at Basel and the London School of Tropical Medicine and Hygiene)

Interest: Cytotaxonomy of sibling species of the Anopheles gambiae complex

Mr. K.J. Njumwa, M.Sc., B.Sc.

Training: Medical Entomology

Interest: Vector ecology - population dynamics

Miss E.O. Lyimo, M.Sc. B.Sc.

Training: Medical Entomology

Interest: Insect control - chemical

Mr. J.N. Ijumba, B.Sc., M.Sc.

Training: Medical Entomology

Interest: Vector ecology - biological control, population biology

Mr. S.M. Magesa, M.Sc., B.Sc.

Training: Medical Entomology

Interest: Not yet determined

b) Technical Staff:

Mr. J.I.K. Mhina

Mr. Msuya

Mr. Mrema

Mr. Malecela

Mr. Rwegoshora

Mr. P. Maggie

Mr. Malima

c) Facilities:

- o Facilities for culturing asexual forms of *P. falciparum*, sterile hood, gases
- o Liquid scintillation analyzer with a computer Unit
- o Bench-top centrifuges

Department of Biochemistry

a) Scientific Staff:

Mr. G.L. Mwaiko, B.Sc.

Training: Biochemistry

(In training at University of Dar es Salaam)

Interest: Seroepidemiology of onchocerciasis

Mr. M.N. Kitundu, M.Sc.

Training: Biochemistry

Interest: Biochemistry of malaria parasites - drug biochemistry

b) Technical Staff:

Mr. R.S. Mtoi

Mr. Mashaka

c) Facilities:

- o HPTLC for malaria drugs detection
- o Slab gel electrophoresis
- o Chromatography
- o Freeze drier
- o Nitrogen facilities for cryo-preservation

Department of Immunology**a) Scientific Staff:**

Mr. Y.G. Matola, M.Sc.
Training: Parasite Immunology
Interest: Malaria Immunology

b) Technical Staff:

Mr. A.R. Mkufya

c) Facilities:

- o Gamma counter for IRMA detection of sporozoites
- o ELISA reader
- o Ultra-low freezer, -80 °C

Department of Helminthology**a) Scientific Staff:**

Miss M.N. Malecela, B.Sc.
Training: Parasitology
Interest: Bancroftian filariasis and onchocerciasis;

Mr. A.I.S. Muro, M.Sc.
Training: Medical Entomology
(In training at London School of Hygiene and Tropical Medicine)
Interest: Sibling species of the Simulium neavei complex

Miss. B. Maaega M.Sc., B.Sc.
Training: Medical Entomology;
(In training at Cornell University)
Interest: Sibling species of the Simulium damnosum complex and dynamics of transmission of onchocerciasis;

b) Technical Staff:

Mr. Machga

c) Facilities:

- o Compound microscopes
- o Dissecting microscopes
- o Facilities for mass rearing of black flies

Common Facilities at the Amani Center:

- o Library; (Mr. M.K. Frank; Mr. J. Gwau)
- o Computer and programs for word processing and biostatistics (Mr. F. Salum)
- o Resthouse - six rooms to accommodate 12 people
- o Animal facilities
- o Insectaries
- o Dark room - Photography
- o Microscopes and dissecting scopes in each department

III. Ongoing Collaborative Activities with Institutions and Agencies from Other Nations

In his presentation at the Fourth Annual Scientific Conference on Malaria Control, organized by the Tanzania Public Health Association and held in Dar es Salaam from 9 to 12 September, 1975, Dr. W.L. Kilama characterized malaria as a critical area for health care efforts in Tanzania. The recommendations from this conference called for recognition of and research on the complex nature of the vector control measures, chemotherapy programs and chemoprophylaxis efforts that will be necessary to control malaria in Tanzania.

Based on these recommendations, the National Institute for Medical Research (NIMR) was established in 1979. Under the directorship of Professor W.L. Kilama, the Institute's mandate was to organize, coordinate, manage, monitor and direct research and control programs for malaria and other vector-borne diseases in Tanzania. It was clear that in order to implement the NIMR program, Tanzania would need to train specialists in vector biology and control, clinical parasitology, basic parasitology, parasite immunology, epidemiology and biostatistics. To implement such an ambitious research and training program, help was solicited from the World Health Organization and other European and North American agencies and governments. The NIMR program is well under way today. Some specialists have already been trained in the above fields and others are receiving the appropriate training.

The countries and organizations currently involved in collaborative research with Tanzanian scientists and the general areas of research are outlined below:

1. **World Health Organization** - especially the TDR special program, from which Tanzania leaders received not only grants for institutional strengthening but also direction in proposed disease control activities;
2. **Great Britain** - collaborative activities in vector control studies, which include mechanical/chemical personal protection by using pyrethrum-impregnated bed nets and chemical control by spraying human dwellings in order to reduce prevalence, incidence and intensity of malaria infection;
3. **Switzerland** - acquiring baseline data on transmission of malaria in a rural area of Ifakara, which can be used in a future malaria vaccine evaluation;

4. **Holland** - collaborative work with Switzerland in Ifakara on malaria transmission blocking vaccine;
5. **Italy** - assistance in evaluation of malaria control project using ELISA and IRMA and other immunological techniques;
6. **Japan** - source reduction and chemical control of malaria and filariasis vectors in the coastal region at Tanga and Dar es Salaam by spraying with fenithrothion;
7. **United States of America** - USAID, chemical control of malaria vectors in Zanzibar.

IV. Evaluation of NIMR Programs for the Control of Vector-Borne Diseases in Tanzania

A. Malaria

1. Malaria - The Problem

Malaria is one of the primary causes of morbidity and mortality in Tanzania. Malaria is hyperendemic and holoendemic in more than three-fourths of the Republic. Very few areas are completely free of malaria transmission. This disease places limitations on the rate of socio-economic development of Tanzania.

Of the three human malaria parasites found in Tanzania (Plasmodium falciparum, P. malariae and P. ovale), P. falciparum is the most dangerous and detrimental to human populations.

Four mosquito species, the principal vectors of malaria in Tanzania, have a regional distribution. From the Anopheles gambiae complex, three species are important vectors: (1) Anopheles gambiae s.str. is a particularly important vector that occurs in the inland areas where the humidity is high; (2) An. arabiensis is found in arid and semi-arid areas and (3) An. merus, which occurs in the coastal zone of Tanzania and on the island of Zanzibar. The fourth species, An. funestus, plays a larger role in transmission of malaria during the dry season because of its breeding in permanent swamps in the country.

2. Ongoing Research at the National Institute for Medical Research.

- a) Monitoring the sensitivity of Plasmodium falciparum to various antimalarial drugs in the country.

P. falciparum shows a considerable resistance to chloroquine and other antimalarial drugs, such as amodiaquin, Fansidar, quinine and mefloquine; however, the most alarming is the resistance of P. falciparum to chloroquine. According to Irare (1985), resistance to chloroquine tested in vivo was as high as 41 percent and in vitro tests show resistance to be as high as 56 percent in some areas of Tanzania (Table 1). The monitoring of drug resistance of P. falciparum includes detection, measuring and mapping of resistance in eight zones of Tanzania: Mwanza, Moshi, Mbeya, Dodoma, Newala, Amani, Dar es Salaam and Ifakara. Both in vivo and in vitro tests are done at two year intervals. The in vivo test is a 7-day test involving schoolchildren. The in vitro test is a 24-hour test and it is done on cultures of infected blood in which growth of trophozoites is observed in the presence of different concentrations of antimalarials.

Table 1. Distribution of Chloroquine and Fansidar Resistance in Tanzanian Schoolchildren

Region	Locality/ District	Percentage Resistance			Year
		<u>In vivo</u> (25mg/kg)	<u>In vitro</u> (1.14)	<u>Fansidar</u> <u>In vivo</u>	
Mara	South	0.0	3.5	-	1981
Tanga	Korogwe	39.5	45.5	0.0	1982
	Pangani	6.0	41.4	0.0	1982
	Tanga	31.8	51.5	0.0	1982
	Muheze	12.6	20.5	0.0	1982
Kilimanjaro	TPC Moshi	14.3	40.5	-	1983
Coast	Gonja	19.0	-	5.3	1983
	Kibaha	20.0	50.0	0.0	1983
Morogoro	Kilosa	12.2	18.8	-	1984
	Morogoro	8.4	12.5	0.8	1984
Mbeya	Kyela	7.7	8.3	0.0	1984
Arusha	Hanang	27.5	-	0.9	1984
Dodoma	Dodoma	18.0	56.0	0.0	1985
	Mpwapwa	41.0	62.0	0.0	1985
Singida	Singida	27.0	62.0	0.0	1985
	Manyoni	29.0	54.0	0.0	1985
Mtwara	Mtwara	14.0	48.0	2.0	1986
	Newala	22.0	42.0	3.0	1986
Ruvuma	Songea	16.0	38.0	2.0	1986
	Tunduru	19.0	29.0	0.0	1986

b) In vitro culture.

A continuous culture system for P. falciparum has been established in order to identify and collect strains of P. falciparum, adapt them to laboratory culture conditions and subsequently study their susceptibility and refractoriness to antimalarial drugs.

c) Malaria chemosuppression in pregnant women.

Chloroquine chemosuppression and chemoprophylaxis (5 mg/kg) was shown to be effective and safe for use by pregnant women. Since the prevalence of parasite resistance to chloroquine is high, new research is underway to find alternatives to chloroquine for the treatment of pregnant woman.

d) Human Red Cell Genetics in Relation to the Management of Malaria in Tanzania.

This study surveys for the prevalence of sickle cell trait and G-6PD in areas of known chloroquine resistance to P. falciparum and assesses the relative risk of using such antimalarials as primaquin to treat individuals with these genetic traits.

e) Entomology, Vector Control and Epidemiology of Malarial Infections.

Most of these studies are carried out at the Muheza Field Station. This program is designed to control malaria by reducing vector-human host contact. Five villages were chosen for this research. In two villages, all residents are provided with permethrin-impregnated bed nets. Conventional chemical vector control is used in two other villages by spraying houses with DDT indoors. The last two villages serve as controls. Density of mosquito population, parity and sporozoite rates are recorded every two weeks. Malaria prevalence and intensity of infection is monitored in schoolchildren. This project is far from completion, but the one-year data show a significant decrease in population density of biting Anopheles, a decrease in sporozoite rates and a decline in the intensity of infection. Prevalence of malaria, however, remains unchanged. It will be interesting to see whether prevalence of malaria will decrease if vector control continues for the next one to two years.

3. Facilities and Personnel

The NIMR has a very active malarial research program. A large percentage of the work is being done at the Amani Medical Research

Center. The personnel who conduct malarial research at the Amani Center are outlined on pages 6-9.

4. Critical Areas of Research and Assessment of Need

Malaria is a widespread and extremely important area of public health concern in Tanzania. The critical areas for research are those that relate to the control of transmission and infection. These include research in vector biology, transmission dynamics, vector control and chemotherapy/chemoprophylaxis of patients.

5. Possible Areas of NIMR/JHU Collaboration

a. Short-term

An accurate assessment of the rate of transmission in different regions of Tanzania will be vital to efforts to identify areas where control measures are most appropriate and to monitor the efficacy of the control programs that are undertaken. The facilities, equipment and personnel are available at the Amani Center for the immunological detection of sporozoites in mosquitoes. However, because of problems in receiving quality reagents as well as other limitations, this assay system is not functioning at the level required to monitor infected vectors. A possible area of NIMR/JHU collaboration could be the transfer of the most up-to-date technology for detection of sporozoites in mosquitoes to the investigators at the Amani Center. This technology transfer could be achieved through an in-country training program in which JHU faculty members Dr. John Beier and Dr. Nirbhay Kumar would visit Amani. This team could establish mechanisms for the most efficient, timely method of exchanging reagents, for ensuring that the personnel of the Amani Center have the proper background information needed to perform and maintain the sporozoite detection system, and for offering technical assistance with the assay procedures.

It should be noted that the same basic technology and information transferred by Drs. Beier and Kumar for sporozoite detection can be used in mosquito blood meal analysis and that the technical ability to do this type of assay can be installed along with the sporozoite assay.

Also in the area of parasite detection in the vector, at some point it may be appropriate to explore the possibility of using stage-specific DNA probes to monitor parasite development in the mosquito.

b. Long-term

There are a large number of research areas where collaboration between NIMR and JHU could be established. These include research on transmission dynamics, vector competence, epidemiology of malaria in the human host, the impact of malaria infection and chemotherapy on the immune response, the impact that other parasitic infections have on the course of malaria and the genetic basis for drug resistance, just to mention a few.

JHU faculty members Drs. John Beier, Nirbhay Kumar and Clive Shiff are acknowledged experts in these areas of parasite research and are interested in initiating collaborative research projects with Tanzanian investigators.

B. Onchocerciasis

1. Onchocerciasis - The Problem

The last comprehensive survey of onchocerciasis in Tanzania was conducted in the late 1960s (Wegesa 1970). At that time, six foci of onchocerciasis had been identified, with major endemic areas in Mahenge, the Eastern and Western Usambaras of the Amani district, and Liuli in the Ruvuma Region. Within the six foci, it was estimated that 320,000 of the 1 million inhabitants would harbor onchocercal infections. The prevalence of infection in some areas exceeded 60 percent. As recently as 1973, it was reported that for schoolchildren living in these endemic foci, the prevalence of Onchocerca infections ranged from four to more than 80 percent (Abaru 1973).

Pruritus, skin depigmentation, atrophy of skin, onchocercomata and hanging groin appear to be the most common manifestation of onchocerciasis in Tanzania. Eye pathology, a common manifestation of Onchocerca volvulus infections in other parts of Africa, does not appear to be a widespread problem in Tanzania. However, it should be noted that there has been no comprehensive survey for Onchocerca-caused eye damage and blindness in these areas and that the degree of ocular damage due to Onchocerca volvulus infections may be seriously underestimated. The most debilitating aspects of Onchocerca infections in Tanzania are filarial fevers and intense, prolonged itching, both of which are severe enough to prevent patients from carrying out their normal daily activities.

Three species of Simulium have been reported to transmit O. volvulus in Tanzania: S. woodi, S. damnosum and S. neavei.

These data and observations indicate that onchocerciasis has been a significant problem in Tanzania. Since no onchocerciasis control measures

have been undertaken since the last major survey, it is likely that onchocerciasis remains a significant public health problem in Tanzania.

2. Ongoing Research at the National Institute for Medical Research

The ongoing research activities of the NIMR toward the control of onchocerciasis is centered on studies of the Simulium vector. Two individuals are being trained at the advanced graduate level as vector biologists to study the taxonomic and transmission dynamics of Simulium species that carry Q. volvulus. The research projects required to complete the degree programs are being conducted in Tanzania.

At present, there are no research activities addressing problems in the epidemiology, parasitology and immunology of Q. volvulus infections in human populations.

3. Facilities and Personnel

The NIMR has a research center or station in or near two of the major foci of onchocerciasis in Tanzania -- the Amani Center and the Tukuyu Station. The Tukuyu Station has been dedicated to carrying out research on the Simulium vector in that area. There are no ongoing projects on Q. volvulus at the Amani Center, but these facilities could easily serve as a laboratory station from which research and control measures could be based. The Amani Center is in the immediate area of a major focus of onchocerciasis. The center appears to have adequate space to house a major research/control effort. Funds will be needed to equip the laboratory for parasitological, biochemical and immunological analysis of samples.

As mentioned above, two NIMR staff members are being trained in vector biology. At this time, no member of the NIMR staff is working on the parasitology or immunology of Q. volvulus infections in humans.

4. Critical Areas of Research and Assessment of Need

Since efforts have already been undertaken by NIMR to train personnel and gain information about the vector, the next critical area would be gaining the epidemiological, parasitological and immunological information necessary to design programs that would lead to control of the disease in the human host. The critical areas for onchocerciasis research in Tanzania are:

- a. Defining the scope of the problem. A reevaluation of the epidemiological parameters that define onchocerciasis in Tanzania, including information on the geographic distribution of the disease, the prevalence of infection, the intensity of infection and the

extent of pathology. These data can be used in the rational design of control strategies for onchocerciasis.

- b. Designing and implementing a program to control onchocerciasis in Tanzania. As outlined below, a strategy employing ivermectin may be appropriate in this regard.

It should be noted that both of these areas of research are included in the NIMR Council's approved research programs for the 1986-1991 quinquennium.

In order to do productive work in both of the areas mentioned above, it will be necessary to train personnel. Formal training of scientific and technical staff in the theory and practice of epidemiological survey techniques, parasitology and immunology would appear to be the most desirable course of action. The School of Hygiene and Public Health at The Johns Hopkins University has strong training programs in all of these areas and, assuming funding can be identified, could offer assistance in training personnel in onchocerciasis research.

5. Possible Areas of NIMR-JHU Collaboration

a. Short-term

Since the staff members who will work on the Simulium vector are still being trained and no personnel have been identified to carry out parasitological/immunological research in Onchocerca infections at this time, it is difficult to define topics for short-term NIMR-JHU collaboration in these areas.

b. Long-term

It would appear from the status of onchocerciasis in Tanzania that chemotherapeutic intervention could result in a significant decrease in morbidity and a reduction in the amount of transmission of O. volvulus in endemic areas. A possible area of collaboration between the NIMR and JHU could be the design and implementation of an onchocerciasis control program employing ivermectin treatment of infected individuals to reduce the number of microfilarial available for transmission and the larvacidal treatment of waters used as breeding sites by the vectors. Evaluation of the efficacy of such a program would require the coordinated efforts of personnel working in the areas of epidemiology, vector biology/transmission dynamics, parasitology and immunology.

The circumstances surrounding onchocerciasis in Tanzania, especially the focal nature of the disease, appear to lend themselves quite well to chemotherapeutic intervention with ivermectin. In

general, ivermectin treatment would be desirable because it is a quick, safe and effective way to reduce the number of microfilaria, which should reduce morbidity and at the same time reduce the rate of transmission of the parasite. The available data indicate that the level of microfilaria is generally low in Tanzania, thus reducing the chances for the severe side reactions that afflict a certain percentage of the patients receiving ivermectin. Ivermectin is administered as a single dose given once every year, which reduces the logistical problems often associated with drug therapy for onchocerciasis. In addition to the immediate and long-term benefits to the human host, ivermectin treatment may also have an impact on transmission through its effects on the vector. Imbibing blood containing ivermectin may reduce the viability of the black fly vector, thus reducing the number of infective bites and decreasing the number of progeny produced as a result of a human blood meal.

In the field of onchocerciasis, JHU faculty can offer expertise and assistance in the areas of immunology (Dr. Alan Scott), transmission dynamics (Dr. Milan Trpis) and epidemiology (Dr. Alfred Buck).

C. Bancroftian Filariasis

1. Bancroftian Filariasis - The Problem

Bancroftian filariasis is highly endemic along the coast of Tanzania. The parasite is transmitted in both urban and rural areas; in the former by Culex quinquefasciatus and in the latter by Anopheles sp. The clinical symptoms include filarial fever, elephantiasis and a high prevalence of individuals with hydrocele.

2. Ongoing Research at the National Institute for Medical Research

As part of a project designed to control vectors of malaria and Bancroftian filariasis in the coastal regions at Tanga and Dar es Salaam by chemical spraying and source reduction, surveys are being conducted to determine the impact that these measures have on the filariasis transmission in urban areas.

No research is being done in the areas of parasitology and immunology of Bancroftian filariasis at this time.

3. Facilities and Personnel

The Amani Medical Research Center, with its Tanga and Ubwari Field Stations, is located within the endemic area for Bancroftian filariasis.

Please refer to the section on personnel of the Department of Helminthology of the Amani Medical Research Center for details on the staff for filariasis research.

4. Critical Areas of Research and Assessment of Need

The critical areas for research in Bancroftian filariasis are essentially the same as for onchocerciasis

- a. Epidemiological assessment of the prevalence and intensity of infection in the endemic areas.
- b. Designing a program that would result in a reduction in parasite load and a decrease in the rate of transmission in both rural and urban areas. Again, an ivermectin treatment program may prove to be the most effective and appropriate course of action.

5. Possible Areas of NIMR-JHU Collaboration

a. Short-term

Until personnel can be identified to work in the area of Bancroftian filariasis, it would be premature to identify areas for short-term collaborative projects.

b. Long-term

As with onchocerciasis, it appears that the area where a collaboration between the NIMR and JHU could be most productive would be in the area of design and implementation of a chemotherapy-based control program for Bancroftian filariasis. Ivermectin, which has been shown to be an effective and safe microfilaricide in patients infected with *W. bancrofti*, would be the drug of choice for such a program. The advantages of this drug are essentially the same as those outlined above for onchocerciasis.

In the field of Bancroftian filariasis, JHU faculty can offer expertise and assistance in the areas of immunology (Dr. Alan Scott), transmission dynamics (Dr. Milan Trpis), and epidemiology (Dr. Alfred Buck).

D. Schistosomiasis

We had no opportunity to assess the schistosomiasis situation in Tanzania. schistosomiasis at this time.

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Chronology

- Aug. 14-15** Travel from Baltimore to New York to Geneva.
- 16-17** Travel from Geneva to Dar es Salaam; briefing at the USAID Office in Dar es Salaam; meeting with the health officer, Ms. Paula A. Tavrow; travel from Dar-es-Salaam to Arusha.
- 18-23** Meeting with Professor W.L. Kilama, Director General, National Institute for Medical Research, and Dr. S.G.M. Irare, Director NIMR Malaria Research Station at Amani, to discuss research activities of NIMR and assistance in research that could be provided by the Johns Hopkins University through the Vector Biology and Control Project.
- 24** Travel from Arusha to Amani.
- 25** Discussion of research programs and recent research activities of the Malaria Research Station at Amani and Muheza with Dr. S.G.M. Irare, Director of the Malaria Research Station, NIMR.
- 26** Visiting the Field Station of the Malaria Control Project at Muheza and discussing problems of vector control related to changes in prevalence and intensity of infection with Plasmodium falciparum in human populations as well as changes in sporozoite rates.
- 27** Travel from Amani to Dar es Salaam.
- 28-31** Further discussions on malaria, filariasis and onchocerciasis problems with Dr. W.L. Kilama and Dr. S.G.M. Irare; writing report on our mission in Tanzania.
- Sep. 1** Meeting with Dr. Kilama and staff at the NIMR headquarters in Dar es Salaam to prepare a list of priorities of critical research areas and needs for technology transfer.
- 2** Meeting with USAID representatives Ms. Paula A. Tavrow, Dr. Clive Shiff and the General Director of NIMR, Dr. W.L. Kilama; debriefing at USAID Mission in Dar es Salaam.
- 3-4** Travel from Dar es Salaam to Baltimore.

Annex 1

National Institute for Medical Research

Background Information and Approved Research Program 1986-91

NATIONAL INSTITUTE FOR MEDICAL RESEARCH

Telephone 30770
Telegrams: MEDSEARCH



P.O. Box 9653
Dar es Salaam
Tanzania

Your Ref:
Our Ref: USAID/I/7

Date 5th May, 1988

Dr. Clive Shiff
USAID Mission
DAR ES SALAAM

Dear Dr. Shiff,

Please refer to our conversation in my office, which were also attended by this Institute's Research and Training Officer and one Research Scientist (Dr. T.K. Matabingwa).

For your information and possible use, I am attaching some background information on this Institute, its staff list, and our approved research programme for 1986-1991.

As discussed, the Institute wishes to train researchers in a number of lines, particularly in epidemiology and biostatistics. Other important areas would include for example behavioural sciences, microbiology, parasitology, entomology, etc.. The required training would be at the masters or doctoral level. In many of these lines, we might be able to secure sponsorship from e.g. WEO/TDR, STI, etc..

The outline of the Institute's approved research program identifies areas in which our staff are working; although some of the projects are yet to start. We would wish to establish working links in these or related areas. As discussed the Institute would benefit from knowing what areas on your side are open for collaboration.

Lastly may I say how happy I was to see you again. Hopefully from your visit you have identified our weaknesses and strength - if any.

Looking forward to future collaboration.

Yours sincerely,

Prof. W.L. Kilama
DIRECTOR GENERAL

enclosure as stated above

WLE/aak.

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INTRODUCTION

The National Institute for Medical Research was established by Act No. 23 of 1979, which enables the Institute to coordinate, manage, undertake, promote, train for, monitor, control and register medical research especially that undertaken in Tanzania. The Institute became officially functional in October 1980.

The first NIMR quinquennal research programme covered the years 1981 to 1986, and was for the most part a preparatory phase during which great emphasis was placed on manpower recruitment and training, establishment of managerial norms, and undertaking research within the given limited capabilities.

The diseases covered during the first five years were malaria, schistosomiasis, onchocerciasis, bancroftian filariasis, plague, tuberculosis and trypanosomiasis.

During the second quinquennium emphasis will continue to be placed on the development of research manpower and providing/conducive research a environment. Besides the diseases listed for research during the first quinquennium, additional areas for research will include diarrhoeal diseases, intestinal helminthes, and sexually transmitted diseases.

In the following pages we outline the research programmes and projects to be undertaken by each of the Institutes' constituent centres and stations, during the years 1986-1991.

1. AMANI

1.1. MALARIA

1.1.1. Protozoology

- 1.1.1.1. Detection, measuring, mapping and monitoring of the sensitivity of Plasmodium falciparum to various antimalarial drugs in the country.

This is an on going programme intended for the evaluation of the parasitological response of falciparum malaria to antimalarials all over the country. Both in vivo and in vitro tests are undertaken. Drugs under current evaluation include chloroquine, amodiaquine, Fansidar, quinine and mefloquine (in vitro only). Monitoring will be limited to several indicator areas, and where regional health authorities are willing to collaborate.

- 1.1.1.2. Continuous Culture of Plasmodium falciparum

This centre intends to collect malaria parasite isolates from the field with different drug responses and adapt them to culture. These isolates will be further characterized in the laboratory and studied on a range of drugs. The same strains will be induced to produce gametocytes and studied for their easiness or refractoriness to infect mosquitoes in the laboratory. Another set of experiments involving such strains will include biochemical changes in the host red blood cells and the parasites in relation to their drug response.

- 1.1.1.3. Studies of Optimum Treatment Schedules for Plasmodium falciparum with Alternative Drugs in Areas of Chloroquine Resistance.

These studies which will be carried out in an area of Tanzania with documented chloroquine resistance, intend to look into and establish the efficacy of:

- a) the new drug mefloquine, used alone or in combination with other drugs;
- b) the traditional potent schizontocidal drugs (i.e. chloroquine, amodiaquine, quinine) either used alone or in combination with other drugs;

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- c) Fansidar used alone or in combination with other potent schizontocides.

It is hoped that this will identify satisfactory drugs and drug schedules for the treatment of chloroquine resistant malaria. This should later lead to the selection of the cheapest and acceptable regimens which offer the lowest risk of adverse effects and the emergence of resistance to new drugs.

1.1.1.4 Malaria Chemossuppression in Pregnant Women.

Pregnant women constitute a major group vulnerable to malaria attacks. Previously chloroquine chemossuppression/chemoprophylaxis at 5 mg/kg weekly was advocated, but the advent of chloroquine resistance has made it almost useless. There is therefore pressing need to search for alternatives to chloroquine, within the prevailing epidemiological conditions.

1.1.1.5 Human Red Cell Genetics in Relation to the Management of Malaria in Tanzania.

This study will survey for sickle cell and G-6PD in areas of known endemicity for chloroquine-resistant P. falciparum, with the ultimate aim of assessing the risk of using such antimalarials as primaquine.

1.1.2. Immunology/Entomology

1.1.2.1 Application of radioimmunoassay (RIA) and ELISA in the detection of sporozoites in mosquitoes.

One of the most important epidemiological parameters for the assessment of malaria transmission is the sporozoite rate. The conventional method for this determination entails individual salivary glands dissection of freshly killed/captured female anophelines and the subsequent microscope examination for the sporozoites. This is laborious and suffers several limitations. Recently two tests (immunoradiometric assay and ELISA) have been developed. These are highly sensitive and

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species - specific. The Amani Centre which determines the sporozoite rates in various epidemiological situations in Tanzania proposes to apply these newly developed sporozoite immunoassays in the detection and identification of human malaria sporozoites in the mosquito vectors. Future investigations would aim at using these or similar tests in epidemiological evaluations in Man.

1.1.3. Entomology

1.1.3.1. Field Trials of Vector Control.

There has been a long history of field trials of residual house-spraying for malaria vector control in Africa. Studies in different regions have varied greatly in their degree of success. Very recently it has been contemplated that personal protection may be more appropriate on a community wide scale. Studies in Tanzania on permethrin-impregnated nylon bed-nets have indicated that impregnation not only restores effectiveness to a torn net, but also inflicts considerable mortality on mosquitoes which come to feed. It is moreover proposed to reinvestigate residual house-spraying and compare its efficiency with that of community use of permethrin-impregnated bed-nets.

1.1.3.2. Study of the Malaria Vectorial System in Tanzania in relation to different epidemiological stratifications.

One of the reasons for failure of some malaria control programmes in Africa was the lack of knowledge on the existence of heterogeneity of the An. gambiae complex vector population. Therefore the demonstration of heterogeneity of the vector population in any area is a pre-requisite for the planning of vector control measures. The present study is intended to update our knowledge on malaria vectorial system with regard to different epidemiological stratifications. In addition, it will also provide base-line data for the future planning of appropriate vector control strategies in the country.

1.1.3.3. The Control of Malaria and Filariasis Vectors.

The control of mosquito vectors of malaria and/or filariasis is problematic, and mosquito-borne diseases are rampant. There is therefore need to develop new tools, and to test those available against mosquitoes. These studies will test and compare under varying settings:

- naturalistic vector control measures;
- new insecticides as and when they become available;
- biocontrol agents;
- the potential role of community participation in vector control.

1.1.3.4. Studies on the "Competitive exclusion" of Anopheles merus.

Recent studies in Tanzania have shown that An. merus extends further inland sometimes up to about 200 km. from the Tanzania coast. However its frequency in such areas is very low. Factors governing its distribution and frequency are yet to be established. Among them is the hypothesis that An. merus is competitively excluded by An. gambiae and An. arabiensis in areas of sympatry. It is therefore proposed to study this aspect in view of controlling malaria by eliminating vectors (An. gambiae and An. arabiensis) and introducing a less vector specie (An. merus).

1.2 BANCROFTIAN FILARIASIS

1.2.1. Parasitology

- 1.2.1.1 Testing the efficacy of new filaricides. Diethylcarbamazine (DEC) the drug used in the chemotherapeutic control of bancroftian filariasis was discovered during the 1940's, and its use is problematic. Recent research efforts elsewhere have focused on the development and testing of new filaricides - e.g. centperazine, ivermectin, flubendazole, etc... NIMR, Amani Centre intends to test new filaricidal drugs locally when they become available.

1.2.1.2. Biology of *W. bancrofti*

W. bancrofti in Tanzania is transmitted by both *Anopheles* sp. and *Culex quinquefasciatus*. Moreover there are variances in the pathology caused, and whether these relate to the human host or parasite is not known. In this study *W. bancrofti* will be studied, focusing on the elucidation of zymodemes.

1.2.2. Entomology

The only planned project here is the same as that listed under 1.1.3.3.

1.3. ONCHOCERCIASIS

1.3.1. Parasitology

1.3.1.1 Medico-socio-economic importance of onchocerciasis in Tanzania.

The distribution of onchocerciasis in Tanzania is well documented. However, the medic-socio-economic importance of the disease has not yet been established. It is therefore recommended that before embarking on other major investigation on the disease, this aspect should first be clarified. This work will then establish the:

- a) medical (especially ophthalmological) importance of the disease at selected areas of Tanzania;
- b) stratification of Tanzania as to the severity or otherwise of onchocerciasis;
- c) socio-economic importance of the disease in those areas;
- d) intensity of the infection in the affected people;
- e) immune response in the target population.

1.3.1.2 Efficacy of newer filariacides

Currently Diethylcarbamazine is the only drug used in the treatment of onchocerciasis—the use of this old drug, may also be accompanied by severe side effects, which has dictated development of newer drugs e.g. ivermectin. The Amani Medical Research Centre, intends to test these new drugs when they become available.

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1.3.1.3. Identification of Onchocerca volvulus

O. volvulus is transmitted by various Simulium sp. in various geographical areas in Tanzania. These vectors, may also harbour other Onchocerca sp. whose separation from O. volvulus on morphological grounds may be rather difficult especially during early larval instars. This study aims at developing or testing simpler identification techniques, e.g. a biochemical key. Further studies would aim at establishing biochemical differences between parasite populations.

1.3.2 Entomology

1.3.2.1. Biology of Simulium onchocerciasis vectors

This study will investigate the:

- bioecology of Simulium damnosum in various parts of Tanzania;
- susceptibility of S. damnosum larvae to various larvicides
- establishment of S. damnosum laboratory colonies.

1.3.2.2. The identification of vectors and transmission dynamics of onchocerciasis in Tanzania.

Although considerable entomological knowledge on Tanzanian Simulium vectors of human onchocerciasis exists, it is still not possible to identify these vectors accurately to the species level. During the quinquennium, efforts will be invested in:

- identifying S. damnosum vector species using cytotaxonomic and biochemical techniques;
- assessing the intensity of biting and transmission of O. volvulus by calculating for each vector species the:
 - monthly and annual biting rates;
 - monthly and annual transmission potentials;
 - relation to seasonal human activities;
 - factors influencing vector distribution and disease transmission.

2. MWANZA

2.1 SCHISTOSOMIASIS

The broad objective will be to test various low cost methods for field investigation of the disease particularly for:

- 1) its quantitative diagnosis;
- 2) demonstration of its public health importance;
- 3) identification of intermediate snail hosts and transmission sites;
- 4) evaluation of various methods for the control of the disease and its transmission;
- 5) evaluation of new antischistosomal drugs for tolerance, compliance and efficacy;
- 6) evaluation of various logistics for optimum utilization of community participation in the control of the disease.

2.2. INTESTINAL HELMINTHIASES

The research programme on intestinal helminthiases, will have the following objectives:

- 1) establishing the public health importance of various intestinal helminthiases;
 - 2) identification of communities with moderate to severe problems of hookworm anaemia;
 - 3) evaluation of the effects on prevalence and intensity from regular standard treatment of hookworm anaemia with anthelmintics and iron at the lowest levels of FHC services;
 - 4) evaluation of control of ascariasis through targeted chemotherapy;
 - 5) evaluation of the available and new anthelmintic drugs for broadspectrum activity against the endemic helminthiases; and
 - 6) evaluation of various logistics that could be utilized for effective primary health care control of the transmission of the endemic helminthiases, including sanitary interventions.
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2.3. DIARRHOEAL DISEASES

The Centre's research objectives in diarrhoeal diseases will include:

- 1) search for improved formulations of oral rehydration solutions, their clinical and community trials, and their delivery logistics;
- 2) identification of diarrhoeal related factors having a bearing on maternal and child care, water supplies, and environmental sanitation;
- 3) evaluations of dietary interventions during and after diarrhoea that will best reduce the nutritional damage resulting from diarrhoea, with special reference to breast-milk formula, and semi-and solid foods;
- 4) clinical trials of new antidiarrhoeal drugs with antisecretory and/or absorptive properties;
- 5) factors related to the effectiveness of measles vaccination; and
- 6) local case prevalences by aetiological agent to facilitate FHC control of the diarrhoeal diseases.

2.4 SEXUALLY TRANSMITTED DISEASES

The broad objective for the research programme on STDs, would be to monitor the spectrum of these diseases on high risk groups consisting of the sexually promiscuous bar maids and prostitutes. The specific objectives will be:

- 1) identification of the locally prevalent STDs;
 - 2) clinical trials of antimicrobial drugs to determine those giving optimum efficacy;
 - 3) sensitivity testing on H. gonorrhoeae isolates against available antibiotics, and
 - 4) collaborative studies on the local epidemiology of AIDS.
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