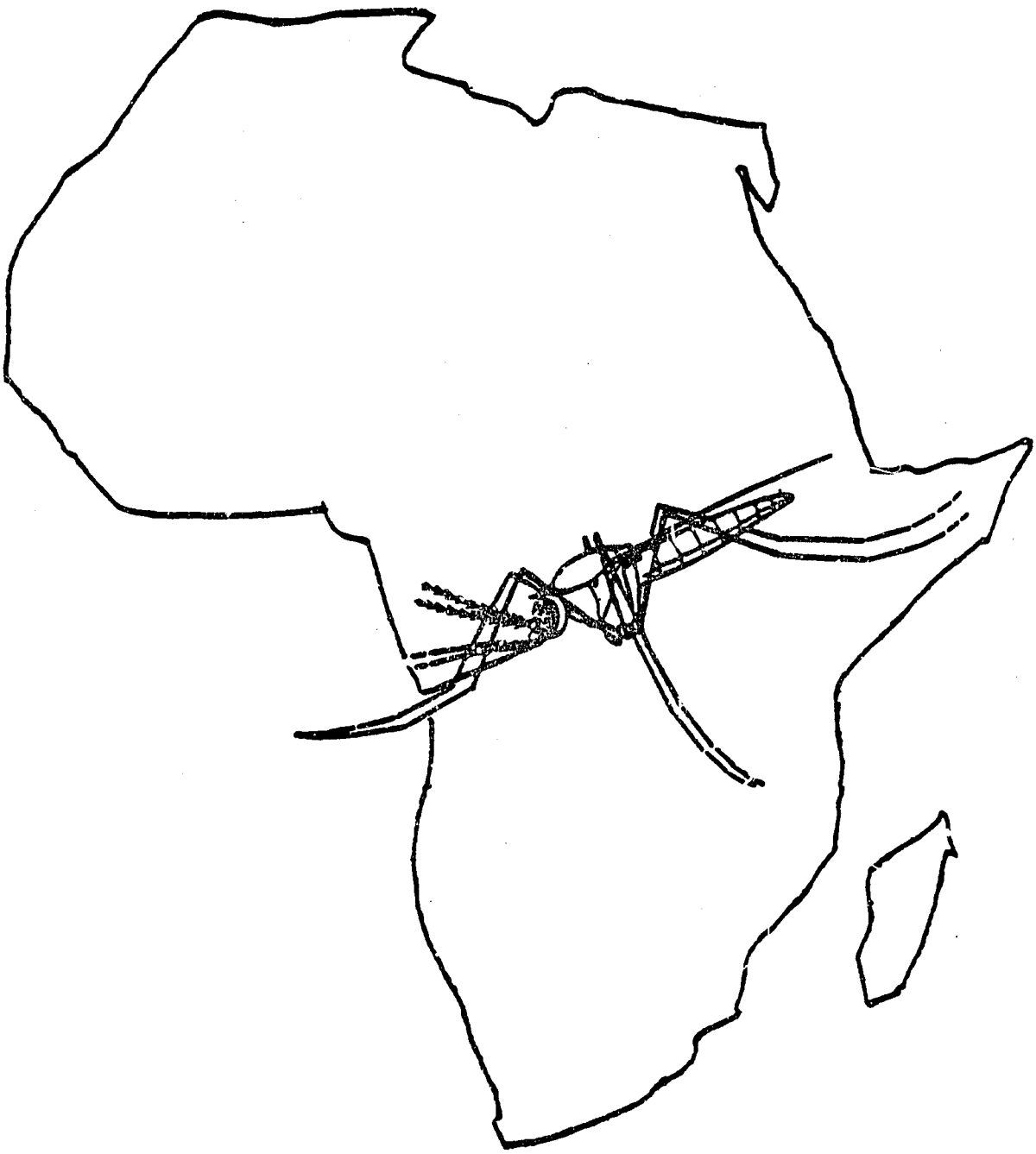
PN-AAN-439/62
ISN-31256

MANUAL ON

MALARIA CONTROL IN PRIMARY HEALTH CARE IN AFRICA



Bureau for Africa
Agency for International Development
Washington, D.C. 20523

December 1982

MANUAL ON MALARIA CONTROL

IN PRIMARY HEALTH CARE

IN AFRICA

Produced for the Bureau for Africa, Agency for International Development, under ADSS Contract AID/DSPE-C-0053, by the American Public Health Association, 1015-15th Street, N.W., Washington, D.C. 20005.

12/82

MALARIA CONTROL IN PRIMARY HEALTH CARE

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FOREWORD

This manual examines the degree to which a malaria control program can be implemented within the framework of a national Primary Health Care system, and attempts to indicate the relative costs, in money and manpower -- trained manpower -- which are inherent in each of several levels of program activity. It indicates which kinds of malaria control lie outside the scope of Primary Health Care. It is pragmatic: evaluate the available malaria problems and the assets available, then adopt the best control program which is affordable, and, to the maximum extent possible, capable of being carried out within PHC.

Some of the concepts involved in a malaria control effort conducted within a PHC framework (and recommended in this manual) represent marked departures from previously accepted practice. For example, the unquestioned administration of a single dose of the chosen antimalarial drug in an amount sufficient to kill all *P. falciparum* malaria parasites in the body of the patient *solely on the basis of fever*, without laboratory confirmation that the fever is malaria-related, breaks new ground.* Similarly, the manual's recognition that wide-spread chemoprophylaxis is frequently not feasible within the resource constraints of national health budgets may appear inconsistent with the position set forth in highly regarded textbooks. Other departures from "conventional practice" are to be noted.

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* It must be acknowledged that the manual's prescription of single-dose treatment of symptomatic malaria, without laboratory confirmation of the presence of malaria parasites, is keyed to the fact that the overwhelming majority of malaria in Africa is caused by one malaria parasite -- *P. falciparum* -- the most dangerous of the four malaria parasites. *P. vivax*, less dangerous, is rarely encountered in Africa, although it is common in Asia. Single-dose treatment at the level of 10 mg. of chloroquine (base) per kilo of body weight, up to a maximum of 600 mg., is normally blood-clearing for *P. falciparum* infection; relapse is possible after single-dose treatment of *P. vivax*. The savings in manpower, in equipment and in training requirements made possible by an adequate single-dose treatment of all symptomatic but unconfirmed malaria warrant the assumption that *all* African malaria is caused by *P. falciparum*. Should experience in any area demonstrate an appreciable percentage of *P. vivax* infection, it would be necessary to consider a regimen of as much as 1500 mg. of chloroquine (base) over a three-day period.

A group of more than 50 expert participants assembled from around the world reviewed the first draft of this document and debated the major issues until consensus was reached. The document was revised to incorporate their conclusions and recommendations,* and may therefore be said to represent the current "state of the art" with respect to malaria control activities that can be pursued within the context of primary health care systems.

Some of the malaria control tactics described in this manual -- and in particular, those in Chapter IV -- should not be confused with the ultimate in what can be done to control malaria. These tactics to control malaria represent the best response possible, given the constraints of very low health budgets which cannot be expected to grow and training levels among those who must plan, administer, evaluate and execute anti-malaria efforts which can be raised only slowly.

The manual takes account of the fact that few African countries are so homogeneous (with respect to the distribution and severity of malaria incidence, or with respect to capacity to deal with the problems of malaria) that one kind of program will be appropriate for application across the board. The manual does indeed describe one kind of program in each of the chapters devoted to the WHO-defined "Tactical Variants." In practice, it is often possible to have elements of two or more Tactical Variants in any country -- depending on the appropriate response and the capacity to respond to the challenge of the several malariological situations in the country. There is no inconsistency in recommending a program which is limited to chemotherapy in most of the country, but which may involve residual spraying in key agricultural areas and larviciding in and around urban areas -- provided that the program can be shown to be technically and administratively feasible and financially supportable beyond the period of external support.

In some areas of many countries of tropical Africa, it may be impossible to conduct any malaria control program more costly than mortality-preventing chemotherapy, the drugs to be purchased by the patient. Even a program as limited as this has the capacity to prevent a million malaria deaths annually.

The manual is organized by broad category or program.

Chapter I describes the functions of the manual, its background, and its underlying rationale.

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* A summary of the conclusions and recommendations of the expert participants in the workshop appears in Annex XIV to this report.

Chapter II reviews briefly the concept of Primary Health Care, the relationship between PHC and malaria control and the general characteristics of malaria in tropical Africa.

Chapter III describes the disease, its causes, and the several points in the disease cycle where effective intervention is possible. It also describes the range of potential control efforts, defined in terms of the goal to be attained and the kinds of intervention needed to attain such goals, and the principles which should underlie the planning for such control efforts.

Chapters IV-VI describe the local considerations that must enter into the formulation of anti-malaria programs appropriate for each of the Tactical Variant situations described in Chapter III; indicate the kinds of actions to be taken prior to or as initial parts of plan formulation; describe supply and equipment needs; show the kinds of staff needed; and identify those elements in each Tactical Variant which could be carried out by appropriately trained, supervised, supplied, and motivated PHC workers.

Chapter VII addresses an element common to each of the Tactical Variant situations -- the role of operational research.

Chapter VIII outlines the actions to be taken by a potential host government which are the prerequisites of external assistance to malaria control efforts.

SUMMARY

I. At the request of the Bureau for Africa, a working group of malariologists, public health specialists, medical officers, social scientists and medical economists was convened in Washington between June 28 and July 2, 1982. The group of 53 health specialists, representing a wide range of geographic, institutional and disciplinary origins, met to advise the Bureau for Africa on:

A. The possibility of conducting, within the framework of national primary health care efforts, successful efforts to control the ravages of malaria in the countries of Sub-Saharan Africa.

B. The kinds of malaria control programs appropriate to implementation within a PHC framework.

C. The goals of such programs.

D. The constraints to the success of such programs.

E. The need for specialized malaria support services in such programs.

F. Areas of program implementation in which conventional wisdom derived from prior malaria control efforts provided inadequate guidance.

G. Risks and dangers associated with malaria control programs.

H. The desirability of providing external support for national malaria control efforts within a PHC framework, and the essential pre-conditions for such support.

I. Guidelines to assist AID field health officers in the development of anti-malaria support projects.

II. The conclusions and recommendations of the group include the following:

A. PHC is considered an appropriate vehicle for malaria control in Sub-Saharan Africa, and often in fact is the only vehicle for control that exists. Available techniques make it possible to conduct a variety of selected anti-malaria efforts within a PHC system.

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B. The nature of a malaria control effort and the tactics employed will vary from country to country, or even within a country. The effort must be related to the severity of the problem, the level of control sought and the indigenous capacity to achieve that level. Mortality control through chemotherapy, morbidity control through chemoprophylaxis and possibly limited vector control were identified as being potentially suitable for implementation within PHC programs.

C. Limitations on resources are such that any activity undertaken to reduce the impact of malaria must be designed to produce maximum results for minimum expenditures of resources in money, manpower and material.

For this reason, the working group concluded that maximum extension of cost-efficient mortality reduction through chemotherapy takes the highest priority among available tactical options. Chemoprophylaxis to provide morbidity protection to high-risk populations (pregnant women and children age 0-5) and to economically valuable populations, and, where technically appropriate, limited vector control activities may also be suitable for implementation within PHC. Vector control which includes wide-spread chemical control will in Africa be appropriate only in localized areas; it should be considered only where appropriate infrastructure and economic conditions permit.

D. In a program conducted within the framework of PHC, it may not be practical to require laboratory confirmation of clinically diagnosed malaria before administering a curative dose of antimalarial drug, nor is it considered to be practical in most situations to administer the drug over a period of days. Specific treatment regimens were recommended for different population sub-groups.

E. Training in drug administration must be extended to the periphery of the PHC system. Supervision from higher levels in the system is an essential element of support to the PHC. Emphasis on education of the population regarding malaria control was stressed.

F. Malaria control programs are not time-limited; they have costs which (especially for programs with the limited objective of reducing mortality) may not decline over time. Yet external assistance is normally time-limited, and the impact on Ministry of Health budgets at the end of external inputs may cause retrenchment or even termination of the control activity. To minimize this strain, the group recommended a policy to encourage that a charge be levied for drugs.

III. The conclusions and recommendations of the working group have been incorporated into the attached malaria control planning manual. This manual is designed to provide guidance to AID field missions in Africa in discussing problems of malaria control with host government counterparts and in formulating proposals for support of malaria control efforts.

I. Introduction

A. Purpose of the Document

The purpose of this document is to provide USAID Health Officers and their counterparts with a comprehensive understanding of how (and the extent to which) malaria can be controlled through the efforts of the primary health care (PHC) system. Inherent in this understanding is an appreciation of the transmission of malaria and its public health significance. The guideines set forth in this document represent flexible methodologies by which malaria control activities can be planned, initiated and maintained via local, regional and national primary health care systems. The limitations of these systems with respect to malaria control are analyzed, and those control activities for which the systems may need to be reinforced are discussed.

B. Objectives

The major objectives of this document are:

1. To present summaries of malaria control activities that can be pursued via the PHC system and conducted at the community level, if given effective supervision, technical guidance and managerial and financial support;

2. To address the concept of variations in the tactics employed in carrying out a strategy of controlling malaria and to indicate the order of their priority within the practical framework of PHC;

3. To provide technical information on malaria transmission, epidemiology and control and to emphasize the attributes and limitations of drug therapy and prophylaxis and limited vector control;

4. To indicate the financial, material, logistic and manpower requirements for each type of malaria control activity;

5. To address the problems of drug resistance and potentially compromised host immunity associated with the implementation of chemotherapeutic and/or chemoprophylactic interventions; and

6. To convey to the user enough basic information about control to enable appropriate decisions on various levels of control activities. Such information will also help in the development of long-term assistance plans.

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C. Background and Rationale

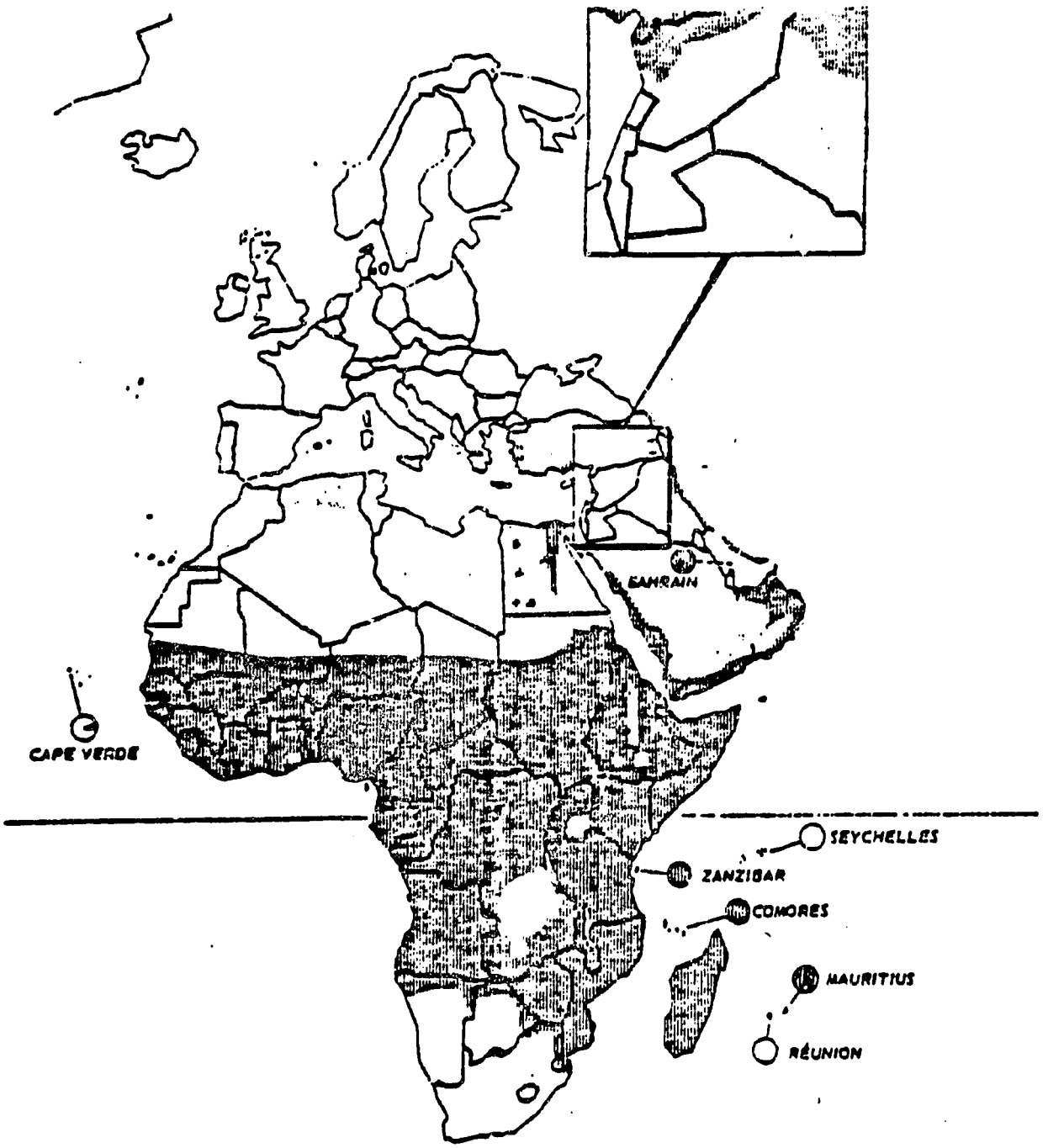
This document responds to the concern of AID's Africa Bureau for the need to identify the most cost-effective way of limiting the impact of malaria on the people of tropical Africa. Malaria remains a devastating disease in Africa and one that inhibits progressive development in the agricultural and economic sectors. Since the inception of the worldwide malaria eradication programs in the 1950s, hundreds of millions of dollars have been spend by AID to combat malaria. Relatively little of this has been in Africa. Although success in eradication has been less than hoped for, many areas around the globe have been made malaria-free. Even where malaria persists, programs have been very successful in reducing drastically the amount of mortality and morbidity caused by malaria. Africa is the conspicuous exception; the World Health Organization (WHO) states that more than half of the world's remaining malaria is concentrated in sub-saharan Africa, where an estimated one million "malaria deaths" occur annually.

In 1978, the conference at Alma Ata emphasized the importance of a basic services approach to improve health in the developing world. Primary health care emerged as the recommended mechanism by which disease could be controlled. To date the majority of the PHC effort has been oriented towards curative services. Recognizing the potential for improvement in the curative and preventive service capacity of PHC systems, the Africa Bureau is formulating a health sector strategy which includes the control of malaria and other major endemic diseases through existing or planned primary health care systems and other country health services.

Widespread government support for the pursuit of malaria control activities at the community level has been evidenced recently. A current report of the General Accounting Office, an arm of the U.S. Congress, recommends that malaria control remain a priority activity for AID support and stresses the need for recognition of circumstances in which malaria control can be incorporated into general health care services (GAO, 1982). Two years ago, an international conference (convened at the direction of the Africa Bureau) formulated a strategy for malaria control in Africa, and identified the manpower, technical, material and logistical requirements for malaria control activities. The participants identified the essential role of PHC in malaria control (APHA 1980). The AID policy of supporting health care and its role in the prevention and control of disease was recently reinforced by the commitment to pursue cost-effective preventive services to reduce the toll of communicable and vector-borne diseases (McPherson, 1982).

MAP 1

Malaria in Africa - 1982



AREAS IN WHICH MALARIA HAS DISAPPEARED, BEEN ERADICATED, OR NEVER EXISTED
ZONES DANS LESQUELLES LE PALUDISME A DISPARU, A ÉTÉ ÉRADIQUÉ OU N'A JAMAIS SÉVI

AREAS WITH LIMITED RISK
ZONES À RISQUE LIMITÉ

AREAS WHE E MALARIA TRANSMISSION OCCURS OR MIGHT OCCUR
ZONES OÙ L A TRANSMISSION DU PALUDISME CONTINUE OU RISQUE DE SE PRODUIRE

The Africa Bureau is committed to assist in efforts to reduce malaria's adverse health impact, using PHC programs as the implementing vehicle as far as possible. This implies an approach at the community level. It places confidence in the community's participation in and support of control activities. Much of the burden of responsibility should be assigned to the residents. The terms of reference of this document encourage well-designed, expandable activities that can be implemented at the community level -- given effective supervision, technical guidance and managerial support. The document is expected to assist AID health officers in Africa in their collaboration in the development of locally appropriate malaria control assistance projects that can be integrated into the missions' and countries' primary health care program.

II. PHC and Malaria Control in Africa

A. PHC

The term Primary Health Care (PHC) describes an approach or strategy, not rigid adherence to a single health delivery system. For many years, at least some aspects of the PHC approach have been in place in a variety of countries, but it was not until the conference at Alma Ata in 1978 that the concept of PHC received universal recognition and forceful approval. Since then, most countries have taken steps to develop and implement a PHC strategy within the context of their own resource and organizational constraints.

The PHC approach endorsed at Alma Ata promotes eight basic services. These are:

1. education concerning prevailing health problems and the methods of preventing and controlling them;

2. promotion of food supply and proper nutrition;

3. an adequate supply of safe water and basic sanitation;

4. maternal and child health care, including family planning;

5. immunization against the major infectious diseases;

6. prevention and control of locally endemic diseases;

7. appropriate treatment of common diseases and injuries; and

8. provision of essential drugs.

These objectives clearly expand the scope of health concerns beyond medical care. In doing so, the delegates of Alma Ata recognized that centralized, curative facility-based and physician-dominated health care systems could not meet the world's pressing basic health needs. The Alma Ata Declaration further recognized that certain major principles need to be followed in order to succeed in providing these basic services. Those principles are:

- Essential health care should be made available to all people.

- Communities have a critical role to play in improving their own health, and they should be actively involved in the design, implementation, and financing of health programs.

- Coordination with other sectors is critical, because many improvements in health depend on economic and social development.

- Programs should be affordable.

- A minimum range of basic health services should be made available at the village level, and the emphasis should be on preventive care.

- The national health system should be designed to support primary health care, by providing both adequate supportive services and access to more complex care when needed.

- Health care at the village level should be provided by persons from the community.

AID's commitment to PHC was in evidence well before the Alma Ata Declaration. In Africa, AID now assists some 22 PHC activities in 15 countries, in addition to a regional activity in Central and West Africa.

Many of these projects are pilot or demonstration efforts that the governments concerned intend to expand or to use as models for nationwide PHC expansion. Other projects are national efforts to strengthen institutional capabilities to support PHC programs nationwide.

Malaria control programs, often with features similar to those of PHC projects, are active in many of the same countries. Indeed, PHC projects in Kenya, Mauritania, Niger, Sudan and Swaziland are planned to incorporate malaria control. Both malaria control and other PHC functions work at the household level and depend upon extension services. Both involve medical diagnosis, treatment and patient education. They are dependent upon community understanding and support from local leaders and citizens. Both have similar support requirements--manpower, training and supervisory needs, logistics--all requiring effective organizational structure. Finally, both PHC and malaria control require a continuity of service within each community and program area, the kind of continuity that is essential for maintaining the respect and support of staff and the people they serve.

Differences exist as well. There are various levels of malaria control activity, some of which require high levels of laboratory support and intensive surveillance; a higher degree of specialized expertise may be required from personnel not directly assigned to the PHC system. Particular care must be taken to monitor all programs involving chemoprophylaxis to detect possible parasite resistance which may emerge following improper drug dosage.

Other problems will have to be faced if primary health care systems are to be utilized as an effective vehicle for malaria control. Recent studies by the General Accounting Office have shown that AID-supported PHC projects face serious difficulties in obtaining inexpensive ground transportation and fuel, in distributing drugs as required, in supervising community health workers, in developing effective community organization and health education programs, and in securing on-going government commitment, including multi-sectoral coordination. Expanding the responsibilities of PHC systems to include more vigorous malaria control can serve to strengthen the appeal of PHC programs by making workers more effectively responsive to a serious health need of the public. There is, conversely, a risk of further inundating PHC field workers who may already feel overworked and under-supported.

Malaria is too important a disease to be ignored or underemphasized. Its challenges (extremely high prevalence, high levels of disability, high mortality among infants and young children) and the factors favoring a decentralized approach (rapid response to chemotherapy, the lack of need for a cold chain and the stability of anti-malarial drugs over time, the present susceptibility of the malaria parasite to chloroquine, the relatively low cost and the low risk of side effects from treatment with chloroquine) all argue for more vigorous malaria control efforts -- within the context of PHC.

B. Malaria in Africa

The general characteristics of malaria in most of tropical Africa are well known and need no major elaboration: high endemicity with only minor seasonal or annual changes in most areas, seasonally high endemicity in savannah areas, early and repeated infection of most individuals, accompanied by rising but never total immunity, a toll in human life that is paid largely by infants, the very young and pregnant women, although periodic epidemics cause death to adults as well, and grossly inadequate statistical information.

The worldwide malaria eradication campaign of the 1950s and 1960s was not implemented on any major scale in most of tropical Africa; the challenge of malaria eradication in Africa was demonstrably beyond the capacity of most African nations in terms of the need for meticulous planning, regional cooperation and coordination, technical expertise of a high order, efficient administration, detailed evaluation, adequate financing, and virtual perfection in execution. Malaria control, which permits more modest goals in keeping with available inputs, represents a realistic and practical strategy for Africa, as indeed it does for other parts of the world.

Various malaria control activities, including the distribution of drugs for prevention and treatment of malaria infections and urban vector control programs, are indeed being carried out in many urban and a few rural areas in Africa, but the overall malaria situation in tropical Africa has not changed appreciably from that which existed a generation ago. A number of African countries face serious constraints in applying the technical skills needed to prepare a long-range malaria control plan; to produce training materials and to undertake necessary levels of training among personnel within the Ministry of Health (including but not limited to the PHC system) which will play a part in controlling malaria; and to monitor and evaluate progress. Some countries may have no anti-malaria effort at the national level, although malaria control efforts are being conducted by municipal authorities in the larger cities.

C. The Disease; Control Interventions Within PHC

1. The Parasite and its Life Cycle[1] *

Malaria in humans is normally transmitted by the bite of a female *Anopheles* mosquito that is infected with one of four species of the genus *Plasmodium* -- *P. falciparum*, *P. malariae*, *P. ovale*, or *P. vivax*. *P. falciparum* is the most dangerous species in terms of the level of mortality and the species most commonly encountered in Africa. As the mosquito feeds from the human bloodstream, it releases malaria *sporozoites*, which enter liver cells (exoerythrocytic stage). After the parasite develops, the liver cell ruptures and releases numerous *merozoites*. These merozoites invade red blood cells (RBCs) and start the erythrocytic stage of an infection. Within the RBCs the parasites develop further, become *schizonts*, and divide again into merozoites. Finally, the infected RBCs rupture. The merozoites then repeat the erythrocyte cycle by invading other RBCs. The release of merozoites from erythrocytes initiates the characteristic chills and fever. Figure 1 shows a simplified version of the life cycle of the malaria parasite.[2]

2. Clinical Features of Malaria[3]

Malaria is an acute disease, clinically typified by chills, fever, and heavy sweating. The clinical

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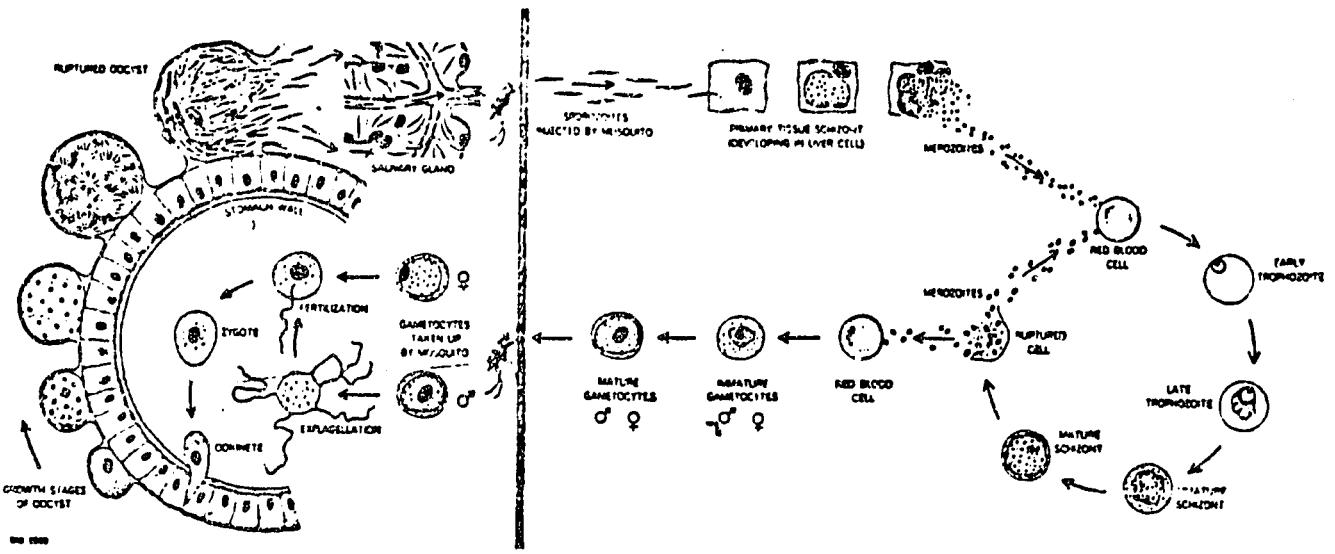
* Throughout the text of this manual, numerical footnotes are keyed to the list of references on page 111.

FIGURE 1

THE LIFE CYCLE OF MALARIA PARASITES
(AFTER ALVARADO & BRUCE-CHWATT, 1962)



features of malaria vary from mild to severe, according to the species of parasite present, the patient's state of immunity, the intensity of the infection, and the presence of concomitant conditions such as malnutrition or other diseases. Malaria tends to be particularly severe in infants, children and pregnant women.

Fever may persist for several days, accompanied by headache, aching joints, and malaise. The classic malaria phases of chills, shivering, high fever, and sweating may not occur. The onset of a malaria attack can resemble an influenza-like illness. In infants the symptoms of malaria can be subtle and quite variable and may be limited to poor appetite, restlessness, and lethargy. The typical clinical course of malaria consists of several phases; these are described in Annex 1.

3. Technical Approaches to Attacking Malaria

Interventions against malaria are directed against either the malaria parasite or the mosquito vector. Drugs are used against the parasite to treat acute illness (chemotherapy) or to prevent symptomatic infection (chemoprophylaxis). Various methods of vector control, such as residual spraying, larviciding, source reduction and water management, have been used to decrease and prevent the transmission of the disease by the mosquito.

Vector control was the major technique used in the global malaria eradication program in the 1950s and 1960s. National programs that relied mainly on vector

control proved to be very costly and were difficult to maintain, particularly in rural areas. They required (and still require) a level of staff training, logistic support, and attention to a single disease -- malaria -- that is rarely available in village-oriented PHC programs in Africa.

The earlier worldwide eradication campaign was keyed to the recognition that, for the first time, techniques were available to interrupt the transmission of malaria by breaking contact between man and the parasite-infected mosquito, and between parasite-infected man and the uninfected mosquito: DDT, used as a residual spray on the walls of inhabited dwellings, would kill infected mosquitoes after they had taken a blood meal, and cheap, effective antimalarial drugs would cure the already infected patient. Recognizing that both the vector mosquitoes and the malaria parasites would eventually be selected for resistance, WHO urged the mounting of ambitious malaria eradication efforts that required very large proportions of nationalhealth budgets, but were considered tolerable as time-limited programs that, once completed successfully, would not have to be repeated or even maintained beyond "simple" surveillance. AID supported these "investment efforts" and has contributed nearly $1 billion since they were first launched.

In the face of the remarkable resilience that vectors and parasites demonstrated under attack, as one insecticide and/or drug after another were found to become less effective (and more expensive) over time, WHO (and AID, too) in recent years began to urge a return to a strategy of malaria control, rather than eradication, in areas where eradication may not be feasible for technical, operational or administrative reasons.

A malaria control program does not demand the rigid timeframe that characterizes malaria eradication. Its objective is to reduce the impact of the disease through an organized effort to institute, conduct, and evaluate measures appropriate to the prevailing epidemiological and socioeconomic conditions, and to achieve the greatest practical improvement in the health condition of the population subjected to the burden of malaria. A program of malaria control need not be applied uniformly throughout a country, depending on the goals deemed feasible in different parts of the country (e.g., concentration on the target groups to be protected, the areas of highest population density, or the areas of greatest economic importance). In its simpler applications, and with the establishment of relatively modest goals of reducing malaria mortality, or mortality and morbidity, malaria control programs

may presently be more acceptable than eradication to national health authorities with limited manpower and financial resources. The more complex forms of malaria control, involving large-scale vector control through the use of insecticides, are technically and administratively demanding.

4. Identification of Malaria Infections

The definitive diagnosis of malaria infection is based on the microscopic examination of a blood smear. Unfortunately, however, laboratory facilities are not usually readily available in rural areas of developing countries, and the allocations of resources to establish diagnostic laboratories may not be justified. Furthermore, the time that elapses between collection of the blood smear and return (from the central laboratory to the collection site) of the examination result is, in many cases, so long that the victim has either died or has been actively transmitting the disease within the community.

An alternative approach is to provide single-dose treatment at the level to clear parasite infection (radical drug treatment) to all persons in the target population who have the clinical symptoms of malaria. Studies in highly malarious areas of Africa and the Americas have demonstrated that the specificity of self-diagnosis is quite high.*

Still another approach is to provide chemotherapy to all fever cases, especially in high-risk areas.

The PHC worker does not have the training to confirm a diagnosis of malaria, but he or she usually does have sufficient training to treat an individual who has fever.

The PHC worker must assume that: any child (age 0-5 years) or pregnant woman who has a fever or who has had fever within the last ten days has malaria as part of his or her illness and must be treated for malaria; any adult with fever of unknown origin or who has had fever of unknown origin within the last two days must also be treated for malaria.

The only "verification" of diagnosis at the PHC worker level would be the favorable response to treatment. Clearly, this implies that the PHC worker should follow-up patients and document the results of treatment.

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* Participant at Malaria Meeting (Centers for Disease Control). Personal communication, June 28-July 2, 1982.

III. Options in Goal Selection: Planning Principles

The choice of interventions to be employed in malaria control must be made in the light of local conditions: characteristics and severity of the disease, host-government commitment, availability of resources, and technical and managerial capacity. Alternative interventions and combinations of interventions may be selected on the basis of the local disease situation, the state-of-the-art potential, and the constraints faced in any particular situation -- or, conversely, to take advantage of the capacity of selected areas of countries to undertake forms of control that would be too sophisticated for countrywide application.

A. The Tactical Variants[4]

WHO has identified four levels of malaria control intervention, designed to accommodate the full range of gradations of national commitment to control malaria (including, ultimately, its eradication). Each level is designed to yield the maximum level of protection against the burden of malaria, using all currently available human and material resources. Known as the four Tactical Variants, they differ in the tactics to achieve that goal.

1. Tactical Variant I

The goal of Tactical Variant I is to reduce and prevent mortality due to malaria by chemotherapy. This variant should be used in areas with a high prevalence of malaria, severe clinical illness and high death rates, low socio-economic status, and limited experience in the administration of malaria programs. The PHC system (general health services) would be responsible for the distribution of drugs to treat acutely ill persons. If for reasons of cost or administrative incapacity, a therapeutic dose of the drug of choice cannot be administered to all presumptive malaria cases, primary attention is to be given to infants and children (age 0-5) and pregnant women.

2. Tactical Variant II

The goal of Tactical Variant II is to reduce and prevent both mortality and morbidity. In addition to treatment of acute malaria cases, special attention is given to the reduction of morbidity in high-risk groups and in the most economically productive groups through the use of chemoprophylaxis: the administration of an antimalarial drug sufficiently often to maintain a minimal lethal blood drug concentration which will prevent clinical illness.

This variant may be used in situations similar to those of Variant I. However, an effective organizational structure is needed for systematic distribution of antimalarial drugs for chemoprophylaxis to selected groups of the population (e.g., infants and young children, expectant mothers, school children, and special labor groups). Where appropriate, limited protective and vector control measures may also be applied by individuals, entire communities, or employers, with the assistance and collaboration of the PHC system and with technical guidance and support from units with special expertise.

3. Tactical Variant III

This variant, in addition to attempting to reduce malaria mortality and morbidity, seeks to reduce the prevalence of malaria (the reservoir of infection within the population) by reducing contact between man and vector, thereby reducing disease transmission.

This variant requires the existence of an organizational malaria control nucleus in some part of a country, or throughout the country, and a sufficient number of trained personnel to apply the methods (treatment of cases of clinical malaria, chemoprophylaxis, and selected methods of vector control) and to undertake epidemiological evaluations of the actions taken and results achieved. Countries may choose this variant when there is strong commitment to control, when resources permit, and when the level of control sought is technically and administratively feasible.

4. Tactical Variant IV

The immediate goal is to achieve countrywide malaria control. The long-term objectives are eradication, keeping countries or areas where the disease has been eradicated free from malaria, and vigilance in countries that are naturally malaria-free but that are threatened by the introduction of the disease. The tools available are those employed for Tactical Variant III; the scope is of course increased.

B. Selection of Tactical Variants

As with other infectious diseases that are transmitted from man to man by obligatory passage through an intermediate host, malaria has multiple points of attack, both in man and in the intermediate host, or vector, at which transmission

may be blocked. The selection of one of the four tactical variants as a vehicle for a malaria-intervention strategy is, in practice, identification of the method that offers the maximum anti-malarial impact, using available resources, and of the best way to use, where possible, the chosen vehicle of intervention, the PHC system.

In this document, more extensive coverage is given to Tactical Variant I than to the other tactical variants. This has been done because each tactical variant subsumes both the goals and the requirements for implementation of all the preceding tactical variants, and because Tactical Variant I is expected to prove to be the most generally applicable to the African context.

1. It is not only appropriate that PHC should serve as the vehicle for malaria control in subsaharan Africa; PHC is often, in the view of most observers, the only vehicle available.

2. The state of the art of malaria control is such that it is possible to mount selected anti-malaria efforts within a PHC framework -- depending on the goals of such efforts.

3. Of the four WHO-defined "tactical variants" -- selections of control techniques which relate malaria control tactics to the nature of the problem, the level of control sought and the capacity to achieve that level -- only those attempting mortality reduction (through chemotherapy) and morbidity reduction (through chemoprophylaxis and, possibly, limited vector control) are at this time suitable for implementation entirely within the PHC system.

4. Individual countries must establish their own goals and priorities with respect to malaria control.

5. Limitations on resources (in money, manpower and materiel) are such that any activity undertaken to reduce the impact of malaria must be planned and implemented in a manner that will produce maximum results for minimum expenditure of resources.

6. The level of control envisioned under Tactical Variant I -- reduction of malaria-related mortality -- is fully consistent with implementation within the PHC system, is far more cost-efficient than a program to reduce malaria-related morbidity, and would constitute an enormous advance toward the goal of "Health for All by the Year 2000" if it could be achieved continent-wide.

C. Stratification

As was pointed out above, the choice of interventions to be employed in malaria control must be made in the light of local conditions, including the characteristics and severity of the disease. The characteristics of the disease and its severity are not necessarily uniform throughout any country in Africa, nor is the indigenous capacity to administer control efforts.

To assist in selecting the most appropriate intervention and in determining the areas where intervention is most needed, a technique of analyzing the malaria situation has been devised. Known as "stratification," the technique in its simplest form consists of identifying the areas of the country which possess similar epidemiologic characteristics. Other things being equal, it will then be possible to apply to all such similar areas a single selection of control tactics -- which might well be quite inappropriate for other areas of the country possessing different epidemiologic characteristics, although they may be geographically close.

Malarious areas may be further subdivided to show such sub-characteristics as parasite species, drug sensitivity of the parasites, vector species, insecticide susceptibility of the vectors, areas with seasonal transmission and areas with perennial transmission, intensity of transmission, areas of unusually high mortality, etc.

From a purely pragmatic point of view, one of the most important criteria for stratification may be the local ability to mount, manage and sustain a malaria control effort. Thus, one subdivision of a country's most malarious areas may identify the available malariological infrastructure and program management capacity.

Such subdivision could lead to an unmanageable number of strata; in practice, only a limited number of sub-characteristics will be found to be applicable.

The results of stratification, usually set forth in the form of maps and tables, enable the planner to determine not only <u>what kind</u> of intervention is appropriate for each sub-stratum, but also <u>when</u> intervention is required. In cases where budget stringency or staff limitations prevent implementation at all points simultaneously, stratification enables the planner to pinpoint his limited resources on the points of greatest need.

It should be noted that whereas a simple stratification is appropriate for the planning of a program to limit malaria-related mortality, to provide health education to stimulate and assist in the planning of village-level source reduction efforts, or to encourage the adoption (by individuals or communities) of mosquito-avoidance measures, the selection of appropriate forms of major vector control may require a more refined stratification, keyed to a level of epidemiological and entomological baseline data which is beyond the capacity of many African countries to produce at this time.

D. Planning Principles

1. Tactical Variant I: Chemotherapy

The guiding principles for the achievement of a successful Tactical Variant I program -- a reduction in malaria-related mortality through chemotherapy -- are four:

a. To work with and strengthen the existing health delivery infrastructure.

b. To work to extend primary health care delivery to populations with demonstrated excess mortality.

c. To provide the least expensive (in terms of money and manpower commitment) intervention(s) to achieve the objective.

d. To provide for ongoing assessment of logistics and outcomes (mortality rate in the target populations), to provide a basis for an evaluation of the intervention.

2. Tactical Variant II: Chemotherapy and Chemoprophylaxis

The guiding principles for a Tacticle Variant I program are equally applicable for a program which also includes morbidity reduction through chemoprophylaxis. However, they need to be expanded in light of the preventive as well as curative aspects of a TV-II program.

a. Preventive antimalaria care is extended through (or with the assistance of) the PHC system to carefully defined groups whose composition is centrally determined. Care must be taken that protection is actually extended to the designated groups.

b. The effectiveness of a program of chemoprophylaxis is a direct funtion of the outreach capacity of the PHC system. In the absence of an effective outreach system, chemoprophylaxis cannot be extended to more than a fraction of the target groups, nor can health education be effective in stimulating other interventions, at either the individual or the community level.

3. Tactical Variants III and IV: Comprehensive Malaria Control

The techniques for achievement of the goals of TV-I and II programs are relatively simple -- the administration of anti-malarial drugs in carefully specified amounts -- and are fully within the capacity of the PHC to deliver. Comprehensive malaria control involves the application of one or more additional, locally determined but objective-specific measures among a wide range of choices.

Comprehensive malaria control seeks not only a reduction in deaths and illness, but also a reduction in the actual prevalence of the parasite in the human malaria reservoir. Intelligent application of this form of control is technically demanding; it requires the availability of technical expertise not merely at the central planning and evaluation unit, but also at the periphery. Decentralized decision-making calls for a measure of training at the periphery of the system which may exceed that required for eradication programs.

Rarely if ever will it prove necessary -- or desirable -- to employ all vector control methods at any single location, although all may be employed at one point or another in a country. When vector control applications are being considered, it is essential to stratify (see Chapter III-C, above) the areas selected for program activity and to identify ecological similarities and differences, enabling the selection and application of specific technical methods which offer the possibility of cost-effective success. The entomological and epidemiological baseline data must be location-specific, not generalized; they are essential to method selection and subsequent monitoring and evaluation. Both data collection and methodology selection should be performed by trained specialists.

It is appropriate to consider vector control operations when the prevalence of malaria infection and incidence of morbidity and mortality are high

in an area where, for whatever reason, it is politically or economically necessary to reduce the malaria burden on the entire population affected. Decision to undertake such operations must be keyed to the availability of a suitable technology (and a determination that the technology proposed is suitable), the availability of the administrative and technical infrastructue to carry out the effort, and a reliable long-term financial commitment and capacity to carry the effort forward for as long as may be required.

The first step, then, is to determine whether or not to undertake vector control, and at what level. The major considerations in reaching this decision and identifying appropriate areas for vector control include:

a. Malaria prevalence, seasonal variations, area infected.

b. Vector species and breeding sites.

c. Vector density and number of infective bites.

d. Vector habits including biting and resting patterns.

e. Vector susceptibility to insecticides.

f. Human population density, mobility and behavior patterns.

g. Type of housing and relation to breeding sites.

h. Cost of alternative interventions.

i. Availability of structures, personnel, funding and management systems for implementation.

If chemical vector control on a large scale is being seriously considered, specialized technical advice is needed from the earliest planning stages. Coordination between USAID and WHO at country level may facilitate obtaining such support, where it is not available within the country.

Cost effectiveness of vector control is dependent on the method of control used and on the type of locality concerned. In urban areas of Africa the malaria prevalence may be low and source

reduction or larvicidal methods (see VI-C, below) represent practicable and cost effective techniques. On the other hand in rural areas, where malaria prevalence is usually high, the only practicable method of effective vector control may be a well-organized and conducted program of residual spraying, normally the only cost-effective measure.

There is, in any event, a need to compare cost effectiveness of alternative programs of malaria control.

As distinct from cost effectiveness (i.e., securing a desired result at minimum cost), it is also possible to consider the benefit-to-cost relationship of vector control efforts (i.e., financial return of an investment in comparison with the financial return from alternative uses of the money invested), even if the cost of such efforts is high in relation to other PHC services. In certain specific circumstances in Africa -- labor camps, certain urban areas and island situations -- the benefit-to-cost ratio of major vector control may well prove to be favorable. For the vast majority of rural areas, vector control activities should be limited to simple measures which can be implemented by the local population, with PHC advice, at minimal costs.

Conprehensive malaria control programs, once initiated, must be carried forward if the initial investment in time and money is not to be wasted. Some actions may require simple maintenance; others require regular and timely repetition. A very few actions, not in themselves likely to have any effect on reducing the malaria reservoir, can be carried out by individuals; their impact is solely on the comfort and health of the individual and his family. For the most part, however, it must be faced that comprehensive malaria control is beyond the capacity of PHC in almost all circumstances to plan and carry out.

PHC can plan a role in the framework of a comprehensive malaria control effort. It can administer therapeutic and prophylactic drugs. It can, through health education, clear the way for vector control by securing village cooperation, acceptance of, participation in and even execution of some of the simpler forms of vector control. It can provide the over-all managerial and supervisory functions already in place through its provincial, district or related health officers

and their staffs, assuming these have in fact been established. But PHC at the periphery will not have the engineers, the parasitologists, the entomologists or the other technical specialists whose expertise is required for the on-the-spot decision-making which is the hallmark of decentralized, comprehensive malaria control.

IV. Mortality Reduction through Chemotherapy (Tactical Variant I)

A. Planning

1. Goal and Targets

a. Goal

The goal of a Tactical Variant I program is to reduce, and to the extent possible, prevent mortality due to malaria. Such a program saves lives and, in the process, reduces the duration of morbidity associated with an acute infection. Given the high rates of malaria prevalence in the population, the high incidence of acute malaria, and the high case fatality rates, many African countries would, reasonably, opt initially to adopt this approach. It requires the availability and the correct use of antimalarial drugs in communities where deaths are occurring. The primary health care system and its outreach elements can be used to dispense drugs. Every effort must be made to get patients to come promptly to treatment units, be they health centers or the homes of volunteer community health workers (CHW). Innovation is essential when providing service in areas where there are no existing health facilities. It is essential, too, to measure the effectiveness of the methods that are used.

Throughout the primary health care system, and in the communities, it must be understood that where chemotherapy is employed, lives will be saved, but the transmission of malaria will not be reduced. As initial goals are achieved, it may be possible, in some epidemiological settings at least, to broaden the strategy to include measures from Tactical Variants II and III, depending on the resources available to the community and the country.

b. Intermediate Targets

Although the overall goal of Tactical Variant I is to reduce mortality due to malaria (within the broader framework of reducing mortality from communicable diseases), it is not only possible, but also essential to define the targets the program seeks to attain. These will be influenced by the epidemiological situation when the program is initiated, including the malaria mortality rate, the geographic extent of the proposed program; and the effectiveness of all elements contributing to program implementation.

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Targets may vary among regions of the country, depending on resources available and the estimate of malaria mortality. Further, targets need not necessarily focus solely on intervening in malarial infections. Other disease interventions (e.g. community oral rehydration programs for diarrheal disease control; prenatal care) share common targets, base populations, reliance on a basic health worker, and simple therapeutics. The simultaneous pursuit of the goals of these several components of the PHC effort is characteristic of the "horizontal" organization of PHC.

It is important to set achievement targets. Although there may be difficulties in defining achievable targets, this exercise is essential because the extent of target attainment serves as an indicator of how well the system is working, and indicates whether changes in protocol are necessary or whether the investment in the program is justified.

Both process and outcome targets need to be set. Process targets give estimates of coverage; they include such activities as training to be given, the number of people to be treated, and the number of pills to be distributed. Outcome targets include indices such as deaths associated with fever treated by PHC workers and deaths associated with fever and parasitemia as documented in higher health facilities.

During the first one or two years of project activities, only process indicators should be used to measure project effectiveness. However, both process and outcome data should be collected from the beginning of malaria control activities.

Analysis of outcome data will be valuable in later evaluations of project effectiveness. An example of an outcome target in a population which has not previously been exposed to aggressive malaria control would be a 50% reduction in mortality associated with malaria over a five year period.

2. Training

Peripheral-level personnel require special training to locate, identify and treat "suspected" or "presumptive" malaria cases; in turn, those who support and backstop the peripheral-level personnel at whatever level of the infrastructure may and probably will

require some degree of training in one or more additional areas, such as planning, entomology, parasitology, epidemiology, administration, health education, surveillance, and evaluation. Few African nations currently have the capacity to provide this range of training in-country. An appropriate program to "train the trainers" may be among the various training opportunities offered by WHO. It may also be possible to provide training through programs which can be mounted in African institutions.

Such training opportunities may not be practical in all African institutions. Where they do exist or can be created, they may also be made available to personnel from other countries -- an appropriate form of intercountry African assistance.

3. Logistics

The inability to provide a system that can deliver the necessary commodities, at point of use and upon request, is the most frequently encountered constraint against success in anti-malaria programs. Control efforts of any kind must be keyed to the availability of an adequate supply chain which can guarantee timely procurement, safe storage, stock control, and delivery at point of use in advance of need.

The ideal is to use an existing system of procurement, storage, and delivery, either that of the Ministry of Health, some other government entity, or commercial distribution facilities, if these are available. It should be noted that in some African countries, only the commercial distributor is a (relatively) reliable source of antimalarial drugs. National anti-malaria programs should not bypass such channels if continuity of drug supply beyond the period of external program support cannot be ensured otherwise.

In any event, the selection of a delivery mechanism will depend upon what is available in-country. It is important to ensure that such a mechanism is adequate and reliable.

The volume of commodities to be moved to reduce malaria-caused mortality is not large. However, transportation is needed to move supervisory personnel from the center to the periphery, to make possible timely reporting, or to make spot surveys which can be used to verify conclusions reached from an analysis of reports (e.g., correlation between symptomatically diagnosed malaria cases and scientific confirmation of acute malaria infection, using microscopic examination of blood smears or other techniques for assessment).

Alternatives have to be considered, and the needs for vehicles (or other means of transport) met.

An adequate (and adequately maintained and managed) logistics system is essential for malaria control. Assurance of the capacity to provide commodity support is critical to the expansion of PHC into areas not previously served.

4. Demographic Considerations

a. Urban and Periurban Areas

In each African country, several demographic situations must be considered that have implications for malaria control and reduction of mortality. Urban areas (defined as areas with populations in excess of 5,000) may be sites of active malaria transmission and excess mortality. Antimalarial drugs can be distributed in these areas through school teachers, neighborhood health posts or block volunteers trained in basic emergency care. The supervision of drug distribution, the establishment of supply lines, and the epidemiologic evaluation of the impact of drug distribution on malaria-related mortality are considerably easier to undertake in urban areas than in rural areas with dispersed populations.

b. Rural Areas

In most rural areas, a well-developed, supervised, and supported health care network is not likely to be found. Therefore, the initial step should be to provide materials and training for drug distribution to the most peripheral level of the health system. In unserved areas where the initial epidemiologic assessment of mortality in children and pregnant women demonstrates an excess of deaths, efforts can be made to extend basic health resources. The PHC extension may take one of several different forms.

(1) Village or Community Health Worker

Generally, in this approach, a volunteer is used who has received minimal training to recognize symptoms, provide health education, promote environmental sanitation, and administer simple remedies (e.g., antimalarial drugs, oral rehydration solutions, and penicillin for yaws). Support for the village worker comes from the nearest fixed health facility.

(2) Mobile Health Workers Based at a Fixed Facility

In this approach, PHC is immediately available only periodically. Mobile health workers based at a fixed facility are used. Although this approach is preferable to no PHC services, it does not adequately address illness where early treatment may be required to prevent death. In short, mobile services are not well suited to the objectives of a malaria control program which is limited to chemotherapy.

c. Migration Phenomena

(1) Temporary Residents

Malaria-related deaths are possible any time persons with limited previous malarial infections are intensively exposed to malaria (e.g., when temporary laborers are brought into a highly malarious area for agricultural or hydroelectric construction work). In such a population, intense malaria epidemics with high mortality can ensue in any age group.

Rapid response, specifically the provision of drug therapy, is essential to reduce mortality. Intervention may require that services be provided outside the PHC system, using hired workers or volunteers. The same principles of epidemiologic assessment and planning as were described for permanent populations are nevertheless applicable.

2. Seaports and Airports

Visitors to countries where malaria is a recognized problem will frequently have their first exposure to *P. falciparum* infection (including infection by chloroquine-resistant strains of the parasite) at the seaport or airport point of entry. These entry ports may also be the points where chloroquine-resistant strains may first be introduced into areas previously free of resistance.

It would unquestionably be highly desirable to provide a mechanism to detect drug-resistant strains of *P. falciparum* among malaria patients who had recently entered the

country, to sensitize the health delivery system to the possibility that chloroquine-resistant P. falciparum had been introduced and to apply emergency measures, including, if necessary a change in the chemotherapeutic drug being employed. In practice, a mechanism to follow up malaria incidence among recent arrivals would be, at a minimum, expensive, and technically impracticable.

Yet the impact of such a drug-resistant strain of parasite upon non-immune populations (including tourists) could have serious consequences. A minimal step, which should be taken at locations where drug-resistant strains of P. falciparum are known to exist, is to provide a printed notice to each arriving passenger of the existence in the country of the chloroquine-resistant parasite strain of the drug known to provide protection and cure, of the drug dosage for prophylaxis during the passenger's stay and of the therapeutic dose to effect radical cure. The transit passenger should be advised to seek medical attention if, within the ensuing two weeks, the clinical symptoms of malaria become apparent, and to show the printed notice to the attending physician. Such a notice may be made available by the carrier, or by national health authorities at the point of entry or transit.

5. Assessment of Feasibility

The decision to administer an antimalarial drug (usually chloroquine) in an amount sufficient to provide radical cure of all symptomatically diagnosed cases of malaria does not end the planning process for mortality control. The feasibility of the proposed course of action must also be tested. An illustrative list of the issues that need to be considered to determine the possibility of a successful malaria mortality control effort is provided below.

a. Disease Characteristics

Is the transmission of malaria perennial? Intermittent? Are outbreaks related to weather patterns? To seasonality? If this relationship is not known, can it be determined? Is endemicity uniform? Are fever and death investigated? Are all areas equally important?

b. Parasite

Which form or forms of malaria are encountered in country? In areas of immediate concern? What percentage of the population is carrying malaria parasite infection (whether showing symptoms of acute malaria or not)? Is a parasite prevalence survey needed? Has the parasite developed known resistance to drugs? Which drugs? What level of resistance? What are the program implications of such resistance?

c. Existing Health Facilities

What are the locations of existing health facilities? PHC? Other MOH? Private?

d. Accessibility

Can the target population be reached? How? During what months of the year? Can curative drugs reach the target group? Who is affected? How many people are affected?

e. Manpower

Is the required manpower presently available? Where are the personnel located? What is the present level of training?

(1) Supervision and Management

Does the existing PHC system possess effective management? Is it capable of supervising remote areas where the program may be implemented? Should the antimalaria effort include management training?

(2) Technical Support

Does the capacity exist to provide the essential epidemiological and parasitological data needed for initial baseline data and to measure progress? Where is this capacity located?

(3) Logistic Support

Is there a demonstrably adequate supply chain, capable of supplying and resupplying the elements in the PHC system which will diagnose, treat, and educate? If not, how can logistic support be improved? Is it

possible to rely on the existing PHC support system? The MOH system? Some other ministry system? Is it desirable to establish a malaria control drug distribution system which can also provide logistic support for the entire PHC system?

(4) Maintenance

How adequate are the commercial facilities for vehicle and equipment maintenance? Is there a need for an in-house vehicle maintenance system? For the MOH? For Malaria control? For PHC?

(5) Diagnosis; Drug administration; Reporting

What is the knowledge of the PHC worker? The CHW? Is the reporting system adequate to provide information needed for evaluation? Is the reporting system within capabilities of the PHC worker?

(6) Health Education

Is health education provided by the PHC program? What is the extent of knowledge of health education within the PHC? How is this knowledge provided? How is it supplemented?

f. Training

Is training needed for senior technicians and managers? For workers at the periphery? Are facilities available, in-country or nearby, to provide the necessary training? Are faculty available? Is there a capability to develop essential curricula? Is there a need for training outside Africa?

g. Supplies

Are the required drugs available? Is the drug of choice produced locally? Could it be produced locally or regionally? Would local production result in a saving? Could it be tabletized from bulk-purchased powder? What are the relative costs?

h. Equipment

Are laboratory facilities available? Are they adequate, given need? What additional equipment is needed?

i. Acceptance

Does earlier experience lead to a conclusion that drugs would be refused where Tactical Variant I is applied (i.e., treatment of active illness)?

j. Monitoring

Does the proposal provide for follow-up activities to detect failure of treatment? To determine the cause(s) of failure? To detect the sites of malaria outbreaks? To identify potential problems of development of resistance?

k. Evaluation

Has adequate provision been made for an evaluation of progress? What measures, beyond prescribed reports, are considered to be necessary? Will sample surveys be conducted to cross-check conclusions derived from PHC reports? Will spot-checks, by slide examination, be made to establish the validity of symptomatic diagnoses of malaria? How will information collected be used?

l. Financial

Can the cost be met, given the resources expected to be available? Is the program cost-effective? Can the same results be achieved with less money, men, and materiel? Can the effort be supported by the country after external inputs have been withdrawn? Can some percentage of costs be met by the village? By the individual?

6. Cost Calculations

In the test of feasibility, an effort should be made to identify all the factors that determine the cost of the proposed intervention, the proportion of costs to be borne by the host government (and, in some cases, by the communities and individuals), and the amount, kind, and cost of external support required.

Wherever the several manpower components of the program may be located, all manpower costs for a proposed malaria control program should be identified and included in the malaria proposal. The number of workers (and other resources) attributed to the program is one of the indicators of the importance assigned to the disease and the host government's commitment to its control.

Costs will vary, depending on the kinds and numbers of personnel required; the structure of salaries and allowances; the kinds and numbers of personnel to be trained and the training loci; the number of people to be served; the number of illnesses anticipated annually; the choice of drug and the prescribed dosage for radical cure; and logistic requirements, including vehicles, maintenance costs, spares, etc. Salary costs must include travel and allowances.

Where malaria treatment is provided by polyvalent PHC workers, the proportion of the cost of those workers' salaries which will be attributed to malaria will be a function of the time they devote to malaria. Even when treatment is provided by voluntary community health workers, such workers are supported by paid employees within the PHC system.

The calculation of drug costs appears to be deceptively simple: the number of individuals to be protected multiplied in turn by the number of drug tablets per radical treatment and the number of anticipated treatments required per person per year. This figure, divided by 1000 and multiplied by the cost of the drug of choice per 1000 tablets (at catalog prices), plus a safety factor of 10%, would appear to provide the annual drug cost.

Drug costs delivered to the end user may be expected to represent a multiple of catalog prices. The cost of ocean freight, storage, and in-country transportation, added to the cost of the drug, import duties, and profit, frequently produce a commercial drug cost to the end user which is up to six times the advertised catalog price.

The cost of a government-maintained drug distribution system would appear to be substantially lower; elimination of the import duty and the distributor's profit could save an appreciable element in the final cost, and governments have access (on the basis of pre-payment) to very low-priced UNICEF drugs. Without assurance of continuity of such purchasing practices beyond the period of external assistance, however, it is probable that the commercial distributor will again become the only reliable source of supply, and long-range plans will have to take this probability into account.

It should be noted that at current (1982) commercial prices in West Africa, for example (4¢ per 100 mg. base chloroquine tablet), a family of six which required three radical treatment courses (single dose) per year per family member would spend over $4.00

annually for chemotherapy; chemoprophylaxis for the mother and two of the children would cost over $18.00 per year. These figures compare with present Ministry of Health budgets which provide, on the average, less than 15% for non-salary costs and which in at least one country provides only 5¢ per person for all drug procurement in 1982.

Clearly, African government health budgets will not accommodate the requirements of free drug distribution, and long-term external support of such costs is neither probable nor desirable.

Two of the tasks which demand priority attention during any period of external support are the strengthening or indeed the creation of a viable supply network and the consideration of a policy of charging fees for drugs (or, possibly, for "treatment service," in countries where free drug distribution is a legal right).

An illustrative costing exercise is shown in Annex XIII.

B. Technical Aspects

1. Tools Available: Chemotherapy

Within a Tactical Variant I program, the sole tool available to reach the goals and targets of reduced mortality is chemotherapy. This involves the administration of an effective antimalarial drug, to those persons "identified" as having acute malaria infections, in a dosage adequate to clear the victim of infection, NOT MERELY TO SUPPRESS INFECTION. This strategy requires the ability to identify acute infections before the blood parasite density reaches high levels (in the first 3-5 days of symptoms) and to provide immediate therapy effective enough to clear the blood of parasitic infection -- that is, to kill the parasites. Such therapy is termed "radical treatment."*

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* Throughout this manual, such therapy is termed "radical treatment". Specifically, the term "radical treatment" as used in this manual describes the dose necessary to clear at least 99.9% of parasitic trophozoites in the blood of the patient.

Several critical issues must be considered in planning programs of malaria chemotherapy.

a. Objectives of Drug Therapy

The prompt treatment of symptomatic infections should at least diminish the risk of death. The choice of antimalaria drug and the dose will influence whether the therapy suppresses the blood parasitemia temporarily (clinical cure) or, alternatively, eliminates the parasite from the body (radical cure). It is desirable to cure infections completely, especially *P. falciparum* infections, to minimize the possibility of killing only the more sensitive parasites, thereby selecting parasitic strains for their drug resistance capacity. Radical cure also avoids the added morbidity that can result from a renewed malarial attack following incomplete (suppressive) drug therapy, and helps to limit continued transmission of the disease to other members of the community.

b. Antimalarial Drugs For Chemotherapy

(1). Chloroquine

Chloroquine is a synthetic 4-aminoquinoline that acts on the red blood cell stage (blood schizont) of the parasite. The drug is normally given by mouth and is absorbed within 4-6 hours of ingestion. The therapeutic concentration of the drug persists in the blood for many days. The action of chloroquine on the malaria parasite in the blood is rapid, and the parasite density decreases in the first 24 hours after therapy. In chloroquine-sensitive malaria infections, the parasites are cleared from the blood within 2-3 days.

(a) Side Effects. Chloroquine is remarkably safe and usually is a well-tolerated drug. Minor side effects include nausea and vomiting, which can be minimized by administering the drug with food. The most serious side reaction associated with chloroquine is itching-allergic dermatitis, which has been noted principally in Africa. Studies in Nigeria indicate that as many as 15 percent of Africans treated orally

with chloroquine experience some degree of allergy.[5] Some reactions are severe (See Annex 2), and many persons subsequently refuse further therapy. It is not clear whether allergic reactions stem from impurities in the drug or a peculiar host response to the drug.

Occasional retinopathy has been reported in individuals who have taken high doses of chloroquine for long periods for the treatment of chronic diseases other than malaria. This retinopathy is extremely rare and has only been reported in cases where the cumulative amount of chloroquine administered was 50 grams or more. Retinopathy has not been observed in individuals who have taken the much lower doses of chloroquine used for malaria treatment.

(b) Impact on Drug Resistance and Natural Immunity. Any use of a drug for antimalarial purposes involves the exposure of the parasite to the drug, and therefore opens the theoretical possibility of selection of drug-resistant parasite strains. To refrain from all use of an effective drug because of resistance selection potential is neither practical nor justified. When chloroquine is employed for malaria chemotherapy and in proper dosage to effect radical cure of malaria, the parasite is killed. Such use has no impact on the process of selection for resistance.

There appears to be no evidence to indicate that therapeutic dosage of acute malaria interferes with the development of immunity.

(c) Single-dose Treatment. Especially in cases where the victim is remote from the site of treatment, it is important to provide curative malaria therapy in a single dose of drugs. Where multiple doses of drugs are required, patient compliance will be appreciably lower than with single-dose therapy.

Single-dose treatment with chloroquine, the normal drug of choice, can clear parasitemias, fever, and symptoms attributed to malaria as effectively as multiple-dose treatment.[6] It has also been demonstrated that single dose treatment can be particularly effective in treating P. falciparum malaria among semi-immune Africans (those who have developed a measure of partial immunity in the course of previous exposure to malaria.[7]) The single dosage of chloroquine required to clear the blood of P. falciparum malaria parasitemia is normally considered to be 10 mg per kg of body weight, up to a maximum of 600 mg. Studies in Tanzania* indicate, however, that over the past 25-30 years, the amount of chloroquine required to effect a radical cure of P. falciparum malaria among semi-immunes has increased significantly. The dose of chloroquine needed to clear 50 percent (clinical cure) or 99.9 percent (radical cure) of trophozoites (TCD_{50} or $TCD_{99.9}$) in children has been found to have increased in the following proportions:

Year	Amount of Chloroquine (mg. base) per kg body Weight	
	To Obtain Clinical Cure	To Obtain Radical Care
	Mg. Base	Mg. Base
1953-1956	1.0	2.5
1968	1.5	-
1970	2.0	5.0
1979	3.5	15.0

These observations indicate that the amount of drug needed to kill parasites is slowly increasing. It is essential to monitor in each country (through controlled laboratory testing) the amount of antimalarial drug needed to obtain a radical cure, to ensure that the correct curative dosage is being administered.

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* Participant at Malaria Meeting (Centers for Disease Control). Personal communication, June 28-July 2,1982.

The amount of chloroquine for the single-dose treatment may have to be increased when the chloroquine susceptibility of P. falciparum declines. Other factors which might indicate a change in the recommended dosage include the degree of immunity in the population and age variation in endemicity. Because of the various forms of drug toxicity, the maximum tolerable single dose is probably in the range of 10 mg. to 15 mg. of chloroquine base per kg. of body weight, but this dosage may vary by age and in the presence of other host factors, and needs to be better determined. If the amount of chloroquine in the single-dose treatment to achieve a radical cure exceeds the maximum tolerable dosage, a multi-dose regimen must be considered.

(d) Prescribed Dosages. Guidelines for administration of prescribed dosages of antimalarial drugs must be clearly outlined in the training for the PHC worker. The normal prescribed dosage for radical cure is 10 mg. of chloroquine (base) per kg. of body weight, up to a maximum of 600 mg.

Although the dosages of chloroquine prescribed for malaria therapy are extremely safe, special care must be taken not to overdose infants. A suspension of chloroquine sulfate (Nivaquine), containing 5 mg. (base) per ml., is required for infants.

Alternative guidelines on dosages by age group instead of weight are summarized in Table 1.[8] Note that when this table is used as a guide, scored tablets (150 mg. base) permit a reliable 37.5 mg. dose for children one year of age and older. Table 2 lists the proprietary names and oral formulations of selected antimalarial drugs.[8]

(e) Dosage for Pregnant Women. The placenta is a significant reservoir for malaria parasites for pregnant women and the standard single dose of 600 mg may not be curative. In the case of the

TABLE 1: ADAPTATION OF DRUG REGIMENS TO AGE*

Drug	Type of Treatment	Timing	Unit	Age (Years) 1	1-3	4-6	7-11	12-15	16+
Chloroquine	single dose (s.1) (1)	-	mg base	37.5-75	225	300	450	450-600	600
			tab. 150mg base	¼ - ½	1½	2	3	3-4	4
	full treatment (2)	0 hours	mg (tablet)	75(½)	75(½)	150 (1)	300 (2)	450 (3)	600 (4)
		6 hours	"	37.5 (¼)	"	75 (½)	150 (1)	150 (1)	300 (2)
		24 hours	"	"	"	"	"	"	"
		48 hours	"	"	"	"	"	"	"
amodiaquine (3)	single dose (s.1) (1)	-	mg base	50-100	200	300	400	400-600	600
			tab.200mg base	¼ - ½	1	1½	2	2-3	3
	full treatment	0 hours	mg (tablet)	50(¼)	100 (½)	150(3/4)	300(1½)	400 (2)	600 (3)
		6 hours	"	"	50(¼)	50(¼)	50(¼)	100(½)	200 (1)
		24 hours	"	"	"	100(½)	200(1)	300(1½)	400 (2)
		48 hours	"	"	"	"	"	"	"
primaquine	gametocytocidal	once	mg base	-	7.5	15	15-30	30-45	45
			tab. 15mg base	-	1/2	1	1-2	2-3	3
	antirelapse (p.v)	daily for 14 dys (4)	mg base	-	2.5	5	7.5	15	15
			tab. 15 mg base	-	-	-	1/2	1	1
			tab. 2.5 mg base	-	1	2	-	-	-
sulfadoxine + pyrimethamine	all	once	mg		250+12.5	375+19	500+25	1000+50	1500+75
			tab. 500 + 25mg	-	1/2	3/4	1	2	3
quinine	full treatment	daily for 7 dys (4)	mg	100-200	200-300	400-500	500-1000	-	-

*Approximations of weight-based dosages, to be used in absence of ability to make accurate weight determination.

[redacted] Centers for Disease Control

SOURCE: CDC

TABLE 2: SOME PROPRIETARY NAMES AND SOME USUAL ORAL FORMULATIONS OF SELECTED ANTIMALARIA DRUGS

International Non-Proprietary Name	Proprietary Names	Some Usual Oral Formulations
chloroquine (diphosphate)	Aralen, Arechin, Avloclor, Bemaphate, Chinamine, Chlorochin, Chlorochina, Delagil, Feroquine, Gontochin, Imagon, Iroquine, Klorokin, Luprochin, Malaquine, Malarex, Noroquine, Paraquine, Resochin, Resoquine, Resorchin, Sanequin, Tanakan, Tresochin, Trochin	Tablets containing 150 or 300 mg base
(sulfate)	Nivaquin, Nivaquin B	Tablets containing 100 to 150 or 300 mg base
amodiaquine (dihydrochloride)	Cam-aqi, Camoquin, Camoquinal, Flavoquine Fluroquine, Miaquine	Tablets containing 200 mg base
(base)	Amodiachin, Basoquin	
primaquine (diphosphate	Neo-Plasmochin, Neo-Quipenyl	Tablets containing 2.5 or 7.5 or 15 mg base
sulfadoxine + pyrimethamine	Falcidar, Fansidar	Tablets containing 500 mg of sulfadoxine + 25 mg of pyrimethamine
sulfadoxine (1)	Fanasil, Fanasulf, Fanzil	Tablets containing 500 mg of sulfadoxine
pyrimethamine (1)	Chloridin, Darapram, Daraprim, Erbaprelina, Malocide, Tindurin	Tablets containing 25 mg of pyrimethamine
quinine		Tablets or capsules containing 125 or 200 or 300 mg of sulfate, or (tablets) 300 mg of various other salts
tetracycline	Achromycin, Aeromicina, Ambramicina, Cyclomycin, Hestacyclin, Omegamycin, Panmycin, Polycycline, Purocyclina, Sanclemycin, Tetrabon, Tetracyn, Tetradecin	Capsules containing 200 or 250 mg of hydrochloride

(1) sulfadoxine and pyrimethamine should be used together only.

pregnant woman, the recommended curative dose is 1500 mg. of chloroquine over a three day period. In addition, it is desirable that, even within a Tactical Variant I program limited to mortality reduction, pregnant women be given 300 mg. of chloroquine (base) per week chemoprophylactically until the end of pregnancy.

(f) Treatment Failure. Most individuals treated for malaria with 10 mg. of chloroquine (base)/kg of body weight will be cured; there are exceptions in certain localized areas of East Africa where chloroquine resistance at the R-I level has been demonstrated and an increased dosage may be required. In cases where fever continues beyond two days and symptoms worsen, or where fever improves initially but recurs within 28 days, treatment may have failed. The failure may be due to incorrect diagnosis of the disease, to the fact that the patient did not take the drug, or that the dosage was incorrect, to a new infection -- or to drug resistance.

If chloroquine therapy has not achieved the desired results, diagnosis should be reevaluated in accordance with the fever protocol used at that level of the PHC system. If no alternative diagnosis can be made, the PHC worker should refer the patient to the next level of the PHC system. When the person is referred to the next level, the cause of the treatment failure should be determined with attention to possible incorrect dosage, possible drug resistance or incorrect diagnosis. Injectible chloroquine and intravenous quinine should be available where competent staff are found in the referral system to treat complicated cases.

(2) Alternative Antimalarial Drugs

(a) Amodiaquine (Camoquine)

Amodiaquine is a 4-aminoquinoline, similar to chloroquine both structurally and in its effect as an antimalarial agent, and equally free of serious

side-effects. In areas where P. falciparum is sensitive to chloroquine, there are few advantages to using amodiaquine, which costs more than chloroquine. In areas with emerging chloroquine resistance, however, there is good evidence to suggest that amodiaquine may be more effective than chloroquine. Field-testing is required in each project to document the relative efficiency of amodiaquine compared to chloroquine. Amodiaquine should not be considered as a simple substitute for chloroquine. Amodiaquine should be reserved for special situations (i.e. where serious parasite resistance to chloroquine has been demonstrated, or where the side effects of chloroquine have made its acceptability questionable).

(b) Pyrimethamine (Daraprim)

Pyrimethamine blocks the ability of the parasite to synthesize the critical molecules required for replication of cells. The drug once was used extensively in Africa, both for prophylaxis and therapy. Resistance to the drug developed rapidly, however, and today, in many areas of Africa, P. falciparum remains pyrimethamine-resistant. Pyrimethamine should no longer be used alone as an antimalarial drug in Africa, although when combined with other drugs, it proves highly effective.

(c) Pyrimethamine in Combination with Other Drugs

Fansidar is a prototype combination of pyrimethamine (25 mg. per tablet), and sulfadoxine (500 mg. per tablet). Two other similar combinations, Maloprim (pyrimethamine and dapsone) and Metakelfin (pyrimethamine and sulfalene), have been used in Africa. All three drugs are designed for use against chloroquine-resistant P. falciparum.

The two components in the drug combinations act synergistically against the parasite, and they are highly

effective against parasites which are resistant to pyrimethamine alone. Resistance to Fansidar can develop when the drug is used extensively (such a problem has emerged in Southeast Asia, New Guinea, and Brazil) and not carefully controlled. Because pyrimethamine has the potential to produce birth defects, these combinations should not be administered to pregnant women. Also, persons with a history of sulfa allergy should not be given these drug combinations.

c. Drug Selection

Selection of the drug of choice should be based on the following criteria; safety and freedom from serious side effects, simplicity in administration, effectiveness, acceptability to patients, availability, and low cost.

These criteria should be applied to drug selection before a malaria control program starts; they should continue to be applied during program implementation to permit appropriate drug choice changes in response to changes in the local situations (e.g., lowered acceptability, lessened effectiveness, cost changes, etc.). Chloroquine is the antimalarial drug of choice in Africa because it best satisfies the above criteria. The PHC worker should have chloroquine in two forms - tablets and syrup for children. In PHC systems where protocols have been developed for the treatment of fever, the protocol should be adapted to add chloroquine if fever due to malaria is suspected.

d. Drug Costs

While chloroquine has been synthesized on a large scale, and with high quality, in developing countries, such production has not been uniformly cost-effective. Tablet formulation from imported chloroquine powder, on the other hand, is not technically difficult. Efforts should be made to encourage pharmaceutical companies that can process chloroquine at the country or regional level in Africa.* The commercial price of imported chloroquine sold at retail in Africa currently (1982) ranges up to 25¢ for the 600 mg. (base) dose required for single-dose adult

* See Annex IV for information concerning manufacture and/or tableting of chloroquine.

therapy. This includes a number of non-drug costs -- shipping, storage, distribution, and, quite probably, customs duties -- and provides a rather startling comparison with the current UNICEF bulk-purchase price of the drug alone -- about 5¢.

Approximately 20 percent of the population of Africa is under five years of age. In highly malarious areas it is estimated that approximately three febrile illnesses per year per child will require chloroquine therapy at 10-15 mg. per kg. For the average child, this would amount to 9¢ per year at 1982 prices -- again, exclusive of shipping, storage, distribution, etc. Actual delivered cost would be far higher.

Where amodiaquine must be used because of chloroquine resistance, the cost is approximately twice that for chloroquine. Currently, amodiaquine is not produced in the U.S., and alternative sources (e.g., regional production in Africa) will have to be explored. Fansidar or Maloprim are even more expensive; their use in PHC programs cannot be advocated at this time because of the cost, potential complications, and the threat of emergence of drug resistance resulting from premature or indiscriminate use.

e. Prioritization

There may be times when it becomes necessary to distingush among categories of fever patients because there is not sufficient chloroquine to treat all suspected malaria fevers. When priorities are necessary due to limited availability of chloroquine, first preference should be given to treating the most seriously ill patients whose fevers may be malaria. The next consideration should be given to the high-risk groups -- children 0-5 years of age and pregnant women. Children in the 6-15 year old age group may be considered an intermediate risk group and should be treated in preference to adults.

f. Drug Procurement and Usage

(1) Wherever possible, generic names should be used for procuring, prescribing, dispensing and labelling drugs.

(2) In procurement of antimalarials, attention should be given to the packaging of bulk supplies (e.g., tins, strips) to optimize utilization in relation to cost. Optimal utilization of drugs must be encouraged at all levels (from consumer to the central ministry) through education and supervision.

(3) While drug presentation and formulation should be as uniform as possible, it should be recognized that the 150 mg. (base) chloroquine tablet usually cited as "standard" is not commmonly encountered in the countries of Francophone Africa, where the 100 mg. (base) tablet is the norm.

(4) The use of injectable antimalarials should be restricted to the referral levels of the PHC system. While injectable quinine and/or chloroquine in trained hands are particularly valuable because of their capacity to produce quick response, they arenormally unnecessarily costly and in untrained or inadequately trained hands have reportedly produced serious side effects, including paralysis.*

(5) As part of its PHC assistance, AID should consider funding to strengthen existing pharmaceutical supply networks in such areas as improved drug procurement, stock control, and in-country distribution.

(6) Wherever possible, consideration should be given to the policy that antimalarials should be sold. Consumer antimalarial prices should be lowered as far as possible by procuring from UNICEF or other low-cost suppliers, by inducing host government to grant custom exemptions on antimalarial drugs, and by improved distribution networks; in some instances, it may be desirable to rely on private or parastatal distribution organizations. Subsidized distribution of antimalarial drugs for sale, (pioneered by subsidized distribution of contraceptives) may be considered.

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* P. Knebel, personnal communication.

2. Baseline Data

Baseline and periodic data needed for a malaria mortality reduction program include:

a. Demographic data: age and sex structure, births, migration, etc.

b. Mortality (overall).

c. Availability and consumption of drugs.

d. PHC structure and coverage.

e. Prevalence of malaria in the population served.

f. Seasonal variation in transmission.

g. Susceptibility of the parasite to chloroquine.

In collecting these data the following must be considered.

- Previous studies, especially those defining mortality, parasite prevalence and response to chloroquine treatment.
- Resources available.
- A study zone to define some of the foregoing indices more precisely may be desirable.

Initial information on the epidemiologic situation in a country is often spotty, derived from whatever sources are available. Among the sources may be village records (if any) on deaths, units reporting to the national health services (e.g., the village clinic or hospital, mobile teams, and special disease control programs), independent groups (e.g., churches, philanthropic organizations, and international organizations); and special studies, which usually are done by expert groups. When incomplete initial baseline data are expanded to cover additional areas where control activities have been mounted, or when initial assumptions are proven erroneous, baseline data must be updated and progress measured against appropriately adjusted targets.

As disease control activities are mounted, it is important to improve the efficiency and quality as well as the quantity of data collection. This can be done by establishing a system of regular surveillance to

estimate the effect on health status of control activities and to determine selected benefit/ cost estimates for the measures that are used. Studies by experts in malaria and other diseases should provide information that national officials and local communities can use to formulate policies, alter program strategies and obtain and use resources.

3. Record Maintenance

Malaria is recognized as a priority problem by most, and perhaps almost all, communities in tropical Africa. When antimalaria activities (and other actions) are initiated in a community, the objectives of those activities should be known to all, including the community, which should have participated in forming the objectives and designing the program of action. The objectives should be quantified, to the extent possible, and a periodic evaluation should be made to determine what progress has been accomplished and how improvements can be made.

Whether the control program is community-based or village-based, the primary health care record maintenance system must be designed to produce data systematically and regularly. Such records inform the community, and higher echelons within the MOH, of the extent to which the facilities of the system are being used, and of the effectiveness of the treatment given. When records are maintained, it is possible to monitor progress throughout the country, or, at any rate, in all areas served by the primary health care system. Certain technical and administrative skills are required to design but also to maintain a useful record system.

Monitoring -- a significant element in program supervision -- is a vital part of the feedback mechanism, which is essential to measure the attainment of goals in terms of expectations, cost-effectiveness, and the possible need for modified implementation techniques. It is essential to analyze the data collected in order to know the reasons for a shortfall from the anticipated achievement of targets (e.g., late delivery of supplies, use of inadequate intervention measures, or rejection of treatment for unanticipated reasons) and to revise measures to overcome constraints to success. The reporting format must be kept as simple as possible, to avoid a situation where reporting overburdens the PHC worker, but it must be adequate to measure progress. Analysis of the reports should reveal the reasons for shortfalls from targets.

4. Evaluation

Evaluation is a systematic examination of the effect of a chosen course of action, using the outcome of the examination to verify the effectiveness of the tactics chosen to attain a goal, to improve on the use of those tactics, to modify the tactics themselves where necessary, and to identify the need for possible alternatives for future action. Evaluation is, therefore, a vital element in the decision process.

For programs designed to reduce malaria-related mortality, the evaluation mechanism has two principal elements: a continuous appraisal of program implementation and an interpretation of the results obtained. Such interpretation leads to judgments as to the adequacy of measures being taken to achieve expected goals, benefit-to-cost analysis, and the possibility of a need for alternative courses of action.

Evaluation is also a tool to determine how well the program of mortality control is being carried out, qualitatively and quantitatively. This in turn influences the kinds of reports being prepared by the peripheral elements of the PHC; reporting formats may vary from country to country, depending on the sophistication of the PHC system. In many countries, reporting may be limited to the kind of records which can be maintained by a CHW who has a very limited education. Such records may take the form of checked boxes on a pictograph chart which would show, for example, numbers of individuals seeking treatment, age, sex, presumed reason for treatment, treatment given, outcome (survival or death), and referrals to succeeding levels in the PHC system.

Such a record would, over time, produce records which would show:

a. A measurable change in mortality following fever. Such a change can be equated to and would probably be at least in parallel with a change in malaria-related mortality.

b. Number of fever episodes recorded: number of fever victims seeking treatment.

c. Number of deaths (among those seeking treatment) by age and sex.

d. Quantity of drugs dispensed (to all fever victims)

e. Drug dosage administered (per case) -- and in consequence, a measure of evaluation of proper drug usage.

f. Number of clinically diagnosed cases which failed to respond to treatment.

g. Cost of services; benefits derived.

h. Effectiveness of method used.

i. Projected mortality prevented.

Clearly, such interpretation of pictograph records involves a thoroughly skilled central planning/evaluation unit.

As a check on the accuracy of the conclusions drawn from the records submitted from the field, sample surveys conducted by expert teams in "indicator" communities (or, indeed, hospitals and dispensaries) may prove to be essential. Sample surveys for evaluating mortality trends may be the only practical way of collecting additional data; they may produce significantly more sophisticated information; they make smaller demands on PHC personnel; they may prove to be more reliable; and they can be undertaken and completed quickly. If the sample survey technique is adopted, the sample must cover seasons systematically and must be repeated often enough to reveal annual as well as seasonal trends. They run the serious risk that the results from an indicator community may <u>not</u> be representative of the country as a whole. Such surveys are, however, made from time to time; field records are maintained, submitted and interpreted throughout the year. The results are used not only to check progress and to guide future planning; they are also fed back to field personnel, to confirm the validity of the chosen control method or to make possible a determination of the causes of possible treatment failures.

From time to time, evaluations are performed by expert teams representing the host country, WHO, and other sources of technical expertise, AID included. <u>Provision for such evaluation should be incorporated into the plan of malaria control which is an essential element of the request for external support</u>.

C. Role of Primary Health Care

1. Historically, antimalaria activities in Africa, as in other countries, have involved basic health services, but only to the extent that drugs were provided to dispensaries, maternal child health (MCH)

units, hospitals, mobile health teams, etc. Sporadic availability and incorrect administration of antimalarial drugs have been major obstacles to success. Another problem is that most of Africa is rural; 80-90 percent of the population lives in villages and towns with fewer than 5,000 persons; health services are remote (more than five km.) and not readily accessible to most of the population. The strategy of incorporating malaria control into PHC must address the important issues of expertise, priority, and training, even when the goal is limited to reduction of malaria-caused mortality.

a. Essential Expertise

In the absence of technical and administrative skills, it is no more possible to plan, implement, and evaluate an antimalaria program within the parameters of primary health care than to operate a vertical malaria program with a separate identity. The numbers and kinds of technical experts required will vary, depending on the extent of the disease and the level of control to be attained, but technical expertise commensurate with both the challenge and the goal must be available within the Ministry of Health. If it is not available, it must be developed.

Even the most elementary control effort -- single-dose drug cure (radical treatment) of clinically identified (even self-diagnosed) malaria victims requires a supply line which ensures the availability of the drug when it is needed, and where it is needed, and a logistical system that meets the requirement for timely ordering of essential supplies, safe storage, and delivery to points of use. It can involve everything from central and regional warehousing to motor fleet operation and maintenance to the use of public transport to move supplies.

Therefore, and because malaria control may be an added task for the already burdened primary health care system, managerial adequacy must be assessed particularly carefully.

b. Priority

The priority assigned to the malaria control effort, by the PHC worker, by the volunteer at the community level, and by the PHC system itself, will affect the chances of success. Malaria is indeed important, but it is only one of many

health problems of African populations. Health workers must be able to deal with many disease problems at once while simultaneously seeking to reduce mortality, morbidity, and disability. A malaria control program must include promotional and educational training for all PHC workers to establish and maintain a high priority for malaria control.

c. Adequacy of Training and Supervision

The importance of active popular participation in local health activities, in villages and cities alike, cannot be allowed to obscure the need for informed participation.

Success in reducing mortality and morbidity due to malaria (and other diseases) will depend upon (1) the prompt presentation of sick individuals to the person who can render effective care; (2) the ability to make a correct clinical diagnosis, administer the correct treatment, record the diagnosis and, to the extent deemed necessary, confirm the diagnosis; and (3) assurance that the patient will take the drugs. Prompt presentation of cases for treatment makes community awareness of and participation in health matters a necessity. Peripheral health care workers, whether they are in villages or larger towns or cities, must be well trained and supervised, have adequate supplies, and be visited frequently in the field.

Lack of competence in successfully "diagnosing" and treating malaria (as well as other priority diseases) will result in a loss of credibility in the community. Patients will not seek medical care, will come late, or will revert to traditional healers.

Because Africa is primarily rural, the use of village or community health workers (CHWs) to treat cases of malaria is especially appropriate. It has even been suggested that in rural areas, the CHW could be a member of the family of the affected patient. In any case, the CHW should be a member of the community, properly trained in the simple fundamentals of diagnosing and treating acute malaria, and with an adequate supply of drugs. However, the CHW should be advised, supervised, and supplied by the nearest health dispensary or other similar facility. Additional backup should be provided by experts at hospitals and other units at the intermediate and national levels.

2. Manpower for Mortality Reduction Program

The PHC delivery system is the main manpower resource, and it can be used to control malaria and reduce mortality if it can be extended to the remote periphery. Support from the existing health infrastructure is needed.

a. Village Level PHC Workers

Personnel are needed to administer drugs and to report the results of activities. PHC workers can perform both tasks. PHC workers are the frontline personnel who can diagnose suspected malaria, administer radical cure, maintain presribed records, provide health education, and promote elementary environmental modification and mosquito avoidance measures.

The extent to which a targeted attack on mortality from malaria will represent a major new burden on the PHC system may vary from country to country; some PHC systems might already be treating presumptive malaria cases. A program that uses Tactical Variant I will emphasize assured drug availability, recordkeeping, and insistence on use of radical, and not suppressive, treatment. As outreach is extended, or as the clientele increases with observed success in treatment, the workload will grow. Additional PHC polyvalent workers (including volunteer workers) may be needed.

b. Referral System

To perform an effective job, the PHC worker needs training, supplies, supervision and a referral system to treat complicated cases of malaria. The referral system should be within a reasonable distance from the village and should have the following functions:

(1) Diagnosis and treatment of complicated cases;

(2) Technical support;

(3) Basic training, supervision and retraining;

(4) Supply of drugs and equipment as they are needed;

(5) Evaluation and monitoring of the effects of malaria control; determination of the correlation between fever cases and acute malaria;

(6) Monitoring for, and detecting evidence of, increasing parasite resistance to drugs.

c. National Level

At the national level, there should be a core of individuals who have malaria expertise. They should collaborate with other members of the PHC system.

The main objectives at the national level are to provide a resource of malaria expertise; to establish national policy; to provide program development, management support and evaluation capabilities; and to incorporate malaria control activities into the primary health care system. The functions of the central locus of malaria expertise should include:

(1) Planning

(a) Development of treatment protocols;

(b) Planning of supervision;

(c) Determining drug of choice;

(d) Maintaining quality control of drugs (such as stability of drug, contents of active principles, shelf life).

(e) Coordination of the program with any integrated rural development or other intersectoral coordination efforts which may be going on in the country.

(2) Evaluation and surveillance

(a) Evaluate effectiveness of PHC system in achieving reductions in malaria mortality rates;

(b) Monitor for emergence of drug-resistant malaria parasites;

(c) Monitor for adverse side effects of drug of choice.

(3) Control of outbreaks

(4) Data collection and analysis

(a) Epidemiologic;

(b) Clinical response (treatment and referral);

(c) Drug consumption.

(5) Recommend changes in protocol based on analysis of data

(6) Administrative aspects

(a) Finances

(b) Logistic and management support

(7) Training (in-service, facilities, advance training)

The number of existing and planned PHC centers and their extensions through village level workers, the level of malaria in the population and the related achievement targets dictate the manpower which is needed to implement Tactical Variant I. The availability of resources and the relative priority of malaria with respect to other health and development problems will influence the degree to which these needs can be met.

Within each level of the PHC system, extended population coverage should be achieved by bringing existing health care workers into malaria control activities and providing them with adequate training and resources. If resources are limited, emphasis should be placed on maximizing coverage at the periphery and directing treatment at high-risk groups.

Existing PHC systems should be examined to determine what training is needed to support the selected level of malaria control activities, with emphasis on defining the specific tasks of each group of workers.

3. Health Education and Community Participation

The use of educational methods to change individual and community beliefs and behavior is basic to PHC. The educational services associated with chemotherapy and other aspects of malaria control involve not only the provision of information to

patients, but also the understanding and support of the members of the patients' families and the community. In a malaria-education program, as in any health education effort, it is essential that workers with educational responsibilities have an accurate knowledge of existing public attitudes toward malaria, the local severity of the disease and its implications, the consequences of delayed or incomplete treatment, other possible control mechanisms, and local feelings about the primary health care system. Too often, education is viewed as something "to be given" to people, and not as a process of involving people to increase their knowledge and to modify their beliefs and behavior.

To formulate effective educational strategies, a sound knowledge of community values and traditions specific to malaria and its treatment and control is required. The educational planning process becomes especially complex when disease prevention through chemoprophylaxis, vector control, or other measures is included among programmatic goals. Personnel in the existing PHC system will have to collect and use basic social science data for planning. If they cannot, they will have to be trained, or additional staff possessing such expertise will have to be sought for use at the national level.

A useful model of detailed educational planning for malaria eradication was presented by Nyswander et al in 1959; portions of that planning document are included in Appendix 5. Although the document was developed in the context of malaria eradication, it has many implications which are applicable to malaria control.

Health education efforts in support of mortality reduction tend to emphasize patient education in a clinical setting. But the clinic is not the only setting for such activities. Important resources also exist in the community (e.g., primary schools, village councils, rural development activities, and religious organizations) that should be involved in education campaigns. Specialized staff training, community organization and educational techniques may be required to facilitate those efforts. The purposes of educational activities may be to achieve a clearer understanding of the causes of malaria, its possible consequences, and appropriate actions to control the disease. Other goals may be to stimulate appreciation of early treatment, motivate compliance with chemotherapeutic regimens, and, when appropriate, motivate villagers to adopt new patterns of behavior that may reduce the likelihood of infections at a later time.

One caveat should be kept in mind: whenever health education is undertaken, the greatest care should be used in making sure that the services, facilities and actions recommended in the message are in fact readily available. For example, a health education campaign to promote the widespread use of chloroquine in the community should not be undertaken unless chloroquine is actually there and available at a cost which the community residents can afford.

Recent experience has shown that carefully planned radio spot announcements can go far to stimulate changes in attitudes and behavior toward health interventions, and to legitimize the presence of community health workers.

In the final analysis, however, the ultimate success of the program will depend less upon the message from outside the community than upon the extent to which community leaders and organizations are able to develop support for the program and understanding of its details on the part of the community residents. In securing support from the communities in carrying out malaria control programs, it is essential to identify the key individuals such as traditional healers, teachers, agricultural extension workers, leaders of womens' groups, and others working in leadership positions.

D. Conclusion

Control of malaria-related mortality through chemotherapy can be implemented through the PHC system, provided that single-dose radical treatment is accepted as the norm, that no diagnosis is required beyond the presence of fever, and that all fever cases are treated as malaria. Supervision is an essential element of support to the PHC worker, and must be supplied from higher levels of the PHC system. The planning of supervision must take place at the central level of the system.

Some observers familiar with the African scene hold that in certain settings it may be appropriate for a malaria control program to include chemotherapy in the home (see Annex XIV). In such cases the family members responsible for providing chemotherapy would have to be identified, trained and supervised for this responsibility, and the availability of therapeutic quantities of the drug of choice would have to be assured.

At the national level, there should be a core of individuals who have malaria expertise. They bear the responsibility for planning, determination of the drug of choice, data collection and analysis, evaluation and surveillance, training, administration and management .

V. Reduction of Malaria Mortality and Morbidity (Tactical Variant II)

A. Relation to Tactical Variant I

Tactical Variant II represents an increase over the level of control sought in simple mortality reduction (TV-I) programs. Through a combination of chemotherapy, chemoprophylaxis and, as appropriate, limited vector control, this variant seeks to prevent both death and illness. It incorporates all of the actions required for the planning, conduct, management, supervision and evaluation of a mortality reduction program and adds a new set of actions aimed at morbidity reduction. Additional considerations must enter into a decision to mount a program which also attempts to control morbidity; both the initial and the recurrent costs of a chemoprophylactic activity are much higher than those for a TV-I program.

B. Planning

1. Goal and Targets

a. Goal: The defined goal of a TV-II program -- to reduce and prevent mortality and morbidity due to malaria, with special attention to reduction of morbidity in high-risk and economically productive groups -- combines humanitarian and economic considerations. It saves lives and prevents illness. Such a program may open important areas to economic development, effectively lengthen the school year, and decrease absenteeism or increase effective crop yield (by enabling actual harvesting of crops produced). TV-II programs are appropriate in situa- tions similar to those suited to TV-I, but where resources permit a more ambitious goal. Effective host country organizational structure is needed for systematic distribution of antimalarial drugs for chemoprophylaxis to selected groups of the population such as infants and young children, expectant mothers, schoolchildren, and special labor groups. In addition, as appropriate, limited protective and vector control measures might be applied by individuals, whole communities, or employers with the technical guidance and collaboration of units of the PHC system which possess the special expertise required.

Whereas the objective of a malaria chemotherapy program is to save human life and curtail morbidity by destroying parasitic infection after it has reached the acute stage, the principal objectives of a malaria

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chemoprophylaxis program are to prevent human illness either by destroying the malaria parasite during the primary incubation period in the liver or by destroying them once they invade the red blood cells but before clinical illness is produced. For effective prophylaxis, the anti-malaria drug must be administered sufficiently often to maintain a minimal lethal blood drug concentration. Drugs which are eliminated slowly from the body have the advantage of requiring fewer administrations. An effective program of chemoprophylaxis in malaria control requires that, depending on the drug of choice, the target population take drugs regularly (normally weekly) for a prolonged period of time. This means that not only must the PHC post command sufficient manpower but also know the number and location of targeted individuals in the community served. Adoption of a program which includes active chemoprophylaxis among target groups involves major administrative commitments.

Chemoprophylaxis to prevent malaria-related morbidity has been advocated for pregnant women and young children, two target sub-populations at highest risk of mortality and morbidity. During pregnancy, malaria chemoprophylaxis has several distinct objectives:

(1) to prevent maternal mortality by preventing morbidity;

(2) to prevent parasitemia which would result in placental infection, which if chronic can result in impaired fetal nutrition;

(3) to prevent maternal malarial attacks which can result in abortion or stillbirth; and

(4) to prevent maternal anemia and undernutrition which can negatively affect fetal development and infant survival.

Morbidity and mortality are particularly high among children in the 0-5 age group; numerically, this group pays the heaviest malaria toll and is in greatest need of protection. In totally endemic areas, mortality among children from 6 months to two years may <u>average</u> 25%.

A third vulnerable class includes two distinctly different groups -- those engaged in activities of material economic significance to the country and those who are migratory. The first group, composed in large part of workers

from outside the country, may have had little or no previous exposure to malaria and are therefore more susceptible to infection than the semi-immune indigenous population.

The nature of malaria preventive treatment requires regular PHC contact with target groups, maintained through an effective outreach system. This contact can serve as a vehicle for providing services related to problems other than malaria infections. (See Section V-D-2, below).

b. Intermediate Targets: As is the case in TV-1 programs, intermediate targets are necessary to measure program effectiveness. For the group being accorded morbidity protection, a minority of the population in most cases, the ultimate objective is elimination of acute malaria. Intermediate targets may vary by region, depending on resources available and the dimensions of the target groups.

As noted in Chapter IV-A-1b, both process and outcome targets are required; process targets (which would require regular monitoring), would include monthly accounting of the number of tablets dispensed, the number of individuals receiving prophylaxis and the frequency with which they ingest the drug; and, if applicable, community vector control measures taken.

Outcome targets would be the prevention of acute malaria infections among target groups in areas of the country where the program exists.

It should be noted that measurement of this type of target achievement requires a somewhat more sophisticated form of reporting, which would include not only the supply and distribution of drugs but also the occurrence of malaria-like illness in the population being served, vital events (i.e., mortality but also birth data), the number of still-births, individual protective and community vector control measures undertaken, and general mortality. Programs aimed at the protection of migrant labor or other worker groups might include the use of residual insecticide spraying in workers' housing; reporting in such cases would including numbers of houses sprayed, frequency of spraying, insecticide used, quantity applied, etc. (see Chapter VI-C-3, below). Absenteeism from the work force would also have to be reported and evaluated.

2. Training

The approach to training for TV-II resembles that described for TV-I in Chapter IV-A-2.

As is the case with TV-I programs, TV-II efforts can be implemented by using (and extending) existing health delivery facilities. Proper training for administering prophylactic drugs and encouraging appropriate vector control intervention is essential. Opportunities also exist to use volunteer community health workers and to be innovative in areas where there are no health facilities.

Individuals who administer prophylactic drugs and the communities themselves must understand that malaria can be successfully treated, that groups being given adequate protection against malaria will not become ill of malaria, but that unprotected groups will still be subject to malaria attack, and that individuals will be protected only as long as they continue to receive and take their prophylaxis.

The role of a central malaria service unit in chemoprophylactic and vector control activities should be clearly defined, particularly for the evaluation and assessment of the impact on malaria morbidity of chemoprophylaxis and associated control activities.

The training of senior level personnel required for a chemoprophylactic and vector control program must include training in the conduct of epidemiological studies necessary for planning and evaluating a morbidity control program.

Training for middle-level personnel will require particular emphasis on proper administration of antimalarial drugs at prophylactic levels, potential side-effects from the use of antimalarial drugs, problems which may arise from the inappropriate distribution of antimalarials to individuals outside the target groups, and health education, including motivational techniques to stimulate individual and community-level vector control efforts. First line PHC and/or CHW will require similar preparation.

3. Logistics

Beyond the points identified in discussing TV-I (see Chapter IV-A-3, above), it should be noted that whereas estimates of drug requirements for chemotherapy are based upon anticipated febrile illness within the total population, quantities of chemoprophylactic drugs needed will depend upon the size of the target

population to be protectd and the nature of malaria transmission in areas being protected (perennial or seasonal).

The volume of material to be transported is less significant a contraint to program success than the timeliness of delivery. Once a pattern of prophylactic drug administration has been initiated, it is important that it be continued without interruption until the end of seasonal transmission, until the protected individual is no longer a member of a group to which protection is to be extended, or until it is no longer required by the epidemiological pattern of the disease in the affected area.

4. Demographic Considerations

To the extend possible, it is important to extend the benefits of disease prevention to the vulnerable groups which bear the heaviest share of the malaria toll.

The means of extension cited for IV-A-4 -- use of the in-place community health worker, use of the mobile health worker and use of services outside PHC -- could be equally applicable to a chemoprophylactic and limited vector control effot. Funds, personnel, and adequate drug supply, and appreciation on the part of the drug distributor of the need for distribution within the prescribed time frame for effective prophylaxis are essential.

5. Assessment of Feasibility

In additional to the feasibility considerations for TV-I cited in Chapter IV-A-5, the following issues must be considered if chemoprophylaxis and limited vector control are to be added to a mortality control program.

a. Disease Characteristics

Geographic distribution, seasonality and frequency of acute malaria infection must be known, at least in general terms, in order to identity priority areas and times for chemoprophylactic and vector control efforts.

b. Parasite

The forms of malaria and their sensitivity to chemoprophylactic agents, particularly chloroquine, are important determinants of feasibility, which may be greatly reduced if drugs more expensive than chloroquine are required.

c. Existing Health Facilities and PHC Services

The availability of a functioning and accessible network of PHC services and supporting health facilities is an essential prerequisite to undertaking a morbidity reduction effort. Chemoprophylaxis and limited vector control should be considered only after establishment of effective malaria treatment services, and only in areas where services for the chemoprophylaxis target groups -- especially, pregnant women and children up to five years of age -- are being provided on a regular basis by trained personnel. Chemoprophylaxis for workers, school children and groups of high economic importance will normally be less costly to administer, with less probability of rejection.

d. Manpower

The addition of chemoprophylactic and vector control related health education services to existing PHC activities, even where outreach is already being provided, will require a small but noticeable additional effort. If existing services are already overloaded, the addition of a malaria prevention activity will require additional manpower. Analysis of existing workload of the PHC staff should be a part of the feasibility assessment.

If the establishment of chemoprophylactic and health education services requires the creation of a new active outreach system, the manpower requirements become larger by a quantum leap; the costs of such an increase require inputs (and long-term commitments) of a different order of magnitude. See Chapter V-D-2, below.

e. Supervision and Management

Although the addition of chemoprophylaxis and health educaion should require little more supervision and management than other PHC activities, the overall adequacy of PHC management system should be assured before embarking on a morbidity control effort. The time constraints of regular weekly drug administration to a group which may involve over a fourth of the population will require the careful budgeting of time.

f. Technical Support

Specialized malaria expertise, including entomological as well as epidemiological and

parasitological skills, is required at the national level, to guide and support the planning, monitoring and evaluation of chemoprophylactic and vector control efforts. Monitoring must include periodic assessment of drug sensitivity of parasites in the population exposed to chemoprophylaxis.

g. Logistic Support, Transportation, Maintenance

Requirements beyond those of an effective treatment program are minor. The greater number of tablets of the drug of choice does not constitute a major increase in volume of material to be transported.

h. Reporting

The extent to which the more sophisticated reporting requirements of a chemoprophylaxis and vector control program can be adapted to the literacy and numeracy capabilities of community health workers may constitute a contraint to accurate reporting and adequate monitoring.

i. Health Education

Health education and motivation of the public are important determinants of the use of (i.e., compliance with) available chemoprophylactic programs. They are even more significant in bringing about the adoption of individual and community vector control measures. The type, general availability and effectiveness of existing health education efforts are important considerations.

j. Training

Principal training requirements are focused on the availability of decentralized training staff and facilities to augment training for PHC and other peripheral health workers and to develop appropriate training modules. Some training, especially for higher level and supervisory personnel, may have to be carried out in another country, as appropriate.

k. Supplies

Addition of chemoprophylaxis to mortality reduction has major implications on both the quantities and the cost of the drugs required. Since these requirements will continue beyond the point of external support, they must be met by a

major increase in the MOH budget or by sale to the user. The extent to which intended beneficiaries will purchase a drug to prevent rather than cure malaria needs to be assessed.

l. Acceptance

Even the acceptance of cost-free prophylaxis by target populations is normally far below that of case treatment. This is a major limiting factor in overall program effectiveness. Existing knowledge of measures to increase acceptance, short of such disciplined situations as commercial employment, is limited. The feasibility of a morbidity control program should be keyed to a realistic estimate of acceptance, consistent adherence to the prescribed regimen, and coverage.

m. Monitoring and Evaluation

Requirements beyond those of an effective treatment program are minor, although there is need for regular monitoring of drug sensitivity, and for assessing the impact on malaria incidence of the limited vector control methodologies adopted. There is also a need to determine periodically whether the frequency of slide-confirmed malaria cases coming to health facilities is changing.

n. Financial

The costs of a morbidity control program (above those required for mortality control) include major increases for drugs, supplies and personnel, and more modest increases for logistics and management. These costs must be weighed against expected benefits, in relation to total health resources available; to other health priorities; and to benefits which would inure from alternative malaria control efforts.

6. Cost Calculations

See Chapter IV-A-6, preceding subsection V-B-5-n, and Annex XIII.

C. Technical Aspects

1. Tools Available: Chemotherapy, Chemoprophylaxis and Vector Control

In addition to chemotherapy for the reduction of malaria mortality, TV-II programs require the administration of anti-malarial drugs in prescribed

prophylactic doses, on a predetermined, rigid schedule, to a selected portion of the population, and offers the possibility of the use of vector control methodology in appropriate circumstances. The prophylactic dose will suppress infection so that it will not become acute or produce symptoms. Assuming proper dosage of an appropriate drug which is taken at prescribed intervals, there should be no incidence of malaria within the target population. Should a case be found, it should be considered evidence of failure to take the drug, inadequate drug dosage, or parasite resistance to the drug. (It is the function of the monitoring staff to determine which is the cause of each prophylaxis failure but it is the responsibility of the PHC worker to report the failure).

Vector control interventions may include individually applied protective mechanisms such as bed nets, and community efforts such as localized source reduction (environmental management to minimize potential vector propagation), water management, and possibly larva control.

a. Selection of Chemoprophylactic Drugs: The drugs described in Chapter IV-B-1, above, are utilized for malaria chemoprophylaxis as well as for chemotherapy, although the dosages are different. Chloroquine is still the cheapest and most widely used chemoprophylactic anti-malarial drug.* Due to its extended persistence in the blood, chloroquine is a highly effective chemoprophylactic drug, safe and normally well-tolerated. Side effects are relatively minor -- nausea and vomiting, which can be minimized by administering the drug with food, and itching-allergic dermatitis, which has caused chloroquine rejection in some parts of Africa.

Long-term follow-up of persons taking chloroquine in prophylactic doses to prevent malaria appears to indicate that even after 10-20 years of continuous prophylaxis, serious ocular effects do not occur at a significantly higher rate than among individuals of comparable age who have never been exposed to chloroquine.

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* Although some chloroquine-resistant P. falciparum has been found to exist in East Africa, such resistance has usually been at the R I level, and chloroquine is still generally effective. In areas of incipient resistance, however, comparisons with the efficacy of amodiaquine should be conducted.

Amodiaquine, similar to chloroquine but more expensive, may be used in areas where P. falciparum has been shown to be resistant to chloroquine, or where rejection of chloroquine is a probable cause of program failure. Field testing is required to document the relative efficiency of amodiaquine vs. chloroquine.

The pyrimethamine-containing drugs (Fansidar, Maloprim, Metakelfin) should not be generally used for chemoprophylaxis, not only because of their cost but especially in view of pyrimethamine's potential for causing birth defects and the effect on the intestinal tract of long-term use of sulfadoxine.*

(1) Dosing Regimen:

a. Perennial Transmission. The dosing regimen most commonly accepted for the target populations living in areas of perennial transmission is 5 mg. chloroquine base per kg. of body weight once a week, without interruption during the period of protection (for young children, through the fifth year; for pregnant women, through pregnancy). However, the suppressive efficacy of this dose and this regimen should be evaluated initially and periodically thereafter. Lower doses (and even biweekly doses) have reportedly proven effective in Francophone Africa, especially for population groups in which semi-immunity has been established. On the other hand, higher doses may be required over time -- as is indicated by the Tanzanian studies cited in Section IV-B-1, above.

In this connection, it should be noted that the major risk to the community from a program of chemoprophylaxis is the selection of chloroquine-resistant P. falciparum parasites.

On the other hand, there is no evidence that chemoprophylaxis prevents eventual development of the immune response. Discontinuance of a chemoprophylactic program will of course result in a temporary increase in mortality or morbidity levels among the previously protected population, stabilizing at the levels characteristic of the unprotected population.

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* See Annexes II and III.

(2) Seasonal Transmission. In areas where a seasonal transmission of malaria is known to exist, chemoprophylactic activity should be adjusted to match the periods of known transmission.

b. Appropriate Vector Control Methodologies

Chapter VI-C, below, describes in greater detail the four categories of vector control which may be employed, individually or in conjunction, in a program of comprehensive malaria control. A number of these methodologies may be appropriately incorporated into a program which otherwise consists of morbidity and mortality reduction through chemoprophylaxis and chemotherapy. For convenience to the reader, those methodologies are here extracted.

PHC can, through health education, clear the way by securing village execution of some of the simpler forms of vector control. But PHC at the periphery will not have the engineers, the parasitologists, the entomologists, or the other technical specialists whose expertise is required for on-the-spot decision-making.

For the vast majority of rural areas, vector control activities should be limited to simple measures which can be implemented by the local population, with PHC advice, at minimal costs. Such a program, once initiated, must be carried forward. Some actions may require simple maintenance; others require regular and timely repetition. A very few actions, not in themselves likely to have any effect on reducing the malaria reservoir, can be carried out by individuals; their impact is solely on the comfort and health of the individual and his family.

(1) Source Reduction

Source reduction is the modification or management of the environment to minimize or prevent vector propagation. It takes many forms, some of which can be undertaken at the village or community level. Environmental modification -- a permanent transformation to reduce or eliminate vector habitat -- may be relatively minor in terms of the effort involved, the technical knowledge required, the need for specialized equipment and the need for subsequent maintenance. Activities which can be undertaken at the community level, given sufficient interest and

understanding, include the filling and leveling of small water collections in and around villages and the drainage of unwanted water. It is of course important to avoid the creation of new borrow pits when securing fill material; undrained borrow pits are in many areas a major source of focal mosquito generation and disease infection. The role of the PHC health education is apparent.

(2) Environmental Management

Some forms of source reduction involve manipulation rather than modification of the environment. At the level of management which can be put into effect at the level of the community or the individual, the practice of intermittent irrigation is useful in two respects: the periodic drying of the irrigated area can destroy mosquito larvae; and there is evidence that some kinds of crops respond favorably to intermittent irrigation. Again, the role of the PHC health educator is apparent.

(3) Avoidance

"Avoidance" is, for the most part, a use of barriers (physical or spatial) to reduce contact between man and vector. The term has also been extended to the use of repellants. The avoidance of biting mosquitoes can assist in controlling exposure to malaria infection. Several of the techniques of avoidance can be put into effect by individuals, and others by communities.

(a) House screening: With the wide-spread availability of plastic screening, the high cost which was formerly cited as an effective socio-economic barrier to the adoption of this highly effective avoidance device may be more manageable. Even in the kinds of houses not suitable for total screening, screened bedrooms may be possible. For the most part, however, use of screening appears to correlate closely with educational levels.

(b) Bed nets: Like screening, bed-nets have been relatively ignored by most potential malaria victims. They may be used even in housing too open to permit

any effective use of screens, and may also be used by those whose occupations require outdoor sleeping. As in the case of screening, the use of bed-nets may require a vigorous health education effort. Their effectiveness is related to the biting habits of the vector(s) in the area of use.

(c) Repellants: A wide range of chemical repellants -- both topical and fumigant -- can assist in reducing man-vector contact. By African standards they are extremely expensive and will probably be purchased only by those whose exposure to malaria infection is already minimal.

(4) Community initiative: Site selection of new settlements should minimize man-mosquito contact. It may in some instances be possible to identify vector breeding sites and to place new settlements beyond the normal flight range of the vector -- which rarely exceeds 5 km. This avoidance technique is principally applicable to populations being resettled to take advantage of development projects -- or which have been displaced by such projects.

2. Baseline Data

The baseline data requirements for TV-I programs, described in Chapter IX-B-2, are equally pertinent to TV-II efforts. In gathering baseline data, emphasis is assigned to the identification of vulnerable groups (geographically and by sex, age, occupation) as indicated by records of malaria incidence as well as mortality.

It is anticipated that any broad application of chemoprophylaxis and vector control methodologies will await the establishment of a successful program of chemotherapy, and that a data base will have been established. Malaria chemoprophylaxis programs require for their planning, monitoring and evaluation, knowledge of malaria morbidity and parasitemia rates. Such data may in part be derived from malariometric surveys in index areas, but care must be used in assuring the applicability of the data produced. A substantial assessment of malaria-related morbidity in the target populations needs to be conducted prior to and during the conduct of chemoprophylactic activities.

Epidemiologic data will be used, first, to determine the geographic areas which exceed threshold levels of acute malaria infection which are determined to warrant chemoprophylactic intervention, and the timing and the duration of intervention required, and later, the effectiveness of malaria prophylaxis and vector control programs. Achievement of the "process" targets identified in Section V-A-1, above, is not to be considered as a fully adequate measure of success; "outcome" progress should also be demonstrated.

3. Record Maintenance

The approach to record maintenance for TV-II resembles that described for TV-I in Chapter IV-B-3. As was noted in Chapter V-B-1, above, however, the reporting requirements for a program of chemoprophylaxis and vector control are more sophisticated than those for chemotherapy alone.

4. Evaluation

Beyond the points identified in Chapter IV-B-4 for evaluation of a TV-I antimalaria intervention, evaluation of a disease prevention effort requires consideration of additional issues:

a. Number of individuals in population segments selected for protection against malaria;

b. Number of individuals actually protected (by age, sex, protection group);

c. Number of individuals refusing protection. Reasons for refusal;

d. Number of malaria cases among protected groups;

e. Cause of failure within protection effort;

f. Success of health education effort to stimulate personal and community vector control interventions;

g. Need to improve health education;

h. Need to change the dose of the prophylactic drug;

i. Need to change the prophylactic drug; and

j. Whether to undertake more comprehensive malaria control.

D. Primary Health Care System

1. Role of Primary Health Care

There are no technical reasons why the PHC system could not successfully undertake the tasks of administering both malaria chemoprophylaxis and chemotherapy. Ability to implement an outward-looking, anticipatory malaria prevention program as well as a treatment program depends on staffing, competing demands on time, the size of the population groups to be protected and the intervals between prophylactic doses.

Review also Chapter IV-C-1, the thrust of which is even more applicable to antimalaria efforts at the TV-II level.

2. Manpower for A Mortality and Morbidity Reduction Program

While the manpower requirements for TV-I programs described in Chapter IV-C-2 are still pertinent (since mortality reduction remains a goal), the additional effort implicit in a chemoprophylaxis program imposes a significant and measurable additional burden on the PHC system. Malaria chemoprophylaxis and vector control interventions are preventive rather than curative; they anticipate and thereby avert the need to react. At the level contemplated by a Tactical Variant II program, they are selective in coverage rather than comprehensive. Their implementation requires more involvement of the PHC staff.

In addition to the system established to implement Tactical Variant I, there is need for an active outreach system at the periphery to deliver chemoprophylactic doses regularly to target populations, and to provide the health education which can stimulate the adoption of individual and community vector control interventions. This system should utilize dispensary services, MCH personnel, midwives, community health workers and traditional birth attendants. To assure adequate chemoprophylaxis coverage, a concerted program of health education aimed at mothers will again be required.

In many, and probably in most cases, this comprehensive active outreach capacity would have to be developed to pursue a chemoprophylactic and related control activity. This could represent up to a two to three fold increase in support requirements, such as drug costs, increases in use of staff for malaria control, transportation, supply facilities, logistic support, management and administrative support.

A particular problem of health delivery relates to cases in which outreach services are required for pregnant women and children, to be visisted in their homes. Experience in Africa and elsewhere indicates that a paid, full-time worker is able to visit an average of 20 families per day. (A part-time volunteer could be expected to have a smaller coverage potential). This large number of new village level workers would require support from the full-time staff of Ministry of Health, Ministry of Education or other government entities. Experience in West Africa indicates that the cost in paid full-time manpower for recruiting, training, supervising, backstopping and supplying volunteer village health workers may be as high as one paid worker for each four volunteers.

While these new village level workers should serve additional PHC functions -- not merely malaria control -- the cost would be high, and in any event far higher than the cost of malaria mortality control for an equivalent population.

Chemoprophylaxis could, however, be provided to only a portion of target groups -- that portion which voluntarily visits a health center (of whatever nature) -- at a low cost in manpower. The program would have little impact on morbidity.

A program with the purpose of assuring delivery of chemoprophylaxis to target groups would be more expensive in manpower; as a rough-cut figure the reuirement for CHW might be about one per hundred family units to be served, with backstop costs of one paid worker per 400 family units.

While a malaria prophylaxis program with outreach could serve as a vehicle for reaching target groups for the total PHC health service package, no such program should normally be considered for malaria prophylaxis alone. Also, in terms of cost effectiveness, it will rarely prove to be appropriate to establish a free-standing chemotherapy program in the absence of an established outreach system.

The administrative burden may be borne more easily when prophylaxis for economically important elements in the work force is desired; the task of drug distribution can be delegated to employers, whose ability to insist on worker participation is enhanced by control of employment opportunity.

When non-immune labor groups enter a highly endemic area, information can be supplied to the employer (or, conceivably, the government ministry responsible for contract workers) regarding the need

for chemoprophylaxis, the drug of choice, the prescribed dose, the schedule of drug administration, and other methods of malaria control for protection of the labor group.

In brief, it may be possible to provide prophylactic protection to economically important elements in the work force or to non-immune labor grops at low cost in time, money or manpower.

With respect to pregnant women or young children, if prophylactic drug distribution is to be passive (i.e., to persons regulary attending facilities of the curative care system already in place) the administration of chloroquine in prophylactic dosage can be undertaken by existing personnel, since the additional work is limited to individuals within target groups who visit the facility. In some cases there may be a requirement for additional staff, but for passive drug distribution the number will be small.

All PHC staff must receive training in and understand the difference beteen chemotherapy and chemoprophylaxis and in health education.

If distribution is to be active, i.e., designed to reach all or a specified high percentage of members of target groups on a regular outreach basis, the manpoer situation is entirely different. Health education, including motivational techniques to bring about the adoption of individual and community vector control measures, becomes a particularly significant element in PHC training. Such a program when assigned to the PHC system imposes an additional burden that can be overcome only by providing adequate staff.

3. Health Education and Community Participation

Compared with the health education efforts required for a TV-I program, described in Chapter IV-C-3, above, health education needs increase in complexity when people are expected to prevent malaria through chemoprophylaxis and/or vector control. There may be few or no local traditions that would support such concepts. Also, anti-malarial drugs are commonly bitter and may have some discomforting side-effects. Family priorities may not include allocation of scarce resources to prevent illness before it occurs. Further, the motivation for chemoprophylaxis may be weakened when people observe that some get malaria after taking drugs -- which may well happen if individuals in the community purchasee the wrong chemoprophylactic drug or follow an improper dosage schedule. Factors such as these argue for the design of on-going evaluation of

educational efforts which seek to discover why actions to prevent malaria are or are not being followed.

E. Conclusions

There are no technical reasons why the PHC system could not successfully undertake the tasks of administering malaria chemoprophylaxis as well as chemotherapy. Ability to implement a program of malaria prevention as well as curative treatment depends on staffing, reliable logistic and management support, competing demands on time, the size of the population groups to be protected, the intervals between prophylactic doses, and the availability of sufficient funds to cover the costs.

The staffing requirements (which would continue beyond any period of external support) constitute a quantum increase over those for a program of mortality control through chemotherapy.

The costs of a morbidity control program include major increases for drugs, supplies and personnel. These costs must be weighed against expected benefits in relation to total health resources available, to other health priorities, and to benefits which would inure from alternative malaria control efforts.

The national distribution policy will govern the decision as to whether the drugs employed for chemotherapy and chemoprophylaxis will be sold or distributed without charge. In discussing possible assistance to malaria control programs with host country officials, field missions should explore the possibility of having beneficiaries bear the costs of chemotherapeutic and chemoprophylactic drugs -- preferably but not necessarily both.

Vector control at the level which can be conducted by individuals or communities will frequently be a particularly effective form of morbidity control, and encouragement of such efforts is a direct responsibility of PHC health education and sanitation personnel.

It is also possible to undertake more technically demanding forms of vector control in some parts of a country which will elsewhere limit its efforts to chemotherapy and chemoprophylaxis. Such endeavors should be undertaken where entomologic studies indicate the need and where the host country capacity for implementation exists. It should be recognized that vector control of this nature (dealt with in greater depth in Chapter VI) is no longer to be considered "malaria control in PHC"; although PHC retains a facilitating role, it lacks the technical capacity to plan and undertake major vector ocntrol programs. It also lacks the ability to devote such a proportion of its attention to a single problem.

VI. Comprehensive Malaria Control (Tactical Variants III and IV)

A. Relation to Tactical Variants I and II

1. Tactical Variant III

Comprehensive malaria control (Tactical Variant III) moves beyond chemotherapy (to prevent death from malaria) and of chemoprophylaxis (to prevent malaria infection from reaching the acute stage) to reduction in malaria transmission through the interruption of contact between man and mosquito. Such a program makes possible the selection of the forms of intervention from a wide range of available techniques; but it also requires the ability to identify the interventions applicable to a particular area, and the capacity to conduct such interventions.

Comprehensive malaria control incorporates all of the actions required for the planning, conduct, management, supervision and evaluation of programs at the TV-I and II levels. The following chapter will concentrate, therefore, on only the additional considerations which must enter into a decision to mount a comprehensive malaria control program at the TV-III level. Decisions on the feasibility of applying control measures beyond mortality control through chemotherapy must be made with the technical support of malaria specialists.

2. Tactical Variant IV

Comprehensive malaria control at the Tactical Variant IV level contemplates not only a country-wide effort but also an effort conducted with a degee of perfection which makes possible the establishment of a long-term goal of eradication. Such an effort is likely to be beyond the present financial capacity of any country in tropical Africa.

B. Planning

1. Goals and Targets

a. Goals

The goals of a comprehensive malaria control program subsume those for drug programs -- reduction of malaria mortality and morbidity through chemotherapy and chemoprophylaxis -- and include the reduction of the actual reservoir of malaria infection within the population -- the actual prevalence of infection -- through the application of one or more measures of vector control, designed to limit contact between man and vector. As applied to malaria control, vector

control is the reduction of the transmission potential of the mosquito vector population by an amount which is epidemiologically significant in reducing human malaria prevalence -- the reservoir of infection -- and related morbidity and mortality. The goal is to break the contact between infected man and mosquito, and between man and infected mosquito -- not to kill all mosquitoes. An appropriately selected vector control measure may prove to be superior to chemoprophylaxis as a form of morbidity control, in terms of cost efficiency. In such circumstances, resource constraints might dictate a decision to attempt vector control instead of chemoprophylaxis.

Vector control measures range from simple physical barriers (screens, bed nets), to repellants (mosquito coils, pest strips), to long-lasting chemical sprays that kill mosquitoes which subsequently rest on house walls or eaves (residual spraying), to habitat treatment to reduce the mosquito population (larviciding), to environmental management to eliminate breeding foci (drainage, filling), and to biological tools (larvivorous fish).

In Africa at present, major vector control efforts will be appropriate only in areas such as urban and periurban locations, on islands, or under special circumstances (e.g., strategic areas, or areas of particularly high economic, social or political significance, where the benefits clearly warrant the high cost). In such circumstances, operational planning of vector control should be decentralized wherever possible to the responsible administrative units such as municipalities or productive enterprises, with higher level technical support where necessary.

This variant depends upon the existence of an organizational malaria control nucleus (not necessarily with country-wide responsibilities) and a sufficient number of trained personnel to utilize the available tools, (chemotherapy, chemoprophylaxis and selected methods of vector control), and to undertake entomological and epidemiological evaluations of the actions needed and taken and the results achieved.

The goal of a comprehensive malaria control program is to achieve a condition in which malaria-related mortality and morbidity and the transmission of malaria infection are reduced; or even completely interrupted.

b. Intermediate Targets

While mortality targets remain essentially the same as those set forth for TV-I and II interventions, (prevention of mortality among victims of acute malaria), the actual number of patients exhibiting the symptoms of acute malaria is expected to decrease markedly. Moreover, the need to extend chemoprophylaxis to particularly vulnerable and/or economically important population groups should (under ideal conditions) decline or disappear as the comprehensive malaria control program takes effect. In practice, the need for chemotherapy will continue at least until a malaria program of nation-wide scope has shown itself capable of a measure of control not likely to be found in tropical Africa. The spread of disease by nomads, migrants and others can reinfect a malaria-free area unless a rigid surveillance effort can be maintained; and surveillance of such a character is beyond the scope of community-based malaria control.

Sample targets might be:

- Identification of all breeding foci within the flight range of the primary vector from each population center served under the program.
- Application of appropriate form of vector control. Elimination of deaths from symptomatically identified malaria in the immediate areas served by a program.
- Continued reduction annually in the prevalence of parasite infection in the population of the area served by the program.

2. Training

The training requirements for a program of comprehensive malaria control far exceed those for programs keyed to chemotherapy and chemoprophylaxis. The decision to adopt this Tactical Variant must be keyed to the existence of an organizational malaria control nucleus and a sufficient number of personnel trained to utilize the available tools (chemotherapy, chemoprophylaxis, and a wide range of methods of vector control), to select the tool appropriate to each entomological and epidemiological situation, and to evaluate the actions needed and the results achieved.

Application of this form of control is technically demanding; it requires the availability of technical expertise not merely at the central planning and evaluation unit, but also at the periphery. Decentralized decision-making calls for a measure of training which exceeds that required for eradication programs.

In addition to advanced training in epidemiology, entomology and malariology, comprehensive malaria control has a need for a number of men who possess training of an entirely different kind: the ability to handle toxic insecticides without danger to themselves and others. Such training may be provided on the job, provided that spray foremen have themselves received adequate training.

It should be noted that the kind of training required for the decentralized decision making noted above is neither required by nor appropriate for PHC workers at the periphery. Comprehensive malaria control is the province of the specialist; PHC workers in the communities can facilitate but seldom manage such efforts.

3. Logistics

Review Chapters IV-A-3 and V-B-3, above.

Control efforts of any kind must be keyed to the availability of an adequate supply chain which can guarantee timely procurement, safe storage, stock control and delivery at point of use in advance of need. Comprehensive malaria control involves a higher degree of mechanization, a wider range of tools (larvicides, residual sprays, application equipment, possibly heavy earth moving equipment, more vehicles, etc.). It may no longer be possible to rely on existing systems of procurement, storage and delivery. Vehicle maintenance may become a key factor in program performance as the volume of commodities to be moved increases, the number of personnel to be transported grows, and the expansion of activities into areas not previously served puts increasing strain on vehicular capacity.

As was noted in respect to training (Chapter VI-B-2, above) the kind of logistic support required for comprehensive malaria control exceeds any normal requirement of a PHC program. It is representative of the kind of effort more characteristic of categorical disease control efforts. It will, moreover, continue as a need beyond any period of external support.

4. Demographic Considerations

Review Chapters IV-A-4 and V-B-4.

5. Assessment of Feasibility

Review Chapters IV-A-5 and V-B-5.

Clearly, the kinds of tests to be applied to a comprehensive malaria control plan will incorporate those applicable to a mortality and morbidity reduction effort; additional tests will be determined by the nature of the interventions.

One major point of difference between programs relying solely on drug administration and those which attack the vector itself is the extent to which the former efforts can take place in virtual isolation, almost uninfluenced by activities outside the local PHC center, as against the wide range of institutions and activities which may influence, or indeed overwhelm, a program directed at controlling the vector. A meticulously conducted program of source reduction can be offset by a carelessly designed or executed highway project which creates an accidental water impoundment; irrigation projects can provide mosquito breeding sites; carelessly maintained drainage systems can have the same effect. Such "man-made malaria" is not the result of malaria control, but it must be of concern to those responsible for the control effort, whether that effort be national or local.

At the national level some type of coordinating body is needed involving all institutions which may have positive or negative effects on malaria or its control. At intermediate and local levels, specialized coordination of malaria and other related activities must be assured (for example, district or village development councils).

The provision for such coordinating bodies in the malaria control plan is a critical factor in assessment of program feasibility.

6. Cost Calculations

Review Chapter IV-A-6; see Annex XIII

C. Technical Aspects

1. Tools Available

In addition to anti-malarial drugs administered therapeutically and prophylactically, comprehensive malaria control has access to a broad spectrum of

vector control methods, selection among which is influenced by the epidemiology, the vector, its breeding preferences, its biting characteristics, its demonstrated resistance to one or more of the available chemical sprays, the nature of the terrain, the impact of possible control methods on th environment, and, of course, the cost and the requisite knowledge. These intervention methods fall into three main categories, all directed against malaria vectors at different stages of their development, and a possible fourth category which might be termed "avoidance".

a. Chemical Control

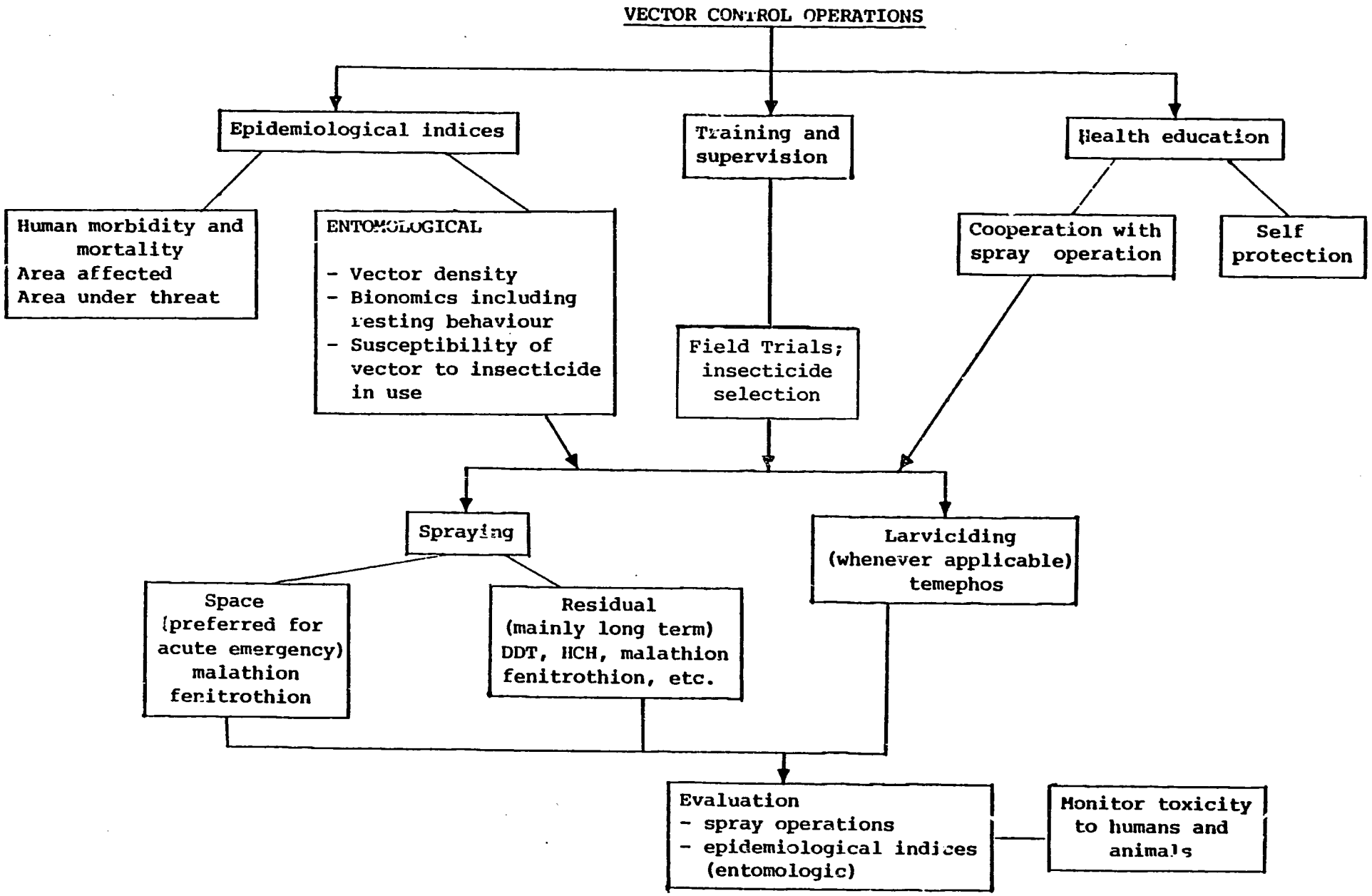
Insecticides are widely used because of their versatility and their quick action; they have the disadvantage of need for regular repetition; their application is very sensitive to local ecological and operational conditions; many chemicals have a relatively short effective period of usefulness before resistance becomes apparent in the vector. Without exception, chemical controls should be initiated only after a suitably organized field trial, required to determine the effectiveness of different pesticides under local ecological conditions. Such trials should be conducted by trained technicians. PHC workers can assist in such trials.

The insecticides used in malaria control (even the "safe" pyrethroids) are at certain doses toxic to man. Some have shown themselves to be lethal when carelessly handled. To avoid danger to spraymen, the protected population and domestic animals, these insecticides should be applied by men trained for the task. Spraymen should have training suitable for the insecticide of choice and be provided protective clothing and proper equipment. Supervision is an important part of any such operation.

Chemical control includes both anti-larval activities and anti-adult measures. Figure 2 outlines the elements of consideration in the determination to undertake a chemical control program.

Certain donors -- specifically, the Agency for International Development -- require an assessment of the environmental impact of the proposed application of the chosen insecticide prior to approval of any project calling for such application. While the application of insecticides in the volume required for public health use has

MALARIA: Figure 3



not been shown to have a damaging impact on the environment, the legal requirement for an environmental impact assessment remains in effect. Such an assessment is normally made by specialists brought to the host country for the sole purpose of performing the assessment -- which is, of course, one of the cost factors in the project.

(1) Larvicides

Anti-larval measures involve the chemical treatment of mosquito breeding sites. The chemical must be selected on the basis of safety to man and environment (including non-target organisms); cost-effectiveness; and ease of application. Most require equipment for application of formulations (e.g., oil, pellets, granules, briquettes). Larviciding can be an effective form of control if properly timed. In practice, the manpower requirements are frequently excessive.

Typical of the range of available larvicides are certain of the organophosphorus compounds (Abate is generally considered the safest and most effective) and mineral oils (time-honored but now expensive). Paris green, an arsenic compound widely used in the U.S. when malaria was still common, is still an easily applied chemical with an excellent safety record but an obvious potential for danger in untrained hands.

Most larvicides may be applied by the standard back-pack spray systems.

(2) Anti-adult measures

Malaria control through anti-adult insecticide attack on the vector mosquito takes two principal forms: residual indoor spraying and outdoor space spraying.

(a) Residual spraying is the application of an insecticide to the indoor surfaces of houses where vector mosquitoes rest before and after feeding. The insecticide should have a long-lasting capacity to kill mosquitoes which rest on it; be safe to man; and be as inexpensive as possible.

The choice of a residual insecticide -- or, indeed, the decision to undertake a program calling for the use of a residual insecticide -- is not purely a function of the known longevity of the lethal effect of an insecticide on mosquitoes. Among other factors which must be taken into consideration are the following:

- The feeding habits of the principal vector or vectors. A mosquito which is primarily or exclusively an out-of-doors biter will not be affected by any residual spray.

- The resting habits of the principal vector or vectors. A mosquito which rarely rests on the inner surfacers of a dwelling after taking a blood meal will not be seriously affected by any residual spray.

- The "excitorepellance" of a particular insecticide which causes mosquitoes to refuse to rest on a sprayed surface.

- The nature of the inner surfaces of the typical dwelling. Some surfaces do not preserve the lethal characteristics of a residual spray over extended periods.

- Cultural behavior patterns which call for periodic resurfacing of all interior walls of residences -- and, consequently, a covering of any residual spray. (Such patterns may be reinforced if the chosen insecticide stains walls or has an objectionable odor).

Typical of the range of residual insecticides are: DDT and similar chlorinated hydrocarbon insecticides; organophosphorus insecticides (malathion, fenthion, fenitrothion); carbamates (Propoxur); and pyrethrins and their synthetic derivatives. (A profile of the most widely used chemical control agents is shown in Table 3). Resistance to specific insecticides has been reported for a number of the major

African vectors of malaria. (Table 4 shows reported vector resistances to insecticides, by vector and by insecticide).

(b) Outdoor space spraying. Especially in emergency situations, such as epidemics, but also in some urban situations, pesticides can be applied outdoors in ultra low volume (ULV) or thermal fog applications, at or near ground level where mosquitoes are abundant. Timing is important; to be effective, such spraying requires the temperature inversion characteristic of early morning or evening and low ambient wind velocity. Outdoor space spraying requires trained manpower, protective equipment for spraymen and mechanical equipment (hand-carried, back-pack or vehicle-mounted machines are available; maintenance can be a problem in many countries). Insecticides of choice include malathion, fenitrothion and the pyrethroids.

b. Biological Control

Biological control of malaria vectors has never, as a single form of intervention, whown itself able to reduce vector density to a point where there is a major long-range (i.e., persistent) reduction in malaria incidence or prevalence. As an addition to other elements in a comprehensive control program, biological control has been utilized in circumstances where chemical attack might prove inappropriate.

(1) Larval control

Three forms of biological vector control at the larval stage have been recognized as theoretically possible -- predators, parasites and pathogens. Only predators (in the form of larvivorous fish) have been used operationally in malaria control programs in Africa. The top-feeding minnow (*Gambusia affinis*) and the guppy (*Lebistes reticulatus*) have been shown to be effective larvivores. Use of local larvivorous species (if available) would be preferable -- to minimize cost and environmental impact. It should be noted that larval control through predator fish is not a practical form of vector control for most of sub-Saharan Africa. The

Table 3. Characteristics of Insecticides Commonly Used in Mosquito Control

INSECTICIDES	Target	Local Application Site	Formulation	Active Content	Dose	Frequency of Application	Equipment	Method of Application	Toxicity	Resistance	Cost	Disadvantages	Advantages
Petroleum Oils	larvae	water surface	w/ 1-2.5% vegetable oil 1% DDT	100%	20-60 l per ha.	weekly	cans sprayers cotton-balls	hands	non-specific fauna/flora kill	none	moderate to high	pollution contamination removes water source	extremely effective easy to apply and store
Pyrethrum and Synthetic Pyrethroids -dimethrin -permethrin -allethrin -decamethrin -tetramethrin	larvae adults	water house (coil) forest (dust) town (fog)	.1-.4% dilution w/ kerosene .2-.4% ducts	.7-3%	.1g/m^2	6x/yr	sprayers foggers smoke coils dusters aerosols (ULVs)	hands truck airplane	kill fish	none	moderate to high	difficult to produce requires equipment	exceptional kill activity for mosquitoes safety
Paris Green	larvae	on water	1-30%	50-55% (arsenious oxide)	6-15g per 100 m^2 water	----	dusters blowers sieves mixers	hand blowers water	no evidence	none	-----	no effect on eggs or pupae constant supervision	low cost high toxicity for anopheline portability
Chlorinated Hydrocarbons													
DDT (dichlorodiphenyltrichloroethane)	adults (larvae w/ oils)	eves walls	50-75%	70-100% (para-para isomer)	2g/m^2	2x/yr	sprayers	hand spray	no evidence to man	A. gambiae A. melas A. pharoensis low		nondegradable toxic to fish and birds nonspecific for insects	low cost

Characteristics of Insecticides Commonly Used in Mosquito Control

INSECTICIDES	Target	Local Application Site	Formulation	Active Content	Dose	Frequency of Application	Equipment	Method of Application	Toxicity	Resistance	Cost	Disadvantages	Advantages
HCH (hexachlorocyclohexane) (lindane)	adults larvae	eves walls	6.5% lindane fumigant and contact	12% (99%-lindane)	.3g/m^2	4x/yr	sprayers	hand spray smoke emulsion	incident free	A. gambiae A. melas A. funestus A. pharoensis	moderate	cross resistance in aldrin shorter residual effect quick resistance	use with DDT in nonresistant FOCI Moderate cost
Dieldrin	adult	eves walls	----	80%	.5g/m^2	3x/yr	sprayers	spray	man animals	A. gambiae A. melas A. funestus A. pharoensis	moderate to high	fairly high toxicity easily produces resistance	quick acting
Organophosphorous Compounds													
Malithion	adults	eves walls	60-90%	50%	2g/m^2	4x/yr	sprayers foggers	hand spray fog	low to none	none	moderate	stores poorly quickly absorbed sprayman precautions	effective on impervious materials effective where there is DDT resistance
Fanthion	adults larvicidal(?)	----	----	----	1.5g/m^2	----	sprayers	----	man animals	none	moderate	higher toxicity	used with some success in Africa
Fenithrothion	adults	eves walls	----	----	2g/m^2	3x/yr	sprayers fumigants	hand spray	man animals cholinesterase depression	----	moderate to high	toxic requires safeguards	long lasting effective in E. Africa

Characteristics of Insecticides Commonly Used in Mosquito Control

INSECTICIDES	Target	Local Application Site	Formulation	Active Content	Dose	Frequency of Application	Equipment	Method of Application	Toxicity	Resistance	Cost	Disadvantages	Advantages
Temephos (Abate)	larvae	water	impregnated granules	1%	1ppm	12x/yr	containers	hand aircraft	very low	none	low	not residual toxic to shrimp resistence develops	highly effective non toxic slow release
Carbamates													
Propoxur (Baygon®)	adults	eves walls	fumigant & spray	----	$2g/m^2$	4x/yr	sprayers	hand	moderate skin reactions	none	high ($12/house)	moderately toxic requires safeguards	residual very effective stable

Table 4

Resistance [1,2] in African Malaria Vectors

Vector	Insecticide			
	DDT	Dieldrin-HCH	Organophosphates	Carbamates
A. gambiae (A&B)	●	●	-	-
A. gambiae (melas)	●	●	-	-
A. funestus	-	●	-	-
A. moucheti	0	0	0	0
A. nili	0	0	0	0
A. pharoensis	●	●	-	-

1. ● = resistance possible; - = no resistance; 0 = unknown
2. Types and quality of resistance may vary with locale.

After Bruce-Chwatt, 1980; WHO Technical Report Series No. 585, 1976.

main vector, Anopheles gambiae, breeds in temporary water habitats, where the fish would not survive. These breeding sites are also too numerous to stock. There are a few exceptions (e.g., Somalia) where there are permanent limited water supplies. Additionally, larvivorous fish have been effective in preventing mosquito production in wells.

Use of parasites and pathogens is still in the research stage as far as malaria control programs are concerned.

(2) Adult control

Measures such as chemical treatment or irradiation of adult male mosquitoes which result in their sterility have been shown to be a control technique which is effective only under very special circumstances where pressure from wild males does not overpower the "treated" males. Genetic manipulation is also in the study stage.

c. Source Reduction

Source reduction is the modification or management of the environment to minimize or prevent vector propagation. It takes many forms, some of which can be undertaken at the village or community level. Table 5, although not specifically keyed to African conditions, suggests the maximum range of community level activity.

(1) Minor Source Reduction

Environmental modification -- a permanent transformation to reduce or eliminate vector habitat -- may be relatively minor in terms of the effort involved, the technical knowledge required, the need for specialized equipment and the need for subsequent maintenance. Activities which can be undertaken at the community level, given sufficient interest and understanding, include the filling and leveling of small water collections in and around villages and the drainage of unwanted water. It is of course important to avoid the creation of new borrow pits when securing fill material; undrained borrow pits are in many areas a major source of focal malaria infection. The role of PHC health education is apparent.

Table 5: Environmental Management Techniques Utilized to Decrease the Population of Man-Biting Anopheline Mosquitoes at the Community Level

	SOURCE REDUCTION REQUIREMENTS[1]					
Technique	Manpower[2]	Equipment[3]	Duration[4]	Maintenance Requirement	Cost	Efficiency[5]
Filling	U/T	L	I	2	1	3
Drainage	U/S/T	L/H	P/A	3	3	3-2
(Open) (Subsoil) (Vertical) (Tidal swamp)						
Water Management	S/T/U	H	P/A	4	3	2
Sluicing and Flushing	U/S	L	A	3	2	2
Intermittent drying	U/S	L	A	1	1	2
Clearing of bush	U/S	L	I	1	1	1
Explosives	S	H	I	1	4	2

1. Numerical grade relates qualitative level: 1=low; 2=moderate; 3=high 4=very high

2. Manpower : S=skilled; U=unskilled; T=Training of supervisory personnel

3. Equipment : L=local tools; H=heavy and/or sophisticated equipment

4. Duration : A=annual upkeep; P=permanent; I=intermittent attention (3-5 years)

5. Efficiency: The efficiency of an intervention is contingent upon its logistical support.

(2) Major Source Reduction

Careful planning and care in the execution of major engineering works -- e.g., highways and irrigation systems -- can reduce the problem of "man-made malaria". Particularly annoying are the water impoundments frequently created by raised highways. Avoidance of man-made malaria is a community problem which must, however, be solved by enlisting support of the anti-malaria effort among those responsible for the planning and execution of development projects.

The exclusion of salt water intrusions in breeding places near sea shores (through tidal gates or thrugh other measures) requires equipment, skill and capital resources not normally available to any but the largest communities.

(3) Environmental Management

Some forms of source reduction involve manipulation rather than modification of the environment. Again, some of these activities are appropriate for application by communities or even by individuals; others require control over major resources, including precautions which should be built into large-scale engineering works from the design stage forward.

For example, some stream-breeding vectors can be controlled by the periodic discharge of a relatively large volume of water, washing away or stranding larvae. An automatic periodic siphoning structure can carry out this procedure, and should be built into plans for the dam which is a prerequisite to a control which relies on flushing.

Similarly, raising and lowering the water level in large reservoirs has the effect of destroying the habitat for some vectors.

At the level of management which can be put into effect at the level of the commuinity or the individual, the practice of intermittent irrigation is useful in two respects: the periodic drying of the irrigated area can destroy mosquito larvae;

and there is evidence that some kinds of crops respond favorably to intermittent irrigation. Again, the role of the PHC health educator is apparent.

(4) Avoidance

Mosquito avoidance, an appropriate form of self-help and community participation effort to reduce the probability of malaria infection within any of the technical variants to malaria control, is covered in detail in Chapter V-C-1-b(3), above.

2. Baseline Data

Since mortality and morbidity reduction continue to be the objectives of a comprehensive malaria control effort, Chapters IV-B-2 and V-C-2, above, remain fully applicable.

Other aspects of a comprehensive effort required specific site examinations for most interventions to determine feasibility. Such data are not likely to exist in usable form; they will require an advance reconnaissance survey which will provide the expertise of the entomologist, the epidemiologist, the parasitologist, the engineer and -- quite possibly -- the social scientist. The baseline data are assembled in the course of the survey. Such a survey may be useful (although it may not always be essential) even for the small-scale activity which can be carried out at the community level. To the extent that technical experts from the center can conduct such surveys, there is a great potential saving in community-contributed labor employed for non-productive efforts -- and in community resentment averted.

3. Record Maintenance

Record maintenance requirements for programs of comprehensive malaria control are more complicated and detailed than those for programs of drug administration. The range of possible activity precludes the simple records suggested in Chapter IV-B-3; literacy is required in the person preparing reports, just as it is in individuals preparing formulations of insecticides. Technical and administrative skills are required to design but also to maintain a useful record system.

In addition to the information produced by the PHC reporting system (see Chapter IV-B-3 and V-C-3, the organization which is responsible for vector cntrol should regularly provide data on, among other things:

- Insecticide of choice for residual spraying
- Application per square meter
- Number and location of houses sprayed
- Number of refusals to authorize spraying
- Number of spraymen employed
- Insecticide toxicity among workers
- Starting and concluding dates
- Amount of insecticide used
- Resistance patterns and levels
- Amount of insecticide on hand
- Insecticide requirements for next cycle
- Date of next cycle
- Sprayers on hand; replacements required
- Nozzle tips on hand; replacements required
- Annual parasite incidence
- Acute malaria incidence
- Larviciding operational data and instructions
- Source reduction activities

Some of this information is needed for operational planning; some for evaluation of results achieved. The nature of required reporting and its prescribed content will be determined by the kind of vector control undertaken.

4. Evaluation

Review Chapters IV-B-4 and V-C-4. Reporting requirements of the PHC with respect to drug treatment will continue under a comprehensive malaria control program, as will the evaluation of those reports.

Additionally, however, the location-specific reporting of the organization responsible for vector control must be evaluated to determine the effectiveness of the measures adopted in reducing annual rates of parasitic infection and incidence of acute malaria infection.

Sample surveys in "indicator" communities are less useful in evaluating progress under a vector control program. The nature of the program will be determined, area by area, in the course of the initial and subsequent stratifications (Chapter III-C), and reporting and evaluation are area-specific.

Communities require information on the social and health impact of their own activities. This may be based on information collected by the community such as numbers of fever cases, general morbidity and mortality, number of cases referred for treatment to hospital or health center, and levels of participation by the community in specific control activities. Such information is needed to insure or increase community support for ongoing activities.

Central managers need additional data derived from both operational information and special collective efforts. The minimum requirement necessary for adequate assessment and replanning calls for an annual general review, with more frequent monitoring of operational information appropriate to the methods in use. Usually the more complex the operation the more need there may be for periodic and detailed evaluation.

Monitoring and evaluation criteria should include the following types of indicators.

- o Prevalence changes - malariometric indices.
- o Vector indicators (appropriate to measures used)
  - vectoral capacity
  - resistance patterns and levels
- o Operational assessment
  - spraying activities and accomplishments
  - environmental changes
  - insecticide toxicity among workers, etc.
- o Cost and effectiveness of the system being used operationally, administratively, and technically.
- o The program budget should make specific provision for evaluation, to insure adequate operational, malariometric and entomologic information for effective planning and replanning.

In addition, it is also vital to examine, give recognition to and quantify the self-help efforts brought about with the assistance of PHC health educators. An evaluation of the educational efforts associated with the comprehensive malaria control effort can provide significant guidance for the design of future health education efforts.

D. Primary Health Care System

1. Role of Primary Health Care

Review Chapters IV-C-1 and V-D-1, above

Where vector control activities are restricted to avoidance and environmental modification measures, they can be applied through appropriate extension of health education and sanitation activities within PHC. These might include individual or general community efforts,

or mobilization of school children for control activities. Where vector control includes wide-spread chemical control such as house spraying, or larviciding, specialized services are likely to be necessary, although they should be linked in mutually supportive relations with PHC activities insofar as possible. Vector control activities beyond avoidance and environmental modification should not be delegated to minimally trained PHC personnel (or for that matter, to minimally trained community personnel) although certain portions of the program may be delegated to minimally trained personnel provided there is technical supervision and guidance. As an example, insecticide spraying can be handled at the community level provided training, guidance and supervision are available. (See, however, Chapter VI-D-2, below.

It is essential, of course, that responsible provincial or district health officials and their staffs be fully involved in coordination and cooperation between the comprehensive malaria control effort and whatever PHC activities are going on in their areas of responsibility. This also relates to the need for the national level coordination body discussed in Chapter VI-B-5, above.

2. Manpower for A Comprehensive Malaria Control Program

With respect to mortality and morbidity reduction, Chapters IV-C-2 and V-D-2, above, remain fully applicable. Manpower for other aspects of comprehensive malaria control is a function of interventions to be made, area to be protected, and the implementing unit. Vector control efforts -- chemical, biological, or source reduction -- involve at the field level technical expertise, management, logistics, training and costs which far exceed such requirements for drug treatment. Moreover, use of some of the residual insecticides involves real dangers -- especially to spraymen -- which make it imperative that such attacks be mounted only by trained manpower, equipped with suitable protective clothing and proper spraying equipment. The timing of interventions, the chemical to be applied, the susceptibility of the vector to the chosen chemical, the interval between insecticide applications, the amount of chemical to be applied, the techniques of application, the duration of chemical effectiveness in killing mosquitoes must be known and built into plans for execution. These factors impose problems of logistics, of rigid timing, of ability to commit staff to single-minded pursuit of a single goal. As such, they fall outside the scope of execution by normal PHC operation.

Community volunteers have been used for vector control activities -- even, it is reported, for major chemical control efforts during the period when chemicals of low toxicity (DDT) were still widely effective. Experience indicates they can be effective initially, but such efforts are unlikely to be sustained, and may not be useful for long-term efforts.

As was noted in Chapter VI-C-3-c, above, however, there are many small-scale projects -- primarily in the field of source reduction -- that can be carried out by communities or even by individuals, without the need for external support. The critical element for execution of such activities is the stimulation to undertake something not visibly and immediately linked to the advantage of the community and its individual members.

The appropriate level of management planning and implementing (supervisory) responsibility depends on the complexity of action to be undertaken, the size of community involved and the level of understanding of persons concerned. Activities such as avoidance and minor source reduction (environmental modification) can and should be planned and implemented at village level and may be supported largely though the PHC structure. More complex measures such as chemical control requires planning at a higher level, with specialized technical inputs. Although there is some limited experience in chemical control using PHC workers, this will usually require support from a specialized vector control unit; moreover, such an effort is beyond the scope of work normally considered appropriate for PHC.

The PHC health educator can serve as the stimulator, the facilitator, and the person through whom additional expert advice may be sought when needed. The health educator may also help secure the full cooperation of the community (as against passivity or even resistance) in relation to measures being executed by other participants in a vector control effort.

Large-scale efforts (development schemes, major drainage efforts, highway construction) are not the responsibility of the community, the PHC or the Ministry of Health, but require at the planning stage the technical inputs of the Ministry of Health malaria specialists to warn of the dangers of "man-made malaria".

In brief, the manpower requirements for comprehensive malaria control are a function of its geographical extent, the nature and number of interventions selected and the entities through which

execution will take place. For PHC, the manpower requirements are those for a program of mortality and morbidity reduction, but with additional burdens to be borne by those responsible for over-all management, supervision and health education.

3. Health Education and Community Participation

Review Chapters IV-C-3 and V-D-3.

Chapter VI-D-2, above, emphasized the role of the health educator in stimulating community participation in vector control activities suitable for community execution and facilitating community cooperation in vector control activities beyond the limited capacity of most communities.

The extent to which community participation can reduce the costs of malaria-related activities as well as activities for the direct control of malaria is an area which warrants careful examination. An increasing amourt of educational effort may be balanced or exceeded by savings in paid personnel needed to carry out activities in the absence of contributed community efforts. In general, for activities in the field of vector control the requirements for the funding of such educational efforts may be as high as 25% of funds available where substantial community inputs are required.

E. Conclusions

Comprehensive malaria control is the province of the specialist. It is inappropriate for implementation through PHC, although PHC cooperation with malaria control activities is essential at all levels. At the local level, PHC can facilitate and create an understanding of measures which it lacks the technical expertise to conduct or direct. Vector control activities may and frequently will be delegated to and financed by the communities which they will benefit. Where they are restricted to minor environmental modification measures, they can be applied through extension of health education and sanitation within PHC. Where vector control includes wide-spread chemical control such as house-spraying or larviciding, large-scale drainage activity or other major source reduction, specialized services will be necessary from initial planning through implementation; such activities should not be supervised by or delegated to PHC personnel unless they have received proper training.

VII. Operational Research

As are all public health interventions, a malaria intervention should be based on the use of available technical knowledge suited to the situation faced. Although much of the technical basis for malaria control is outlined in this document, the applications of control techniques may need to be further refined by study of interventions and their alternatives. This operational research can lead to refinement of specific costed activities on country-specific basis.

Essential features of operational research are: 1) a concise statement of the question to be answered and 2) a detailed protocol describing the study procedure. Without these, the time and effort invested in research may result in no new knowledge. WHO has prepared standard research proposals, which, under certain circumstances, can be externally funded.

In malaria control programs that are integrated with PHC, a wide array of topics for potential research exists. Currently, these topics range from manpower management, to field supply, to logistics, to laboratory support to test for drug sensitivity. Several examples of such operational research topics are listed below. They are keyed to a PHC-executed program of malaria mortality reduction through chemotherapy.

- Use of slide examinations to confirm symptomatic diagnosis of malaria, or to determine the accuracy of self-diagnosis.
- Effectiveness of fixed health units in reducing mortality (overall and malaria-related).
- Importance of the community's contribution to disease control.
- Parasite resistance to drugs (presence or absence).
- Number of tasks that can be performed effectively at the health unit or by a health worker in the field.
- Criteria for initiating a more comprehensive control effort.

Similar illustrations of operational research keyed to a PHC-executed program of malaria chemoprophylaxis include, inter alia:

- What is the maximum effective duration of protection against acute malaria infection for chloroquine? amodiaquine? Does this period of protection tend to decrease over time?

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- Alternative drug regimens which may extend the period between drug distribution?
- Impact on malaria incidence of community vector control methodologies?
- Importance of health education in improving patient compliance with chemoprophylactic drug schedules?
- Effect (in terms of drug misuse) of distributing drugs to recipients on monthly, quarterly, annual basis?
- Effect in terms of failure to secure protection under such a policy?
- Alternative drug distribution mechanisms?

Illustrative of research keyed to a PHC-<u>assisted</u> program which includes comprehensive malaria control:

- Under what conditions may residual spraying operations be safely delegated to community workers? Larviciding?

VIII. Prerequisites for Assistance

External support is not warranted in the absence of a long-term national commitment to a goal-oriented, well-planned, organizationally sound, technically and administratively feasible and costed plan of malaria control which takes full account of the country's physical and human resources down to the community level.

The prerequisites for assistance include, *inter alia*:

A. Request

A request from the host government for assistance in planning, implementing or evaluating malaria control efforts, whatever the level of control sought, must be supported by evidence of national will to carry out the proposed program and of the priority assigned to the problem of malaria..

B. Plan

The request should be keyed to a plan describing the malaria problem, the proposed course of action and the anticipated results. The plan should provide:

1. The area in which the program will be conducted, population affected, and specific population groups and age groups targeted for attention.

2. A baseline of epidemiological data which describes the existing problem in quantitative terms, to enable subsequent evaluation of accomplishment under the program.

3. A description of plans for supervising, monitoring, evaluating and providing essential specialized support to PHC workers.

4. A life-of-project projection of requirements in terms of manpower, money (local currency and foreign exchange) and equipment or supplies, defining in terms of quantity and quality the resources to be provided by the host government and those expected from external sources (AID, WHO or other agencies).

5. Logistic and transportation requirements of the project. This element of the plan should include a description of methods of procurement, warehousing, distribution, stock control, reorder points, etc., and as appropriate, provision for equipment and vehicle maintenance.

6. Training requirements and a plan defining *who* requires training, *where*, *when*, and *by whom*.

7. The relationship of the malaria control project to other PHC activities.

8. Methods of assuring coordination with and the full support of other elements in the Ministry of Health; with other health agencies in the country; and with other ministries or agencies concerned with activities affecting malaria in the country.

9. The social and economic impact of the proposed project.

10. How the project will be continued beyond the period period of external assistance.

C. Counterpart Relationship

From the outset of the project, there should be an identified, qualified officer to whom the host government assigns responsibility for project management, including evaluation. This officer would become the counterpart of the USAID H/N officer, or of the leader of a contractor technical assistance team.

D. Assistance in Plan Preparation

The preparation of a malaria control plan may be beyond the immediate capacity of a number of African countries. International and bilateral assistance in plan preparation, including feasibility studies as embodied in small-scale projects to test the applicability of intervention techniques or assistance in training, warrant support by international and bilateral sources of external assistance.

E. Backstopping

The USAID H/N officer must be able to rely on quick support from the offices of the Africa Bureau and technical backstopping from S&T/HEA.

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ANNEX 1

CLINICAL FEATURES OF MALARIA[3]

I. GENERAL CLINICAL FEATURES

A. The Incubation Period

This occurs between the time of the infective bite and the onset of symptoms; during it, pre-erythrocytic forms are developing in the liver. These cause no symptoms but the end of this incubation period may merge with that of primary fever. Premonitory symptoms such as malaise and chilly sensations may then occur. These are due to the presence in the blood of asexual parasites which have developed from early maturing hepatic pre-erythrocytic forms. The parasites at this stage are too few to be detected in ordinary blood films but they have been demonstrated by inoculating the patient's blood into volunteers.

The duration of the incubation period is 10-15 days, but with some strains of *P. vivax* and *P. malariae* this duration may be exceeded. It is also prolonged by prophylaxis which is inadequate to destroy completely developing parasites.

B. The Primary Fever

1. With Particular Reference to *P. falciparum* Infection

This is marked by paroxysms which correspond to the development of the parasites in the red blood cells. The peaks of the fever coincide with the release into the circulation of successive broods of merozoites.

The primary fever in its first few days is usually irregular or even continuous and then the classical 48-hour periodicity becomes established. In *P. falciparum* infections the fever may continue to be irregular throughout its course and the hot and cold stages, so typical of other malarial infections, are less clearly separated from one another.

The typical attack has three distinct stages: the cold stage, the hot stage and the sweating stage. These are followed by an afebrile period in which the patient feels greatly relieved.

The cold stage. The onset is with lassitude, headache, nausea and chilly sensations followed in an hour or so by rigors. The temperature rises

rapidly to 39°-41°C (102°-106°F). Headache is often severe and commonly there is vomiting. In the early part of this stage, the skin feels cool; later it becomes hot. Parasites are usually demonstrable in the blood. The pulse is rapid and may be weak. The next stage follows in 1/4-3 hours.

The hot stage. The patient now feels hot and the skin is hot and dry to the touch. Headache is intense but nausea commonly diminishes. The pulse is full and respiration rapid. This stage lasts for 1/2-6 hours.

The sweating stage. Profuse sweating follows the hot stage and continues for an hour or so. The temperature drops rapidly to normal and the skin is cool and moist. The pulse rate becomes slower, the patient feels relieved and often falls asleep.

Febrile herpes is common in all malarial patients.

After the primary attack of fever, there follows an afebrile interval of 48-72 hours and then other attacks similar to the first. After each, there is a similar afebrile period.

In *P. falciparum* infections the headache, nausea and vomiting are usually more severe than in *P. vivax* and other malarial infections and there is a greater tendency towards the development of delirium, haemolytic jaundice and anaemia. The mortality is much greater than in other forms of malaria. Those who survive with continuing infection as a result of inadequate treatment or no treatment may suffer several weeks or months of suboptimal health interspersed with febrile episodes, malarial anaemia and sickness.

2. In *P. vivax* Infections

P. vivax is the commonest species of malaria in South-East Asia but is rare in Africa. The primary fever is more severe in non-immune than in partially-immune persons. In areas in which malaria has been controlled, the state of immunity of the population has waned, and if they become infected, as by return of malaria to the region, the symptoms are more severe than they would have been before control took place. Symptoms are as described above but are usually milder and more regularly divided into 'hot' and 'cold' stages than in *P. falciparum* infections.

3. In P. ovale Infections

These differ little from those of P. vivax described. They tend, however, to be milder than those of P. vivax and to cease after a few paroxysms even if no treatment is given. The parasite occurs in Africa and, rarely, in Eastern Asia.

4. In P. malariae Infections

Clinically P. malariae attacks resemble those of P. vivax but the cycle is of 72 instead of 48 hours. The tendency for long-term relapses to occur is marked, and recently it has been suspected that they are not true relapses (that is, arising from release into the blood of a fresh brood of merozoites from exo-erythrocytic forms) but result from the continued presence of parasites in the blood. If this were so, it would explain why there are many records of patients who have had P. malariae infection even 20 years earlier and who have then transmitted the infection by blood transfusion. In these long continued P. malariae infections, there is a special tendency for the nephrotic syndrome to supervene.

C. The Latent Period

In this the patient is usually free of symptoms but exo-erythrocytic forms of the parasite are persisting in the liver. In P. falciparum infections following inadequate treatment, the parasites persist only in the blood and the patient is rarely completely free from symptoms.

D. Short-Term Recrudescences of Fever

These occur within days, weeks, or, in those with a relatively high degree of immunity, particularly to P. falciparum, even months after the primary fever. They result from the continued presence, in the blood, of asexual forms of the parasite. The presence of such forms is a consequence of inadequate treatment or of no treatment in a person who has made a partial recovery by virtue of incomplete immunity. Clinically they tend to be less severe than primary attacks.

E. Long-Term Relapses

These result from maturation in the liver of exo-erythrocytic forms with liberation into the blood of merozoites which then enter erythrocytes. In P. vivax infections, such relapses may occur for approximately three years after the primary fever, and in P. ovale for approximately 1 1/2 years. In P. falciparum infections,

relapses of this type do not occur. In P. malariae infections, attacks of malarial fever, as mentioned above, may occur for 20 or more years after the initial infection.

II. COMPLICATIONS OF P. FALCIPARUM INFECTIONS

A. Cerebral Malaria

This occurs particularly when non-immune persons have remained untreated for 7 to 10 days after development of the primary fever. At this time the patient's condition is liable to deteriorate rapidly with increasing headache and drowsiness which later merge into confusion and light coma. At this stage, even if treatment is given, the condition may deteriorate further into deep coma with stertorous breathing. When the coma is light, the condition may simulate that of delirium in typhoid for the patient may be able to talk and answer questions although later he will have no recollection of so doing. In very heavy infections, delirium and coma may develop suddenly and may even occur early during the course of the febrile illness. Convulsions, hallucinations and maniacal violence sometimes develop. Hyperpyrexia is not unusual and occasionally palsies may develop. Signs of meningeal irritation are rare except in young children. Occasionally malarial confusion and mania may occur in ambulant patients and have sometimes been confused with drunkeness, especially if some alcohol has been consumed and the breath smells accordingly.

B. Acute Renal Failure

The shock-like mechanism associated with severe malaria, particularly when there are cerebral features, may lead to oliguria or anuria and histologically in such cases tubular necrosis will be present. The degree of necrosis or tubular damage depends on the duration and intensity of the renal ischaemia which has to be present for some hours before histological changes become detectable. Oliguria or anuria therefore tend to develop some hours after the patient has become confused or otherwise seriously ill from the P. falciparum infection. Necrosis is most likely to occur when there is a combination of dehydration, vasoconstriction and hypotension. When there is severe vasoconstriction, however, even a minor fall in blood pressure may be enough to cause severe or complete ischaemia. Almost invariably in severe malaria there is a marked fall in blood pressure. An important factor leading to this fall is the loss of water and sodium brought about by the sweating and vomiting from which those with severe malaria suffer. Histologically, the glomeruli usually escape injury even when the tubular lesions are marked.

The tubular lesions usually consist of localized areas of necrosis. Electron microscopy reveals changes in the tubules to be much more marked and extensive than those revealed by ordinary light microscopy. A watch should therefore be kept on urinary output in severely ill malarial patients; except in very hot weather, a drop to 400 ml or less urine per day indicates renal failure. The blood urea in these patients rapidly rises and unless effective treatment is employed it may reach 300-400 mg/100 ml blood (that is, up to approximately 70 mmol/l).

C. Liver Damage

Haemolytic jaundice in this infection may be aggravated by liver damage. The liver is these cases becomes more than usually enlarged and tender.

D. Gastro-intestinal Symptons

Diarrhoea may occasionally occur in severe infections in which there is necrosis or damage to the intestinal wall. Dysentery or even cholear may be simulated.

E. Dehydration

Vomiting, sweating and diarrhoea may comtine to produce dehydration. This may be recognized by the inelasticity of the skin, sunken eyeballs, thin weak pulse and low blood pressure. Dehydration, by increasing blood viscosity, impairs its oxygen carrying capacity and may lead to renal and cardiac failure.

F. Collapse

The patient may suddenly collapse, possibly when the temperature is subnormal. The blood pressure will be low and the pulse weak. Often, there has been much vomiting and possibly diarrhoea. Peripheral circulatory failure due in part to dehydration and in part, in some cases, to lesions in the adrenal glands is thought to be responsible for this complication which was formerly referred to as the algid type of the infection.

G Anaemia

Haemoglobin values encountered in P. falciparum infections are lower than in infections with other species of malaria parasites. This is thought to be due to the greater proportion of erythrocytes which become parasitized in P. falciparum infections and also to be due to release of more malarial antigen with consequently more marked immuno-haemolytic anaemia. Sometimes in pregnant women a sudden and catastropic fall in haemoglobin may occur.

H. Blackwater Fever

Some degree of darkening of the urine is common in severe P. falciparum infections; this is due to the passage of bile pigments resulting from haemolysis. In very severe infections, the urine may become deeply pigmented. Classical blackwater fever consists, however, of a sudden massive haemolytic episode in which the patient who has felt unwell for some time takes a dose of quinine and within an hour or two has an attack of shivering, feels weak and collapses, and the urine, which till then had been normal in colour, is almost black when next passed. Marked anaemia rapidly develops and recurrent rigors and an irregular fever follow. There is almost always a history of having taken small doses of quinine, inadequate to suppress the existing P. falciparum infection.

I Other Complications

Petechial haemorrhages in the skin, mucous membranes and sometimes the retina may occur and may sometimes be related to disseminated intravascular coagulation. The spleen enlarges in all malaria infections, and in chronic malarial infections may becoome very large, especially in children. Rupture from trauma, sometimes slight, may then occur. Pigment-containing gallstones are commoner in those with chronic malaria than in otherwise healthy persons.

III. COMPLICATIONS OF P. VIVAX, P. OVALE AND P. MALARIAE INFECTIONS

A. Anaemia

This may develop in any of these malarial infections, particularly after repeated attacks or long continued untreated infections.

B. Splenomegaly

This is common even after moderately severe attacks and it becomes more pronounced in those who have had much malaria. Gross splenomegaly may occur, especially in longstanding P. malariae infections, and rupture of the spleen may then occur, even from minor trauma.

C. The Liver

Like the spleen the liver may enlarge, partly as a result of erythrophagocytosis by reticulo-endothelial cells within it. It becomes tender and transient biochemical dysfunction may occur.

D. Herpes

Herpes labialis is particularly common and herpes affecting other sites is occasionally reported.

E. Renal Complications

A form of the nephrotic syndrome has been encountered, particularly in longstanding P. malariae infections; it has also very rarely been reported in children with protracted P. ovale infection. It results from deposition on the glomerular basement membrane of immune complexes developed against the malaria parasite. In these cases, gross generalized oedema, with proteinuria and severe hypoproteinaemia, occur. Children, of either sex and about the age of five years, are those most likely to be affected. The prognosis is usually favourable.

IV. MALARIA IN PREGNANCY

Malaria of any form may precipitate miscarriage or abortion and may complicate pregnancy by causing severe anaemia. Pregnancy also appears to impair immunity to malaria and thus in those in whom the disease has been latent a relapse may develop during pregnancy. Fever during the puerperium should always be considered as possibly resulting from malaria. Investigations for malaria should first be carried out, and if the results are negative the patient should be investigated for other causes of pyrexia.

V. MALARIA IN CHILDREN

Children commonly develop high fever even from relatively mild infections. They may develop convulsions during the malarial attack, and dehydration in them develops with greater rapidity as a result of vomiting or sweating than it does in adults.

SIDE EFFECTS AND TOXICITY OF SELECTED ANTIMALARIALS

Dr. Bettie Graham, N.I.H.

The effectiveness of a drug depends not only upon its therapeutic effect but also upon side effects of short- or long-term usage, toxicity from chronic use, and poisoning as a result of a single high dose. The toxicity and effects of chloroquine, pyrimethamine, and primaquine have been extensively reviewed by H. Weniger in three articles published in 1979.

CHLOROQUINE

The recommended dose of chloroquine for adults is 300 mg. base per week for malaria prophylaxis and 1500 mg. base over a three day period for a radical cure of a malarial infection. The side effects of chloroquine taken at this dosage may include itching, anorexia, listlessness, vomiting, vertigo, nausea and double vision. Most of these side effects are not incapacitating and can be reduced by taking chloroquine with food or immediately after a meal.

However, the most serious side effects which appear to be unique among Africans are itching or pruritus. At present it is not clear whether the itching is due to an allergic reaction to chloroquine itself or to a reaction to impurities in different chloroquine preparations. However, the report that sensitivity to chloroquine develops only after several treatments may indicate an allergic response. In Nigeria, it is almost standard practice to treat malaria with a schizonticide and an antipyretic to relieve the itching, such as paracetamol (an analgesic which has been used for years to relieve headache, lumbago and other muscle pains and has no inflammatory action).

The most serious toxic effect of chloroquine resulting from long term use (200 mg. chloroquine or more per day over a period of years) is that involving the visual system. These complications included keratopathy, macular

degeneration and retinopathy. Kerotopathy, or corneal opacities, can lead to problems with accomodation and blurred vision. Upon withdrawal of the drug, corneal opacity is reversed and no permanent visual defects are found. The reported incidence varies from as low as 10% to as high as 70% in patients taking chloroquine for prolonged periods of time. Macular degeneration due to chloroquine is rare and is irreversible.

Retinopathy is a serious complication but is also a less frequent complication of long-term users of chloroquine. Although the actual incidence of retinopathy is difficult to assess because most patients do not receive an eye examination before treatment, it has been reported to vary from 0.5% to 14%. Retinopathy is not reversible upon withdrawal of the drug and some authors have even reported progression of retinopathy after discontinuation of the drug. The pathology shows a destruction of the rod and cone elements of the retina with an accumulation of pigment-laden cells in the outer retinal layers. Total dosage of chloroquine appears to be the principal factor in the development of retinopathy and several investigators have suggested that the risk of retinal damage first appears when the total dose of chloroquine exceeds 100 gram base.

To date, there is no documented evidence to show that chloroquine taken prophylactically (300 mg. per week) causes retinal damage. In a retrospective study involving 57 U.S. Foreign Service personnel who had lived in areas endemic to malaria and who had taken chloroquine base (without primaquine) prophylactically for five or more years, no visual defects were reported. When compared with 30 control subjects, none of the 57 individuals had any demonstrable visual field defects. This information should be interpreted

with caution since this is a small sample and the exact total dosage taken was not given.

Information on the effects of chloroquine on the developing fetus is limited, and those observations which are recorded are limited to pregnant women taking excessive doses of chloroquine for extended periods of time for the treatment of lupus erythematosis. Five reports on twenty-seven pregnancies tend to suggest that chloroquine (300 mg. base per week for malaria suppression or 150 mg. base daily for treatment of lupus erythematosis) does not adversely affect the development of the human fetus. Only one report suggested that excessive doses of chloroquine may be injurious to the developing fetus. For now, the cause for alarm about the effect of chloroquine on the developing fetus is probably unwarranted.

Chloroquine is safe for children when given as a prophylactic and as a radical cure of malarial infection. However, the drug should only be given under supervision, should only be dispensed by trained personnel who can give the recommended dosage, and should not be dispensed in large quantities.

The World Health Organization has recommended a single dose of 10 mg./kg. of chloroquine as being optimal for safety. In a report cited by Weniger, chloroquine toxicity was evident only when two or more times the recommended single dose was ingested. There appears to be a very wide margin between a therapeutic and a toxic dose of chloroquine. In a few cases reported where an individual has received a single high dose of chloroquine and antidotal procedures have been initiated immediately the patients have been revived following lavage of the small intestine.

PYRIMETHAMINE

Pyrimethamine, like chloroquine, is active against the erythrocytic stages of malarial parasites and thus suppresses the clinical symptoms of this infection. The recommended prophylactic dose for adults is 25 mg.-50 mg. per week. Weniger reported no side effects attributable to this drug when taken in doses recommended for malaria suppression. However, acute toxicity can result from ingestion of a single high dose of pyrimethamine and involves the central nervous system and the gastrointestinal tract. Although wide variations in individual response to high doses of pyrimethamine have been recognized in adults, there have been reports of fatal poisoning in children after ingesting only 2-3 times the maximum recommended dose. Administration of high doses of pyrimethamine (50-100 mg.) for more than 2 days can cause gastrointestinal disturbances as well as bone marrow depression. Several reports have suggested that since pyrimethamine is an antimetabolite, it may present a hazard when used in less developed areas where the population, in addition to malaria, may suffer from other types of anemias and folate deficiencies associated with malnutrition.

Although pyrimethamine has been shown to be teratogenic when given to rats, no such observation has been observed in humans In two separate studies involving about 270 African women who had taken pyrimethamine during pregnancy, none were reported to have delivered abnormal infants. Clearly this is a small sample from which no conclusion can be drawn. However, if pyrimethamine does produce abnormalities at a very low incidence, the number of individuals studied might have been too small to detect any abnormalities. Because of the observations in animals it would not be prudent to recommend this drug as an antimalarial to pregnant women.

PRIMAQUINE

Primaquine is effective against the exoerythrocytic forms of *Plasmodium viva* and *P. falciparum* and has been used in some countries as a prophylactic agent. The therapeutic dose ranges from 15-30 mg. per day for adults.

The most frequently-observed side effect following administration of primaquine is gastrointestinal disturbances such as nausea, vomiting, anorexia, dizziness, and cramps. By taking primaquine at meal time, most of these symptoms can be prevented.

The most serious toxic effect of primaquine is acute intravascular hemolytic anemia. Acute hemolysis is characterized by a rapid fall in hemoglobin and erythrocyte counts with simultaneous increase in the leucocyte count, sudden fever, vomiting, jaundice and appearance of hemoglobin in the urine. These symptoms appear suddenly and without warning.

The typical course of primaquine-induced hemolytic anemia has three phases. The Acute Hemolytic Phase lasts seven to twelve days. During this period, approximately thirty to fifty percent of the red cell mass is destroyed. Typically, older erythrocytes are preferentially destroyed. The Recovery Phase occurs between the tenth and fortieth days after the beginning of the primaquine treatment. The red blood cell count rises slowly and reaches normal levels by the fourth or fifth week. The Resistant or Equilibrium Phase begins when the anemia disappears and continues for as long as the same dose of primaquine is administered.

The sensitivity of the erythrocytes to hemolysis is due to an enzyme deficiency, glucose -6- phosphate dehydrogenase (G-6-PD deficiency). There are many variants of the G-6-PD deficiency and the distribution of this enzyme-deficiency varies throughout Africa. The anemia which is produced in enzyme deficient American Blacks and Africans is less severe and the primaquine sensitive erythocytes of American Blacks and Africans are less susceptible to hemolysis than the primaquine-sensitive erythocytes of populations in the mediterranean area.

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ANNEX III

USE OF DRUGS FOR MALARIA CONTROL IN TROPICAL AFRICA

by

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During the past years, technical and financial constraints have led to a considerable reduction in the use of residual insecticides for the control of malaria in tropical Africa. Consequently attention has again been given to the use of drugs for chemoprophylaxis and treatment.

The limitations of existing drugs, their selective action and the diversity of epidemiological and socio-economic conditions in which they are administered do not allow the adoption of a universally applicable strategy regarding drug administration. Today, the place of chemotherapeutic measures for malaria control has to be determined in relation to realistic health targets that can be attained and maintained, taking into account the properties of each type of drug, the versatility of epidemiological and socio-economic conditions and the availability of resources.

Since the time when quinine was first used in Africa, considerable experience has been acquired regarding the use of antimalarial drugs for the protection and treatment of semi-immune African populations. The purpose of this paper is to review this experience, to identify the existing problems and to outline possible solutions.

Historical background

Before 1900, antimalaria measures carried out in tropical Africa consisted mainly of the administration of quinine for the treatment and the prophylaxis of malaria. There is no precise information on the date of the introduction of quinine into Africa.

In tropical Africa, apparently quinine was first introduced by the Portuguese in the 17th century when Cardinal di Lugo instructed the Jesuits to use extensively Cinchona bark in their missionary work (Russell, 1955). On the other hand, it is only towards the end of the 19th century that English, French and German physicians, members of exploratory and military expeditions to Africa, finally recognized the antimalaria properties of quinine (Ross, 1910; Weatherall, 1965).

At this time, access of local populations to drugs was limited to military personnel and to those living in the immediate vicinity of the missionary clinics. After the discovery of the development cycle of the malaria parasite at the turn of the century, the emphasis shifted towards antilarval operations, although quinine and later on synthetic antimalarials (pamaquin and mepacrine) were used both for clinical practice and for individual and collective prophylaxis but mainly of non-African residents. The efficacy of single-dose quinine treatment of semi-immune Africans was indeed demonstrated as early as 1900 (Stephens & Christophers, 1900) but this fact did not receive attention; hence only limited attempts were made to render the drugs more accessible to the population.

Some administrative factors were indeed responsible for the lack of progress in this direction, but, the theory propagated by S.P. James stating

that first attacks of malaria in African children should be left untreated to favour acquisition of immunity and that immune adults rarely need treatment, had a very negative impact (Watson, 1953).

The unsuccessful attempts to stop malaria epidemics by mass distribution of quinine and pamaquin in some small areas also had a discouraging effect. In the 1940's new synthetic antimalarial drugs such as proguanil, pyrimetharine and chloroquine were introduced into the region. However, surveys of anti-malaria activities carried out in tropical Africa at the beginning of 1950 (WHO, 1951) and particularly in the field of malaria chemotherapy (Covell, 1950; Bruce-Chwatt, 1950), indicated that physicians and public health administrators were not often fully aware of the properties of these drugs.

The situation began to change in the 1950s. The evidence accumulated and presented by Wilson, Garnham & Swellengrebel (1950) in their leading article on malaria in tropical Africa, clearly indicated that contrary to prevailing views, malaria in the highly endemic areas was an important cause of suffering and death among infants and children who were the most in need of protection.

Along the same lines, the first Conference on Malaria in Africa, held in 1950, known under the name "Malaria Conference in Equatorial Africa" (WHO, 1951), stated that extensive use should be made as soon as possible of modern methods of malaria control without regard to the original level of endemicity. Later on, even though emphasis was placed on the indoor use of residual insecticides, malaria chemotherapy continued to be developed. Studies on the comparative therapeutic values of single doses of mepacrine, proguanil, pyrimethamine, chloroquine and amodiaquine were carried out by

Handfield-Jones (1949), Archibald (1951), Bruce-Chwatt (1951), Bruce-Chwatt & Archibald (1953), Miller (1954) and Baroda (1955) in semi-immune African people; the efficacy of the treatment in cases of light and moderate malaria infections was fully recognized and single-dose treatment was recommended for outpatient clinics (Covell & al., 1955). All these drugs cleared the peripheral blood in most subjects in two to three days with an average clearance time of about two days, but the results achieved with 4-aminoquinolines appeared to be the best and the most consistent.

Trials aiming at the protection of whole village populations were carried out with success (Clyde, 1954; Jones, 1954; Vincke, 1954; Schneider et al.) malaria epidemic was prevented by chemoprophylaxis in a highland agricultural estate in Kenya (Roberts, 1964).

The first country-wide malaria control programme aiming at the protection of the entire child population by chemoprophylaxis started in Madagascar in 1949 and, by 1955, the distribution centres were treating a total of 760,000 children (Joncour, 1956). According to the documents presented at the Second African Malaria Conference held in 1955, quinine and mepacrine were replaced this time by proguanil, pyrimethamine and 4-aminoquinolines, although quinine continued to compete successfully with chloroquine in the treatment of severe clinical cases. In 1954, resistance of Plasmodium falciparum to pyrimethamine and proguanil was reported for the first time in East Africa where this drug was used in mass drug administration schemes (Jones, 1954; Clyde & Shute, 1954).

The Second African Malaria Conference and the Technical Meeting held in Brazzaville, in 1957, once again drew the attention of malariologists to studies on the effect of residual insecticides on malaria transmission.

As indoor spraying with insecticides failed to interrupt transmission in most of tropical Africa, it was thought that the addition of mass treatment to the spraying operations may lead to eradication of the disease. Subsequently, mass drug administration was carried out as a supplementary measure in a number of malaria eradication pilot projects: (Benin, Nigeria, WHO/AFRO, 1960; Upper Volta, Escudie et al, 1961; Cameroon, Cavalie and Mouchet, 1962; Senegal, Locan & Michel, 1962; and Uganda, Zulueta et al, 1962). Although the interruption of malaria transmission was not achieved anywhere (with the possible exception of Uganda), the effect of these measures on the level of malaria endemicity and on the population's health was considerable, particularly in the young age groups (Kouznetsov, 1977).

Failure to interrupt malaria transmission by residual insecticides alone and/or in combination with mass drug administration in many areas also encouraged the trail of Pinotti's method in Ghana (van der Kaay & Najera, 1962). The overall malaria parasite rate was drastically reduced from 80% to 4%, but the project failed to achieve its targeted objectives and was discontinued.

At the beginning of the 1960s, it became clear that malaria eradication was not possible under the epidemiological and socio-economic conditions prevailing in tropical Africa with the means available and that for financial reasons residual insecticides could not be extensively used; the emphasis once again shifted to chemotherapeutic measures.

By the mid-60s, resistance to proguanil and pyrimethamine was reported from many countries of tropical Africa (WHO, 1965) and as a result chloroquine replaced these drugs in all mass drug administration schemes, (WHO, 1971).

The high effectiveness of single-dose treatment with chloroquine in tropical Africa was further stressed by Clyde (1961) who demonstrated in Tanzania that even very small doses of chloroquine (as little as 4-8 times lower than 10 mg per kg body weight) could be "as efficient in clearing parasitaemias, fever and symptoms attributed to malaria as large doses." The same investigator and later on Kusnecov, et al (1972), and Storev et al (1973) demonstrated that in semi-immune African people, not subject to reinfection, single dose treatment with chloroquine may result in more than 90% radical cure.

The limited choice of effective drugs and the threat of the appearance of P. falciparum resistance to 4-aminoquinolines encouraged studies on the use of sulfones and sulfonamides for malaria treatment.

Painful reaction at the infection site, non-efficacy against strains resistant to proguanil and pyrimethamine led to the discontinuation of trials carried out in Africa with repository drugs (Clyde, 1965; Clyde & Avery-Jones, 1966; Laing et al, 1966; McGregor et al., 1966). Good results were obtained by the administration of single-dose treatment with sulfones and sulfonomides, particularly in combination with dihydrofoliate reductase (DHFR) inhibitors, (Archibald et al., 1963; Laing, 1966; Shute & Dowling, 1966; Michel, 1968; Rey et al., 1968; Lucas et al., 1969; Fasan, 1971; Storev et al., 1973).

These drugs or drug combinations do not have sufficiently obvious advantages over chloroquine or even mepacrine to justify their introduction into practice, as long as malaria parasites remain susceptible to 4-aminoquinolines.

So far, investigations using mainly the WHO standard in vivo field test have failed to substantiate the presence of chloroquine-resistant strains (Bruce-Chwatt, 1970; WHO, 1973). A continuous monitoring of P. falciparum sensitivity to 4-aminoquinolines by the in vitro techniques is required, particularly in areas where these drugs are used extensively and when there is a possibility of importation of resistant P. falciparum strains from known foci; in vivo studies carried out in semi-immune populations can only measure the response of the disease to the treatment and not that of the parasites. The recent reports on the presence of P. falciparum malaria resistance to a standard dose of chloroquine in non-immune visitors who travelled to Kenya and Tanzania (MMWR, 1978) require urgent investigation and action.

Since no more than 20% of the African population have access to the medical services, various approaches for delivery of drugs to the population and vulnerable groups were discussed and recommended by the WHO Expert Committee on Malaria, and by the WHO Scientific Working Group on Chemotherapy of Malaria, WHO, 1961, 1967 and 1973. Consequently, projects aiming at the protection of the most vulnerable groups and even of the entire population, were initiated in some countries.

Programmes aiming at the protection of the child population, through a network of voluntary collaborators, were continued in Madagascar. Weekly administration of chloroquine to nearly 10% of pre-school children resulted in considerable reductions in the spleen and parasite rates. A national programme with the same objectives in view was launched in Senegal. There, drug distribution has been carried out by teachers and the programme drew its financial support from the network of agricultural cooperatives. In Cameroon, school children were protected through drug administration carried

out by teachers and in Zambia by medical assistants specially assigned for this purpose. At the end of the scholastic year the parasite rates and parasite counts of the children who had been receiving chloroquine were lower than those who had not received it. In Northern Nigeria, an attempt was made by the author to make use of local chiefs for the distribution of antimalarial drugs to fever cases. The chloroquine was supplied to the village chiefs by the primary health centre that also carried out overall supervision of these activities, in close contact with the district chief. The scheme was terminated three years later after the chloroquine stock was exhausted.

Country-wide schemes aiming at regular chemoprophylaxis of infants, young children and expectant mothers, and treatment of febrile patients by community primary health workers and political leaders, have been initiated in Tanzania and Mozambique. In Tanzania, at present, it covers more than half of the country's population. In many countries attempts were also made to attract pregnant women and nursing mothers to the health centres so that they might receive the necessary care, including administration or antimalarial drugs.

Malaria chemosuppression by chloroquinized salt has been implanted in remote rural areas of Tanzania (Clyde, 1966) and in an industrial enterprise in Uganda (Hall and Wilks, 1966) with a good degree of success and with the cooperation of the population. The last two trials indicated that in special circumstances Pinotti's method could find its place in malaria control in tropical Africa.

The yearly cost of the chemotherapeutic schemes mentioned above and conducted by government agencies varied from 20 to 80 US cents per protected

person (depending on the type and frequency of distribution) and in chemo-suppression trials with chloroquinized salt it reached US $1.50 (WHO, 1971). Today, the cost would probably be 10 to 20 percent higher due to recent increases in the price of drugs. It is difficult, if not impossible, to calculate the average cost of individual treatment per person as the prices of drugs on the market depend on a number of variables such as initial cost, profits by producer and sellers, import taxes, etc. In countries where importation and sale of drugs are not under government control, selling prices of drugs are often up to 20 times higher than they should be.

Serious consideration should be given to the choice of drug, schedule and mode of distribution, since in Africa funds available for all medical and health services are around US $1.50 per person, per annum (Bruce-Chwatt, 1977). More efforts should therefore be made to reduce the cost of drug administration by involving voluntary collaborators (community leaders, teachers, medical helpers, etc.) in the distribution of antimalarials and by promoting community participation for the purchase of antimalarials and any other essential drugs. It is generally accepted that:

i) importation and sale of antimalarial drugs should be carried out only through government channels at cost price or even subsidized price and,

ii) strict price control of essential drugs on the open market should be imposed.

As observed by Bruce-Chwatt in the 1950s, by Lupascu in the 1960s (Lupascu, 1965) and by Kouznetsov in the 1970s, the price and not the quality of the drug governs its use in many African countries.

In spite of a widespread resistance of Plasmodia to proguanil and pyrimethamine in most countries of tropical Africa, these drugs are still imported, sold and extensively used for treatment of malaria patients by private practitioners, pharmacies and even in state out-patient clinics, as the existing legislation does not consider those drugs to be harmful.

At the same time, combinations of sulfones and sulfonamides with DHFR inhibitors appear on the market in many African countries despite the fact that caution should be taken regarding their widespread use, because of the high frequency of severe side-effects, the risk of quick development of Plasmodium resistance and the possible impact on drug-sensitivity of bacterial flora, such as Neisseria meningitidis and Mycobacterium leprae.

The need for a better definition of government drug policies with respect to antimalarials and other essential drugs is strongly felt especially today when emphasis is being placed on primary health care.

Conclusion

At present, chemotherapy is the main if not the only feasible method of malaria control in countries of tropical Africa, particularly in rural areas. Unfortunately, in almost all African countries, chemotherapeutic measures are still limited with the administration of anti-malarial drugs to sick persons through a limited network of health institutions, with the aim of reducing malaria mortality and alleviating suffering. Only in some countries attempts have been made to extend the coverage by involving collaborators, or to implement activities aimed at reducing malaria morbidity and mortality through the provision of suppressive treatment to selected groups of the population (young children, pregnant and nursing women, school children, etc.). No efforts

should be spared to promote these activities through a greater involvement of collaborators, the development of primary health care systems and the encouragement of community participation in providing antimalarial drugs to sick people free of charge or at a reasonable cost.

Although the review of previous trials and of more recent antimalaria schemes clearly indicates that considerable experience has been accumulated during the present century in tropical Africa in the field of malaria chemotherapy, the experience gained is not fully reflected in the current antimalaria operations. Opinion still differs greatly with regard to the long-term benefits of some chemotherapeutic measures, and a clear answer has yet to be given regarding the interaction between systematic drug administration and malaria immunity. Serious consideration should be given, both at national and regional level, regarding the choice and dosage of the appropriate drug and the elaboration of simple and explicit instructions for their administration addressed to all categories of personnel involved in malaria treatment.

Recent reports suggesting appearance of P. falciparum chloroquine-resistant strains in Africa, make it imperative that national and regional programmes be developed to assess and monitor P. falciparum response to antimalarial drugs and that effective operational countermeasures be urgently implemented.

The uncontrolled use of antimalarial drugs (both old and new) irrespective of their properties and cost demands the development of guidelines for a rational use of antimalarial drugs and the establishment of national policies regarding drugs, their sources of supply, their means of distribution and their cost.

ACKNOWLEDGEMENT

The author wishes to express his gratitude to Dr. T. Lepes, Dr. J.H. Pull, Malaria Action Programme, and Professor L.J. Bruce-Chwatt, for their critical review of the manuscript.

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Length of Treatment: For semi-immunie Africans, a single dose of 10 mg of chloroquine (base) per kilo of body weight, up to a maximum of 600 mg., is normally adequate to clear the blood of P. falciparum parasites. However, recrudescence is possible; multiple doses (1500 mg. of chloroquine (base) over three days may prove necessary. If multiple doses are indicated, patients should be reminded to take all of the drug in order to obtain its full effect.

It must be emphasized that administration of subcritical doses of chloroquine increases selection pressure on the drug.

Administration: Patients should be reminded to take the medicine with meals (to minimize stomach upset). If a patient has difficulty swallowing tablets or if the syrup is not available for children, the tablet may be crushed and mixed with sweetened water to ease administration.

Storage: Although chloroquine in the dosage required for malaria chemotherapy of chemoprophylaxis is safe and free of major side effects, the drug in overdose quantities is toxic, especially to small children, and should be kept out of their reach. It should not be exposed to extreme heat but kept in a cool place when possible.

Interactions: The potential for the pruritis associated with chloroquine therapy is increased if the patient is also on a pyrazolone derivate such as phenylbutazone (e.g., Butazolidin) which is used in the treatment of arthritis.

In planning and implementing the program, there is a time when a decision is made on what drugs are to be given, who will give them, under what circumstances and how much will be given. At that time a decision should be made on the nature and amount of drug-related information which should be shared with the patient. The amount of information shared with the patient at the time of dispensing should depend on the approval of the prescriber, the level of training of the dispenser in handling patient follow-up questions and the ability of the patient to understand the information given.

VIII. QUALITY ASSURANCE

This is a key concern. The manufacturing practices should include steps in quality control. For chloroquine tablets these steps include:

1. Tests for content uniformity
2. Tests for weight uniformity
3. Tests for tablet disintegration
4. Tests for tablet dissolution
5. Tests for tablet hardness
6. Tests for self-life under local storage conditions

Reference sources for selecting appropriate quality control tests for chloroquine tablets and most pharmaceuticals are the International Pharmacopoeia, The United States Pharmacopoeia, The National Formulary (U.S.) or other internationally recognized pharmacopoeia.

IX. PACKAGING AND REPACKAGING

The active ingredient of chloroquine tablets, chloroquine phosphate or chloroquine sulfate, is a white powder, odorless but bitter-tasting. It slowly discolors on exposure to light and is freely soluble in water. Thus containers should be well-closed and light resistant. Tablets should be stored in places where the temperature is no higher than 104 degrees Farenheit or 40 degrees centigrade. When repackaging care should be taken to use moisture-resistant containers (for example, waxed paper or plastic) where possible. Newspaper and paper boxes do not give the tablets adequate moisture protection.

X. LABELLING

Product labels from the local manufacturing source must contain specific information: directions for use, name, quantity of chloroquine (base), contra-indications, lot number, expiration date, and appropriate warnings and precautions. When repackaging, care should be taken to relabel the drug.

In addition, it would be helpful to pre-print the directions for use (pictoral or stroke system for illiterates). There should also be space for entering the patient's name and the date given.

XI. ASSURING APPROPRIATE USE

It is useful to have information about the dosage form of a pharmaceutical as described above, for this assists in assuring proper storage and dispensing. Further, at the time of dispensing, reminder and reinforcing information can be given to the patient. This includes length of treatment, administration, storage and interactions, if appropriate.

ANNEX IV

THE PHARMACEUTICS OF CHLOROQUINE

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Several requests have come in from the field recently for technical information on the components of chloroquine tablets and their manufacture. In addition, several studies (1, 2, 3) have identified the need for information on improving the dispensing of chloroquine, especially at the village level.

Information is presented here to assist programs which seek to support manufacture of chloroquine tablets and to assure their appropriate dispensing and use. However, presentation of this information does not signal a shift of AID's policy away from procurement of the finished dosage product in cases where this is most appropriate.

I. DECIDING TO PRODUCE PHARMACEUTICALS LOCALLY

The production of pharmaceuticals locally may be considered as part of malaria control. The decision to produce should be based first on whether or not the country has pharmaceutical processing (or, indeed manufacturing) capability. If so, the next question is whether that capability can be put to use to produce essential anti-malarials such as chloroquine tablets.

A. Tablets

There must be a sound production cost analysis before embarking on the production of chloroquine tablets in any country. This analysis is not only to cover the cost of raw material and its processing to the finished and packed product, but also the cost of adequate quality control. If local production proves to be more economic than the cheapest price of a high quality brand of a reliable foreign producer it must still be ascertained that adequate supplies will be available whenever required. In the case of chloroquine tablets, the active ingredient, chloroquine phosphate or chloroquine sulfate, is not manufactured in the United States. Therefore any program to support local manufacture would require AID source/origin waivers.

A decision must also be made regarding the drug and form to be manufactured. In deciding what form(s) of chloroquine preparations to produce locally, a great deal will depend upon the dosage forms already

available and how familiar the health workers and people are with their proper use. The present standard doses (100 and 150 mg. base) should be maintained, and probably the pediatric tablet of 50 mg. base content. The invention of new dose formulations should be avoided. [4]

B. Chloroquine Powder

If the manufacture of chloroquine itself, either as diphosphate or sulfate, is envisaged, standards of the International Pharmacopoea will have to be complied with. For a local production below 20 metric tons per annum -- 80,000,000 tablets of 150 mg. (base) -- it will be usually cheaper to buy the raw product from a reliable source.

If a country does not presently manufacture pharmaceuticals or related chemicals, a key question to be answered is: Is the cost-benefit of such an investment reasonable over the long-term? What is the country market (i.e., quantity of drug needed for the population) for the drugs to be produced; what is the government's policy toward regulation of such enterprises, toward pricing, toward the import of raw material and toward market protection; what is the presence of sufficiently trained or trainable manpower; what is the potential for private sector involvement, either domestic or foreign; what are the opportunities for co-financing the project; and what is the availability of necessary facilities and utilities?

II. AID POLICY TOWARD LOCAL PRODUCTION

Given a favorable production cost analysis, a decision is required as to the kind of assistance to request from AID: purchase of raw materials and/or intermediate formulations; purchase of equipment and the training of personnel in its use.

Currently, AID focuses support for local production of pharmaceuticals on the purchase of raw materials and/or the purchase of equipment used in manufacturing. Several requests in this area are under current consideration.

In the private sector, AID programming tends to emphasize the development of private enterprise over support of parastatal organizations (Parastatals are business enterprises that are partly or wholly government owned.)

Should local production be decided upon, project planners need to be aware of the technical aspects of the tablets or other dosage forms to be produced. The following information on chloroquine is presented to highlight the kind of information needed.

III. NOMENCLATURE

Chloroquine is found in pharmaceutical preparations in a combined form as chloroquine phosphate (also called chloroquine diphosphate), chloroquine hydrochloride or chloroquine sulfate (5, 6). The phosphate and sulfate are generally used for oral dosage forms while the hydrochloride is used for injectable preparations.

The term "chloroquine" is often used generically to refer to pharmaceutical preparations whose active ingredient is the combined form. However, the therapeutic portion is the chloroquine itself -- the base.

In French West Africa, a common brand name is Nivaquine[R] whose active ingredient is chloroquine sulfate. However, the active ingredient of an American-made brand, Aralen, is chloroquine phosphate. According to the Food and Drug Administration, chloroquine sulfate and chloroquine phosphate have similar drug safety and efficacy.

IV. COMMON ORAL DOSAGE FORMS IN AFRICA

There are two oral dosage forms of chloroquine commonly available in Africa: syrups, which are usually in a strength of 50 mg. chloroquine base per 5 cc and tablets in three different strengths. In most of French-speaking Africa, chloroquine sulfate is available as Nivaquine[R], which has 100 mg. chloroquine base per tablet. Chloroquine phosphate tablets, available under many brand names in other parts of Africa, generally contain 100 mg., 150 mg. or 300 mg. of chloroquine base. Sugar-coated tablets normally contain 300 mg. of chloroquine (base) and are made of chloroquine phosphate.

It is important to note that (contrary to long-established WHO recommendations), chloroquine tablets are sometimes labelled according to the total amount of active ingredient present rather than to the amount of the base. The dosage listed by all reliable suppliers refers to the base content.

V. CHLOROQUINE TABLET DESCRIPTION

Generic chloroquine tablets are usually white, convex, standard size, compressed tablets. Some manufacturers may score the tablet, making it easier to break in half when needed. Some tablets manufactured under a brand name may have a colored sugar coating. (Aralen, manufactured by Winthrop in the U.S., is such an example.) When the tablet is sugar coated, breaking it in order to give a smaller dose is very difficult and absorption may be compromised. In any event, the sugar coating frequently polymerizes after prolonged storage, the tablets do not dissolve in the stomach, and the dose of chloroquine is voided unused.

VI. CHLOROQUINE TABLET COMPONENTS AND CHARACTERISTICS

Generally the simple compressed tablets without sugar coating are seen in Africa. As compressed tablets they consist of the active ingredient and other ingredients necessary to insure adequate size and weight of the tablet (diluent), to allow proper cohesion of the powders in the tablet (binder), to facilitate the break-up and dissolution of the tablet in the body so that there is a release of the active ingredient (disintegrant), and to aid in manufacture of the tablet (lubricant). A sample formula and component characteristics are presented in the following table.

SAMPLE CHLOROQUINE PHOSPHATE TABLET FORMULA AND COMPONENT CHARACTERISTICS (7, 8)

Ingredient	Function	Amount
Chloroquine Phosphate	Active Ingredient	255 mg.*
Starch	Diluent Disintegrant	23 mg.
Avicel[R]	Diluent Binder	35 mg.
Lactose	Diluent	41 mg.
Ac-Di-Sol[R]	Diluent Binder	12 mg.
Silicon Dioxide	Lubricant	.5 mg.
Magnesium Stearate	Lubricant	3 mg.

* Represents 150 mg. of chloroquine base.

VII. GOOD MANUFACTURING PRACTICES

The World Health Organization (WHO) has produced guidelines (9, 10, 11) on the processing of pharmaceuticals. These documents should be referred to in order to assure that the planned process will comply with these accepted guidelines. The United Nations Industrial Development Organization (UNIDO) can be called upon if technical assistance is needed for the planning of the pharmaceutical plant, its equipment, staffing and operation.

Annex V

ADULT MOSQUITO CONTROL BY RESIDUAL SPRAYING

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I. Background

Indoor residual spraying is undoubtedly the most effective single malaria control method ever devised. Also, it can be usefully employed for the control of vectors of such mosquito-borne diseases as filariasis, dengue, yellow fever, and encephalitis. When conditions for its use are favorable, it offers possibilities for achieving a rapid solution to complex malaria problems. However, the solution is usually temporary unless reinforced by other vector control measures involving prevention and control of breeding places. Experience in the malaria eradication program has made it abundantly clear that malaria may resurge to previous and even higher levels of prevalence after the withdrawal of spraying.

A. The concept of residual spraying for malaria control emerged from findings in South Africa and India in the 1930s that daily indoor spraying with pyrethrum greatly reduced the incidence of malaria in rural villages. Although effective, the method was impractical and costly for large scale use because of the need for almost daily spraying. To obtain a cost-effective, practical result, an insecticide was needed with a long-lasting residual effect against indoor resting malaria vectors. The advent of DDT in World War II met the need. It was demonstrated by repeated experiments in the mid-1940s that a single DDT spraying of walls and ceilings at a low dosage rate of 1 and 2 g/m^2 provided complete control of resting *Anopheles* mosquitoes for 3 to 6 months and longer.

B. The rationale of residual spraying for malaria control was based on the observation that malaria vectors tended to invade human habitations in search of blood meals and to rest on walls, ceilings, and other indoor surfaces before and after feeding. Thus, when these mosquito resting places were treated with an effective residual insecticide, resting mosquitoes absorbed a lethal dose and died before taking another blood meal. In addition to relieving mosquito annoyance in sprayed habitations, DDT spraying reduced malaria rates and frequently interrupted malaria transmission when the spraying was systematically and thoroughly executed over a large area. Other prerequisites of successful control included: habitations suitably constructed for residual spraying, a strong preference for indoor resting by local malaria vectors and a consistent pattern of indoor activity and sleeping by the people after sundown.

C. The creation of the world malaria eradication campaign under the auspices of WHO in the late 1950s basically emerged from three events: (1) the disappearance of endemic malaria in the United States, Puerto Rico, and Italy where DDT house spraying was employed extensively in conjunction with other methods (larval control), (2) the disappearance of endemic malaria from several mainland tropical areas after a few seasons of residual spraying, and (3) the appearance of mosquito resistance to DDT in some malaria control programs.

Resistance posed a serious threat because the indefinite continuation of a malaria control strategy by DDT spraying would predictably intensify and

spread until the insecticide was rendered ineffective for malaria control. An eradication program would conceivably avert this possibility since it would be limited in time and planned and coordinated to complete the spraying phase in a four year continuous coverage operation.

D. Although the malaria eradication campaign evolved into one of the greatest public health endeavors of all times, the eradication objective could not be sustained in most developing countries. The eradication objective was, therefore, changed to control in 1975.

Administrative, managerial, and financial difficulties were major obstacles to the eradication effort, but the residual spraying strategy also encountered difficulties in many situations. Significant problems included:

(1) Extradomiciliary transmission due to exophilic and exophagic behavior of many malaria vectors and/or their opportunistic capability of feeding and resting outdoors and indoors. When combined with a traditional pattern of outdoor activity of people after sundown, including outdoor sleeping, residual spraying had little effect.

(2) Mosquito resistance to DDT and other residual insecticides.

(3) Insufficient knowledge of the ecology, habits, and behavior of many malaria vector species as a basis for planning and predicting the need for supplementary and complementary vector control activities.

(4) Reports on spray operations indicated a tendency to overspray and to overextend spraying into non-transmission areas resulting in excessive expenditures. This problem stemmed from the use of case detection as the criteria for spraying without backup entomological data on the occurrence and distribution of vector populations.

(5) Adherence to rigid residual spraying criteria in carrying out spray cycles, spray rounds, dosage rates, house spraying coverage, without proper evaluation of entomological, epidemiological, and socioeconomic factors contributed to excessive cost and misplacement of resources.

II. *Residual Spraying in Malaria Control*

There is still a world-wide attack on malaria, but the recommended strategy has been revised to adoption of an integrated strategy involving a combination of methods: chemical, biological, cultural, and physical operations directed against adult and immature stages.

A. *Planning a residual spray program*

Geographical reconnaisance, training, and other preparatory activities are necessary for proper planning and organization of the spraying and for determining the total technical, manpower, material, and budget requirements of the program.

B. *Insecticides for residual spraying*

Residual type insecticides are contact poisons which kill adult mosquitoes resting on sprayed surfaces. The toxic effect results from absorption through pores and nerve endings. Some insecticides produce a combined contact and fumigant or vapor effect, although the effective lethal period of vapor disappears long before the contact effect. Criteria governing the effectiveness of residual insecticides are as follows:

Schneider, J., Languillon, J. & Delas, A. (1958) Association chloroquine-pyrimethamine dans la chimioprophylaxie du paludisme; resultats apres 22 mois de traitement (deuxieme note) Bull. Soc. Path. exot., 51, 316.

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Wilson, D. B., Garnham, P. C. C. & Swellengrebel, N.H. (1950) A review of hyperendemic malaria. Trop. Dis. Bull., 47, 677.

World Health Organization, Techn. Rep. Ser., 1951, 38; 1961, 226; 1966, 324; 1967, 357; 1967, 375; 1971, 467; 1973, 529; 1977, 537; 1977, 549.

Zulueta, J. de., Kafuko, G. W., Cullen, J.R., & Pederson, C. M. (1961) The results of the first year of a malaria eradication pilot project in Northern Kigezi (Uganda). E. Afr. med. J., 38, 1.

(1) a high biological activity against the vector mosquito lasting 3 months after application.

(2) producing a high vector mortality after one-half to one hour exposure.

(3) low toxicity to man and animals.

(4) good storage, mixing, and application characteristics.

(5) low application costs.

INSECTICIDES USED IN RESIDUAL SPRAYING

Insecticide	Class	Relative Cost	Hazard	Insecticidal Action	Dosage[a] Rate (g/m^2)	Estimated[a] Effectiveness (months)
DDT	Organochlorine	Low	Slight	Contact	1-2	6-12
Dieldrin[b]	Organochlorine	Low	High	Contact	0.25-0.50	6-12
Lindane	Organochlorine	High	Moderate	Contact & fumigant	0.25-0.50	3-6
Malathion	Organophosphorus	Moderate	Slight	Contact	1-2	2-3
Fenitrothion	Organophosphorus	High	Moderate	Contact & fumigant	1-2	3-6
Propoxur	Carbamate	High	Moderate	Contact & fumigant	1-2	2-3
Landrin	Carbamate	High	Moderate	Contact & fumigant	1-2	2-4
Chlorphoxim	Organophosphorus	High	Moderate	Contact & fumigant	1-2	3-4
Pirimiphos-methyl	Organophosphorus	High	Moderate	Contact & fumigant	1-2	3-4

[a] Dosage rate and period of estimated effectiveness depends on a number of variables such as vector susceptibiltiy, climatic conditions, type surface, and build-up effect of retreatments. If a build-up effect is confirmed after the second round, the dosage rate may be reduced or the intervals between spray cycles increased.

[b] Because of the hazard to man and domestic animals, the use of Dieldrin has been banned by most countries. Experience has shown that after a period of use, spray operators develop toxic symptoms even when veils, caps, and gloves were worn in addition to hats and overalls. Dieldrin should not be used for indoor spraying without full justification and unless strict precautionary measures and medical supervision are ensured.

C. *Spray application*

Although residual insecticides may be applied by a variety of spraying equipment, the hand operated, 3 gallon capacity, compression sprayer continues to be the most effective and commonly used method. The five factors governing the application of a uniform dosage rate are:

--the insecticide concentration or percentage of insecticides in the liquid;

--the air pressure in the sprayer;

--the nozzle tip aperture size;

--the distance from the nozzle tip to the surface being sprayed;

--the speed of application over the surface.

The ultra-low volume (ULV) cold fogger machine may have promise for indoor residual treatments offering the advantage of rapid coverage and the standard compression sprayer. However, the heavy rebound of spray droplets from ceilings and walls may limit the use of ULV for this purpose.

A malaria control program offers opportunities for a much more flexible approach to residual spraying than was allowed under the rigid spraying protocols governing malaria eradication. For example, spray coverage, dosage rates, spray cycles, spray rounds could be adjusted to fit the epidemiological condition governing malaria transmission rather than pursuing a standard pattern of spraying without regard for entomological and epidemiological factors. Using a flexible approach would provide opportunities for realizing economies in material, labor, and transport without loss of effective control. A few examples of such opportunities would include:

(1) *Spray coverage*, the concept of laying a protective barrier of sprayed houses around the perimeter of a village or town to intercept the influx of malaria vectors from outlying rural areas. There is evidence to show that the peripheral treatment would obviate the need for spraying the inner area of the town or village. Treatment of buildings or rooms not used as sleeping places such as kitchens, grain stores, unoccupied houses, shops, schools, churches, and auditoriums, could be omitted from spraying coverage.

(2) *Focal coverage*. Malaria tends to assume a focal distribution associated with the distribution of vector mosquito breeding. Identification and delimination of these areas for spraying coverage could conceivably reduce the spraying workload.

(3) *Selective spraying* implies spraying parts of walls, ceilings, and mosquito resting places rather than treating the entire house according to traditional eradication procedures. There is entomological evidence that partial spraying is effective.

(4) *Dosage rates* could be adjusted to the variables of transmission. Areas of short seasonal transmission could receive a lower dosage rate than areas of long seasonal activity. After the initial

spray round, subsequent rounds could be sprayed at a lower dosage rate taking advantage of the build-up effect.

D. *Safety precautions*

The insecticides recommended for residual spraying are very toxic to mosquitoes and many other insects but need not be hazardous to man if precautions are taken. However, human toxicity is almost certain to arise if small amounts of the material are accidentally taken orally or if skin surfaces are contaminated for several hours. Therefore, special care must be taken to protect spray personnel and the public from possible ill-effects due to unnecessary exposure or accidental ingestion.

E. *Health education*

Experience has shown that residual spraying cannot be forced upon the public. People need to be convinced that spraying will give protection from vector diseases and mosquito annoyance. The education should aim to develop an attitude of cooperation and collaboration of the people with the residual spraying effort.

F. *Mosquito resistance*

Procedures for avoiding the development of mosquito resistance to the residual insecticide should be included in the operational plan.

III. *Entomological Assessment of Residual Spraying*

Residual spraying is an insect control operation and should be planned with the objective of achieving maximum control of the target insect (the malaria mosquito or other disease vector) for the longest possible period with the least expenditure of effort and cost. The most effective and economical programmes are those planned and evaluated on the basis of sound entomological data on the ecology, behavior, habits, host preferences, mosquito susceptibility to the insecticide under varying conditions, and environmental stresses. These are the mosquito factors that govern decisions on proper selection of the insecticides, spray cycles, rounds, spray coverage, and dosage rates. Assumptions and generalizations on mosquito bheavior can lead to inefficient and wasteful operations.

In the pre-spraying phase of residual spraying, the entomological data provides a basis for decisions on the selection of the insecticide, the dosage rate, the spray cycles, spray rounds, and the geographical boundaries of spraying.

After the first and subsequent spray rounds, entomology asesses the (1) impact of the spraying on the vector population; (2) the duration of insecticidal effect; (3) the need for alteration in the spray cycles and rounds; (4) the need to change the dosage rate; (5) the need to change insecticides because of incipient resistance or other problems; (6) changes in mosquito behavior induced by insecticidal exposure; (7) non-target control effects on other household insects such as bedbugs, roaches, fleas, and flies; and (8) harmful effects on beneficial insects (honey bees, silkworms).

In summary, the systematic collection and interpretation of entomological data will not only provide an ongoing evaluation of the progress of control but can lead to improvements and economies in the program. As the operation progresses, the assessment may show that lower dosage rates, fewer cycles, or fewer houses need spraying. to achieve the vector control objective. With many insecticides, spray residues may build up sufficiently after several cycles to allow an increase in the interval between cycles or a decrease in the dosage rate. As insecticides, labor and transport are costly items, economies realized could be substantial and usefully employed for extension of the vector disease control effort.

IV. *Suggestions for Research*

1. If not already available an updated annotated bibliography dealing with the biology, ecology, and ethology of all mosquito vectors of malaria and other diseases vunerable to control by residual spray should be compiled. The bibliography would not only provide an essential reference for planning residual spray programs but would also reveal voids in the knowledge of mosquito vector biology for future study.

2. Examine the efficacy of partial indoor coverage of residual sprays (alternating sprayed and unsprayed swaths on inside walls, spraying lower half of walls, and similar treatment combinations) compared with complete treatment.

3. Investigate and recommend methods of avoiding mosquito resistance to insecticides in residual spray programs, i.e. joint, rotational and sequential use of insecticides, selecting an insecticide not used extensively for local agricultural pest control, not using the same insecticide for both larval and adult control and other procedures.

4. Investigate the feasibility of training and utilizing local village people to perform house spraying operations under supervision instead of relying exclusively on spray operators employed by the organization.

5. Assess the potential for ULV residual spraying application.

6. Investigate the efficacy of house spraying around the periphery of villages and towns surrounded by mosquito sources and malaria transmission as a protective barrier against the influx of malaria infective mosquitoes into the unsprayed central area.

7. Investigate an appropriate role for residual spraying in the development of an integrated malaria control plan.

Annex VI

DRAFT

October 26
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EDUCATIONAL APPROACHES IN THE MALARIA ERADICATION PROGRAM

by

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SCHEMATIC SEQUENCE OF EDUCATIONAL ACTIVITIES IN THE MALARIA ERADICATION PROGRAM

Education Activities	Who is to be educated in the educational operation of the program?	Objectives of the educational operation	Preparatory Phase	Attack Phase			Consolidation Phase			Maintenance Phase
			First Year	Second Year	Third Year	Fourth Year	Fifth Year	Sixth Year	Seventh Year	
A. Program planning 1. at the federal level	a. Heads of federal government agencies. b. Top citizen leadership. c. Appropriate chiefs in administration. d. Appropriate representatives of legislative committees of the government. e. Appropriate members of national health department. f. Medical association. g. Owners and managers of newspapers, radio stations, etc.	a. To secure financial support for duration of program. b. To give thorough understanding of all phases of the program. c. To open up channels for education in official and unofficial agencies which will reach provincial and village levels. d. To form a group of national leaders to support necessary changes in the program. e. To plan for educational materials that may be needed. f. To plan public information activities.	a. Personal interviews. b. National committee. c. Subcommittees. d. Development of plans and policies for the educational operation.	This should be a continuous activity until malaria is eradicated.						Appropriate educational activities developed by Health Dept. staff in collaboration with Malaria Eradication Program staff, national committees and/or other groups.
a. at the provincial level	a. Provincial heads of agencies. b. Provincial administrators. c. Appropriate members of provincial health departments. d. Representatives of any unofficial agency or club that has influence and molds opinion in the province. e. Leaders in industry and agriculture. f. Medical association and hospital representatives. g. Representatives of press and radio.	a. To develop a broad base for financial support. b. To secure fullest cooperation from health department staff. c. To work out details of how each agency or group can promote education and participate in pertinent phases of the program. d. To "firm up" assignments of educational tasks to be done (what, when, where.) e. To develop teaching and informational materials appropriate to the provincial program. f. To use all resources available in any agency for the over-all educational operation.	a. Provincial committee. b. Subcommittees. c. Development of "guide for the educational program". d. Development of educational materials to use in "attack" period.	Evaluation and change of details where necessary.	Evaluation and change of details where necessary.	Development of specific methods to be used in surveillance in the province. Development of educational materials to use in "surveillance" operation.	Evaluation and change of details where necessary as a continuous activity until malaria is eradicated.			•
3. at the local level (the village will be used here as an illustration rather than the town or city)	a. Representatives of education, agriculture, health and other agencies who work in the village. b. Religious leaders, and other indigenous opinion makers such as midwives, "medicine men", storekeepers, leaders of clans, etc.	a. To secure acceptance of spraying and surveillance techniques in the village. b. To develop a few people in the village who will be informed and will influence others through spreading accurate information. c. To make full use of whatever professional people may serve the village on a full-time or part-time basis. d. To get ideas from indigenous leaders as to best ways of doing education.	Training of personnel to do this work in villages should be a priority during the first year. Foremen, sprayers, sanitarians, nurses and community workers are among those who might be given responsibility and trained to secure village cooperation through early participation in planning program details.	Contact needs to be maintained with village leaders, formally or informally, so that they will prepare villagers for successive spraying periods. Although it must be started earlier, it is during the final year of the attack phase that intensive education should be done to help village leaders become competent interpreters of the surveillance techniques to be used. In fact, if adequate time is taken to find and develop true village leadership, some of the problems of training in the surveillance opera-			No matter what techniques are used in reaching surveillance objectives, it will be a wise procedure to have a small committee of villagers who are informed as to the status and findings of the surveillance work; who can correct erroneous ideas and interpretations of the surveillance procedures; who can constantly use their influence to get people in for diagnosis and treatment.			•

SCHEMATIC SEQUENCE OF EDUCATIONAL ACTIVITIES IN THE MALARIA ERADICATION PROGRAM (continued)

Education Activities	Who is to be educated in the educational operation of the program?	Objectives of the educational operation	Preparatory Phase	Attack Phase			Consolidation Phase			Maintenance Phase
			First Year	Second Year	Third Year	Fourth Year	Fifth Year	Sixth Year	Seventh Year	
B. Education to Secure Group Support 1. from professional groups	a. Medical associations. b. Nursing associations. c. Dental associations. d. Engineering associations. e. Social work associations. f. Education associations.	a. To create informed professional allies. b. To get support from governing boards for the m.e.p.* c. To develop professional resources which may be helpful in different ways.	Methods of getting support from groups such as these include (1) participation by representative of association on committees; (2) request by m.e.p. director to speak at board meetings or annual meetings; (3) sending periodic reports to group; (4) sending articles for publication in association's bulletin.	Continuation of active support.			Continuation of active support. Private physicians and hospitals will need to be informed of the methods to be used in the surveillance operation and their respective roles. It is expected that their representatives will participate in developing the policies for their cooperation.			Appropriate educational activities developed by Health Dept. staff in collaboration with Malaria Eradication staff, national committees and/or other groups
2. from management groups	a. Chamber of commerce. b. Industry. c. Mining. d. Agriculture.	To broaden the base for financial support.		*			Continuation of active support.			*
3. from workers groups	c. Unions. b. Cooperatives.	To open channels for interpreting the program through their meetings and publications.		The support of these groups may be more important at the zone or provincial levels.			*			*
4. from citizens groups	c. Men's clubs--Rotary, Lions, etc. b. Women's clubs. c. Church groups.	To broaden the base for financial support. To have informed communicators who operate at a level different from professional workers.		These groups have wide influence in cities and towns. Provincial and local health department staffs might assume responsibility for educating these groups.			*			*
5. from teaching institutions	a. Medical schools. b. Schools of nursing. c. Teachers training institutions. d. Agricultural schools. e. Police schools. f. Army schools. g. Schools for training religious leaders.	a. To develop the over-all support of the teaching institutions for the m.e.p. b. Because of the long duration of the program it is possible to have a great number of persons who will be informed about the m.e.p. before they start to work. These people should give strength to the program later when it may be needed. c. From some of these schools it may be possible to recruit workers either immediately or later.		It is probably better to leave the task of educating the teaching institutions to the zone or provincial levels. The provincial health department staff might assume this task.			*			*
6. from mass media groups	a. Newspapers. b. Publishing Companies. c. Radio Stations. d. Television Stations. e. Advertising agencies.	a. To develop the overall support of owners and employees for the m.e.p. b. To open channels for securing favorable publicity for the program	This is a priority at the very beginning of planning.	Continuation of active support.			*			*

* Malaria eradication program

Note: It is evident that to build a broad base for the m.e.p. such as indicated in (B.) it will be necessary to have competent staff to plan the educational approaches with these varied groups. Good teaching aids should be developed to explain the program succinctly and dramatically.

SCHEMATIC SEQUENCE OF EDUCATIONAL ACTIVITIES IN THE MALARIA ERADICATION PROGRAM (continued)

Education Activities	Who is to be educated in the educational operation of the program?	Objectives of the educational operation	Preparatory Phase	Attack Phase			Consolidation Phase			Maintenance Phase
			First Year	Second Year	Third Year	Fourth Year	Fifth Year	Sixth Year	Seventh Year	
C. Face-to-face education 1. by professional staff and administrators of the m.e.p.	High government officials and top leaders in and out of government at federal and provincial levels.	a. To convince them of the necessity of the program. b. To convince them of its feasibility. c. To demonstrate how, step-by-step, the goal can be achieved. d. To secure their understanding and support.	This is a priority at the very beginning of the program.							Appropriate educational activities developed by Health Dept. staff in collaboration with Malaria Eradication Program staff, national committee and/or other groups.
2. by malaria specialists during surveys, research, evaluation studies	a. Community leaders. b. Health department and hospital staff. c. Householders.	a. To secure understanding and support for the techniques being used. b. To develop confidence in individuals through adequate explanation of the techniques. c. To prepare the community to accept other workers in the m.e.p. who may follow. d. To ascertain barriers which exist to acceptance of the program. e. To locate persons who may be useful later as community leaders, workers, or volunteers.	These opportunities for education are part of the preparatory phase.	Since evaluation of the success or failure of the spraying, the investigation of new cases of malaria and the testing of insecticides in various kinds of houses are continuing functions during the attack and consolidation phases, the malaria specialists are at the center of activity throughout the program. As prestige figures to staff and community alike they have a special obligation toward their educational responsibilities.						"
3. by field workers: foremen, mappers, sprayers, evaluators, volunteers	a. Indigenous village leaders. b. Householders. c. Teachers in village schools.	a. To give simple explanations of the nature of malaria transmission and its eradication. b. To answer questions. c. To give each person a sense of his own responsibility for participating in the program.		As soon as field staff begin their respective operations, their jobs as teachers begin.			The personnel during the surveillance operation will need supervision to be sure that they are not creating attitudes which may defeat the program.			"

SCHEMATIC SEQUENCE OF EDUCATIONAL ACTIVITIES IN THE MALARIA ERADICATION PROGRAM (continued)

Education Activities	Who is to be educated in the educational operation of the program?	Objectives of the educational operation	Preparatory Phase	Attack Phase	Consolidation Phase	Maintenance Phase
			First Year	Second Year Third Year Fourth Year	Fifth Year Sixth Year Seventh Year	
D. In-service education 1. for technical staff of the m.e.p.	a. Heads of divisions. b. Zone chiefs. c. Sector chiefs.	a. To become aware of the importance of the educational aspects of the program. b. To teach methods of education which will produce acceptance of the program. c. To help zone chiefs develop educational policies for their areas. d. To help sector chiefs in methods of working with staff and villagers.	This will be a part of the orientation of staff.	Occasional staff meetings devoted to evaluating the educational activities in zones, provinces and sectors will furnish opportunities for continuing staff education.	Occasional staff meetings devoted to educational problems encountered.	Appropriate educational activities developed by Health Dept. staff in collaboration with Malaria Eradication Program staff, national committees and/or other groups.
2. for field staff (preparatory and attack phases)	a. Foreman. b. Mappers. c. Sprayman.	a. To help each man to assume his educational responsibilities. (1) Appropriate educational content. (2) Appropriate educational methods. (a) Interview. (b) Small group discussion. (c) Use of visual teaching materials. b. To help each man win friends for the m.e.p. through awareness of his public relations functions and his interpersonal relationships.	A priority during the first year.	Because of staff turnover and other reasons it may be necessary to train new staff throughout this period.		•
3. for field staff (surveillance operations)	a. Evaluators. b. Volunteers.	a. To stress their importance as teachers in the m.e.p. b. To give insight into the psychological and cultural barriers which may exist in taking blood samples or reporting cases. c. To show them how to teach, how to interview.	A priority if these persons are used in surveys during the preparatory phase.	If evaluation goes along with the spraying, the training of these workers should be undertaken prior to their work. Intensive preparation will be needed prior to the surveillance operation.	The administrator should review the work of evaluators with great care. This is a crucial phase of the program. The work should be appraised not only in statistical terms. How the evaluator approaches people and is accepted by them is of prime importance. If a few people with residual malaria do not like the evaluator, they will find ways to defeat the purposes of the program.	•
4. for other staff	a. Laboratory workers. b. Maintenance men. c. Drivers. d. Warehouse staff. e. Others.	a. To instruct every worker so that he can give accurate information to his own groups. b. To develop in each worker a sense of his importance to the entire program so that he can see where his work fits into the whole pattern.		This can be done by directors of the divisions concerned in special staff programs. A system of reporting to the workers on achievements and problems will strengthen morale.		•
5. for health dept. staff (because of the important place this agency has in the m.e.p., it has been selected as an example of in-service training of workers other than	Division directors on national and provincial levels.	a. To acquaint them with the objectives, methods and duration of the program. b. To secure their support and active cooperation when appropriate.	This is a priority. It is not sufficient to communicate only with the malaria and laboratory specialists. Every public health worker needs to know and be sympathetic to the aims of the m.e.p.		Health Department staff in local and provincial areas will need precise information as to their responsibilities during the maintenance phase.	•

SCHEMATIC SEQUENCE OF EDUCATIONAL ACTIVITIES IN THE MALARIA ERADICATION PROGRAM (continued)

Education Activities	Who is to be educated in the educational operation of the program?	Objectives of the educational operation	Preparatory Phase	Attack Phase			Consolidation Phase			Maintenance Phase
			First Year	Second Year	Third Year	Fourth Year	Fifth Year	Sixth Year	Seventh Year	
B. School program 1. Administrative channels for communication to the public	School administrators on federal, provincial and local levels.	a. To obtain permission to inform all teaching staff about the m.e.p. through circulars and regular channels of the school system. b. To secure cooperation from the schools in reaching parents of school children through printed material. c. To use school buildings for community meetings about m.e.p. d. To obtain permission to include children in surveys or sampling studies.	High level contacts with federal and provincial school officials should be made during the preparatory period.	Intense efforts to contact school personnel in cities, towns and villages should be made prior to the entrance of the spraymen.			The schools may be key centers during the surveillance operation depending on the methods used. Teachers should be well informed as to the purpose of the surveillance techniques so that they can combat misinterpretations.			Appropriate educational activities developed by Health Dept. staff in collaboration with Malaria Eradication Program staff, national committees and/or other groups.
2. Curriculum development.	a. Teachers	a. Development of units of instruction. (How to develop these units is indicated in a later section of this bulletin.) b. To give teachers a sound basis for teaching about malaria.		Development of teaching units on malaria.	Institutes, summer courses, inclusion in "refresher" activities, special courses.					
	b. Students	a. To develop in children knowledge of the disease, its transmission and methods for eradicating it. b. To give children an understanding of malaria eradication as a part of public health responsibilities and services.				Introduction of new units to school children in regular classes. In this way knowledge and practices are taught to future citizens. This teaching goes on year after year once it has been introduced in accordance with sound educational practice.				

Special Scientific Questions

1. Side Effects

Reactions and side effects to drugs are covered in detail in Annex 2. They are generally not severe enough to prevent adequate treatment or impede a program based on chemoprophylaxis. Monitoring of side effects of drugs is indicated, particularly if drugs are locally produced.

2. Drug Resistance[9-11]

Drug resistance in malaria parasites can be defined in various manners. The principal method is caused by the failure of the parasites to be cleared from the blood following a standard oral dose of antimalarial drug. In recent years, *in vitro* test systems have been developed in which parasitized blood is incubated in the presence of an increasing concentration of the drug in a test tube. The critical point in assessing the efficacy of a malarial drug is to determine whether, at a particular drug dose, the infection is cured permanently, transiently suppressed, or unaffected.

Drug resistance in Africa is an issue only with *P. falciparum*, which is, unfortunately, the predominant malaria species throughout the sub-Saharan region. Resistance to dehydrofolate reductase inhibitors (DHFR) (pyrimethamine, proguanil) developed rapidly in

P. falciparum in most regions of Africa soon after the inhibitors were introduced. Pyrimethamine resistance has persisted in most areas (especially East and West Africa) where such investigations have been made. Since resistance to DHFR inhibitors appears not to be graded, but rather absolute, the use of these compounds alone is no longer recommended.

Since 1976, confirmed chloroquine resistant *P. falciparum* infections have been acquired in Kenya, Tanzania, Madagascar, and Mozambique. A number of travelers to these areas, the majority of whom had no prior history of malaria, contracted *falciparum* malaria while taking adequate (300 mg weekly) chloroquine prophylaxis. In addition, some of the infections were not completely cured by a therapeutic dose of chloroquine; although the parasites initially cleared from the blood, they reappeared. This is the minimal degree of chloroquine resistance. To date, in limited field tests in Kenya and Tanzania, semi-immune inhabitants (generally children) have continued to be cured by chloroquine.

Despite findings of emerging chloroquine resistant malaria parasites in East Africa, chloroquine remains the principal drug for malaria control in Africa. Minimally resistant *P. falciparum* parasites are being transmitted, especially in East Africa. *The awareness of this potential underscores the importance of rigorous surveillance for drug resistance as an integral component of every control program in Africa.* Further, in recognition of the potential for

increasing drug resistance, it is imperative that malaria drug distribution in PHC programs gain the maximum benefit (e.g. mortality reduction) while not unduly exposing the drug to increased selective pressure for resistance. In essence, this may require upward adjustment of minimum effective dosage as experience dictates.

3. Drug Sensitivity Surveillance

Surveillance of drug sensitivity has to be carried out on a national and regional basis. Monitoring the sensitivity of *P. falciparum* requires early reporting of drug treatment failures and longitudinal monitoring of the sensitivity by *in vivo* and *in vitro* testing of the same populations. Standardization of sampling methods and test techniques are essential to obtain comparable information. Only when adequate information about the level and geographic distribution of drug susceptibility is available and a good monitoring system is in place will rational planning and use of reasonable chemotherapeutic and chemoprophylactic measures be possible.

Assessment techniques In vivo tests are used mainly to assess the blood schizontocidal effect of 4-aminoquinolines in patients with P. falciparum infections. The WHO Standard Field Test[12] consists of the administration of 25 mg. of chloroquine base per kg over three days, with an observation period of 7 days. In the "extended" test the observation period is 28 days. Bloodslides are examined daily during the observation period. The Standard Field Test cannot distinguish between sensitive strains and an R-1 (low level resistance) response. Unfortunately, it is usually not feasible to extend the period of the test beyond 7 days and to exclude the possibility of reinfection. The in vivo tests to express the results is the Trophozoite Clearance Dose (TCD) and is expressed as the TCD_{50}, TCD_{98} and the $TCD_{99.9}$.

In vitro tests have been developed to measure the direct response of the P. falciparum parasites to antimalarial drugs. The macro in vitro test has been standardized and measures the schizont maturation in short-term, non-continuous culture. This test requires at least 10 ml. of blood, which limits its application in children and in certain populations. A micro in vitro test has been developed that requires 0.01 ml. of blood; this amount can be obtained from a fingerprick. The micro in vitro test also measures the schizont maturation and is completed in 24

hours. The *in vitro* tests can produce data to estimate the specific *Effective Dosages* (ED) of antimalarial drugs. In addition to the macro and the micro *in vitro* tests, a 48-hour *in vitro* test has been developed that permits measurement of the response of *P. falciparum* to schizontocidal drugs and also to drugs such as pyrimethamine, because the entire developmental stage can be completed. This 48 hour test requires 0.02 ml. of blood, an amount that also can be obtained from a fingerprick.

4. Effect of Drug Distribution on Host Immunity

There has been concern over whether a highly successful antimalarial drug prophylaxis program for infants and young children will so completely suppress malaria parasitemia that children will not acquire antimalarial immunity. To date conclusive field experiments have not been performed. It is possible that excessive concern is being shown; in practice, prophylaxis programs are rarely 100 percent completely effective. Children would still experience occasional parasitemias and gradually acquire protective immunity.

Some have raised the question of whether giving antimalarial chemoprophylaxis to semi-immune populations will decrease their resistance to malaria infection. Further, would interruption of chemoprophylaxis in these populations result in major outbreaks of illness? Unfortunately, there is not a lot of information to answer these questions precisely.

Long-term chemoprophylaxis with chloroquine will decrease the levels of malaria antibody in certain population groups, but will not eliminate antibody completely.[1-3]

Of more serious concern is the effect of abrupt discontinuation of the use of antimalarials on morbidity and mortality among semi-immune populations. There is the theoretical possibility that these persons, particularly young children and pregnant women, might develop severe malaria if drugs were stopped in a heavily endemic area.

Hence, once begun, prophylaxis programs, should be sustained. The use of chemoprophylaxis should be predicated on a long-term commitment to decreasing morbidity due to malaria, as well as mortality. Strong efforts must still be made to provide prompt and accurate treatment to patients with acute illness, following the recommended approach in "Tactical Variant 1", as outlined above.

This requires the necessary material resources to sustain provisions of chemoprophylaxis in communities undertaking this approach. To withhold antimalarial chemoprophylaxis from previously protected persons in endemic areas because of no assurance of a continued supply of drugs will probably

result in a malaria toll equivalent to the usual mortality and morbidity in untreated areas. When drug supplies are limited, the treatment of acutely ill children and pregnant women should have the priority; these same groups have priority when antimalarial drugs for chemoprophylaxis are in short supply.

Additionally, control measures aimed at decreasing human-mosquito contact might be undertaken in selected areas (i.e., urban or peri-urban) in which reduction or interruption of malaria transmission becomes a community objective. In these areas approaches to reduction of mortality and morbidity should have already succeeded before major commitments are made to vector control.

ANNEX VIII

DEFINITION OF LEVELS OF ENDEMICITY

Hypoendemic - Areas where there is little transmission and the effect of malaria on the general public are unimportant.

Mesoendemic - Found typically among small rural communities in the sub-tropical zones with varying intensity of transmission depending upon local conditions.

Hyperendemic - In areas with intense but seasonal transmission where the immunity is insufficient to prevent the effects of malaria on all age groups.

Holoendemic - Perennial transmission of a high degree, resulting in a considerable degree or immune response in all age groups, but particularly in the adult.

Annex IX

Table 1 Vectors of Malaria in Africa

Table 2 The Feeding, Resting and Breeding Behaviors of African Malaria Vectors

Figure 1 Anopheline Bionomics

Figure 2 Synopsis of Vector Control Methodologies

Table 1 Vectors of Malaria in Africa[1]

Vector	Location			
	W. Af.	E. Af.	Cen. Af.	Sudan
A. gambiae (A&B)[2]	●	●	●	●
A. gambiae (melas)[2]	●			
A. funestus	●	●	●	●
A. moucheti	●	●		●
A. nili	●	●	●	●
A. pharoensis	●	●		●
A. sergenti (?)		●		●

1. After Wilcox and Manson-Bahr, 1976.

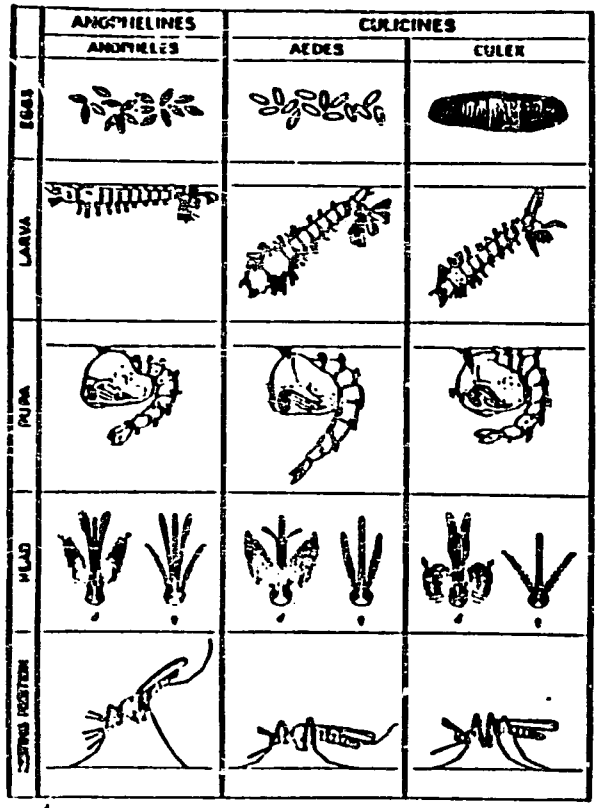
2. *Anopheles gambiae* is described in the nomenclature as being a complex of species presenting genetic variation yet variation not distinctive enough to constitute a separate taxonomic species differentiation.

Table 2 The Feeding, Resting and Breeding Behaviors of African Malaria Vectors[1]

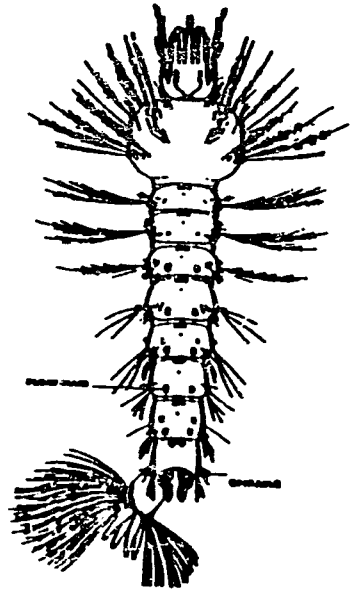
Behavior	Anopheline Vector						
	A. gam. (A&B)	A. gam. (me.)	A. fun.	A. nil.	A. pha.	A. mo
Feeding						
Man (Indoors)	•	•	•			•
Man (Outdoors)					•	
Man & Animals				•	•	
Resting						
Inside (Daytime)	•	•	•			•
Inside or Outside				•	•	
Breeding						
Household utensils	•					
Puddles	•					
Pools, Ponds, Lakes	•		•		•	•
Seepage, Springs			•			
Wells, Cisterns					•	
Rice fields	•				•	
Canals, Running streams	•		•	•	•	•
Brackish marshes		•				
Shade				•		
Sunlight	•				•	

1. After Wilcox and Manson-Bahr, 1976.

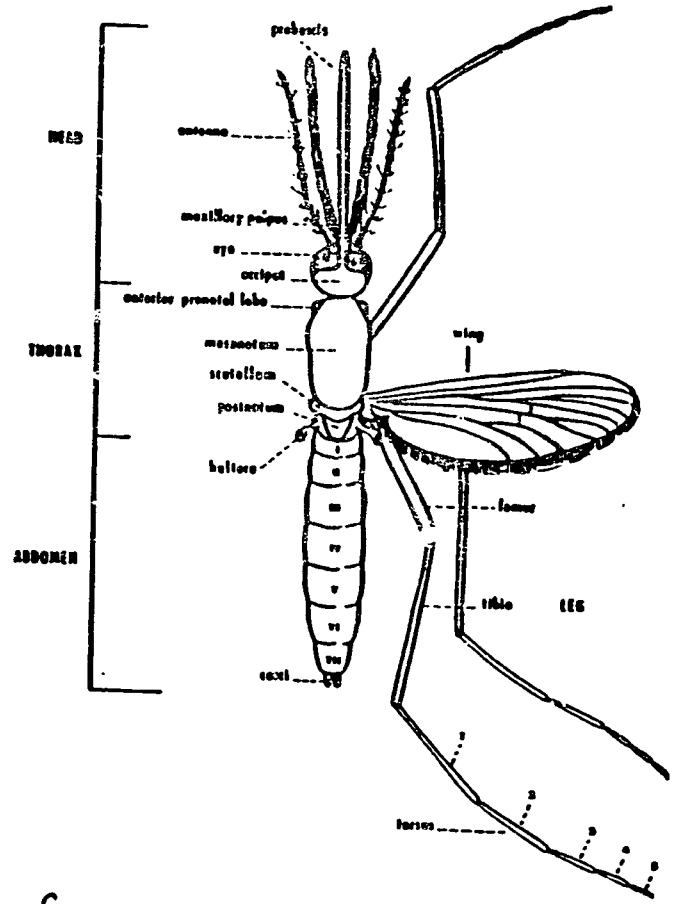
Figure 1 Anopheline Bionomics



A. Differentiation of Anopheles, Aedes and Culex mosquitoes at various stages of their development. Note the length of palpi in female Anopheles in comparison with other tribes of mosquitoes. (Wellcome Museum of Medical Science)



B. Larva of an Anopheles mosquito. (Wellcome Museum of Medical Science)



C. General anatomy of a female Anopheles mosquito. (Modified from WHO, 1972, 'Vector control in international health')

Mosquito (Anopheline) Bionomics

Anopheline mosquitoes belong to the Order Diptera, the Sub-order Nematocera, the Family Culicidae, the Sub-family Culicinae and the Genus Anopheles. Of the 400 species of Anopheline mosquitoes, approximately 50 are important malaria vectors. Vectorial importance is evaluated by preference for human blood, feeding and resting behavior (indoors vs.outdoors), longevity and population density in relation to man (proximity of breeding sites to human settlements).

Anopheline mosquitoes undergo complete metamorphosis in four developmental stages, namely egg, larvae, pupae and adult (Figure 1). Eggs are laid within 72 hours of a blood meal (300-500 eggs per female) (only females are vectors of malaria). Larvae hatch and moult four times. Within 10-14 days they pupate and subsequently emerge as adults.

Adult Anophelines have a flight range of 3-4.5 km.; however, A. gambiae and A. funestus exhibit a slightly smaller range. An Anopheline's lifespan ranges from two weeks to one month.

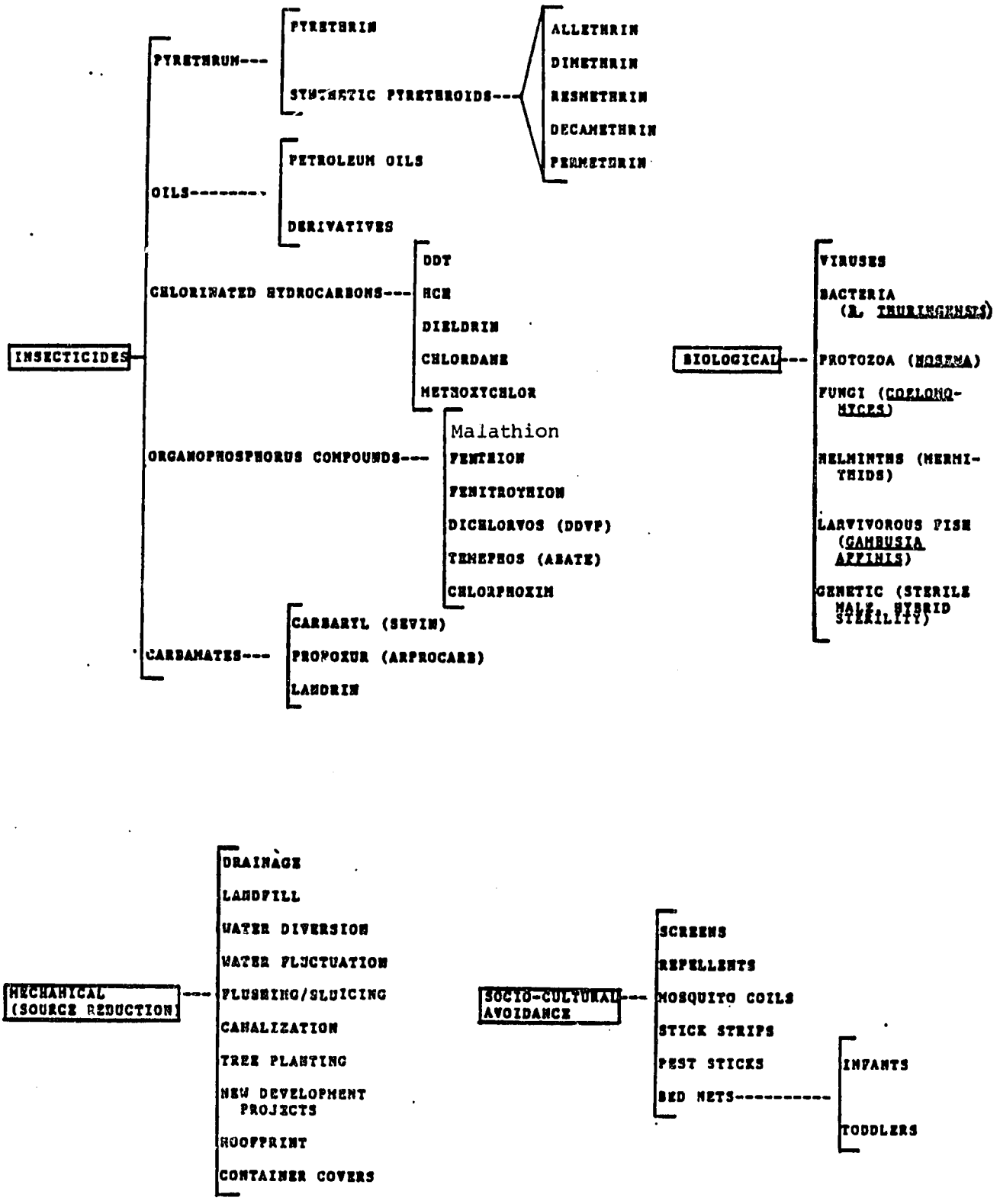


FIGURE 2 SYNOPSIS OF VECTOR CONTROL ACTIVITIES AT THE COMMUNITY LEVEL

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INFO AAAF-01 AFEM-03 AFEA-03 AFSA-03 AFRA-03 AFFW-04 AFCW-03
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GCAF-01 PPEA-01 ICFL-01 CTA-10 OCA-01 PPIA-01 AADS-01
DSME-01 IT-05 CH3-01 AFDA-01 CDC-05 CIA-05 HEW-09 RELO-01
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APPROVED BY AID/A-AA/AFR:WHNORTH
AID/AAA/AFR/DR:JKOEHRING
AID/AFR/DR:LHELLMAN
AID/AFR/RA:JCUMMISKEY (DRAFT)
AID/PPC/PDPR:ABLOOM (DRAFT)
AID/AFR/DR:JHICKS (DRAFT)
AID/DS/HEA:ABUCK (DFT)
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AMEMBASSY DAR ES SALAAM
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AMEMBASSY FREETOWN
AMEMBASSY GABORONE
AMEMBASSY KAMPALA
AMEMBASSY KHARTOUM
AMEMBASSY KIGALI
AMEMBASSY KINSHASA
AMEMBASSY LAGOS
AMEMBASSY LILONGWE
AMEMBASSY LUSAKA
AMEMBASSY MASERU
AMEMBASSY MBABANE
AMEMBASSY MOGADISHU
AMEMBASSY MONROVIA
AMEMBASSY NAIROBI
AMEMBASSY NIAMEY
AMEMBASSY NOUAKCHOTT
AMEMBASSY OUAGADOUGOU
AMEMBASSY PRAIA
AMEMBASSY YAOUNDE
AMEMBASSY LOME
AMEMBASSY SALISBURY
AMEMBASSY BRAZZAVILLE
USMISSION GENEVA
AMCONSUL ALEXANDRIA

UNCLAS STATE 128365

AIDAC AIROBI FOR REDSO/EA, ABIDJAN FOR REDSO/WA

E.O. 12065: N/A

TAGS:

SUBJECT: AFRICA BUREAU POSITION ON MALARIA

STATE 128365 0011 006927 AID3004
REF: REPORT OF STRATEGY ADVISORY GROUP ON AN ANTI-MALARIA SUPPORT STRATEGY FOR TROPICAL AFRICA
WHO FOR BRAZZAVILLE
GENEVA FOR WHO, ORAZZAVILLE AND ALEXANDRIA PASS TO RESPECTIVE ,HO REGIONAL DIRECTORS.

1. SUMMARY, THE PURPOSE OF THIS TELEGRAM IS TO (A) REVIEW T;E EFFORTS TO DEAL WIT, MALARIA; (B) DESCRIBE RECENT DISCUSSIONS CONCERNING MALARIA CONTROL IN AFRICA; (C) POINT OUT THAT, INAFRICA, ADMINISTRATION OF ANTI;ALARIA DRUGS TO TREAT PATIENTS AND TO PREVENT ILLNESS IIN HIGH RISK GROUPS IS TO 3E EMPHASIZED; (D) ADVISE MISSIONS THAT EFFORTS TO ACHIEVE TOTAL INTERRUPTION OF TRANSMISSION BY ATTACKING THE (ECTOR MOSCUITOAT ANTIMALARIA PROGRAMS WHICH CAN B- IMPLE- (E) INDICATE THAT ANTIMALARIA PROGRAMS WHICH CAN BE IMPLEMENTED THROUGH PRIMARY HEALTH CARE SERVICES WILL BE CONSIDERED; (F) ENCOURAGE MISSIONSTO CONSIDER MALARIA W;EN PLANING HEALTH AND RELATED PROGRAMS OR PROJECTS; AND (G) CONFIRM THE AFRICA BUREAU'S WILLINGNESS TO SUPPORT CERTAIN TYPES OF ANTIMALARIA ACTIVITIES. END SUMMARY.

2. BACKGROUND. THERE HAS LONG BEEN A CONSENSUS AMONG PUBLIC HEALTH AUTHORIIES THAT MALARIA IS THE MOST WIDESPREAD INFECTION IN AFRICA. NEVERTHELESS, ONLY LIMITED ANTI-MALARIA ACTIVITIES HAVE BEEN UNDERTAKEN, AND NO IMPROVEMENT IS APPARENT IN THE MALARIA PROBLEM IN TROPICAL AFRICA. PILOT PROJECTS WHICH WERE CONDUCTED DURING THE 1950S AND 1960S GENERALLY DEMONSTRATETHAT MALARIA COULD BE CONTROLLED BUT FAILED TO DEMONSTRATE THE FEASIBILITY OF ERADICATING THE DISEASE BY THE RESIDUAL INSECTICIDE TECHNIQUE WHICH WAS BEING EMPLOYED IN OTHER REGIONS. THE WORLD HEALTH ORGANIZATION (WHO) RECOMMENDED IN 1967 THAT ANTI-MALARIA ACTIVITIES IN AFRICA BE CONVERTED TO HEALTH SERVICE DEVELOPMENT EFFORTS. THE COUNTRIES GENERALLY AGREED AND SOON ANTI-MALARIA EFFORTS WERE GREATLY CURTAILED THROUGHOUT MOST OF THE REGIO. HOWEVER, SINCE 1970, A SUBSTANTIAL CHANGE HAS OCCURRED IN THE INTERNATIONAL PHILOSOPHY TOWARD MALARIA. THIS HAS RESULTED IN A RECONSIDERATION BY BOTH AID AND WHO OF THE DESIRABILITY OF SUPPORTING MALARIA CONTROL IN AFRICA. SIGNIFICANT DEVELOPMENTS HAVE INCLUDED THE FOLLOWING:

A. THE WORLD HEALTH ASSEMBLY (WHA) IN 1975 ADOPTED RESOLUTION WHA 28.87, WHICH INVITED THE ORGANIZATION'S REGIONAL COMMITTEES TO GIVE SPECIAL ATTENTION TO MALARIA IN THEIR RESPECTIVE REGIONS AND TO MAKE RECOMMENDATIONS REGARDING THE ORIENTATION FRAMEWORK.

B. RECOMMENDATIONS FOR GUIDANCE OF MEMBER GOVERNMENTS IN THE AFRICA REGION FOR THEIR PARTICIPATION IN THE WORLDWIDE ANTI-MALARIA CAMPAIGN WERE COMPLETED IN JUNE 1975. (WHO REGIONAL COMMITTEE FOR AFRICA - AFR/RC 25.7)

C. TH. WHO REGIONAL OFFICE FOR AFRICA (AFRO) HAD, BY 1977, COMPLETED PREPARATION OF A PROPOSAL FOR AN ANTI-MALARIA PROGRAM IN THE AFRICA REGION.

D. THE WHO EXPERT COMMITTEE ON MALARIA, AT ITS SEVENTEENTH MEETING EARLY IN 1979, PREPARED GUIDELINES, PARTICULARLY FOR ADMINISTRATORS AND HEALTH PLANNERS, ON THE PLANNING. IMPLEMENTATION AND EVALUATION OF MALARIA CONTROL PROGRAMS.

E. AID/AFR IN 1979 INITIATED THE DEVELOPMENT OF AN ANTI-MALARIA STRATEGY FOR TROPICAL AFRICA. THE STEPS IN THIS PROCESS HAVE INCLUDED:

(1) A REPORT HAS BEEN PREPARED WHICH SUMMARIZES AVAILABLE INFORMATION ON MALARIA IN AFRICA. (GRAHAM, BETTE J., MALARIA ERADICATION/CONTROL PROGRAMS IN SUB-SAHARA

AFRICA, AUGUST, 1979).

(II) WHO STAFF IN GENEVA, SWITZERLAND, ALEXANDRIA, ARAB REPUBLIC OF EGYPT AND BRAZZAVILLE, CONGO HAVE BEEN CONSULTED REGARDING POSSIBILITIES FOR CONTROLLING MALARIA IN AFRICA.

(III) THE FIRST SESSION OF THE MALARIA WORKSHOP IN WASHINTON, D.C., REVIEWED THE AFRICAN MALARIA PROBLEM AND PLANNED STEPS FOR DEVELOPING AN ANTI-MALARIA STRATEGY FOR AGENCY CONSIDERATION.
IV. TWO TEAMS OF MALARIA EXPERTS EXAMINED THE MALARIA PROBLEM AND THE RESOURCES AVAILABLE OR NEEDED FOR CONTROL IN FOUR ENGLISH SPEAKING AND FOUR FRENCH SPEAKING AFRICAN COUNTRIES.
(V) CLOSING SESSION OF THE MALARIA WORKSHOP IN ABIDJAN, IVORY COAST, PRODUCED A RECOMMENDED ANTI-MALARIA STRATEGY WHICH SUBSEQUENTLY WAS DISTRIBUTED FOR REVIEW AND COMMENT BY AFR/W AND FIELD MISSIONS.

3. GENERAL AFR POSITION. THE EVENTS AND ACTIONS DESCRIBED ABOVE HAVE REVEALED A SIGNIFICANT CHANGE IN THE APPROACHES NOW BEING RECOMMENDED TO DEAL WITH MALARIA. CONTROL IS EMPHASIZED. THE ADMINISTRATION OF ANTI-MALARIAL DRUGS TO TREAT SUSPECTED CASES AND TO PREVENT DISEASE IN HIGH RISK GROUPS ARE IMPORTANT ELEMENTS IN THE CONTROL PROGRAMS WHICH ARE RECOMMENDED FOR TROPICAL AFRICA. USING DRUGS FOR CONTROL HAS SPECIAL SIGNIFICANCE IN RURAL AFRICA BECAUSE, IN THESE ENVIRONMENTS, SATISFACTORY LEVELS OF MOSQUITO CONTROL ARE PARTICULARLY DIFFICULT TO ACHIEVE. IN ADDITION, PRIMARY HEALTH CARE PROGRAMS ALREADY ARE BEING SUPPORTED BY A.I.D. SINCE THESE PROGRAMS CAN BE DESIGNED TO INCLUDE ELEMENTS THAT ARE IMPORTANT FOR MALARIA CONTROL, THE NEED FOR SPECIALIZED, VERTICAL ANTI-MALARIA PROGRAMS ARE INNAPPROPRIATE AND MAY BE LARGELY AVOIDED. BECAUSE OF THE CHANGES WHICH HAVE OCCURRED IN THE PHILOSOPHY OF MALARIA CONTROL ACTIVITIES IN HEALTH SECTOR STRATEGIES, MISSIONS THAT ARE INTERESTED IN DEVELOPING A MALARIA CONTROL ELEMENT IN COUNTRY AND HEALTH SECTOR PROGRAMS MAY FIND THE FOLLOWING GUIDELINES HELPFUL:

A. AID ASSISTANCE TO ANTI-MALARIA PROGRAMS SHOULD BE CONSIDERED ONLY IN AREAS WHERE THE DISEASE CONSTITUTES A SERIOUS HEALTH PROBLEM.

B. THE APPROPRIATE STRATEGY FOR MOST OF AFRICA IS ONE OF

MALARIA CONTROL. MALARIA ERADICATION MAY ALSO BE FEASIBLE, BUT ONLY IN SPECIAL CASES, E.G. ON SMALL ISLANDS.

C. MALARIA CONTROL PROGRAMS SHOULD BE CONSIDERED IN THE CONTEXT OF PRIMARY HEALTH CARE. ELEMENTS THAT SHOULD BE CONSIDERED FOR INCORPORATION IN THE PRIMARY HEALTH CARE SYSTEM INCLUDE ADMINISTRATION OF THE SELECTED ANTI-MALARIAL DRUG(S) FOR TREATMENT AND PREVENTION OF ACUTE MALARIA, LABORATORY DIAGNOSIS OF MALARIA, TESTING OF PARASITE SENSITIVITY TO PROGRAM DRUGS, VECTOR CONTROL ACTIVITIES WHEN APPROPRIATE, PARTICIPATION IN THE COLLECTION OF NECESSARY EPIDEMIOLOGICAL DATA FOR PROGRAM PLANNING AND EVALUATION AND HEALTH EDUCATION.

4. TACTICAL VARIANTS. AID SUPPORTED PROGRAMS OF MALARIA CONTROL SHOULD GENERALLY FOLLOW THE TACTICAL VARIANTS RECOMMENDED BY THE STRATEGY GROUP ON ANTI-MALARIA SUPPORT STRATEGY FOR TROPICAL AFRICA (SEE REF). THEY CORRESPOND TO RECOMMENDATIONS OF THE WHO EXPERT COMMITTEE ON MALARIA IN ORDER OF PRIORITY AND ARE:

A. TACTICAL VARIANT 1: REDUCTION AND PREVENTION OF MORTALITY DUE TO MALARIA THROUGH PROMPT TREATMENT OF THE DISEASE WITH ANTI-MALARIA DRUGS WHICH ARE CAREFULLY SELECTED FOR GENERAL PROGRAM USE. NO NEW COMPOUNDS, NOW BEING USED IN AREAS WHERE THERE IS WIDE SPREAD RESISTANCE, SHOULD BE USED IN AFRICA. SUCH DRUGS SHOULD BE HELD IN RESERVE UNTIL THEY ARE NEEDED BECAUSE PARASITE RESISTANCE HAS DEVELOPED TO DRUGS SELECTED FOR GENERAL PROGRAM USE.

B. TACTICAL VARIANT 2: IN ADDITION TO TREATING PATIENTS WITH MALARIA, TACTICAL VARIANT 2 CAN PREVENT AND REDUCE BOTH MORTALITY AND MORBIDITY BY SYSTEMATICALLY DISTRIBUTING ANTI-MALARIAL DRUGS (CHEMOPROPHYLAXIS) TO HIGH RISK GROUPS SUCH AS INFANTS, EXPECTANT MOTHERS, SCHOOL CHILDREN AND SPECIAL LABOR GROUPS. THIS VARIANT MAY ALSO INCLUDE LIMITED PERSONAL PROTECTIVE MEASURES AND VECTOR CONTROL MEASURES THAT CAN BE APPLIED BY INDIVIDUALS, WHOLE COMMUNITIES OR EMPLOYERS WITH TECHNICAL GUIDANCE OF THE GENERAL HEALTH SERVICES.

C. TACTICAL VARIANT 3: REDUCTION OF PREVALENCE, MORTALITY AND MORBIDITY DUE TO MALARIA USING THE MEASURES DESCRIBED IN PARAGRAPHS 4A AND 4B ABOVE THROUGH AN ORGANIZATION WITH A SUFFICIENT NUMBER OF TRAINED PERSONNEL THAT IT CANNOT ONLY APPLY CONTROL METHODS BUT ALSO CAN UNDERTAKE EPIDEMIOLOGICAL EVALUATION OF THE RESULTS ACHIEVED.
D. TACTICAL VARIANT 4: COUNTRY WIDE CONTROL, USING ANY

OR ALL MEASURES FOR CONTROL, AS APPROPRIATE, WITH THE ULTIMATE OBJECTIVE OF ACHIEVING ERADICATION. IN AFRICA, THIS OPTION IS CONSIDERED APPROPRIATE FOR APPLICATION ONLY ON A FEW SMALL ISLANDS AND IN CERTAIN URBAN AREAS.

5. APPLICATION OF CONTROL MEASURES.

A. UNDER CURRENT CONDITIONS IN RURAL TROPICAL AFRICA, IT IS CONSIDERED DESIRABLE THAT FIRST PRIORITY BE GIVEN TO PROGRAMS DIRECTED TOWARD REDUCING HIGH MALARIA DEATH RATES (TACTICAL VARIANT 1) AND SECOND PRIORITY TO PROGRAMS COMBINING EFFORTS TO REDUCE BOTH MORTALITY AND MORBIDITY THROUGH THE ADMINISTRATION OF EFFECTIVE CHEMOTHERAPEUTIC AGENTS (TACTICAL VARIANT 2). UNDER SOME RURAL CONDITIONS, PERSONAL PROTECTIVE MEASURES, E.G. MOSQUITO NETS OR VECTOR CONTROL, MIGHT BE THE MOST COST-EFFECTIVE MEANS FOR DEALING WITH THE PROBLEM.

B. IN URBAN AND PERIURBAN AREAS, GREATER EMPHASIS MIGHT BE GIVEN TO THE APPLICATION OF A BROAD RANGE OF MEASURES TO ACHIEVE A MAXIMUM REDUCTION OF MOSQUITO-BORNE DISEASES GENERALLY, AND NOT MERELY A REDUCTION OF MALARIA MORTALITY AND MORBIDITY. SUCH MEASURES INCLUDE SOURCE REDUCTION, LARVICIDING, ADULTICIDING, SCREENING OCCUPIED BUILDINGS, ETC. SPECIAL ATTENTION NEEDS TO BE GIVEN TO THE DETECTION OF DRUG RESISTANT STRAINS OF MALARIA PARASITES, PARTICULARLY IN CITIES WHICH HAVE INTERNATIONAL PORTS OR AIRPORTS.

C. UNUSUAL SITUATIONS: UNUSUAL SITUATIONS NOTED BY THE STRATEGY ADVISORY GROUP INCLUDED SMALL ISLANDS, WHERE ERADICATION MAY BE POSSIBLE, AND NOMADS, WHICH PRESENT SPECIAL PROBLEMS OF CONTROL. DEVELOPMENT PROJECTS PRESENT OTHER EXAMPLES. MALARIA TRANSMISSION SHOULD BE CONSIDERED FROM THE EARLIEST PLANNING STAGE OF CAPITAL DEVELOPMENT PROJECTS. PROJECTS DESIGNS SHOULD MINIMIZE BREEDING OF VECTOR MOSQUITOS. SINCE DEVELOPMENT PROJECTS ATTRACT PEOPLE, PRECAUTIONS ARE NEEDED TO PREVENT MALARIA EPIDEMICS THAT CAN FOLLOW THE MIXING OF MALARIA CASES WITH SUSCEPTIBLE POPULATIONS.

D. DECISIONS CONCERNING ORDERS OF PRIORITY FOR MALARIA IN RURAL/URBAN, OR SPECIAL SITUATIONS CAN BEST BE MADE IN THE FIELD.

5. CONSIDERATIONS IN PLANNING AND IMPLEMENTING SUPPORT OF MALARIA CONTROL.

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C. COUNTRY DEMONSTRATES AN ABILITY TO SUPPORT AN EFFORT OVER THE LONG-TERM, WHICH MEANS BEYOND THE PERIOD OF EXTERNAL ASSISTANCE.

D. THERE IS SUFFICIENT INTEREST OF OTHER DONORS TO COVER THE REQUIREMENTS FOREXTERNAL ASSISTANCE; AND THOSE DONORS WHO AGREE TO PARTICIPATE EXPRESS WILLINGNESS TO PROVIDE SUPPORT FOR A MINIMUM OF FIVE (5) YEARS.

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Department of State

OUTGOING TELEGRAM

BUDGET CONSTRAINTS, (B) EXISTING OR PLANNE COUNTRY PRI-
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MULTI-DONOR INVOLVEMENT. CLARK

ANNEX XI

WORLD HEALTH ORGANIZATION

Regional Office for Africa

ORGANISATION MONDIALE DE LA SANTÉ

Bureau régional de l'Afrique

ANTIMALARIA STRATEGY AND PRIMARY HEALTH CARE

Report on an internal meeting

Brazzaville, 26-30 October 1981

1. INTRODUCTION

1.1. Background

The meeting on antimalaria strategy and primary health care was held at Brazzaville from 26 to 30 October 1981. The participants are listed in Annex 1 and the agenda of the meeting in Annex 2.

The Regional Committee at its thirtieth session in 1980 invited the Member States to formulate their national antimalaria strategies and send them to the Regional Office in early 1981. This was done by 28 countries. On the basis of the documents received the Regional Director submitted a draft regional strategy to the thirty-first session (Annex 3).

By resolution AFR/RC31/R11 the Regional Committee approved the report and invited Member States to formulate, by 15 January 1982, plans of action for implementing their national strategies. This could enable the Regional Plan of Action to be prepared. The Committee firmly reitrated its political will to strengthen malaria control.

The Director General and the Regional Director therefore decided that the Secretariat would hold a preparatory meeting to discuss possible orientations of the Plan. From earlier exchanges of letters agreement on the following had emerged:

- TCDC provides the best framework for implementation of this plan and PHC is the best approach;
- in the initial phase, support should be given to a few countries where the chances of success are high;
- a multidisciplinary team bringing together expertise from Regional Office and Headquarters will meet to discuss theproblems arising:

The team in question accordingly met and produced the present report based on its discussions and conclusions. The meeting had the following terms of reference:

- review the overall regional antimalaria strategy and propose activities to be carried out in the context of PHC;
- identify and propose an initial group of countries for such action, specifying relevant approaches and related financial implications;

- explore the kind of collaboration suitable for the islands in the Region with a view to attaining the final goal of eradication.

1.2. Malaria and PHC: summary of the present situation

Malaria is one of the five principal causes of mortality and morbidity in Africa, and is endemic in about 90% of the African continent. It accounts for 15%-20% of hospital admissions. Stable malaria is rife and attains hyper- and holo-endemic levels in most of the countries. In certain climatic conditions, malaria exists at hypo- and meso-endemic levels. Few countries in the Region are naturally malaria-free.

The high mortality rate is particularly high among children in the 0-5 year age group (approximately one million deaths per annum). The harmful effects of malaria may also be seen in the reduced output of workers, which hampers socioeconomic development.

By the end of 1976 three countries in the Region had launched PHC programmes, while 14 included specific PHC activities in their health programme. Others had expressed interest in the PHC approach. By 1980, all except four of the countries had formulated policies to ensure the development, promotion and implementation of PHC.

The Regional Office continues to promote this programme and support the countries through the exchange of information, workshops, seminars and financial contributions. An evaluation of the programme in the African Region is under way.

After its discussions the meeting agreed on the following guidelines for antimalaria activities.

2. IMPLEMENTATION OF ANTIMALARIA ACTIVITIES IN THE CONTEXT OF PHC

The following approaches and activities were formulated to meet the needs of an antimalaria programme. In most cases they are applicable both at regional and national levels.

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2.1. Approaches

- To raise awareness among policy-makers and concerned technical departments of the socioeconomic repercussions of malaria and of the need to include malaria control in the health ministry's budget.
- To further elaborate the malaria profile of the countries.
- To step up public information concerning the causes, occurrence, prevention and treatment of malaria.
- To strengthen the countries' capability to train personnel skilled in malaria control in the contex f PHC and at all levels.
- To carry out applied research in order to pinpoint appropriate techniques.
- To provide technical and logistic support to countries having implemented malaria control programmes.
- To make regul. evaluation of malaria control programme activities.

2.2. The activities mentioned in the present document are given merely as examples and are not limitative.

Activities that should begin in 1982

1. Setting-up or strengthening of a department charged with malaria control at the Ministry of Health.
2. Collection of data: morbidity, mortality. Extent of target groups, drugs needed.
3. Preparation of a national plan of action for malaria control.
4. Dissemination of information to policy-makers and concerned departments.
5. Information and education of the public regarding malaria.
6. Introduction of malaria-control components into study curricula.
7. Retraining of staff already at post.
8. Definition of duties of each type of personnel at all levels

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9. Organization of courses and workshops at country and regional levels (TCDC).

10. Advisory services for formulation of the malaria control plan and the training programme.

11. Preparation of teaching modules for training programme.

12. Identification of extrabudgetary resources as a support to the programme.

13. Identification of budgetary resources from other departments at country level.

14. Strengthening of the countries' technological capability (drugs, insecticides, technical equipment).

15. Exchange of information, experiences and results achieved regarding appropriate technology.

16. Use of ICP/MPD intercountry project forward posts (planning, implementation and evaluation of activities).

17. Use of regional advisory panel experts.

18. Regional meeting on malaria.

19. Supply of scientific equipment.

20. Study-trip and training fellowships.

2.3. Specific activities

2.3.1. Health information and education

Mass approach is a key element, making full use of mass media, particularly radio, and of information/motivation campaigns organized at national, community, family and individual levels with the active participation of various political and sociocultural organizations.

In order to develop the educational component, the following actions should be taken:

- intercountry workshops;
- similar workshops at national level.

In turn these meetings will allow the mobilization of the community in favour of the programme. For the implementation of these activities, the extrabudgetary financial

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contribution must be promoted, particularly for training, production of educational material in malaria, applied social research and various community actions.

Some detailed suggestions may be found in Annex 4.

2.3.2. Essential drugs

Provison of essential drugs which includes antimalarial drugs such as chloroquine should be part of the action programme on essential drugs. These drugs will be obtained in the following ways:

(i) by direct purchases by Member States using their own resources;

(ii) by procurement through TCDC utilizing such mechanisms as group bulk purchasing of UNICEF/WHO/Member States;

(iii) by free donations from such organizations as UNICEF, etc., which supply free drugs to least developed countries;

(iv) through bilateral arrangements between governments;

(v) through local production which aims at strengthening self-reliance.

The sixteenth WHO Expert Committee on malaria worked out the cost of single dose treatment of malaria and chemoprophylaxis, based on the following:

- single dose treatment of febrile cases (10 mg/kg of weight - US $10 000 000 per year;
- chemoprophylaxis of vulnerable and high risk groups (10% of the general population) once every two weeks (5 mg/kg weight) US $15 000 000.

2.3.3. Applied research for the implementation of antimalaria strategy.

The Regional antimalaria strategy emphasizes that applied research should be an integral part of malaria control programmes. It should support national malaria control programmes by searching for solutions to problems encountered.

WHO support to malaria research is channelled mainly through the Tropical Diseases Research Special Programme (TDR), of which malaria is one of the six targe diseases. Field research activities are dealt with by the Scientific Working Group on Applied Malaria Field Research (SWG/FIELDMAL).

Global expenditure on malaria research by TDR in the 1982-1983 biennium is esti

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mated at $9.4 million, of which $2 million is for applied field research. The amount that will be spent in the African Region will depend on the number and quality of research proposals made by the Member States. Judging by the paucity of such proposals in the past, it can be safely assumed that funds will be available for any reasonably costed project that is relevant to a national malaria control programme. Fuller information on TDR funded malaria research projects in the African Region is given in Annex 5.

Considering the role of drugs in the regional antimalaria strategy, it turns out to be urgent to set up a regional surveillance programme on the sensitivity of P. falciparum to antimalaria drugs.

2.3.4. Manpower training

Three centres (Ethiopia, Nigeria, Togo) train manpower in malaria control. The revision of programmes in relation to present needs, the development of educational modules, the renovation of teaching material require particular attention. Financial means for developing this programme can only be estimated after an inventory of available resources and activities to be undertaken has been made.

MAL/PHC programming workshops are essential if we want to strengthen the malaria component in the framework of primary health care. To this end, two workshops have been arranged:

- Workshop 1: Gambia, Ethiopia, Tanzania - September 1982
- Workshop 2: Madagascar, Mozambique, Togo - January 1983

Each workshop will last 10 working days and will cost about US $30 000.

3. PROPOSED COUNTRIES FOR INITIAL IMPLEMENTATION

3.1. Choice of countries

Extensive discussions took place on the selection of countries that would be supported on the lines indicated above. It was that consideration should be given to: the willingness of a country to allocate necessary resources to the implementation of this programme; the existence of a reasonable health infrastructure; the willingness of the country to participate in the programme.

Many countries were considered suitable. For the initial phase it was agreed to propose the following countries: Gambia, Ethiopia, Mozambique, Madagascar, Tanzania, Togo.

3.2. Activities in selected countries

- Setting up or strengthening of the service charged with malaria control.
- Determination of epidemiological features and malaria stratification.
- Working out of methodologies.
- Assessment of needs in supplies, equipment, drugs and personnel.
- Planning and identification of national resources and other funding sources.
- Drawing up of implementation schedules.
- Ordering of logistic equipment and drugs.
- Health education and community sensitization.
- Setting up of a system for distribution and storage of antimalarials.
- Continued evaluation of activities.
- Applied research on the health, epidemiological and socioeconomic impact of measures applied.

4. ACTIVITIES IN THE ISLANDS

The Region has three kinds of situations:

(i) islands where the eradication campaign has not yet been considered: the antimalaria strategy applies as on the continent;

(ii) islands where an eradication campaign has been considered and/or planned: this is therefore the preparatory stage of an eradication campaign;

(iii) islands where a campaign is taking place: PHC must allow an effective epidemiological surveillance/monitoring.

Financial support and manpower training are vital to the three groups, although in varying degrees.

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5. FUNDING

5.1. Needs expressed by the countries

Preliminary needs expressed by the countries in their national strategies are given in the following table (annual expenditure in US dollars):

Countries	Drugs	Insecticides	Logistic equipment	Operation	Consultants or training
Angola	460 000	240 000	700 000	200 000	+
Benin	85 000	300 000	2 400 000	3 000 000	+
Burundi	-	-	-	-	-
CAR	125 000	200 000	2 000 000	100 000	+
Comores	16 000	160 000	197 000	10 000	+
Congo	200 000	55 000	70 000	20 000	+
Ethiopia	5 480 000	-	442 000	-	-
Gabon	-	-	-	-	-
Ghana	-	-	-	-	-
Guinea	600 000	55 000	115 000	65 000	+
Equat. Guinea	120 000	10 000	30 000	10 000	+
Upper Volta	152 000	50 000	-	-	-
Malawi	-	-	-	-	+
Mali	-	-	-	-	+
Mauritius	-	-	-	-	+
Niger	5 100 000	-	-	650 000	+
Nigeria	-	-	-	-	-
Uganda	200 000	-	100 000	45 000	+
Rwanda	8 800	15 000	30 000	-	+
Sao Tome	2 000	102 000	100 000	45 000	+
Senegal	-	-	-	-	-
Seychelles	-	-	-	-	-
Sierra Leone	-	-	-	-	+
Swaziland	-	-	-	-	+
Tanzania	-	-	-	-	-
Togo	15 000	-	-	-	-
Zaire	1 500 000	4 000 000	1 300 000	1 000 000	+
Zambia	-	-	-	-	+

5.2. Cost of activities in the six countries

In view of these needs and estimates, the following were regarded as being necessary for the development of MAL/PHC activities in the six above-mentioned countries:

	US $
- Intercountry workshops	75 000
- Similar workshops at national level	160 000
- Contribution to promote training, production of educational materials on malaria, applied social research:	
- at regional level	5 000
- at country level	50 000
- Drugs	7 710 000
- Logistic equipment	18 750 000
- Operation and applied research in the field	2 100 000
Total	28 850 000

5.3. Cost of regional activities

(in thousands)

	1982	1983	1984	1985
1. Advisory services	60	62	65	70
2. Supply of drugs	25 000	25 000	25 000	25 000
3. Supply of insecticides	1 750	1 750	1 750	1 750
4. Grants (research)	2 750	2 750	2 750	2 750
5. Study fellowships, training seminars	2 000	2 000	2 000	2 000
Total	31 560	31 562	31 565	31 570

To this must be added the US $30 000 planned in paragraph 2.3.4. above.

6. CONCLUSIONS AND RECOMMENDATIONS

The PHC approach with its emphasis on community participation, intersectoral action and reorientation of the existing health system so that it can plan an effective role in the delivery of essential care to all citizens, is the key to tackling of the malaria problem in Africa.

A number of proposals have been made on the implementation of antimalaria activities within the PHC context. These proposals related to the Region as a whole selected countries, islands and the mobilization of resources.

At this meeting, certain approaches and mechanisms were proposed. These will be reviewed in the light of plans of action to be presented by the countries in January 1982. In the main, the proposals should stimulate reflexion on the concept of the regional plan of action to accelerate the implementation.

A specific decision is requested on the following:

(i) proposed countries and the initial activities;

(ii) programme of support to islands in the control/eradication of malaria;

(iii) mobilization of extrabudgetary resources particularly for antimalaria drugs. It will be necessary to initiate contacts with the various donor agencies.

Several administrative issues concerning training are summarized in WHO/AFR/RC30/18, Item 28.

(28.) Manpower training deserves the highest priority. This involves training specialists for directing national programs. But supervisors and operational staff are also required for anti-malaria work in the context of primary health care. Training specialists (malariologists, operational technicians) and professional supervisors is more economical and effective when it takes place in the Region. Such training must therefore be continued at the Lagos and Lome health manpower training centers Operational staff should be trained at country level by the personnel trained at Lome and Lagos. This should be part of training for the development of primary health care. Training in malaria control should also be extended to all health manpower categories at all levels. Appropriate teaching material will be prepared. (Emphasis added)

COST ESTIMATING

Whereas cost calculations for drug administration programs consist very largely of relatively predictable elements (personnel, training, and drug procurement and its ancillary costs), similar calculations for a program which also incorporates vector control are substantially more complicated. The following are calculations for three kinds of effort -- all without labor costs:

1. Chemotherapy

Population to be served	1,000,000
Adult population (12^+)	750,000
Child population (1-12)	250,000
Drug price	chloroquine in 150 mg. base tablets $15.00 per 1000 tablets
Presumptive fevers/year	
Adults	1
Children	3
Average body weight	
Adults	60 kg.
Children	30 kg.

Drug requirement

Adults:	750,000 x 600 - 150	=	3,000,000 tablets
Children:	250,000 x 300 x 3 - 150	=	1,500.000 tablets
	Total		4,500,000 tablets

Drug cost:	4,500,000 - 1000 x $15	=	$67,500
Cost per person			$0.0675

To this must be added shipping, storage, in-country transport, and (paid by host government) import duties -- figures which will differ from country to country.

The other factor, which will vary depending on salary structure, extent of paid staff (including those required to support voluntary workers), extent of travel allowances for evaluative and supervisory personnel, and training costs, is personnel costs.

2. Chemoprophylaxis

Population to be served (20% of total)	200,000
Adult population (pregnant women)	50,000
Child population (0-5)	150,000
Drug	Chloroquine in 150 mg. base tablets tablets
Drug price	$15.00/1000 tablets
Prophylactio dose	5 mg. chloroquine base/ kg body weight
Treatment frequency	Weekly
Endemicity	Perennial
Rounds	52/year
Average body weight	
Adults	60 kg
Children	15 kg

Drug requirement

Adults: 50,000 x 300 x 52 - 150 = 5,200,000

Children: 150,000 x 75 x 52 - 150 = 3,900,000

Total 9,100,000

Drug cost: 9,100,000 - 1000 x $15 = $136,500

Cost per person treated = $0.6825

To this must be added the same kinds of ancillary drug costs and salary costs noted in Section 1. Note that for a program of chemoprophylaxis, the personnel levels may be increased by a factor of 2 or more, and salary costs will be very appreciably higher than those associated with a program of chemotherapy.

3. Vector Control: Reduction of Prevalence through Residual Spraying Operations

Population to be served	1,000,000
Houses	200,000

a. <u>Insecticide</u>: Malathion at $2500 per ton of wettable power 50% technical product

Application: 2 gm. technical product/square meter

Frequency: Twice annually

Duration of spray rounds:	1 1/2 months
Average surface to be sprayed/ house	250 square meters
Work rate per sprayman	8 houses/day

Insecticide requirements per round:
200,000 x 250 m^2 x 2 gm - 50% = 200 metric tons

Cost: 200 tons x $2,500	= $500,000
Add reserve and/or wastage	$ 50,000
Total	$550,000
Annual insecticide cost (2 rounds)	$1,100,000

b. <u>Sprayers</u> (Hudson 4 gallon @$100.00)
(Nozzle tips @$ 1.25)

Area to be sprayed 200,000 x 250 m^2	50,000,000 m^2
Rate per sprayman/day 250 m^2 x 18	2,000 m^2
Work days per round	40
Sprayers required	625
Reserve - 20%	125
Total required	750
Cost @$100 per sprayer	$75,000
Spare parts - 10%/year	$7,500/year
Nozzle tips - 3 per round, or 6 per year x 750 sprayers x $1.25	$5,625/year
Annual cost (average 5 year sprayer life)	$15,000/year
Total	$28,125

(Note, however, that all sprayers are required for <u>every</u> round, including the first. <u>Initial</u> funding requirement is therefore $88,125)

c. Transportation

1) Pick-ups: 2 per 5 squads of 5 spraymen - 625 x 2 - 5 - 5 = 50
1 for entomology 1
1 for mechanic and/or reserve 1
Total required 52 x $12,000 = $624,000

Annual cost (average 5 year pick-up life) $124,800

Spare parts - 10% per year $ 62,400

Annual cost $187,200
(Note, however, that all trucks are required for every round, including the first. Initial funding requirement is therefore $686,400)

2) Light field vehicles:

Operational sector chiefs	5
Senior supervisor	1
Sanitarian	1
Entomology	1
Epidemiology	1
Province malaria officer	1
Reserve	1
Total 11 x $7,000	$77,000
Annual cost (average 5 year life)	$15,400
Spare parts - 10% per year	$ 7,700
Annual cost (average)	$23,100
Initial funding cost	$84,000

3) Motorcycles

Field operators	150	
Reserve	15	
Total	165 x $700	= $115,500
Annual cost (average life 3 years)		$ 38,500
Spare parts - 10% per year		$ 11,550
Annual cost (average)		$ 50,050
Initial funding cost		$127,050

Transportation per year (average)	$260,350
Initial funding cost	$837,850

d. Laboratory Equipment and Supplies

Oil immersion microscopes (10 year life)	
12 x $500	$ 6,000
Annual cost	$ 600
Entomological (10 year life)	
3 x $800	$ 2,400
Annual cost	$ 240
Dissecting (5 year life)	
3 x $600	$ 1,800
Annual cost	$ 360
Laboratory supplies	$ 1,200
Annual cost	$ 2,400
Initial funding cost	$11,400

e. Antimalarial drugs

On the assumption that during the initial period of operation, chemotherapy would continue to be required for 10% of the population annually, chloroquine at a level of 10% of that required for a program of chemotherapy alone (see item 1, above).

Drug cost	$ 6,750

f. Fuel, Lubricants, Maintenance -

g. Personnel

As is apparent from the foregoing, the initial funding for a vector control program is high; ensuing years (for the life of the equipment) are for that reason lower, although maintenance costs will rise with the age of the equipment.

Drug, insecticide and equipment costs are continuing to rise; figures used in the foregoing illustrative exercise are for 1982, are derived from various sources, are (especially for equipment) approximations, and are in some instances already outdated. In General, the costs of insecticides will increase from DDT to malathion to fenitrothion, not only on a per ton basis but also on the basis of the proportion of technical product (DDT - 75%; malathion - 50%; fenitrothion - 40%), and (for fenitrothion) a 50% shorter period of residual effectiveness.

ANNEX XIV

SUMMARY CONCLUSIONS AND RECOMMENDATIONS

At the request of the Bureau for Africa, Agency for International Development, and advisory group of malariologists, medical officers, public health specialists, social scientists and medical economists was convened in Washington, D.C., between June 28 and July 2, 1982. Fifty-three in number, and coming from 10 countries and a wide range of international agencies, U.S. government agencies and private organizations, the group members gathered to advise the Bureau for Africa on:

- the possibility of conducting, within the framework of national primary health care efforts, successful programs to control the ravages of malaria in the countries of sub-Saharan Africa;
- the kinds of malaria control programs appropriate to implementation within a PHC framework;
- the goals of such programs;
- the constraints to the success of such malaria control programs;
- areas of program implementation in which the "conventional wisdom" derived from prior anti-malaria efforts provided inadequate guidance;
- the risks and dangers inherent in a program which, for reasons however persuasive, operates without the safeguards hitherto deemed essential; and
- the desirability of providing external support for national malaria control efforts within a PHC framework, and the essential preconditions for such support.

As was to be expected, a group so diverse in geographic, institutional and disciplinary origins, sometimes found more than one answer to these challenges. Yet the extent to which the group reached consensus was both remarkable and encouraging; conclusions reached and recommendations advanced were, in some instances, sharply different from established practice.

The Advisory Group concludes:

A. Primary Health Care: An Appropriate Vehicle for Malaria Control?

1. PHC is considered an appropriate vehicle for malaria control in sub-Saharan Africa, and often in fact is the only vehicle for control that exists.

2. The state of the art is such that it is possible to mount a variety of selected anti-malaria efforts within a PHC framework -- depending on the goals of such efforts.

B. Kinds of Malaria Control Programs Suitable for Implementation Within A PHC Framework

1. Of the four WHO-defined "tactical variants" -- selections of control techniques that relate malaria control tactics to the severity of the problem, the level of control sought and the indigenous capacity to achieve that level -- mortality control (through chemotherapy) and morbidity control (through chemoprophylaxis and possibly limited vector control) appear suitable for implementation within PHC at this time.

2. Where vector control activities are restricted to minor environmental modification measures, water control and mosquito avoidance techniques such as the use of bed nets, screens and repellants, they can be encouraged through appropriate extension of health education and sanitation activities within PHC. Vector control which includes wide-spread chemical control will in Africa be appropriate only in localized areas, for protection of urban and periurban populations; in some of the coastal islands; or under specialized circumstances such as the need to protect strategic areas or groups for economic, social or political reasons. In such circumstances, operational responsibility of vector control should wherever possible be decentralized to such administrative units as municipalities or productive enterprises. Such activity as chemical control or large-scale environmental management will usually require planning at a higher level, with technical inputs and support from a specialized vector control unit.

3. Whatever the goal and the selection of malaria control techniques, there is need for a central core of technical and managerial expertise that can plan, train, direct, supervise, support and evaluate malaria control efforts at the periphery. Vector control programs would increase such needs.

4. Peripheral elements in the PHC system require guidance and support from higher levels in the system. To perform effectively, th PHC worker needs training and supplies, supervision and a referral system to treat complicated cases of malaria.

C. Program Goals

1. Individual countries must establish their own goals and priorities with respect to malaria control. The most pressing need is to reduce malaria-related mortality in rural areas. It must be recognized, however, that in economically important parts of developing countries, malaria morbidity may do even more damage than mortality, since morbidity affects the working economically valuable population whereas mortality has its primary impact on infants.

2. Limitations on resources (in money, manpower and material) are such that any activity undertaken to reduce the impact of malaria must be so implemented as to produce maximum results for minimum expenditure of resources. In practice, this means that one form of malaria control within the parameters of technical feasibility -- chemoprophylactic morbidity control -- will probably not be widely employed because the same amount of resources devoted to chemotherapy can provide mortality control to far more people. Chemoprophylaxis and limited vector control to reduce morbidity should be restricted to high risk-populations including the labor force in development areas, and only be considered where appropriate infrastructure and economic conditions permit.

3. The level of control envisioned under Tactical Variant I, reduction of malaria-caused mortality, can be implemented within PHC systems, and would constitute an enormous advance toward the goals of "Health for All by the Year 2000" if it could be achieved continent-wide throughout Africa.

D. Drug Selection

1. Six criteria should govern the selection of either a therapeutic or a prophylactic anti-malarial drug: (1) safty and freedom from serious side-effects; (2) simplicity in administration; (3) effectiveness; (4) acceptability to patients; (5) availability; and (6) low cost.

Recommendations

a. These criteria should be applied to drug selection before a malaria control program starts and should continue to be applied during program implementation to permit appropriate drug choice changes in response to local situations (e.g., lowered acceptability, lessened effectiveness, cost changes, etc.).

b. Although limited chloroquine resistance (R 1 level) has been found in some parts of East Africa, chloroquine continued to be the anti-malarial drug of choice in Africa. The development of chloroquine resistance in Africa requires constant monitoring.

c. Amodiaquine, although more expensive, is also satisfactory. It should not be considered as a simple substitute for chloroquine. It should be reserved for special situations (emergence of serious resistance or drug rejection by patients because of side effects) in which chloroquine would no longer be fully acceptable.

E. Constraints to Program Success

1. Among identified constraints to successful malaria control, the following ranked high.

a. Failure to establish baseline data; to stratify the area to be served according to the levels of malaria endemicity and the patterns of excessive mortality (to determine the tactical variant(s) to be used); to anticipate management, logistic, manpower and financial requirements; to provide for regular evaluation of results attained; and to replan the program on the basis of evaluation results.

b. Inadequate knowledge of cost-effectiveness of control measures.

c. Assignment of anti-malaria responsibilities to a health infrastructure inadequately prepared to assume the burden.

d. Shortages of both trained manpower and essential training capacity; inadequate training facilities at all levels.

e. Poor administrative, managerial and general services support, including coordination of and cooperation between all malaria and related control efforts, agencies and institutions.

f. Structural inadequacy of the anti-malaria effort at the center. (Seven of the eight Task Forces into which the Advisory Group was subdivided indentified a central malaria service within the Ministry of Health as an absolute need to support the "front line" elements of the PHC system.)

g. Difficulty of access to malarious areas.

h. Limited resources to cope with the many problems faced (of which malaria is only one).

i. Inflation of all costs in the face of declining per capita resource availability throughout much of Africa.

Of these nine key constraints to program success (others were also cited), the first three can be averted or contained by proper initial preparation and planning; the second three are in fact part of the problem to be overcome; and the final three are the hard facts of life that must be recognized and taken into account in setting program goals -- including such goals as the assumption by the host government of all costs beyond the period of external support.

F. Diagnosis and Treatment

1. Current practice in many malaria control programs often requires a time-consuming, equipment-intensive and skill-demanding series of steps prior to parasite-killing (as opposed to parasite suppressing) treatment of confirmred malaria: blood slide preparation and microscopic examination for all suspected malaria cases; and preliminary suppressive treatment pending laboratory confirmation of malaria. Only then is chemotherapy administered at the curative level -- over a period of three or more days.

2. In a program conducted within the framework of PHC, (but, more particularly, in a situation where 80 percent of the population may have parasites in their blood):

   a. The PHC worker should have sufficient training to provide chemotherapeutic treatment, at a prescribed dosage for a parasite-killing cure of malaria, to an individual who has fever, even if the worker has not been trained to confirm the diagnosis.

   b. Single-dose chloroquine treatment of clinically diagnosed malaria at the level of 10 mg. of chloroquine (base) per kilo of body weight, up to a maximum dose of 600 mg., has been demonstrated in Africa to be both safe and effective; additionally, the PHC worker can supervise the actual use of the drug.

c. The only required verification of a clinical diagnosis of malaria normally is a successful patient response to treatment. Failure of the patient to respond to chemotherapy indicates at least the need to reconsider the diagnosis following the local fever protocol; this may lead to prompt referral to the next level of supporting health service. (Such failure may also indicate that the patient did not take the drug, that dosage actually taken was insufficient to clear the blood of parasites, or that a new infection has taken place. It may also flag a case of drug resistance.)

Recommendations:

a. PHC worker training should establish as mandatory the single-dose treatment of all fever cases by administration of a prescribed blood-clearing (radical) level of chloroquine (or other drug of choice). It is entirely appropriate to waive laboratory confirmation of acute malaria prior to radical treatment, in view of constraints imposed by shortages of time, laboratory facilities and skills.

b. Supervision from higher levels in the system is an essential element of support to the PHC worker.

c. Education of the population regarding malaria control should be stressed.

G. Training

1. It is essential to revise training cirricula for PHC workers to incorporate the required level of knowledge of their role in the anti-malaria effort.

2. There are at present no comprehensive training facilities in Africa that provide for the range of skills required for the leadership of a successful anti-malaria program. WHO's demonstration activities, seminars, study tours, support of a post-graduate course in public health and a training center for health personnel have been useful but do not meet the anticipated requirement for trained leadership.

3. Development and strenthening of national training centers constitute a critical need for most of Africa.

Recommendation: While such centers should have African direction at the earliest possible time, they may require initially (and as long as is needed) the stimulus of external technical inputs.

4. Training programs for administrative and operational personnel must be available to each country undertaking an anti-malaria effort. Training must be keyed to the level of control sought.

5. The success of malaria control efforts depends on the availability of trained personnel at all grades. The investment of funds of the external donor and the host government is endangered if technical personnel are improperly or inadequately trained to carry out the program.

Recommendation: National institutions that provide training in control of malaria in countries that receive external support for anti-malaria programs should also receive external technical and financial assistance whenever improved training is regarded as critical to the success of the relevant programs. The level of assistance will depend on the extent to which the countries themselves are unable to provide training appropriate to the demands of the program.

6. The importance of training cannot be allowed to obscure the fact that investment in training facilities will prove unproductive unless there is a will to utilize the facilities. WHO regional malaria training centers in Lome and Lagos were reported to have discountinued their programs because of lack of interest on the part of the nations of Africa in providing candidates for training.

H. Program Continuation Beyond External Assistance

1. Malaria control programs are not time-limited; they have costs that (especially for programs with the limited objective of reducing morbidity and mortality) will not decline over time. Yet external assistance is normally time-limited, and the impact of continuing costs of Ministry of Health budgets after the termination of external inputs may be such as to cause retrenchment or even termination of the malaria control activity.

2. The continued private-channel sale of anti-malarial drugs throughout most of tropical Africa, even at high prices, demonstrates both the awareness of the ability of such drugs to cure malaria and the willingness of Africans to pay for chemotherapy.

Recommendations:

a. To minimize the strain of malaria control on national health budgets, and to make possible the continuation of control efforts beyond the conclusion of external assistance, most if not all countries of sub-Saharan Africa should consider the adoption of a policy under which chemotherapeutic drugs would be provided at cost to the users.

b. Such a policy, if adopted, should be embodied in the plan for controlling malaria, and should constitute a significant element in the host government support commitment which could be used as one element in the basis for any external assisistance.

Note: The Advisory Group was unanimous in its conclusions that: (1) administering a dosage lower than that required to clear the blood of parasites would encourage parasite selection for drug resistance, (2) single-dose treatment at a blood clearing level should replace multiple-dose treatment, (3) the drug of choice should be administered by an individual trained to prescribe the proper dosage for the body weight of the victim.

A vigorous minority held that the trained individual who administers drug treatment of malaria should for the time being be a member of the PHC system, but that ultimately it will prove desirable and even necessary to have trained individuals in every home, to permit immediate self-medication or home medication of malaria. Such a policy should be geared to the continuous availability of the drug of choice in every home, the ready availability of resupply, the availability of supervisory and of back-up services to take care of cases that do not respond to home drug medication, and the adoption of a policy of unrestricted sale of the drug of choice (versus a policy of free drug distribution).

Adherents of this position recognized the high initial drug cost, but believed that the combination of (1) reduced requirements per location for PHC workers to adminster drugs, and (2) revenue generation through sale of anti-malarial drugs would enable maximum extension of mortality reduction through chemotherapy within the confines of an

inevitably limited Ministry of Health budget. This would be especially true where the chemotherapy program was part of an integrated rural development effort which had local capital generation as one of its objectives.

The ultimate success of such a home-based program of malaria control through self-financed chemotherapy would depend substantially upon: (1) the extent to which community leaders and organizations are able to develop support for the program among community residents and an understanding of its details, and (2) the degree to which integration with capital generation activities can be pursued.

I. Preconditions for External Support

1. External support is not warranted in the absence of a long-term national commitment to a goal-oriented, well-planned, organizationally sound, technically and administratively feasible and costed plan of malaria control activity that takes full account of the country's physical and human resources down to the community level. (See, however, Section I-4, below).

Recommendations:

The prerequisites for assistance include:

1. Request

A request from the host government for assistance in malaria control, whatever the level of control sought, must be supported by evidence of national will to carry out the proposed program and of the priority assigned to the problem of malaria.

2. Plan

The request should be keyed to a plan describing th malaria problem, the proposed course of action and the anticipated results. The plan should provide:

a. The area in which the program will be conducted, population affected, specific population groups and age groups targeted for attention.

b. A baseline of epidemiological data that describes the existing problem in quantitative terms; this will enable subsequent evaluation of accomplishment under the program.

c. A life-of-project projection of requirements in terms of manpower, money (local currency and foreign exchange) and equipment or supplies, specifying the quantity and quality of the resources to be provided by the host government and those expected from external sources -- AID, WHO or other agencies.

d. Logistic and transportation requirements of the plan, including a description of methods of procurement, warehousing, distribution, stock control, reorder points, etc.

e. Training requirements and a plan of <u>who</u> required training, <u>where</u>, <u>when</u>, and <u>by whom</u>.

f. The relationship of the malaria control project to other PHC activities and to integrated rural development or similar projects.

g. Methods of assuring coordination with and the full support of other elements in the Ministry of Health with other health agencies in the country, and with other ministries or agencies concerned with activitis affecting malaria in the country.

h. A plan for continuing the project beyond the period of external assistance.

3. <u>Counterpart Relationship</u>

From the outset of the project, there should be an identified, qualified officer to whom the host government assigns responsibility for project management and evaluation. This officer may be the counterpart of the USAID H/N officer.

4. <u>Assistance in Plan Preparation</u>

The preparation of such a plan may be beyond the immediate capacity of a number of African countries. International and bilateral assistance in plan preparation, including feasibility studies as embodied in small-scale projects to test the applicability of an intervention technique, or assistance in training, warrant support by international and bilateral sources of external assistance.

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