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AID MALARIA STRATEGY WORKSHOP

JUNE 7-10, 1983

COLUMBIA, MARYLAND

By Eugene J. Gerberg
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African mothers line up with their babies to let a rural doctor in Tanzania check them for signs of malaria.

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1330 Dillon Heights Avenue
Baltimore, Maryland 21228

Project Director: Dr. Eugene J. Gerberg
Chairman: Dr. Donald E. Weidhaas
Rapporteur: Mr. Albert E. Farwell

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Executive Summary

Malaria continues to be the leading deterrent to development of human and natural resources in vast areas of the world. It is the leading disease in terms of mortality and morbidity. As a direct result of the adverse impact of the disease, countries with serious malaria problems cannot become economically viable.

The existing policy of the Agency for International Development (AID) with respect to anti-malaria programs, ten years old and interpreted differently in each of AID's regional bureaus, requires revision if the Agency is to have a coherent world-wide approach to a problem of world-wide scope. Existing policy and its implementing support criteria are exessively rigid with respect to insistence on a purely economic rationale for AID support of malaria programs. These criteria pay inadequate attention to the need to identify and anticipate constraints to successful long-term malaria control; in addition they are silent on the relationship between malaria control and an increasingly important but widely variant mechanism for the delivery of health services, Primary Health Care (PHC).

The AID Malaria Strategy Workshop recommends a firm AID requirement that a country requesting assistance in controlling its malaria problem (1) be fully aware of the need for and (2) make a commitment of long-term support of the proposed program. With respect to the tactical approach to malaria control and the degree of control sought, the Workshop recommends maximum AID flexibility -- subject to an epidemiologically established plan of operation, a determination of the plan's technical feasibility and a careful assessment of administrative capacity and long-term financial affordability. Malaria's negative impact is such that properly supported requests for assistance warrant immediate consideration.

Economy of execution demands that all malaria programs make the maximum use of existing and potential PHC systems, consistent with the capacity of such systems to carry out their assigned roles. Conversely, in those countries where malaria is endemic and uncontrolled, a concentrated attention on primary health care without including an appropriate effort to reduce the toll of (if not the incidence of) malaria is irrational.

The degree adequacy of AID's malaria staff, in Washington and in the field, is of grave concern. It lacks both the numbers of personnel and the technical capacity to discharge its responsibilities. Especially in the field, AID staff has little or no malaria control training and operational experience. Specific suggestions for increased staffing and training are advanced.

While commodity supply will continue to be vital to early success of anti-malaria efforts, the Workshop report singles out research and training as the keys to long term success, and identifies specific areas of both research and training.

AID's malaria policy should take cognizance of the need for increased research; continued support (through to the conclusion of field testing) of malaria vaccine research, but also other forms of applied research, vital if the PHC system is to play its full role. Effectiveness of available anti-malaria drugs and insecticides is threatened by wide-spread and growing parasite and vector resistance; replacements are urgently needed.

While recognizing AID's long-established encouragement of collaboration among AID, international financial sources and other donor nations in support of malaria control activities, the Workshop sees little likelihood of increased multidonor support of malaria control without positive AID action. Such a course of action is suggested.

Workshop Conclusions

Major conclusions and recommendations emerged from the deliberations of the AID Malaria Strategy Workshop. Reports of sub-group Task Forces underlie these recommendations (which were debated within the entire Workshop, serving as a Committee of the Whole, to reach consensus). These Task Force reports appear in subsequent sections of this study.

A. AID Malaria Policy

1. Country Commitment.

AID's policy in responding to requests for assistance in dealing with the problems of malaria should be firm with respect to a requirement that the requesting county must recognize and commit itself to the long-term control of its malaria problem.

Without such a commitment, no amount of external support and no plan of operation, however well conceived, can assure long-term success in controlling malaria.

2. Tactical Flexibility.

AID's policy should be flexible with respect to the requesting country's tactical approach to malaria control and the degree of control to be attained and maintained.

A plan for malaria control must, however, be appraised on the basis of its technical feasibility and the country's administrative capacity and long-term financial responsibility. This appraisal must provide a reasonable anticipation that the assistance requested will lead to a

supportable and self-sustained malaria control activity -- whatever its scope -- which can be expected to continue beyond the termination of external assistance.

3. Priority.

Malaria's negative impact on economic and social development, its effect in shortening life expectancy, its toll in morbidity and the concentration of its effects on children and pregnant women give the disease a priority so high that properly supported requests should be given immediate consideration.

4. Use of PHC System.

Economy of execution demands that all malaria programs make the maximum use of existing (and potential) PHC systems, consistent with the capacity of such systems to carry out their assigned roles. However, the presence or absence of a PHC system should not determine whether or not support should be given to an anti-malaria program.

In some countries the PHC system, supported by a mandatory core of malaria expertise within the Ministry of Health, may be the only vehicle for malaria control.

5. Research.

AID's malaria policy should take cognizance of the need for increased research and field training.

Support of necessary research would include but would not be limited to continuation (through to the conclusion of field testing) of AID's long-standing support for basic research leading to a malaria vaccine (or vaccines). Other forms of research are needed: applied research and operational research to determine the effectiveness of innovative as well as conventional control measures and combinations of measures.

B. Criteria for AID Assistance to Anti-Malaria Programs

AID support of a country request for assistance to a malaria control effort is warranted when the country makes a long-term national commitment to a goal-oriented, well-planned, organizationally sound, technically and administratively feasible and costed plan of malaria control. This plan should take full account of the country's physical and human resources down to

the community level, take into account any recognized constraints to program success, and include proposals for overcoming or accommodating to such constraints.

The prerequisites for assistance include:

1. 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.

2. 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:

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

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

c. A description of plans for supervising, monitoring, evaluating and providing essential specialized support to workers at the periphery.

d. 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).

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

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

g. The relationship of the malaria control program to other activities of the Ministry of Public Health

h. 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 (including those in the private sector) concerned with activities affecting malaria in the country.

i. The social and economic impact of the proposed program.

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

3. Review

The request for assistance may be approved only on the basis of an AID review which is specifically designed not only to to identify the program's technical, administrative and economic feasibility but also its affordability beyond the point of external support. The review should also examine the extent to which long-term goals of the plan take into account the known constraints to the attainment of such goals.

4. Assistance in Plan Preparation

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

C. Role of PHC and Community Participation in Malaria Control

1. Use of Most Effective Vehicle.

While non-specific AID support to develop and strengthen country-wide PHC systems might in time be sufficient to assist in achieving malaria control, in endemic areas where malaria is a major threat to economic development or

quality of life, AID should provide selective support of malaria control using the most satisfactory available vehicle. In many countries, this will be the PHC system.

2. Time Constraints.

While all PHC systems require training, supervision, logistic support and a referral system, the need for quick response, (in particular the need for ready availability of chemotherapy and ability at the system's periphery to determine and administer an adequate dose of a curative drug) inherent in successful treatment of acute malaria warrants AID's particular attention to these factors in evaluating malaria control proposals within PHC systems.

3. An AID strategy of assisting malaria control through PHC should be complemented by:

a. Professional Core Group.

Support as needed to the development, through in-country training or training abroad, of a strong central core of experienced national malaria professionals, capable of the planning, designing, management and evaluation of appropriate interventions.

b. Diagnostic Tool Research.

Support of research to develop the simplified yet accurate diagnostic tools essential to enable quick and accurate diagnosis of malaria by individuals who possess very low levels of technical training.

c. Community Participation.

Support of operational research into techniques for eliciting increased and improved community participation in malaria control.

d. Complementary Projects

Support of malaria control in development projects and programs outside the health sector, especially those which could be adversely affected by malaria (e.g., education, settlement and rural development projects) or those which could themselves contribute to the malaria problem (e.g., irrigation, highway construction, land reclamation).

4. Conversion from Vertical System.

Types of malaria control activities proposed for transfer from a vertically administered system to the PHC system should be very carefully selected in the light of the geographical coverage of the PHC system and the adequacy of the preparation of the PHC staff to assume the new burden, and the potential weakening of an existing malaria program.

D. Multidonor Assistance

AID Health and Development policies already advocate the encouragement of collaboration between AID and other donors. The following added specificity is suggested:

1. Donor Collaboration and Coordination.

AID should continue its ongoing efforts in collaborating/coordinating with other donors of health assistance at the country, regional and international levels.

2. Professional Staff Coordination.

Regular contact for research and country program coordination between AID professional staff and other financial and technical agencies should be maintained.

3. Acceleration of Multi-donor Support.

For purposes of accelerating the rate of international financial support for malaria, four levels of action are suggested:

a. AID country health representatives should continue to encourage governments to identify needs for external cooperation to formulate these needs within project proposals which merit the approval of the national planning authority, and to seek multisource funding for malaria. AID should support (through the use of short-term consultants) the efforts of WHO field representatives to help in project formulation and justification.

b. In view of regional differences in the approaches for control of the malaria problem, AID should maintain close consultation with WHO Headquarters and Regional

Offices with respect to status of programs, requirements, and project formulation.

c. AID should continue to support WHO Headquarters in Geneva in its periodic consultations among donor groups for exchange of views on malaria program status and anticipated requirements for external cooperation.

AID should also explore comparable mechanisms with other multilateral and bilateral funding institutions.

d. AID should cooperate with WHO and other international development cooperation organizations, at both central and regional levels, to identify both potential donors and appropriate recipients; should provide such information to countries seeking external assistance; and should cooperate, as appropriate, in the formulation of proposals for multi-source external financial and technical support.

E. Research

The greatest successes in anti-malaria programs have been achieved through anopheline mosquito control to prevent spread of malaria. Research on these vectors of malaria must be intensified in order to improve control methodology. Such research should include study of the vectors themselves, improved insecticides and insecticidal application equipment, biological control and integrated or comprehensive vector management.

1. Vaccine Research.

AID should continue to support malaria vaccine research at a level which will permit completion of this important project.

2. Other Centrally Funded Research.

Because of current operational difficulties, especially drug resistance in malaria parasites and insecticide resistance in mosquito vectors, new research activities should be initiated in the following areas:

a. Simplified malaria diagnostic and survey methods.

b. Identification, clinical evaluation and field testing of new anti-malarial drugs, through to registration and approval for human use.

c. Identification and testing of new insecticide compounds and biological agents, as alternatives for insecticides to which resistance has developed or which may in some situations be unsuitable because of vector behavior.

d. Development and testing of improved insecticide formulations.

e. Development of test methodology for use in specifications necessary to ensure delivery to the field of high quality insecticides, application equipment and packaging.

f. Development of a variety of alternative, possibly novel, malaria control measures.

g. Further investigation of epidemiological determinants of the malaria problem which affect human ecology and therefore the severity of the malaria problem or the feasibility of its control.

3. Operational Research.

As trained professionals emerge, AID should support operational research at the program level, essential to ensure effective malaria control programs. Provision should be made in country programs for an operational research component, to develop the area-tailored vector and parasite control programs upon which effective anti-malaria measures must be based. Such a technical research component would determine the optimum curative drug, the proper dosage and the high-risk populations. It would also monitor drug sensitivity in association with PHC activities.

4. Review of Proposed Research.

AID should maintain an effective system of review for malaria research proposals, especially at the central and regional levels, to assure against duplication of effort. The review process should include a cross-check of planned research with WHO's Special Programme for Training and Research in Tropical Diseases (TDR), and with bilateral research organizations. Maintenance of close contact

with agricultural operational and research interests in insecticides may avoid later problems.

5. Research Funding

The intrinsic nature of present malaria control programs is such that research in support of effective, operational programs is an absolute necessity for long-term success. The investment in control-related research should be commensurate with the investment in the total program.

F. Training.

1. National and International Training.

A material expansion of AID sponsorship of training related to anti-malaria programs is essential. Such training should apply to all levels of malaria program personnel with host countries. Strengthening of national training capability is a proper and indeed a priority matter for AID support.

It may also prove feasible for AID to support (as it is already doing in Asia) the development and functioning of collaborating institutions at the regional or interregional level to provide a better utilization of training resources.

2. Core Skills Training.

Key national personnel, especially in scientific, operational, public health and administrative positions, should be provided with the necessary skills required to carry out the functions of their positions. Such training may be provided in their own countries, in the U.S., or in a third country, as is deemed appropriate. Degree-level training should be encouraged and funded in selected cases.

3. Training Materials.

AID should support the development and production of training materials at all levels.

4. Training for Research.

A more specialized need is the strengthening of the capabilities of research workers in the developing countries,

if technology transfer is to be most effective. Training of this nature should be coordinated with WHO's TDR, but AID can and should play a role as well, particularly in longer-term training of such personnel in U.S. educational institutions.

5. Training for AID Personnel.

See Section I-4 below.

G. Epidemiologic Assessment, Diagnosis, Malaria Drug and Insecticide Use

1. Program Design.

Malaria control programs must be designed and evaluated using adequate epidemiologic data on malaria, its transmission and its health consequences in the area.

2. Local Drug and Insecticide Manufacture.

While local drug and insecticide manufacture may in some instances be technically feasible and consistent with AID policy to encourage and support local formulation of antimalarial chemicals, careful quality control and uniform packaging of these products are mandatory to ensure both efficacy and safety to humans.

3. Control Over Antimalarial Drugs and Insecticides.

In the design and operation of malaria programs, the quality control, supply and use of current and new antimalarial drugs and insecticides should be regulated in coordination among national governments, AID, other sources of assistance and international organizations and industry to maintain the efficacy of available tools as long as possible and to ensure product safety to humans.

H. Vector Control

1. Role of Vector Control

Many malaria control programs must continue to be based entirely or in great part on vector control: chemical, environmental or biological, or a combination of these methods.

2. Entomological Surveys

Entomological surveys to determine the vector species or strain, breeding sites and breeding habits are absolutely essential to successful vector control.

3. Insecticide Selection

Determination of the most cost effective insecticide can only be made by field-test comparison of usage under local conditions.

I. AID Staffing

AID must reconsider its overseas staffing priorities, which currently stress managerial skills rather than malaria technical skills. Only with the expansion of training programs which cover both technical and management skills, for national but also for AID staff, will malaria programs be adequately designed and implemented.

1. Mission Staffing.

AID should provide a malaria-trained U.S. advisor to each AID-supported malaria program.

2. Regional Staffing.

AID should establish for each region a particularly well-qualified U.S. malaria specialist to serve as coordinator and technical backstop to country-level malaria advisors and as a consultant in the formulation of initial plans to establish malaria programs.

3. Washington Staffing.

AID should strengthen the malaria control expertise in its headquarters offices, both in regional offices and in the Office of Health, to provide expeditious review of and support to country programs.

AID's current patterns of organization in Washington and assignment of responsibility deprive malaria programs of technically qualified review of project proposals, and multiply contact points between AID and Centers for Disease Control (CDC) unnecessarily, to the detriment of effective relations.

a. The responsibility for the design review, technical coordination and evaluation of malaria (and other vector-borne diseases) control and research programs should be centralized and assigned to technically qualified and trained personnel in the Office of Health, Science and Technology Bureau.

b. The Regional Bureau should continue to be responsible for project management. Individuals with direct responsibility for the malaria programs in each region should be trained in malaria control.

4. Training for AID Personnel.

Given the shortage of trained and experienced malaria control personnel in the U.S., AID should cooperate with one or more U.S. educational institutions to establish suitable training programs to address this real and growing problem. Only with the expansion of training programs for AID staff as well as for national staffs will malaria programs be adequately designed and implemented.

J. AID Environmental Guidelines

1. AID's basic policy of concern for the environmental impact of some malaria control activities is sound and is in no need of change at this time. However, until new and yet unproven alternative methods of vector control are developed and tested, the use of pesticides in many and possibly most vector control programs must be considered a sine qua non.

2. Residual pesticide interior treatment of dwellings has litte or no impact on the environment. In terms of its absolute effectiveness (in terms of results achieved) and its cost-effectiveness, residual pesticide treatment remains the most efficient method of malaria vector control. AID should not discontinue support for vector control through the use of residual pesticides; in fact, the rising costs of presently available insecticides and the progressive spread of anopheline resistance to the present array of such insecticides may require that AID support research leading to the development of new, effective, equally safe and hopefully cheaper alternative insecticides.

3. AID should also encourage and finance research leading to the development of alternative methods of vector control

that would be as effective as residual insecticides, and as environmentally sound.

Foreword

Malaria is a highly debilitating and frequently fatal disease, caused by any of four protozoan parasites, of the genus Plasmodium, and transmitted from person to person by the bite of Anopheles mosquitoes. While progress in the diminution of malarial infection has been made in many countries, and the disease has been eradicated in a number of countries (or areas within countries) where it had been historically prevalent, endemic malaria continues to be a major public health problem, of particular importance because of its resurgence in many areas where it had been controlled.

Malaria-caused morbidity has a negative impact on economic growth in many developing countries, restricts food production, labor productivity and educational attainment in most tropical and subtropical countries, and adversely affects the well-being of some twelve hundred million people.

Malaria is also the world's most killing disease in terms of total mortality. However, its burden is borne to an overwhelming degree by the very young and by pregnant women. It is estimated that in Africa alone, malaria contributes to the death of a million children a year.

Malaria's economic impact is tremendous. In humanitarian terms, its impact is immeasurably great.

AID MALARIA STRATEGY

I. Introduction

The practical intent of a revised AID strategy is to provide updated, officially-approved program guidance for use by AID personnel in Washington and in the field, many of whom will not have received specialized malaria training. Such guidance will also serve as an approved AID position which may be shared with other participating governments, other U.S. institutions, and with international organizations such as the World Health Organization (WHO).

AID's purpose in convening the AID Malaria Strategy Workshop was to elicit from an expert group a series of recommendations which could provide guidelines for a new AID policy in respect to criteria for the review and approval of anti-malaria programs which merit AID support, with specific relation to:

o Criticisms of AID's existing program selection and approval criteria contained in a 1982 report to the AID Administrator by the General Accounting Office (GAO).

o The essential foreign policy functions of U.S. programs of economic assistance. AID's efforts to advance economic development are designed to strengthen the economies of countries receiving assistance, to contribute to their political and economic stability, to help meet basic human needs, and to express U.S. humanitarian concerns.

o The essential elements of economic assistance projects to which AID's interests are directed. These elements are considered to represent the most effective forms of assistance to the economic advance of the "poor majorities" in developing countries. They include the policy framework within which development activities take place; increased reliance on the potential contribution of the private sector; increased attention to scientific and technical cooperation with the developing countries, including support of research and training, the development of new technologies and technology transfer; and assistance in institutional development, critically important to the achievement of self-sustaining economic and social change.

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II. Background

A. From Malaria Eradication to Malaria Control

In the developing countries to which it extends technical and economic assistance, the U.S. has consistently shown a willingness to support efforts to reduce the impact of malaria on both the quality of life and the potential for economic development. Since the early 1950's, the U.S. has provided over $1 billion in bilateral assistance to support anti-malaria programs, in contributions to the malaria efforts of the World Health Organization (WHO), and in support of research, including development of mosquito control methodology, epidemiological research, improved insecticides and application equipment, malaria vaccines, and anti-malaria drugs.

The initial results of these programs were dramatically successful: eradication of the disease in many countries, and striking reductions in malaria-related mortality and morbidity in virtually every country where programs were initiated. Yet the successes of the early years of the program could not be maintained everywhere; in some countries, malaria resurged with alarming rapidity when anti-malaria efforts slackened. It soon became apparent that the techniques of the eradication effort could not in many countries guarantee a quick elimination of the disease nor assure a quick termination of the heavy annual costs. By 1969, WHO reluctantly concluded that, however desirable the eradication of malaria might be as an ultimate goal, in countries where eradication was not yet feasible due to financial or technical constraints, a program of malaria control -- the degree of control not specified -- should be considered. Whereas malaria eradication programs were, by design, of a limited duration, malaria control programs had no predictable end. The principal differences between a malaria eradication program and a malaria control program are briefly stated in Table 1.

Expenditures for the salaries and wages of the independent malaria eradication staffs which were considered tolerable for programs with an anticipated short life span often proved to be too high to be borne for control programs with no visible termination date, and efforts were made in a number of countries to combine the responsibilities of these staffs, especially at the field level, with those of the basic health services. Efforts to devolve the responsibilities of vertically organized malaria eradication programs to the basic health services were generally unsuccessful; malaria incidence usually rose promptly. This is hardly surprising; basic health services were usually not as well-developed as were the highly organized malaria eradication services. Where health services existed, they were for the

TABLE 1
Differences between a Malaria Control Programme and a Malaria Eradication Programme

	CONTROL PROGRAMME	ERADICATION PROGRAMME
OBJECTIVE	The reduction of malaria to a prevalence where it is no longer a major public health problem.	The ending of the transmission and the elimination of the reservoir of infective cases in a campaign limited in time
AREA OF OPERATIONS	Not necessarily covering all the area where malaria transmission takes place.	Must cover all the area where malaria transmission takes place.
MINIMUM STANDARDS	Good	Perfect
DURATION OF OPERATIONS	Without limits	Programme ends when certain requirements are met
COST	Constantly recurring	Expenditure represents a capital investment and is not a permanently recurring cost
CASE-FINDING	Superfluous	Of paramount importance
EPIDEMIOLOGICAL INVESTIGATION OF POSITIVE CASES	Superfluous	Necessary in the late stages
EPIDEMIOLOGICAL EVALUATION OF RESULTS	By usual malariometric surveys	Proof of disappearance of indigenous new malaria cases
IMPORTED CASES	Do not deserve particular attention	Important and dangerous when effective attack measures have been withheld
TOTAL COVERAGE	Unnecessary	Indispensable both for the attack measures and the case-finding
ADMINISTRATION OF THE PROGRAMME	May not be the best and still be sufficient	Must be fully efficient and speedy; if not, danger of failure

The above table, a modification of that appearing in WHO's Expert Committee on Malaria Sixth Report (1957). page 9, is drawn from "A Textbook of Malaria Eradication," Emilio Pampana, Oxford University Press, New York, 1969.

most part oriented toward treatment rather than prevention of disease, were multi-purpose rather than specifically designed to combat malaria, and the pesonnel usually lacked sufficient training. Moreover, they were frequently Moreover, they were frequently seeking the goals of malaria eradication without possessing the resources of the former eradication program, and their results were measured against earlier eradication targets. Malaria control was widely regarded as a poor man's eradication program.

In 1970, AID noted that since the early 1950's both AID and WHO had provided training for national malaria personnel in the skills required for malaria eradication, and reached three questionable conclusions: that individual countries had adequate cadres of trained professional personnel, that WHO would continue to provide such technical advisory services as might be necessary, and that it was no longer necessary for AID to do so. The underlying assumption of this new policy -- that cadres of personnel trained in the techniques of country-wide and centrally directed intensive malaria eradication could readily assume the quite different problems of decentralized malaria control -- went substantially unchallenged for a number of years.

B. AID Malaria Policy

By 1973, AID found it necessary to reassure its own field missions as to the Agency's willingness to support anti-malaria programs. The Agency issued guidance to its missions which (AID Circular A-733, July 3, 1973) which indeed assured them of willingness -- on a case-by-case basis -- to support country malaria programs, but with a number of carefully defined preconditions:

- Country interest and concern for malaria, as evidenced by "an adequate budget and staff".
- A need to protect the gains of substantial prior U.S. investment in development assistance, or to prevent malaria from inhibiting further development.
- A technically, administratively and financially sound malaria plan (approved by both WHO and AID).
- Evidence that the country had mobilized available internal resources and explored the availability of other (non-AID) external assistance.

These strictures still constitute the only Agency-wide guidance to USAID Missions, although they have in fact been

superseded by regional instructions issued by the Bureaus for Asia and Africa.

C. AID Auditor General's Report

In 1976, AID's Auditor General issued a report which drew attention to:

- The resurgence of malaria in countries where the disease had been controlled or, indeed, virtually eradicated.

- The decline in the level of the overall attack on malaria, since the program machinery to combat malaria had been essentially disassembled.

- Failure in many countries to integrate malaria services into health systems, leaving malaria technicians and workers without job security or career potential and causing them to seek careers elsewhere.

- Declining AID inputs into malaria programs, with consequent threat to developmental gains achieved and potential future gains.

- AID-supported research to produce a malaria vaccine -- a laudable effort that merited continued high priority.

The report urged, inter alia, the assembly of a task group of specialists to review the malaria situation and recommend essential modifications in AID's policy.

AID's response to the Auditor General's recommendation was positive. Both the Bureau for Asia, representing the region which had the most to lose from a resurgence of malaria, and subsequently the Bureau for Africa, representing the region which the "global" eradication program had virtually by-passed, convened expert panels to advise on the criteria which should govern the extension of AID assistance to country malaria programs.

The two reports, issued in 1977 and 1982, respectively, have many features in common. Both groups attempted to bridge the gap between country-wide malaria eradication programs, conducted by essentially independent vertical organizations, and malaria control programs integrated into the overall public health systems. The Asia Bureau report concluded that, where basic health services are adequately developed and effective, many malaria control operations, (e.g. drug distribution, health education) can be devolved to the local health infrastructure. The Africa Bureau report, however, adopted the more radical approach of prescribing the manner in which (particularly in Africa), the Primary Health Care (PHC) system can play

the key role in programs designed to reduce malaria mortality and morbidity, primarily through the use of anti-malarial drugs. Both of these advisory groups concluded that program success depended upon the presence within the Ministry of Health of a strong core group of malariologists, epidemiologists, entomologists, logisticians and administrators who could plan, supervise, provide essential training, supply, backstop and evaluate the efforts of the PHC system at the periphery. Finally, both rely to a greater or lesser extent on the availability of a functioning PHC system. AID has pledged itself to the support of the idea of PHC, but PHC as an instrument is not precisely defined. In many countries, it has received more lip service than solid national backing, and seems to owe its principal support to the self-evident fact that hospital-based, centrally located health delivery systems are not only unable to serve the health needs of people outside urban areas, but also are clearly beyond the capacity of many developing countries to support and maintain. This is true even if the bulk of initial investment in such health delivery systems is externally provided.

The Bureau for Latin American and the Caribbean also chose (in 1980) to issue its own restatement of the 1973 Agency position on malaria, although it did not feel the need for an external advisory group. In essence, Bureau policy reiterated the 1973 criteria, but directed that support to malaria programs be considered in the context of rural health-care delivery goals, and that such support be competetive, in terms of benefits attained, with other options for assistance.

To restate: the essential abandonment of the global effort to eradicate malaria forced AID to give serious consideration to the instrument through which malaria control efforts could be carried out -- in essence, the mechanism which could deliver this basic health service. It also forced AID planners to concentrate on such key factors as a malaria control programs' affordability, and the will and ability of a host country to maintain the control effort beyond the period of external assistance.

D. Primary Health Care

The findings and recommendations of the two expert groups, but in particular, of the Africa group, are consistent with AID's position (as enunciated in two successive Health Policy Papers) in support of Primary Health Care (PHC).

In 1978 the WHO and the United Nation's Childrens Fund convened in Alma-Ata an international conference on Primary

Health Care -- the outcome of which has been a world-wide acceptance of PHC as the recommended mechanism for delivery of health services and, indeed, prevention and control of endemic diseases. By 1982, half of AID's development assistance budget for health supported the delivery of PHC services in developing countries.

The term Primary Health Care describes an approach or strategy, not a rigid adherence to a single health delivery system, and the Alma-Ata deliberations, as set forth in the conference report, make it plain that the PHC system must be able to depend upon the support of other levels of the health system to provide specialized services not available from the PHC system at the periphery. The central level provides planning, evaluation and managerial expertise, specialist staff, training, research, laboratory facilities, and logistic and financial support.

E. GAO Report

In April 1982 the U.S. General Accounting Office (GAO) drew to the attention of the AID Administrator the fact that the criteria which determined AID's willingness to consider assistance to country malaria programs had been established in 1973 -- nine years earlier -- and had not been revised since that time, although they were often being honored in the breach. GAO observed, however, that some of AID's Regional Offices had established their own criteria for program approval, but that there was need for a revised agency-wide statement of policy with respect to support of malaria programs. In urging the need for policy revision, GAO noted two critically important changes since issuance of the 1973 approval criteria: (1) the emergence of PHC as the key mechanism for the delivery of health services and (2) the potential role of PHC in conducting malaria programs. GAO also drew attention to the decline in levels of AID support of anti-malaria efforts, to the rapidly rising costs of the drugs and insecticides used in malaria control, and to the drastic reduction in AID's ability to provide, from its own personnel resources, either technical, operational and management assistance at its overseas posts or program review and management advice at its headquarters offices.

Finally, GAO advised AID that while malaria project designs should take full cognizance of inherent constraints to successful anti-malaria activities and to their long-term effectiveness, and while AID's review and approval processes should ensure that programs are not undertaken where constraints preclude progress, AID needs the flexibility to meet

humanitarian needs on a case-by-case basis. GAO also took favorable note of AID's support of research leading to the development of an effective malaria vaccine (or vaccines), which could, if successfully commercially produced, prevent illness and/or limit transmission.

GAO's Summation:

o Malaria is still a major public health problem in many developing countries; some 1.8 billion people live in areas of countries still at risk to the disease, and some 214 million people are infected annually.

o AID's current program guidelines are in fact outdated and in need of revision, but must provide sufficient latitude to enable AID to meet humanitarian needs.

o AID-assisted malaria control programs have been generally successful in meeting short-term goals, but progress toward long-term targets has been inhibited by factors which must be taken into consideration in program formulation, review and approval.

o No single check-list approach to the identification of programs which merit U.S. assistance will be applicable to every situation; nevertheless, a standard is still required to prevent the commitment of scarce foreign assistance resources to projects which offer little hope of sustained progress when viewed in the light of known constraints.

o A recurring theme throughout the report: AID faces difficult decisions concerning future support of malaria programs -- yet such decisions must be made.

F. Workshop Composition

The AID Malaria Strategy Workshop was convened to bring to bear the collective advice of some 27 scientists, educators, medical entomologists, public health specialists and medical economists in helping AID resolve the questions raised by GAO. Participants from AID Regional and Technical Offices were joined by health research directors, distinguished faculty members from four universities, senior personnel from such international organizations as the World Health Organization, the Pan American Health Organization and the World Bank, and such U.S. governmental entities as the U.S. Department of Agriculture and the Centers for Disease Control, and malaria-experienced private sector participants. The group also included participants from two assistance-donor nations, Japan and the United Kingdom.

G. Workshop Procedures

The participants in the AID Malaria Strategy Workshop considered that their responsibility transcended the consideration and recommendation to AID of a revised list of criteria which should underlie the approval of AID support of anti-malaria programs at the country level, especially since such criteria are usually a device for screening out unacceptable proposals rather than for identifying programs which should be encouraged. Moreover, the GAO report criticizes not only what it considers obsolescent or inappropriate criteria of malaria program approval; it also points to factors which inhibit achievement of program goals, to the changed institutional framework for anti-malaria programs, and to the growing need for anti-malaria effort in the light of wide-spread malaria resurgence.

To enable AID to discharge the responsibility of even selective malaria support during a period of rising malaria endemicity in many countries, limited availability of resources (including AID resources), competing demands of other claimant programs (including other programs in the health field), and the need to tailor and adapt malaria programs to the varying forms of PHC as it emerges in the developing countries, the Workshop participants perceived a clear need for numerous changes, not only in AID's screening system but also in its response and implementation mechanisms.

The Workshop participants also examined and reached conclusions on those program elements where AID's inputs may achieve maximum return on investment; on areas where AID's inputs can and should be augmented from other sources of support; on the desirability of development of new tools for malaria control, and the role which AID can play in their development; and, inevitably, on the singular importance of PHC to malaria control and the malaria-related needs of this still inadequately explored mechanism for distribution of health services.

III. AID's Malaria Policy

A. Past and Current Policies

U.S. involvement in international anti-malaria activities can be traced in an unbroken line from participation in the Pan American Health Organization's Third International Sanitary Conference (1907) to the present, peaking in the global malaria eradication effort of the late 1950's and 1960's, but continuing in the form of support to malaria control programs in the 1970's and 1980's.

The levels of investment during the eradication period -- by AID, by WHO, by other donors and by the host countries -- were recognized by all as bearable only under the assumption that they could be cut radically after the disease had been eliminated from a country and the only remaining function was vigilance to prevent reintroduction. As it became apparent that eradication was unachievable in the foreseeable future for many countries, it also became apparent that the costs of large, independent malaria organizations could no longer be tolerated.

Malaria control, anticipating the continued presence of at least a low level of malaria, would of course have recurring costs -- to be borne, it was expected, from the augmented national revenues which would follow the economic development made possible by control over the leading cause of morbidity and mortality, malaria. Four principal factors combined to thwart such expectations.

- Overconfidence as a byproduct of dramatic initial success. Malaria resources (personnel, funding, materiel) were diverted to other programs in many countries, thereby allowing malaria to recrudesce.

- The development of insecticide resistance in vector mosquitoes, rendering them no longer susceptible to safe, cheap DDT, and often requiring the development and use of more highly toxic, more expensive and shorter-lived chemicals for use as residual sprays.

- The emergence of malaria parasites capable of surviving the once universally effective therapeutic drug, chloroquine, requiring the development and use of new, more expensive chemotherapeutic and chemoprophylactic drugs.

- The almost vertical rise in the costs of all petroleum-based chemicals, of fuels, of supplies and equipment, following OPEC's assault on the world's energy price

structure, from which the developing countries have particularly suffered.

Other factors also contributed to the inability of malaria control programs to attain -- and maintain -- their long-term goals; and in conjunction, these factors now make it difficult if not impossible for any but the most successful of the developing countries to be able to afford from their own resources the continuing costs of integrated malaria control -- the kind of effort which had succeeded malaria eradication in many countries, and which involved vector control, chemotherapy and, as appropriate, chemoprophylaxis. Recommended by the Asia Bureau Malaria Strategy Study in 1977, integrated malaria control remains the most effective technique for reducing and maintaining at a low level the actual incidence of malaria, and is still recommended for those countries where health resources are adequate to support its commodity costs, technical and administrative demands, and requirements for trained staffing. The Asia Bureau's policy emphasizes that malaria control is a part of national health planning, not an independent program; that PHC has a key role to play in program implementation; but that the presence of a malaria-trained core group within the Ministry of Health is of crucial importance to the planning, management, training, support, backstop and evaluation functions. While concurring on the need for malaria expertise in the Ministry of Health, the Africa Bureau has moved even further toward the integration and the incorporation of malaria control into PHC. The Bureau's instructions to its field missions indicate the degree to which a malaria control program can be implemented within the framework of a national PHC system, and the costs in money and trained manpower inherent in each of several levels of malaria control. The Africa Bureau in essence defines the desirable program as the affordable program -- which, for most African situations, limits anti-malaria activity to control over malaria-caused mortality through chemotherapy. Limited vector control is recognized as a suitable and, in fact, a highly desirable malaria intervention, primarily in urban areas, but the limitations of health budgets in most countries make vector control activities on any major scale unaffordable.

The Africa Bureau's strategy, not of preventing but of curing malaria attacks as they occur by providing chemotherapy to the greatest number of malaria victims who can be reached through the PHC program, represents the ultimate in low-cost malaria "control", given the present state of the art. Its costs are further lowered by its reliance on a single clinical diagnostic indicator -- fever -- as evidence of acute malaria, thereby avoiding both the time loss and the costs involved in slide preparation and laboratory examination, the normal diagnostic evidence of malaria. Finally, treatment is defined as the administration of a single dose of chloroquine in

an amount adequate to clear the patient's blood of parasites -- for a fee, or a "user charge", to the patient, wherever possible.

This bare-bones approach to malaria control is feasible in Africa where the overwhelming percentage of malaria cases is caused by a single parasite, Plasmodium falciparum. Plasmodium falciparum in Africa is generally still susceptible to chloroquine treatment (although resistance has now been confirmed in some areas of East Africa). The patient's blood can be cleared of Plasmodium falciparum infection by the administration of a single adequate dose of chloroquine or other chemotherapeutic drug.

In other areas of the world, where malaria may be caused by any one of a number of Plasmodia, (e.g., Plasmodium vivax, the common malaria parasite of South Asia) which are not susceptible to single-dose treatment, the Africa strategy will prove to be less readily applicable, and possibly inapplicable. Not only may the disease be expected to recur after single-dose treatment; in some areas, the parasite has shown itself to be resistant to drug after therapeutic drug. In such areas, vector control will probably remain the principal mode of malaria control -- hopefully augmented by new anti-malarial tools. The ideal such tool would be an affordable malaria vaccine which is both polyvalent and capable of providing protection for a year or more. Promising as are the developments in AID-supported malaria immunology research, several years of continued research and development will be required to satisfy Food and Drug Administration (FDA) requirements.

In short, there is no present successor to the formula approach of the malaria eradication period: a single short-run program believed to be applicable to any country (excepting, of course, tropical Africa). Rather, malaria programs must be tailored to the epidemiological situations which they are designed to combat. It is ironic that tropical Africa may remain the exception to the general rule; there appears to be an inexpensive, affordable if Spartan program which is generally applicable throughout the area, and which has the capacity to save lives and shorten the duration of malaria-caused morbidity, even though it may not reduce malaria incidence.

B. AID's Appropriate Role

As AID has recognized, there is a marked correlation between improved health and economic development. At one time, the argument was advanced that improved health would and indeed should follow economic development. This thesis ignores three critical factors: the degree to which a healthy populace can accelerate economic development; the degree to which some kinds of epidemic disease can not merely inhibit development, but in fact thwart it entirely; and, not least important, the human-

itarian considerations which attach a value to the protection of both life and quality of life. In fact, AID's Health Assistance Policy Paper points out that the development success stories of the past twenty years have taken place in countries which made a systematic investment in the health of their people.

It is an entirely tenable thesis that AID support of health programs -- malaria control included -- should be restricted to those countries which are making or are prepared to make such a systematic investment in health.

C. Malaria Control's Relationship to AID Priorities

In those countries where malaria and/or other vector-borne diseases constitute a serious health problem, control of these diseases represents an integral part of AID assistance to improvement of health care. Control programs relate directly to each of AID's major development priorities: technology development, adaptation and transfer; institutional development; influence on host country policy reform; and, in many instances, increased use of the private sector. A strong case may be made that malaria control is the ideal program to attain AID objectives in many of the developing countires.

Conclusions and Recommendations

1. Country Commitment.

AID's policy in responding to requests for assistance in dealing with the the problems of malaria should be firm with respect to a requirement that the requesting country must recognize and commit itself to the long-term control of its malaria problem.

Without such a commitment, no amount of external support and no plan of operation, however well conceived, can assure long-term success in controlling malaria.

2. Tactical Flexibility.

AID's policy should be flexible with respect to the requesting country's tactical approach to malaria control and the degree of control to be attained and maintained.

A plan for malaria control must, however, be appraised on the basis of its technical feasibility and the country's administrative capacity and long-term financial responsibility.

This appraisal must provide a reasonable anticipation that the assistance requested will lead to a supportable and self-sustained malaria control activity -- whatever its scope -- which can be expected to continue beyond the termination of external assistance.

3. Priority.

Malaria's negative impact on economic and social development, its effect in shortening life expectancy, its toll in morbidity and the concentration of its effects on children and pregnant women give the disease a priority so high that all properly supported requests should be given immediate consideration.

4. Use of PHC system.

Economy of execution demands that all malaria programs make the maximum use of existing (and potential) PHC systems, consistent with the capacity of such systems to carry out their assigned roles. However the presence or absence of a PHC system should not determine whether or not support should be given to an anti-malaria program.

In some countries the PHC system, supported by a mandatory core of malaria expertise within the Ministry of Health, may be the only vehicle for malaria control.

5. Research.

AID's malaria policy should take cognizance of the need for increased research and field testing.

Support of necessary research would include but would not be limited to continuation (through to the conclusion of field testing) of AID's long-standing support for basic research leading to a malaria vaccine (or vaccines). Other forms of research are also needed: applied research and operational research to determine the effectivness of innovative as well as conventional control measures and combinations of measures.

Section IV, below, describes and defines the criteria which determine whether particular requests warrant approval under the foregoing policy. See, also, Section VI, which defines more specifically AID's existing policy on multi-donor assistance.

IV. Criteria for AID Assistance

A. Existing AID Criteria

Since 1973 AID's announced policy with respect to malaria has been that to receive AID support, a country anti-malaria program must meet four criteria. Assistance may be considered when:

1. The country demonstrates its own interest and concern for malaria through the provision of an adequate budget and staff to carry out the program;

2. There is a critical need to protect a substantial U.S. investment in terms of gains already made or a need to prevent malaria from becoming a deterrent to other country development programs;

3. The country provides a malaria plan which is technically, administratively, and financially sound and is based on an AID review of the recommendations of a joint WHO/Host country evaluation team;

4. Available resources within the country have been mobilized and available external sources of assistance have been explored.

B. GAO Criticism

GAO's report to the AID Administrator is critical of only one of these criteria -- the second -- and its criticism is that AID has failed to follow its own self-imposed strictures. A second criticism is that the criteria as stated do not adequately identify those programs which merit U.S. assistance. Finally, GAO observes that AID needs the flexibility to meet humanitarian needs on a case-by-case basis.

In point of fact, criterion No. 2, which drew GAO's unfavorable attention, is a particularly useful device for signalling countries where AID should be particularly alert to the need for an appropriate malaria program. The criterion should not, however, be understood as a necessary precondition for program consideration; as GAO notes, AID needs the flexibility to meet humanitarian needs on a case-by-case basis.

GAO is quite correct, however, in observing that the existing criteria are silent with respect to guidance to AID reviewers to approve malaria program proposals only in light of their capacity to overcome identified constraints to program success -- and that failure to take such constraints into consideration could preclude sustained progress. Recognition of

such constraints is explicit in the advice of the expert groups to both the Asia and Africa Bureaus; both of these groups have identified lists of constraints like that in GAO's report, although substantially more detailed. In particular, the Africa Bureau's Malaria Manual identifies nine such constraints or groups of constraints. Their application is world-wide; and the AID Malaria Strategy Workshop hereby incorporates them by reference[1]

Such constraints will vary from country to country; no single standard will apply to all. The Workshop Group did not attempt to provide a new checklist of possible constraints; it did recognize, however, that insistence on a "technically feasible" plan would not preclude program failure as a result of factors which the plan could not itself overcome -- as, for example wide-spread insurgency. However recognition of such constraints is indeed a function of examination for administrative feasibility and for evaluating the degree to which plan targets may be attained.

Thus, while the Workshop Group believes that the 1973 approval criteria have in the main served AID well, and have (through constructive interpretation) permitted the discharge of AID's responsibility for meeting humanitarian needs, the Workshop Group concludes that AID would be better served by a single set of approval criteria than by the present somewhat conflicting regional patterns and an admittedly obsolete overall Agency policy in respect of malaria assistance.

The Workshop Group also concludes that one focus of the GAO report is itself in need of critical attention. The GAO report concludes -- or rather, is keyed to its assumption -- that all malaria programs should be designed to achieve long-term reduction of malaria. While this is a consummation devoutly to be wished, it must be recognized that the long-term costs of a program which will reduce malaria are beyond the present and at least in the short-term, projected capacity of many countries to support beyond the period of external assistance. It is indeed possible, however, to project the capacity of many such countries to support indefinitely the costs of a program designed to reduce malaria-caused mortality, through the administration, to clinically-diagnosed malaria victims, of an effective antimalarial drug at an appropriate dosage. Such an effort, which meets the criteria established by WHO[1] for the

[1]Manual on Malaria Control in Primary Health Care in Africa, December, 1982. These constraints are reproduced in Annex 4.

simplest form of malaria control, Tactical Variant I, would have little or no impact on the reservoir of parasitic infection within the populace (malaria prevalence) or the annual number of cases of acute malaria (malaria incidence). It would, however, save many lives, particularly among pregnant women and young children; it would abbreviate the periods of malaria-caused morbidity, especially critical in the economically important adult population. Especially in countries where the malaria parasite remains susceptible to single-dose treatment of inexpensive chloroquine, it appears that a sustained and sustainable reduction in the mortality and abbreviation of morbidity caused by malaria constitute entirely acceptable goals.

C. Proposed AID Criteria of Approval

The Workshop's recommendations to AID concerning AID policy in dealing with the problems of malaria are set forth in Section IV, above. To implement this policy, there is need for specific criteria for evaluating requests for AID assistance.

Conclusions and Recommendations

The AID Malaria Strategy Workshop concludes that AID support of a country request for assistance to a malaria control effort is warranted when the country makes a long-term national commitment to a goal-oriented, well-planned, organizationally sound, technically and administratively feasible and costed plan of malaria control. This plan should take full account of the country's physical and human resources down to the community level, take into account any recognized constraints to program success and include proposals for overcoming or accommodating to such constraints.

The prerequisites for assistance include:

1. 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.

2. 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:

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

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

c. A description of plans for supervising, monitoring, evaluating and providing essential specialized support to workers at the periphery

d. 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).

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

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

g. The relationship of the malaria control project to other activities of the Ministry of Public Health

h. 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 (including those in the private sector) concerned with activities affecting malaria in the country.

i. The social and economic impact of the proposed program.

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

3. Review

The request for assistance may be approved only on the basis of an AID review which is specifically designed not only to identify the program's technical, administrative and economic feasibility but also its affordability beyond the point of external support. The review should also examine the extent to which the long-term goals of the plan take into account the known constraints to the attainment of such goals.

4. Assistance in Plan Preparation

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

V. Role of PHC and Community Participation in Malaria Control

A. Alma-Ata Declaration

In 1976, the countries of the world declared in the 30th World Health Assembly that the world's social goal should be "the attainment by all citizens of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life." In 1978, a joint WHO/UNICEF sponsored world conference held in Alma-Ata, endorsed the view that the provision of primary health care (PHC) to the mass of the world's people should be seen as the highest international priority in the health sector and agreed that the PHC approach is the key to attaining the goal of health for all.

The Alma-Ata Declaration further recognized that 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 finance of health programs.

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

- A minimum range of basic health services should be made available at the community levels, with emphasis on preventive care. The national health system should be designed or reoriented to support primary health care, by providing both adequate supportive services and access to more complex care when needed.

Countries implementing the primary health care approach are recognizing the need to expand and strengthen the community-based health infrastructure and to improve planning, management practices, logistic support, training of personnel supervision and referral systems. PHC programs have shown no uniformity in the actual implementation of the PHC approach. There are serious administrative deficiencies which need to be addressed if the PHC approach is to be efficiently and effectively implemented.

B. PHC: A Vehicle or THE Vehicle

The basic objective of AID health programs is to help the developing countries to achieve self-sufficiency in providing popular access to cost-effective curative and preventive health services; to lower rates of mortality and morbidity, especially among the vulnerable population groups, particularly children, women in the reproductive age, and other priority groups.

In planning the national use of available and usually limited financial and manpower resources, identification of those health problems which are responsible for most of the mortality and morbidity of the population is imperative. Among endemic diseases which adversely affect the majority of third world countries in the tropics, malaria is paramount.

Even in the absence of major epidemics, malaria is an insidious, ever-present infection which in Africa alone annually contributes to the death of at least 1 million infants and young children. Malaria interferes with education and training, and saps the energy and strength of the community attempting to free itself from the vicious circle of disease, disability, and poverty. In such countries, a focus on primary health care without a simultaneous effort to reduce malaria is irrational.

Primary Health Care is, in fact, considered an important vehicle for implementation of malaria control activities and in countries where malaria is endemic, malaria control should become an essential component of PHC. If the implementation of PHC matched the idealized concept, an AID policy limited to providing support to develop and strengthen country-wide PHC systems might in time be sufficient to assist materially in achieving malaria control.

AID has invested heavily (up to 50% of its total health budget in 1982) in supporting the development of PHC, recognizing the extent to which a well-executed PHC program can improve health delivery services, especially to the rural poor. The Agency has also recognized that PHC means different things in different countries; that it must be judged by its performance rather than its mystique; and that its goals are sometimes over-optimistic. Many countries have failed to take advantage of existing systems of health service delivery, private and public. PHC has sometimes been treated as a separate, competing, overlapping health system.

Where an in-place PHC system exists, it should provide such delivery services as the administration of chemotherapeutic treatment of malaria, health education, and guidance and encouragement to communities as to limited vector control

activities which they can perform. It is less likely that PHC can successfully discharge all of the complex functions of integrated malaria control, particularly in those countries where such programs are already in place.

From a strategic standpoint, and depending on the extent and severity of the malaria problem and the extent and capacity of the PHC system, it is appropriate for AID to support malaria control selectively within the primary health care program as well as to support malaria control per se in selected areas of a country when justified by malaria's potential for frustrating developmental activities or by catastrophic malaria incidence.

In implementation of malaria control activities within PHC, careful consideration must be given to the types of activities which can be cost-effectively incorporated. Where the PHC system is weak, further overburdening of primary health care workers with additional malaria control tasks without training, adequate logistics and supervisory support can be expected to lead not only to further weakening of PHC services, but also to ineffective malaria control activities. AID support to malaria control within the primary health care program should therefore also include strengthening the key elements: training, logistics and support from a competent, malaria-trained core group.

PHC adds to the number of approaches to be used for malaria control activities. The simplest and cheapest program is the reduction of malaria-related deaths through timely chemotherapy. This form of malaria control is identified as Tactical Variant 1 in the Seventeenth Report of the WHO Expert Committee on Malaria; it is the approach to malaria control in tropical Africa, recently adopted by AID's Bureau for Africa. Such a program has little effect in reducing malaria incidence or prevalence but it can save many lives. Moreover, while there are recurrent costs, they are small. The technical demands of this variant on the PHC staff are relatively low; it presents no time constraints other than prompt treatment. In most cases, it should be possible to pass on at least a portion of the drug costs of chemotherapy to the affected individual.

Malaria's challenge includes its high prevalence and incidence, relatively high levels of disability, and (especially in the case of falciparum malaria) high rates of mortality. A vigorous application of Tactical Variant 1 is possible within PHC because of malaria's rapid response to chemotherapy, the stability of anti-malaria drugs over time, the lack of need for a cold chain, the relatively low cost of chemotherapy, and the low risks of side effects from treatment with chloroquine, to which malaria parasites in many areas remain susceptible. The utilization of PHC to implement Tactical Variant 1 is par-

ticularly appealing in countries with minimal technical expertise. This could serve as a preparation for an expansion of the PHC system and for the more sophisticated subsequent control efforts which can reduce malaria incidence to what the country may consider tolerable levels -- when such efforts become technically feasible and affordable. It is in such cases that PHC as a vehicle for anti-malaria efforts has its greatest potential. While PHC will also have a role to play in source reduction and other vector control programs, that role is quite probably of a limited nature, e.g., education.

One aspect of malaria control through PHC which has been particularly appealing to budget-restricted Health Ministries is the apparent potential savings inherent in a program which relies heavily on voluntary help, relatively low levels of required training, and an approach to logistics which may depend on other, existing systems for deliveries of supplies and equipment.

It should be clearly understood that the peripheral health system is not free-standing. It requires adequate supervision and logistic support. The "savings" which are expected to flow from a malaria control program executed by the PHC system are easily overestimated, and may prove to be illusory. While experience will vary from country to country, there appears to be a considerable degree of correlation between the number of voluntary workers in PHC system and the additional number of full-time employees required to instruct, supervise, backstop and provide logistic support to the volunteers. Community participation in malaria control (and other local-level health programs) will not automatically lead to a reduction in the need for technical personnel or even in financing; the immediate result may be an actual increase in the required Ministry of Health investment in personnel, time and money. The ultimate target, of course, is better delivery of health services. There are, however, cost considerations, which must be anticipated by health and malaria program planners and provided for.

The AID strategy of supporting malaria control within a PHC context should not be interpreted as a constraint to support of malaria control by other means. The AID strategy clearly must encompass support of appropriate basic and applied research. Additionally, malaria control can and should be pursued in development projects and programs outside the health sector. For example, a development program in a malarious area might appropriately undertake malaria control activities carried out by rural development, irrigation, hydroelectric or agricultural technicians, with the advice and support of the same core group whose presence is inherently essential to

successful malaria control within PHC. To insure the effectiveness of AID's support for selected anti-malarial activities within its health sector assistance or through PHC delivery mechanisms, the existence within the host country of a strong central core of experienced technicians capable of planning, design, accurate diagnosis, management and evaluation of appropriate interventions is essential.

C. Community Participation

The importance of community involvement and participation has been recognized widely, not only by proponents of PHC, but by the entire social and economic development community. The mechanisms through which this participation can best be elicited must quite literally be developed on a case by case basis, with the cooperating country clearly taking the lead. While AID cannot profitably try to assume resonsibility for developing community participation, a strategy of supporting efforts to stimulate the AID-assisted country to take the leadership in developing community participation is appropriate, as is the full support of country initiatives in developing and encouraging community participation. In planning malaria control operations, it is important to include studies of communities' local physical environment; socioeconomic and cultural patterns; knowledge and attitudinal factors which can influence program effectiveness; available resources which can be used to provide logistic support; and the prospects for continuity of operations. Appropriate educational approaches should be developed which can emphasize preventive and protective actions that individuals and communities can take for malaria control, such as reduction of sources for vector breeding, physical personal protection techniques (screens, bed nets, repellents), effective use of drugs and early notification to and contact with primary health workers and malaria workers for treatment.

AID support for national training of primary health care and malaria workers in concepts and methods for developing and implementing these educational approaches is appropriate; suitable educational training materials will need to be developed. The implementation of the training and information activities related to community participation must be an integral component of general training strategy developed within the overall malaria control strategy.

Conclusions and Recommendations

1. Use of Most Effective Vehicle.

   While non-specific AID support to develop and strengthen country-wide PHC systems might, in time, be sufficient to assist in achieving malaria control, in endemic areas where malaria is a major threat to economic development or quality of life, AID should provide selective support of malaria control using the most satisfactory available vehicle. In many countries, this will be the PHC system.

2. Time Constraints.

   While all PHC systems require training, supervision, logistic support and a referral system, the need for quick response inherent in successful treatment of acute malaria (in particular, the need for ready availability of chemotherapy and ability at of the system's periphery to determine and administer an adequate dose of a curative drug) warrants AID's particular attention to these factors in evaluating malaria control proposals within PHC systems.

3. An AID strategy of assisting malaria control through PHC should be complemented by:

   a. Professional Core Group.

      Support as needed to the development, through in-country training or training abroad, of a strong central core of experienced national malaria professionals, capable of planning, designing, management and evaluation of appropriate interventions.

   b. Diagnostic Tool Research.

      Support of research to develop the simplified yet accurate diagnostic tools essential to enable quick and accurate diagnosis of malaria by individuals who possess very low levels of technical training.

   c. Community Participation

      Support of operational research into techniques for eliciting increased community participation in malaria control.

   d. Complementary Projects.

Support of malaria control in development projects and programs outside the health sector, especially those which could be adversely affected by malaria (e.g., education, settlement and rural development) or those which could themselves contribute to the malaria problem (e.g., irrigation, highway construction, land reclamations).

4. Conversion from Vertical Systems.

Types of malaria control activities proposed for transfer from a vertically administered system to the PHC system should be very carefully selected in the light of the geographical coverage of the PHC system, the adequacy of the preparation of the PHC staff to assume the new burden, and the potential weakening of an existing malaria program.

VI. Multidonor Assistance

Multidonor assistance refers to cooperative effort on the part of donors of assistance to support specific activities in developing countries, through normal government-to-government or institution-to-government agreements. The precise transfer mechanism will depend on the nature of the project agreement(s), which may involve separate bilateral agreements or varying degrees of joint funding (such as co-financing, parallel financing or the establishment of special funds) and the provision of commodities and services.

A. New Donors To Development Programs

While the growth of national economic and social development planning over the past three decades has often affected malaria program financing adversely by increasing the competition for development funding both at the national and international level, the U.S. no longer overshadows the support efforts of other developed countries to the degree it did in the 1950's and 1960's. There are today, in addition to the U.S., at least 15 national and international sources of technical and financial cooperation[1], many of which have displayed active interest in the health sector if not in malaria control as such.

The annual levels of concessional aid to developing countries reached $35 billion in 1981, with an estimated 10 per cent flowing into health programs ($3 billion). By way of comparison, the average annual cost to the United States of U.S. assistance to malaria programs over the period 1950-1981 was $32 million. Studies of the experience of present and potential donors suggest that most national ministries of health have not yet begun systematically to explore potential financial cooperation for health, let alone for malaria.

The international economic crisis of the past decade has contributed to the increase in commodity import prices (drugs and insecticides). This has seriously affected some countries which have been highly dependent on external aid, e.g. Haiti and Nepal. However, the relative costs of malaria programs,

[1]A 1980 review of international donor funding, by L.M. Howard, indicated participation by the following external sources 1976-1978: Australia, Belgium, Denmark, France, Germany, Fed. Rep., Japan, Netherlands, Norway, Sweden, Switzerland, United Kingdom, United States. Multi-lateral and other international institutions have included WHO, UNICEF, the World Bank and the Asian Development Bank.

for both affected countries themselves and for external agencies, have been relatively small in comparison with measures of national wealth. For example, public and private sector health costs combined infrequently exceed 3 per cent of Gross Domestic Product in developing countries. National public sector budgets are characteristically small. Public sector health budgets rarely exceed 5 per cent of the national public budget. Malaria programming from a country's own resources -- independent of external assistance -- has in recent years not frequently exceeded 5 per cent of the health budget.

Prior to the intensive programming, since the late 1960's, of water, sanitation, family planning and medical care services, malaria programs were frequently the most expensive national health efforts in the public sector. Today, malaria programs, even programs of a dimension and composition which might offer the chance of a major reduction in malaria incidence, would require a lower proportion of available resources, both internal and external, than programs of twenty years ago. In comparison with total national resources of developing countries as measured by their Gross Domestic Product (more than $400 billion for the 68 poorest countries) and by the annual magnitude of external concessional flows for health (more than $3 billion), malaria programming might appear to present a somewhat less formidable financial challenge than is generally assumed.

This somewhat optimistic projection gives inadequate attention to the fact that average financial capacity is of little help to the sub-average countries. Additionally, there is a heavy competition for both national and external funding. The Minister of Health who recognizes the danger of resurgent malaria faces a greater need to demonstrate to his superiors an economic justification for an adequate malaria budget than that faced by his predecessor of the 1950's, when eradication was a holy crusade. To pose the problem in its bluntest terms, the first and most serious problem of the concerned Minster of Health may be to couch his proposal in national development terms understandable to the Finance Ministry, the Development Planning Commission, or a similar authority which has the power to allocate funds.

Assuming careful attention to the most efficient use of national and external support for malaria, the magnitude of costs per se is not likely to pose the most serious obstacle to sustained support if there is well-documented, credible justification in national development terms.

Although policy statements of external financial organizations and agencies are not usually oriented to malaria, health sector proposals, including malaria, are generally acceptable,

provided that such inclusion represents an official government request which is channelled through the appropriate national planning or financial authority. The potential number of external sources is larger than the current participating number.

B. Current AID Policies On Multidonor Funding

Development policy, based on Congressional legislation, is explicit in its encouragement of international financial collaboration in multisource funding.

The 1982 AID Health Assistance Policy Paper underscores the importance of donor coordination, and draws attention to the responsibility of WHO for attracting and coordinating international funding.

At the country level and in limited regional or interregional programs of health, AID has participated in multidonor efforts. However, there does not yet exist a systematic cooperative effort among AID and other principal donors in support of malaria (or for health in general) on a global scale. To give effect to AID's concept of serving as a donor-of-last-resort, an active system of joint consultation with other donors may be essential in the health sector.

Since total AID health programming represents only 10-15 percent of total world-wide concessional aid for health, more systematic collaboration with other sources of assistance becomes increasingly important.

C. Assessment of Financial Requirements

With respect to international multi-source financial cooperation, AID's strategy should take into consideration the need for a joint assessment of financial requirements at the country level by the host government, AID, WHO and other cooperating agencies. Such an assessment should take into account all of the factors set forth in Section V, above; in particular:

Epidemiological status

Program status (administration, proposed and ongoing strategy, assessment of progress, costs, national and external financing)

National commitment
- -- at Ministry of Health level
- -- at Development Planning Commission level
- -- legislation

Nature of program justification in development terms

Status of requests for external cooperation

Potential alternative sources of financial/ technical cooperation for malaria

In view of the spectrum of potential external financial sources, specific assessment should be made of efforts by host governments to formulate proposals for external assistance and of the response to such requests. From an administrative point of view, proposal preparation and clearance at the national level may pose greater potential constraints than the actual availability of external concessional financing.

At the Ministry of Health level, governments may not be fully aware of the sizeable number of donors with policies favorable to health programming. Lack of information on sources of potential financing and difficulties in project preparation are constraints to mobilization of external financial assistance.

D. Financial Resource Mobilization

External sources confirm that the number of officially presented health proposals is small in comparison with the dominant flow of well-prepared projects presented on behalf of the agriculture, industry, transportation, and energy sectors.

The practical process of financial resource mobilization involves the following procedures:

1. Identification and documentation of potential external concessional sources, with attention to their policy, program, funding, organization, and process procedures.

2. Identification and development of national malaria projects in a systematic way which specifies objectives, requirements, schedules, alternative sources of financing, and external financial and technical requirements. Project justification, for approval at the national planning authority level, needs to be stated in terms which relate credibly to national economic and social development ob-

jectives, to technical and administrative feasibilities, and to capacity to evaluate results.

3. Analysis of total requirements against potential sources.

4. Presentation of proposals by requesting governments to representatives of external financial organizations, usually in the country of origin. Varieties of channelling mechanisms exist.

5. Training of health sector personnel in international resource procedures, an administrative/management art which is often unfamiliar to technically oriented personnel.

In summary, there appear to be 40 or more potential donors who may take an interest in malaria programs. These sources have not been canvassed systematically. The task of resource mobilization is sizeable and unlikely to succeed as an incidental activity of existing personnel within the AID -- or, indeed, the WHO malaria program. AID strategy will require an active policy to mobilize resources for malaria in collaboration with WHO and other external sources.

E. WHO Role In Financial Resource Mobilization

The World Health Assembly has repeatedly exhorted WHO to mobilize financial support for anti-malaria activities and urged member states to coordinate their efforts with WHO. These actions reflect international consensus that WHO should actively promote the mobilization of support of anti-malaria activities.

Other than the Geneva Health Resources Group for Primary Health Care, which is initiating exploratory activities in mobilization of international funding, it would appear that there is as yet no systematic, organized focus for financial resource mobilization for health on a global scale, let alone for malaria. Specialized WHO programs such as TDR do indeed convene their own international funding meetings, however, and at the regional level, the Pan-American Health Organization and other WHO Regional offices have initiated the identification of principal sources of concessional funding for health (including malaria) and the provision of guidelines for resource mobilization in the Americas.

Conclusions and Recommendations

AID Health and Development policies already advocate the encouragement of collaboration between AID and other financial sources. The following added specificity is suggested:

1. Donor Collaboration and Coordination.

   AID should continue its ongoing efforts in collaborating/coordinating with other donors of health assistance at the country, regional and international levels.

2. Professional Staff Coordination.

   Regular contact for research and country program coordination between AID professional staff and other financial and technical agencies should be maintained.

3. Acceleration of Multidonor Support.

   For purposes of accelerating the rate of international financial support for malaria, four levels of action are suggested:

   a. AID country health representatives should continue to encourage governments to identify needs for external cooperation, to formulate these needs within project proposals which merit the approval of the national planning authority, and to seek multisource funding for malaria. AID should support (through the use of short-term consultants) the efforts of WHO field representatives to help in project formulation and justification.

   b. In view of regional differences in the approaches for control of the malaria problem, AID should maintain close consultation with WHO Regional Offices with respect to status of programs, requirements, and project formulation.

   c. AID should continue to support WHO Headquarters in Geneva in its periodic consultations among donor groups for exchange of views on malaria program status and anticipated requirements for external cooperation.

      AID should also explore comparable mechanisms with other multilateral and bilateral funding institutions.

   d. AID should cooperate with WHO and other international development cooperation organizations, at both central and regional levels, to identify both potential donors and

appropriate recipients, should provide such information to countries seeking external assistance; and should cooperate, as appropriate, in the formulation of proposals for multi-source external financial and technical support.

VII. Research and Training

A. Research

Paul F. Russell, the architect of AID's malaria eradication program, stated in 1968 that "there does not appear to have been a logical or practical ratio between the $500 million spent trying to eradicate malaria and the $25 million spent to find out how to do this most effectively and economically."

The strategies as well as the tactics of anti-malaria programs have had to be changed to take advantage of technological advance and changed again as the vectors of malaria and the disease-causing parasites have demonstrated remarkable resistance against insecticides and drugs. Some vectors have changed their resting and feeding habits, rendering previously effective control methods obsolete. (Or, quite possibly, the vector strain which was susceptible to control has been replaced by another strain, less amenable to the control methods employed). Control techniques which have been shown to be effective in one country fail in another. Investments in Research and Development play as great a role in malaria control as they do in industrial development.

Some of the questions to malaria control remain unanswered. Funds to find answers to such questions may spell the difference between success and failure of control programs in many countries.

Moreover, the lack of trained malariologists, epidemiologists, entomologists, parasitologists, sanitary engineers and other technicians is hampering the application of technologies already shown to be effective.

AID's major contribution to worldwide malaria control programs may well be the long-lasting effects of funds invested in research. Although significant funding is required for purchase of commodities -- such as insecticides, laboratory supplies, anti-malarial drugs, insecticide application equipment, and vehicles -- such expenditures appear to be disproportionate to amounts spent upon research. The combined effect of AID expenditures for research and training will be to reduce permanently the threat of malaria through the development of improved control methodology, and to upgrade technical expertise within each country assisted.

One of AID's areas of comparative advantage, among international cooperation agencies, is its capability of supporting research activities. Such activity should be further strengthened to develop new tools for malaria control. Continued coordination with international research funding organizations,

such as WHO's Special Programme for Training and Research in Tropical Diseases (TDR) as well as bilateral research organizations will be necessary to prevent duplication and to strengthen certain research activities as appropriate.

AID should continue its long-range efforts to develop malaria vaccines, but should also diversify its research activities to include a comprehensive, expanded program in vector control methodology as well as parasite control, designed to solve serious gaps in the knowledge and the tools necessary to deal with problems already identified or yet to emerge.

1. Vaccine Development.

AID has shown commendable foresight, persistence and courage in supporting development of an anti-parasite vaccine -- a feat never before accomplished. Given the remarkable progress of the last few years, there can be no question that continued support should be provided for vaccine research at a level which will ensure the completion of this extremely important project.

Yet even under the best of circumstances that Workshop members can presently envision, a vaccine will not provide the sole method of achieving malaria control. Research over a broadened spectrum is required, including further development of integrated comprehensive malaria control methodology.

2. Vector Control.

The greatest successes attained in anti-malaria efforts to date have usually been achieved through measures taken to control the anopheline mosquitoes that are responsible for the spread of malaria. However, many unsolved vector control problems still require intensive study, if these vectors of the disease are to be effectively controlled. These problems include need for additional knowledge of the biology of these insects, especially as pertains to mosquito suppression.

The following are examples of vector-related research which should be undertaken, and which would warrant AID support:

a. Environmental control methodology

b. Development of new and/or improved insecticides

c. Improved methods of insecticide application

d. Improved packaging of insecticides

e. Improved biological control methods

f. Increased knowledge of vector taxonomy, biology and ecology

g. Novel control methods

3. Epidemiological Studies.

AID should support research programs to develop improved and simplified malaria diagnostic and survey methods -- particularly important in view of the role to be played by relatively unskilled PHC workers in diagnosis, not merely of the presence of acute malaria infection, but of the particular plasmodial parasite responsible, and the appropriate therapy.

4. Anti-Malaria Drugs.

In cooperation with other agencies and with private industry, AID should support the development of new anti-malarial drugs, especially the clinical and field testing of new compounds through to registration and approval for human use.

5. Socio-economic Studies.

Interactions among human cultural and social practices and malaria should be studied by qualified, health-oriented research workers.

6. Operational Research.

Support should be given to operational research at the program level, focusing on malaria epidemiology and control issues. A technical research component in any approved program would (a) determine the optimal curative drug dose regimen and the high-risk populations to be targeted for drug therapy programs, (b) monitor drug sensitivity in association with PHC activites, and (c) determine the level of insecticide resistance of vector species. It may also be possible to develop area- or culture-specific methods to increase community participation in malaria control operations.

7. Development of Health Delivery Systems.

The integration of malaria control into PHC units requires additional research.

B. Training

Training is the single most important requisite for the institutional development which is essential to the generation or improvement of national capabilities needed to plan and execute malaria control programs. Training is equally essential to ensure the development, adaptation and transfer of the new technologies of malaria control to which reference was made in Section VII-A above.

AID should recognize the importance of training in malaria and other vector-borne diseases as an essential and cost-effective activity to promote disease control. Past U.S. participation, as exemplified by the joint AID-PAHO sponsorship of the Jamaica Malaria Eradication Training Center (METC), provides a good example of the "ripple effect" of such an effort. From 1958 to 1967, twenty courses were presented with 337 persons receiving training. Subsequently, large numbers were also trained during the 1964-1973 period at the METC/Manila. Many of these individuals are now in key positions in malaria and other public health programs throughout the world.

U.S. training facilities presently available for malaria courses are scarce. However, the newly organized International Center for Public Health Research of the University of South Carolina now offers both short courses and degree courses (MPH) in Comprehensive Vector Control with emphasis on malaria. MPH programs at other Schools of Public Health (California, Harvard, Hopkins, Tulane, etc.) also offer applicable courses, particularly in epidemiology and biostatistics.

Conclusions and Recommendations: Research

The greatest success in anti-malaria programs have been achieved through anopheline mosquito control to prevent spread of malaria. Research on these vectors of malaria must be intensified in order to improve control methodology. Such research should include study of the vectors themselves, improved insecticides and insecticidal application equipment, biological control and integrated or comprehensive vector management.

1. Vaccine Research.

AID should continue to support malaria vaccine research at a level which will permit completion of this important project.

2. Other Centrally Funded Research

Because of current operational difficulties, especially drug resistance in malaria parasites and insecticide resistance in mosquito vectors, new research activities should be initiated in the following areas:

a. Simplified malaria diagnostic and survey methods

b. Identification, clinical evaluation and field testing of new anti-malarial drugs, through to registration and approval for human use.

c. Identification and testing of new insecticide compounds and biological agents, as alternatives for insecticides to which resistance has developed or which may in some situations be unsuitable because of vector behavior.

d. Development and testing of improved insecticide formulations.

e. Development of test methodology for use in specifications necessary to ensure delivery to the field of high quality insecticides, application equipment and packaging.

f. Development of a variety of alternative, possibly novel, malaria control measures.

g. Further investigation of epidemiological determinants of the malaria problem which affect human ecology and therefore the severity of the malaria problem or the feasibility of its control.

3. Operational Research

As trained professionals emerge, AID should support operational research at the program level, essential to ensure effective malaria control programs. Provision should be made in country programs for an operational research component, to develop the area-tailored vector and parasite control programs upon which effective anti-malaria measures must be based. Such a technical research component would determine the optimum curative drug, the proper dosage and the high-risk populations. It would also monitor drug sensitivity in association with PHC activities.

4. Review of Proposed Research

AID should maintain an effective system of review for malaria research proposals, especially at the central and regional levels, to assure against duplication of effort. The review process should include a cross-check of planned research with WHO's TDR and with bilateral research organizations. Maintenance of close contact with agricultural operational and research interests in insecticides may avoid later problems.

5. Research Funding

The intrinsic nature of present malaria control programs is such that research in support of effective, operational programs is an absolute necessity for long-term success. The investment in control-related research should be commensurate with the investment in the total program.

Conclusions and Recommendations: Training

1. National and International Training

A material expansion of AID sponsorship of training related to anti-malaria programs is essential. Such training should apply to all levels of malaria program personnel within host countries. Strengthening of national training capability is a proper and indeed a priority matter for AID support.

It may also prove feasible for AID to support (as it is already doing in Asia) the development and functioning of collaborating institutions at the regional or inter-regional level to provide a better utilization of training resources.

2. Core Skills Training

Key national personnel, especially in scientific, operational, public health and administrative positions, should be provided with the necessary skills required to carry out the functions of their positions. Such training may be provided in their own countries, in the U.S. or in a third country, as is deemed appropriate. Degree-level training should be encouraged and funded in selected cases.

3. Training Materials

AID should support the development and production of training materials at all levels.

4. Training for Research

A more specialized need is the strengthening of the capabilities of research workers in the developing countries, if technology transfer is to be most effective. Training of this nature should be coordinated with WHO's Special Programme for Training and Research in Tropical Diseases (TDR), but AID can and should play a role as well, particularly in longer-term training of such personnel in U.S. educational institutions.

5. Training for AID Personnel

See Section X below.

VIII. Epidemiologic Assessment, Diagnosis, Malaria Drug Use

Malaria control in the 1980s must contend with hard realities and changing priorities. The monetary resources available for malaria programs are static or shrinking while the problems are expanding. Well-trained manpower is scarce, in the developing countries but also in both bilateral and international assistance agencies.

In contrast to these obstacles, there are developments which generate optimism for future malaria control efforts. Many countries now consider malaria control as a health priority within the context of expanding health services, especially in the framework of PHC. Additionally, while many new technical problems in malaria control have emerged in recent years (e.g. drug and insecticide resistance), innovative approaches to malaria control are also being developed (e.g. malaria vaccines). The critical challenge in the 1980s will be to define malaria issues clearly and to design programs which effectively and efficiently address the control of the disease. Adequate malaria data bases are essential to decision making, at this time and in the future. Only with an understanding of the epidemiology of malaria in a country or geographical area can rational programs be designed, intervention be assessed, and resources be used with the highest efficacy.

A. Epidemiologic Assessment and Diagnosis

While it is of essential importance, financing should not form the only basis for decisions on the form and the extent of a malaria control program. An epidemiologic profile of malaria (morbidity and mortality) must be compiled, prior to the design of any program. Such a profile should identify the factors involved in malaria transmission, seasonal variations and geographical differences in transmission potential within the area, consequences of the disease (impact on the quality of life, social and economic aspects), and the socio-economic and human ecologic and cultural features (e.g. seasonal migration) which may determine or at least influence malaria transmission.

Currently available parasitologic and seroepidemiologic methods are cumbersome, and costly when applied on a wide scale, since they require adequately equipped and trained laboratory staff. Parasitologic diagnosis and surveys are nevertheless essential. Serologic or immunologic assessment in the human population can be extremely important in assessing the malaria experience and acquired immunity in whole populations or in specific age groups at various degrees of malaria risk. Such immuno-epidemiology is of crucial importance in

current program planning and for the planning and assessment of malaria vaccination in the future.

B. Malaria Drug Use

Irrespective of other control measures, antimalarial drugs will continue to be an essential means to limit mortality and suffering from malaria and to minimize loss of productivity. However, the distribution of drugs, either to treat or prevent malaria, does not have an appreciable role in limiting malaria transmission, except for the use of gametocytocidal medicaments under well defined circumstances. Worldwide, resistance to available antimalarial drugs is increasing dramatically. Furthermore, the available range of alternative drugs for countries where drug resistance is either a risk or already well-established, is quite limited. In comparison to first-line drugs such as chloroquine and amodiaquine, the alternative drugs are expensive and have a greater risk of adverse reactions. Some of these drugs cannot be used in various high-risk groups such as young children and pregnant women. Considering these limiting factors, it is critically important to use antimalarial drugs in the most efficient, targeted way possible, while limiting the risk of development and spread of resistance.

In the context of malaria control programs, therapy of malaria infections should, to the greatest extent possible, be reserved for persons who meet precise diagnostic criteria. Ideally, only persons with a confirmed malaria parasitemia should be treated. When parasitologic diagnosis is not possible, drug therapy should be distributed to persons satisfying at least a clinical diagnosis of malaria, including fever.[1]

[1]It should be noted that the classical response to the question of drug therapy in the absence of parasitologic confirmation of a clinical diagnosis of malaria is unquestionably in the negative -- a fact which underscores the need for research leading to the development and use of simplified malaria diagnostic and survey methods. In fact, the classical prescription for integrated malaria control asserts that antimalarials should not be used for malaria control as an alternative to effective measures directed against transmission. Among the countries described by the phrase "the poorest of the poor", however, a program keyed to the use of chemotherapy may be the maximum program which is affordable, and as was noted in Section III, the maximum affordable program is the desirable program.

In all cases, treatment should achieve the complete elimination of asexual malaria parasites from the blood. This can be achieved by using an adequate dose regimen of a blood schizontocidal drug. This will not compromise the immune status of the individuals and communities. A lower dosage may for a short time lower the density of blood parasites and suppress symptoms, without actually curing the infection. Such suppressive therapy favors the development of drug resistance.

In areas with low or moderate transmission, the program may also aim at the radical treatment of P. vivax infections.

Epidemiologic data must be collected via in vivo and in vitro drug testing to define which drug and dosage will radically cure infections. Clearly, the objective is to maximize the cure rate with the least expensive and least toxic drug.

Presumptive therapy (using a subcurative dose of drug prior to receipt of parasitologic confirmation) and mass drug administration (MDA) - periodic drug therapy to an entire population irrespective of illness, using subcurative dose) are not advised in the absence of effective measures against malaria transmission.

Malaria chemoprophylaxis (the administration of a blood schizontocidal drug on a regular, periodic schedule to suppress malaria symptoms) has been advocated in the past and extensively practiced in many malaria programs. Mass chemoprophylaxis, however, has many negative consequences, and is not advocated under most circumstances. Weekly administration of subcurative doses of a drug is expensive, both in terms of drug cost and manpower requirements. Of equal or even higher importance, subcurative dosing of large segments of a human population in an area with active malaria transmission actively favors the selection of drug resistant parasites. Malaria chemoprophylaxis should be provided, however, to pregnant women in the 2nd and 3rd trimesters of pregnancy in areas with intensive malaria transmission and well-supervised MCH programs.

The provision of effective curative drug therapy at the local level, ideally as part of PHC and combined with diagnostic services, is far more efficient and cost-effective than drug prophylaxis in limiting malaria mortality and illness. The development of therapy programs will strengthen emerging PHC programs, particularly those emphasizing maternal education and child health promotion.

While the development of resistance is, to an extent, an inevitable consequence of drug use within and outside malaria programs, such resistance is retarded by assuring that drugs receive controlled and efficient administration, especially if malaria transmission can be controlled at the same time. Moni-

toring of the drug response, particularly in *Plasmodium falciparum*, is essential in all malaria control programs. Combined *in vivo* and *in vitro* drug sensitivity surveys during the program design phase will permit a reasoned decision on drug therapy strategy. Throughout the program, systematic follow-up of the parasite response is required to monitor for changes in drug response. Such monitoring should be integrated into the health care system in the form of post-treatment follow-up, in order to detect promptly any deterioration of *in vivo* drug response. A more systematic assessment, including *in vitro* testing for current and alternative antimalarial drugs, will be required to determine quantitative changes of drug sensitivity, to monitor the geographical extent of resistance, and to select the optimal alternative therapy.

Conclusions and Recommendations

1. Program Design

Malaria control programs must be designed and evaluated using adequate epidemiologic data on malaria, its transmission and its health consequences in the area.

2. Local Drug and Insecticide Manufacture

While local drug and insecticide manufacture may in some instances be technically feasible and consistent with AID policy to encourage and support local formulation of anti-malarial chemicals, careful quality control and uniform packaging of these products is mandatory to ensure both efficacy and safety to humans.

3. Control Over Antimalarial Drugs and Insecticides

In the design and operation of malaria programs, the quality control, supply and use of current and new antimalarial drugs and insecticides should be regulated in coordination among national governments, AID, other sources of assistance and international organizations and industry to maintain the efficacy of available tools as long as possible and to ensure product safety to humans.

IX. Vector Control

A. Forms of Vector Control

Many malaria control programs will continue to be based entirely or in great part on vector control. This is particularly true where the vectors are primarily endophilic, or where larviciding is effective, as well as in areas where parasite resistance to antimalarials has appeared. Such control may be based on chemical, environmental or biological methods or any combination of these.

Chemical control may be directed against either the adult or the aquatic stages of the vector mosquito. In most cases malaria vector control programs are based on the indoor application of residual insecticides. In many instances these have proven to be remarkably effective. Where vectors are still susceptible, the insecticide of choice continues to be DDT, the safest and most economical compound available, and the least harmful to the environment when used as an indoor spray. In a number of areas of the world, physiological resistance and/or governmental regulations preclude the use of DDT; alternative compounds must be used, once their cost effectiveness and safety to man and the environment have been established.

Insecticides used as residual sprays offer many advantages as tools for vector control. They are widely used because of their versatility and their unique combination of quick action and effectiveness over extended periods. They also have disadvantages. There is a need for regular repetition of the application of the insecticide; their application is very sensitive to local ecological and operational conditions; and 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. Such a trial can not only determine the relative effectiveness of different pesticides under local ecological conditions; it can also establish the amount of a given insecticide which has to be applied per square meter, the amount of surface which must be sprayed, and the period during which each insecticide retains its ability to kill mosquitoes. An insecticide which retains its effectivness through an entire malaria season will be more cost-effective than a second insecticide costing half as much per pound if the second insecticide must be reapplied during the season, or if the second insecticide must be applied at a greater amount per square meter or over a greater amount of surface.

The insecticides employed in malaria control are safe to man when used according to directions, but can be dangerous when carelessly handled. To avoid harm 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.

In some instances, especially in periurban and urban areas, larvicides may be utilized. Space sprays have also found limited use against certain urban vectors.

Environmental management practices, although at times involving larger initial investments, may offer long range effectiveness; they merit special consideration in water development projects such as hydro-electric or irrigation systems. In any event, malaria control must be considered in planning any major agricultural development projects in endemic areas.

Biological control measures currently enjoy popular acceptance, although they clearly constitute no panacea. They include such agents as larvivorous mosquito-fish, and a number of still-being-tested agents including bacteria and nematodes. None of the presently-available biological control agents can presently be seriously considered for operational use except in experimental areas.

Integrated vector control should consider and include a judicious combination of any of the above methods most appropriate against the target vector species.

B. Vector Control in PHC

Whatever the methods utilized, AID should encourage cooperating governments to include malaria control within the design of their national PHC systems as they are developed. Many of the vector control activities must, by their very nature, depend on community participation and support. However, the successful involvement of the community will require training of the PHC workers responsible for health education and the simpler aspects of vector control. For major efforts, vector control specialists from the central core group will be required for program planning, worker training, timely provision of appropriate equipment and supplies, and frequent evaluation of the quality of the work, including periodic insecticide susceptibility tests.

The blending of malaria control activities into PHC programs will require considerable planning, training, and the availability of well-trained PHC workers and, especially, professional core groups to ensure the support that the extensive PHC programs will require. Unfortunately, in most countries such core groups do not yet exist. There are simply

not enough professionally prepared vector control specialists who must, in the long run, bear the responsibility for the planning, implementation, supervision, and evaluation of the vector-control of national malaria control programs. Such groups, once formed, can also progressively be involved in, and be responsible for, control efforts against other vector-borne diseases, such as filariasis, Chagas disease, yellow fever, dengue hemorrhagic fever and Japanese encephalitis.

Conclusions and Recommendations

1. Role of Vector Control

Many malaria control programs must continue to be based entirely or in great part on vector control: chemical, environmental or biological, or a combination of these methods.

2. Entomological Surveys

Entomological surveys to determine the vector species or strain, breeding sites and breeding and feeding habits are absolutely essential to successful vector control.

3. Insecticide Selection

Determination of the most cost-effective insecticide can only be made by field test comparison of usage under local conditions.

The Vector Control Work Group also concurs with the broad conclusions of other work groups: training, research and malaria-qualified advisory services are absolutely critical elements in AID's malaria control strategy. The Group's specific recommendations in these respects appear in Section VIII, Research and Training, and Section X, AID Staffing.

X. AID Staffing

A. Current Staffing

The inadequacy of AID's current staffing, from the standpoint of its physical limitations, its lack of experience and, in some instances, its total absence, proved to be, of all the topics considered by the AID Strategy Workshop, troubling to the greatest number of the Work Groups and the area on which unanimity of opinion was most immediately reached. A group of malaria specialists -- AID's combined field and Washington staff -- which was at one time, arguably the most able ever assembled has been allowed to shrink to a handful. Few of AID's desk officers have a technical background adequate to enable them to ask intelligent questions of any of the few remaining malaria experts.

In the field, AID relies, almost without exception, on WHO to provide technical expertise in malaria control, assistance in planning and initial review of program proposals. Yet WHO's capacity to discharge these important functions has decreased even as AID's capacity has virtually disappeared. Fifteen years ago, WHO warned AID of WHO's inability to take up the burden left by the drastic reduction in the number of AID's technically qualified advisors -- to no avail. Today, AID has malaria-experienced contract advisors in two countries; and in two others, has been able to locate malaria-experienced local residents who can monitor the use of U.S. - provided insecticides to assure effective use and safety of both spray teams and project beneficiaries.

Malaria specialists convened to advise AID on malaria policy for Asia and Africa have urged the need for a technically qualified and experienced AID officer (or contract employee) in each malaria program receiving AID support. The Asia Strategy Group also noted the need for a particularly well qualified specialist, preferably posted in his region of assignment, to serve as coordinator and technical backstop for country-based malaria advisors. His ready availability could assure the sharing of experience and information among the countries of the region. The regional position, created after the report of the Asia Strategy Group, had the predicted effect, but is now vacant.

B. Need for Technical Expertise

The strategy of controlling the impact of malaria by eradicating the disease everywhere is no longer advanced, by AID or by WHO, as a practical solution to this major problem.

The alternative is to control the disease by reducing malaria's incidence in a particular country (or at least malaria-related mortality and morbidity) to a level which the country considers tolerable. But whereas the techniques of eradication were conceptually simple if operationally difficult, the techniques of malaria control are more complex; they are tailored to the epidemiological situations, area by area; they are therefore more complicated to plan, require greater numbers of malaria-trained people throughout the nation's health delivery system, and rely far more on collaboration at the community level than on mere acceptance of a delivered service from the central government.

Yet despite the foregoing, the current spectrum of technology, subject to financial and administrative feasibility, offers practical alternatives to decrease the risk of serious illness when the program design is tailored and pre-tested to deal with the country- and even area-specific malaria status. The design task, because of its complexity, requires technical advice based on experience and expertise in malaria. AID is ill-equipped today to provide either the experience or the expertise for such advice. WHO's capacity to provide such advice is also limited. AID has found it necessary to overload its thin line of Washington-based expertise in responding to field requests for assistance in planning and in project performance evaluation.

C. Promotion of Multi-donor Assistance

1. Although the number of potential sources of external support for malaria is large, the development of such support has to date been subject to only limited exploration. While the responsibility for the mobilization of the required support is clearly and unambiguously assigned to WHO, an expression of AID's willingnesss to participate in the resource mobilization effort by supporting the costs of an assigned AID-recruited officer (with secretarial support) would represent a high leverage, low-cost investment in an activity which could show a major return toward a long-term AID goal.

D. Appraisal and Evaluation of Program Proposals

AID no longer possesses the in-house staff, in its Washington headquarters or within its geographic regions, to make more than a fraction of the mandatory on-site examinations of new malaria control program proposals. Such examinations are essential to evaluate the immediate capacity of host country

nationals to implement proposals, to identify possible gaps in proposals and in listed constraints to the achievement of stated goals, or even to establish that the proposed programs constitute well-considered solutions to identified, epidemiologically defined problems.

Washington-based expertise is already stretched to the breaking point. The utilization of field-experienced retired personnel and borrowed WHO and CDC staff, sometimes in combination, has been a relatively effective appraisal mechanism, but one which relies on longevity of retirees and the ability of WHO and CDC to release key staff to participate. The answer to the need for appraisal and evaluation of program proposals -- and, indeed, for help in the formulation of proposals -- has frequently been and will for the foreseeable future continue to be the contract consultant or contract team.

The number of malaria and vector-borne disease specialists, especially those possessing field experience in the planning and operational aspects of malaria control programs, has declined markedly in recent years. The field experience of personnel identified in responses to AID requests for proposals in the area of malaria program appraisals is a criterion for contractor selection fully as important as their academic qualifications -- a factor to be taken into account in contractor selection.

Conclusions and Recommendations

AID must reconsider its overseas staffing priorities, which currently stress managerial skills rather than malaria technical skills. Only with the expansion of training programs which cover both technical and management skills, for national but also for AID staff, will malaria programs be adequately designed and implemented.

1. Mission Staffing

   AID should provide a malaria-trained U.S. advisor to each AID-supported malaria program.

2. Regional Staffing

   AID should establish for each region a particularly well-qualified U.S. malaria specialist to serve as coordinator and technical backstop to country-level malaria advisors and as a consultant in the formulation of initial plans to establish malaria programs.

3. Washington Staffing

AID should strengthen the malaria control expertise in its headquarters offices, both in regional offices and in the Office of Health, to provide expeditious review of and support for country programs.

AID's current patterns of organization in Washington and assignment of responsibility deprive malaria programs of technically qualified review of project proposals, and multiply contact points between AID and CDC unnecessarily, to the detriment of effective relations.

a. The responsibility for the design review, technical coordination and evaluation of malaria (and other vector-borne diseases) control and research programs should be centralized and assigned to technically qualified and trained personnel in the Office of Health, Science and Technology Bureau.

b. The Regional Bureau should continue to be responsible for project oversight and management. Individuals with direct responsibility for the malaria programs in each region should be trained in malaria control.

4. Training for AID Personnel

Given the shortage of trained and experienced malaria control personnel in the U.S., AID should cooperate with one or more U.S. educational institutions to establish suitable training programs to address this real and growing problem. Only with the expansion of training programs for AID staff as well as for national staffs will malaria programs be adequately designed and implemented.

XI. AID Environmental Guidelines

In accordance with the National Environmental Policy Act of 1969 (NEPA), the Agency for International Development, on March 24, 1976, proposed regulations to amend Title 22 of the Code of Federal Regulations (CFR), by adding a new Part 216 entitled "Environmental Procedures", which became effective when published in the Federal Register, June 30, 1976.

The new procedures were developed to ensure that environmental factors and values are integrated into the decision-making process of AID, and to assign responsibilities within the Agency for assessing the environmental effects of its actions. The regulation states that it is AID policy:

> "To ensure that the environmental consequences of proposed AID-financed activities are identified and considered by AID and the host country prior to final decision to proceed, and that appropriate environmental safeguards are adopted;
>
> "To assist in strengthening the indigenous capabilities of developing countries to appreciate and evaluate the potential environmental effects of proposed development strategies and projects, and to select, implement and manage effective environmental protection measures, and;
>
> "To identify impacts resulting from its actions upon the environment including those elements of the world biosphere which are the common natural and cultural heritage of mankind."

The Regulation defines various elements of environmental procedures including initial environmental examination, threshold decision, environmental assessment, environmental impact statement, negative determination, and negative declaration.

The Regulation describes AID activities which may not be "major Federal actions significantly affecting the human environment" and will, therefore, not normally require the filing of an environmental impact statement or the preparation of an environmental assessment. Examples given include certain research; education or training activities; projects in which AID is a minor donor to a multidonor project without potential effects on the environment of the U.S. or areas outside any nation's jurisdiction; and disaster and emergency relief activities.

Also identified are the types of AID projects which may constitute "major Federal actions significantly affecting the quality of the human environment" and will, therefore, require evaluation under

the environmental procedures. "Significant effects" to be considered include "those which adversely affect such aspects of the human environment as air, water, land, flora and fauna, and socioeconomic conditions." Special attention must be given to problems involving, among other things, hazardous substances.

The Regulation sets forth general and detailed procedures for the initial environmental examination, threshold decisions, preparation of environmental assessment or environmental impact statement, intra-agency processing and review, monitoring of environmental impact statement, intra-agency processing and review, monitoring of environmental impact during implementation of projects or programs, and revisions of previous assessments when new facts or information become available. It also assigns responsibilites within AID for carrying out the environmental procedures.

Pesticides or pest management activities are not specifically mentioned in any part of the "Environmental Procedures," but are clearly included by definition in the AID activities to be considered under this regulation.

In May 1977 AID filed with the Council on Environmental Quality an Environmental Impact Statement on its pest control program. AID adopted a policy of placing greater emphasis on research and technical assistance and less on the procurement and use of pesticides. AID would also provide funds for training, protective clothing and equipment, application equipment, technical supervision, emergency medical treatment, monitoring pesticide use and disposal of unused pesticides and pesticide containers.

While AID specifically recognized the need to continue to use pesticides to control malaria and other vector-borne diseases, AID also announced its intention to seek to reduce pesticide dependence by encouraging the use of other materials for pest control, where applicable. Special attention would be given to malaria control by experimenting with non-chemical pest control methods, e.g. source reduction; by applying environmentally acceptable chemicals; and by developing alternative disease control methods that avoid pesticides, such as a malaria vaccine.

In April 1983 AID issued a policy determination which was an update of 22 CFR Part 216 of 1976 and Section 118 of the Foreign Assistance Act. These new procedures are designed to obtain an appropriate level of flexibility in the environmental evaluation process and to reduce the potential for delays in program approval. AID has eliminated from review the categories of projects with little or no likelihood of environmental impact. AID also announced its intention to offer assistance in overseeing development projects which may potentially aggravate problems such as schistosomiasis, malaria and trypanosomiasis due to alteration of habitat by human activities.

Basically, so far as malaria or other vector control programs are concerned, AID realizes that the use of pesticides will continue to be necessary, until supplementary and alternative methods are developed. AID's strategy is to continue to de-emphasize excessive dependence upon pesticides; to concentrate the Agency's efforts on an integrated approach to the control of vector-borne diseases; and to promote the use of new or alternative methods which do not depend on the use of persistent pesticides, including such methods as source reduction, water management, larviciding and biological control. It should be pointed out at this time, however that the first three methods are neither new nor original. They have been previously used in many malaria control programs. Biological control, with the exception of the use of mosquito-eating fish, has not yet been proven to be effective in an operating malaria program.

Conclusions and Recommendations

1. AID's basic policy of concern for the environmental impact of some malaria control activities is sound and is in no need of change at this time. However, until new and yet unproven alternative methods of vector control are developed and tested, the use of pesticides in many and possibly most vector control programs must be considered a sine qua non.

2. Residual pesticide interior treatment of dwellings has little or no impact on the environment. In terms of its absolute effectiveness (in terms of results achieved) and its cost-effectivness, residual pesticide treatment remains the most efficient method of malaria vector control. AID should not discontinue support for vector control through the use of residual pesticides; in fact, the rising costs of presently available insecticides and the progressive spread of anopheline resistance to the present array of such insecticides may require that AID support research leading to the development of new, effective and hopefully cheaper alternative insecticides.

3. AID should also encourage and fund research leading to the development of alternative methods of vector control that would be as effective as residual insecticides, and as environmentally sound.

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ANNEXES

AID's Present Role in World-Wide Malaria Programs

AID is actively involved in malaria control activities in Africa, Asia, and Latin America. This involvement ranges from support of training and operational research to the provision of commodities and technical services. Support of the local costs of malaria control is not normally a part of AID-supported malaria control projects, but contributions are made from PL 480-generated local currency or, in rare cases, from project funds, to meet a portion of local costs in on-going host country research efforts to assist in development of new technologies. In addition, AID provides considerable central funding in support of malaria research.

A Region by Region summary of AID-assisted overseas programs is presented to provide details on individual programs and to illustrate the range of malaria control activities in which AID is currently involved.

A. Africa

The principal malaria control assistance efforts by AID in Africa are related to projects in Primary Health Care (PHC). At the end of 1982, AID was providing assistance to 22 PHC projects in 15 countries in the Africa Region. Most of these projects lie in endemic malaria areas where only rudimentary health delivery systems exist, so control of malaria is included as an activity of these PHC projects. The major malaria control intervention used in these PHC projects is the provision of anti-malaria drugs, primarily for chemotherapy, which provides individual clinical relief, but does not greatly affect transmission. Manpower and resources are in short supply, and vector control through a variety of interventions in not normally included in PHC projects. The number of malaria cases in Africa is not known; it is conservatively estimated that there are upwards of 10 million cases per year with over a million deaths. In June 1982, the Bureau for Africa sponsored a workshop on "Malaria Control in Primary Health Care," held in Washington, D.C., to organize planning and project implementation guidelines for African situations corresponding to WHO's four tactical variants in malaria control. A manual based on the recommendations of this workshop has been sent to USAID units to provide guidance in strengthening the malaria control components of present and future PHC projects.

AID is supporting only one specific malaria control project in Africa, located on Zanzibar and Pemba in Tanzania. A six-year, $11.7 million loan-asissted activity, the goal is to provide malaria control services to approximately 500,000 people living in this area. This

project provides: (1) technical assistance in the form of one long-term contract project scientist and a number of short-term consultants; (2) commodities (primarily insecticides, sprayers vehicles, laboratory supplies and anti-malaria drugs); (3) support of operational research; and (4) provision of long and short term training. The project is now focussed on baseline surveys, training, and creating workable management systems for field operations and administrative responsibilities.

Suitable regional malaria control training faciltiies for Africa are very limited. The malaria training centers established by WHO in Lome and Lagos are no longer providing specific long-term training in malaria control. AID attaches high priority to training of malaria and public health workers in the use of basic and alternative methods of malaria control. Efforts are made to increase attention to such training at the national and at the regional levels.

In Africa, operational research on malaria control is limited primarily to the role of anti-malarial drugs, especially chloroquine, plus some small studies on the Anopheles gambiae complex. AID is promoting applied field research, but the limitations of staff and resources are great. There are almost unlimited possiblities for the transfer and use of technologies which would be of great assistance in controlling this disease, which has such an important social and economic impact.

B. Asia

AID provides major assistance to country malaria control efforts in the Asian area. Assistance is provided to Pakistan, Nepal, Thailand, Sri Lanka and Indonesia. India has recently completed an AID-assisted malaria control project and some residual activity continues in that country. Burma has a malaria control component in its AID-assisted PHC project which supports procurement and distribution of anti-malaria drugs.

1. Pakistan. A five year, $41.0 million grant project was approved in mid-1982 for malaria control support to the Government of Pakistan. AID inputs include technical assistance, commodity support, establishment of a new Training and Research Center, and operational research support. Malaria incidence in Pakistan in 1982 is reported to be below 20,000 cases. The principal purposes of the U.S. assistance are: (1) to allow for orderly transfer of malaria control responsibilities from the present vertical program to the horizontal general health service organization, and (2) to increase urban malaria control activities. Vector resistance or tolerance to the insecticide used, malathion, has not yet become a problem in the operational sense although there are indications of increasing tolerances to this insecticide in some parts of the Punjab. Chloroquine resistance has not been confirmed in Pakistan, but can

be expected to appear in the future. Special malaria problems relate to increased waterlogging conditions in some areas, and to the presence of 2.8 million Afghan refugees within the country. Special control procedures in the Afghan refugee camps have minimized this major malaria threat. U.S. assistance to malaria control is programmed up to 1986.

2. Nepal. AID-assisted malaria control in Nepel is implemented through the Integrated Rural Health and Family Planning Project. Approximately $4.8 million is provided for assistance over the five year period of 1980-1985. The funds support procurement of required commodities, training, research support and limited technical assistance within the over-all project. Field monitoring of the use of U.S.-supplied malathion is provided through a locally hired malaria officer. AID assistance is coordinated with WHO, the U.K., and UNDP which provides technical assistance and additional support for training, research and commodity procurement.

In recent years, malaria incidence in Nepal has been reported at between 12,000-16,000 cases. Approximately 70% of the 1982 cases came from nine districts along the Indian border. The terai malaria vector, Anopheles annularis, is resistant to DDT, but is reported susceptible to malathion. Large scale malathion spray operations were carried out in 1981 and 1982 in the terai, with only limited success in reducing transmission and lowering case rates. There have been no reports of chloroquine-resistant parasites from indigenous cases, although such parasites have been found in patients with a history of travel to various parts of India. Yearly program evaluations have been carried out by the Government of Nepal and external malaria consultants provided by the donor agencies.

Six districts in Nepal have integrated malaria control activities into their general health activity, and five more districts are scheduled for integration in the 1983-1984 period.

3. Thailand. The malaria control program in Thailand has experienced increasing difficulties due to wide-spread parasite resistance to both chloroquine and Fansidar, increasing vector resistance to DDT, and changes in behavior patterns of the major mosquito vectors. For three years, AID assistance has dealt primarily with malaria control training for both malaria and public health workers, limited operational research; and commodity support, construction of research facilities in Bangkok, Pakchong and Chiang Mai, and three unit offices as well as additional training buildings at the National Training Center. This AID project will be completed in September 1983. In 1982, approximately 421,000 cases of malaria were detected and reported in Thailand, only a portion of the actual cases in the country. Widespread availability (from the private

sector) and misuse of antimalaria drugs has led to a very serious and explosive resistance situation. especially in SE Thailand. The westward spread of chloroquine-resistant malaria into Burma and India is to some extent due to the lack of a viable malaria control operation in Thailand. Operational research to identify optimal drug schedules is in progress, as is an effort to increase the efficiency of spray operations. AID assistance is coordinated with the efforts of the three-man malaria advisory team supplied by WHO.

4. Sri Lanka. From 1978 through 1983, AID has provided some $16.0 million to the Government of Sri Lanka (GSL) for malaria control support. This funding has provided training, commodities, technical assistance, and support for research facilities. The program has resulted in a dramatic lowering of malaria incidence from well over a half million cases in 1977 to under 40,000 in 1982. The program uses only malathion in its residual spray operations, because the major vector, Anopheles culicifacies, is resistant to DDT. No chloroquine-resistant parasites have yet been detected, but such resistance is expected to appear within a few yeras. Yearly evaluations of the program have been carried out by the GSL with external malaria consultants provided by donor agencies.

AID efforts are coordinated with WHO and with British and Netherlands Offices of Development Assistance. WHO provides three full-time technicians, plus limited training and research support. The British Government has provided approximately $2.0 million in assistance to GSL anti-malaria activities, mainly in vehicles and transport. The Netherlands contribution of $4.0 million has been primarily for insecticides and construction. This program is presently characterized by excellent multi-donor coordination and is presently succeeding in accomplishing its objectives.

5. India. Recent AID assistance to India for malaria control was completed in 1982. Some $38.0 million has been expended, primarily for insecticides and ULV spray equipment. The project was originally planned for a five year period, to supply external assistance to the Government of India (GOI) in meeting insecticide requirements for malaria control until national production capacity could meet those needs. By the end of the second year of the project, the GOI informed AID that its national production capacity was sufficient to meets its expected malathion requirements, and only a short-fall in DDT availability was foreseen. AID has performed a series of Project Evaluation Summaries, based on records and field observations of India's National Malaria Eradication Program, primarily in Gujarat and Maharashtra States. Special attention was given by AID to training in the application of organo-phosphorus insecticides and to effective health safeguards for field operation personnel.

6. Indonesia. For three years AID has provided assistance to a malaria control project in Timor, plus some consultant services in Java for vector control in focal malaria problem areas. The Timor Malaria Project is directed at a serious disease problem, but working conditions in the area do not allow full utilization of the available assistance. One long-term contract advisor was assigned to the project, and commodities were provided. The contract project advisor's assignment has been completed and the advisor has returned to the U.S.A. The Outer Islands of Indonesia have a number of urgent malaria problem areas which affect orderly development and human well-being. The World Bank is considering some limited malaria control assistance in Suluwesi over the next several years. Malaria case records are valid only for the Java-Bali areas of the country. The Outer Islands reporting systems are not complete. Approximately 100,000 cases of malaria occur in Java-Bali alone each year.

WHO provides technical assistance and training/ research support to the Indonesian malaria effort, coordinated with AID activities.

7. Malaysia. When WHO, AID, and CDC realized that malaria eradication was not an immediately achievable goal, particularly in hyperendemic areas of the world, a reorientation of national and international efforts against the disease was recommended and malaria control efforts based on epidemiologic variables were clearly mandated. This policy/strategy shift from eradication to control involved the establishment of attainable goals, the employment of available resources, and the application of a combination of anti-malaria measures appropriate to the problem in any given area.

In 1978, an assessment of the malaria situation in Asia by an international team of experts concluded that an extensive reorientation of malaria programs in the region was required and that training at all levels of personnel would be the most appropriate means to achieve this goal. The experts observed that malaria control is a much more complicated and complex issue than the single-method approach of malaria eradication. The paucity of trained personnel in virtually all malaria control programs, even those which were well designed, was recognized as the fundamental problem hindering success in many countries of Asia.

The Agency concurred with the expert group that the most productive approach in addressing these needs was through the development of a training program directed toward this most pressing problem. In 1982, in collaboration with the Center for Diseases Control (CDC) and WHO, AID provided special funding for the establishment of a Regional Malaria Training Program at Kuala Lumpur, Malaysia. This International Secretariat for Malaria Training was

developed to address individual country needs in the region and to increase malaria program effectiveness through seminars and workshops at various levels of program organization.

C. Latin America and The Caribbean (LAC)

Malaria control is a component in several AID-supported PHC projects in Latin America, but only in Haiti is there an AID-supported program specifically aimed at malaria control. There are an estimated 200,000 cases of malaria in Haiti each year, although only 50,000 cases were reported for 1981. AID has assisted this program for many years. In mid-1982 AID approved a new five-year, $8.5 million malaria control project for 1982-1986 to assist Haiti in its anti-malaria program, providing technical assistance, commodity support, operational research and training, and 35% of the field operations costs. Attention is directed specifically at providing proper epidemiological studies, and operational stratification of the program. The insecticide used, fenitrothion, in spray operations to control the principal vector, Anopheles albimanus, is provided free of charge by the Government of Japan. Health safeguards for spray personnel are implemented through training and the provision of protective equipment.

WHO/PAHO has a team of three malaria advisors assigned to Haiti, and also supports training and research efforts in the program.

The dominant malaria parasite in Haiti, Plasmodium falciparum, is treated successfully with chloroquine, administered primarily through volunteer collaborators and health institutions. The presence of chloroquine resistance will be carefully monitored.

In the Washington offices of LAC and in field positions alike, there are no direct-hire AID personnel trained in malaria control with operational experience although the single contract advisor in Haiti has extensive field experience. Malaria cases in LAC have increased by 50% during the past five years, wide-spread insecticide resistance to a number of compounds occurs in Central America, and there are serious needs for training and research support. The rising incidence of malaria in Latin America has serious health implications for the U.S. PAHO is assisting a number of countries in Latin America and in 1981 provided 24 professional and technical staff to field programs. In 1973, PAHO had 65 such staff assigned to Latin American country programs.

D. Near East

The AID Bureau for Near East has no specific AID-assisted malaria control programs in countries which it serves. A number of countries in the Near East area have malaria problems, but most can afford to provide their own services. Some consider malaria as a health problem not

requiring external bilateral assistance. Chemotherapy is extended through various PHC projects.

E. AID/Washington

Technical assistance in malaria control is provided to the various regional bureaus of AID by the Office of Health, Bureau for Science and Technology (S&T/H), which has three scientists available in its Tropical Disease Unit, and several officers assigned to PHC projects. During 1982/1983 S&T/H provided direct overseas consultant assistance to country malaria control field projects in eight countries, and assisted in obtaining the services of short-term consultants for specific country requests in the fields of entomology, malariology, management and operations. In addition to field services, technical information and advice is provide to the country desks and regional bureaus through project reviews, response to field inquiries and preparation of project documentation.

F. Centrally Funded Research

Since 1966, AID has provided major support of malaria immunity and vaccination research, and has created a cooperative research linkage system consisting of various projects located in a number of U.S. universities and research centers. Although the development of a viable malaria vaccine will not constitute a single solution to the entire complex malaria problem, such a vaccine would add greatly to the arsenal of weapons which can be employed against the disease, to complement the use of chemotherapy, vector control, and other interventions. Two new technologies -- hybridoma technology and genetic engineering -- now provide helpful tools in the development of a vaccine. AID now provides over $2.0 million each year for research support for vaccine development and is linked with the efforts of the WHO malaria immunology program.

AID funds are also channeled to projects,in the U.S. and abroad, in various other aspects of malaria research, such as anti-malaria drugs, entomology, insecticide testing and operational vector control. Such support may be provided by central funding or by use of special project funding at the country level.

Summary

AID continues to provide substantial assistance to numerous countries in support of national efforts to control malaria. Such support is justified not only on the basis of the economic but also the social importance of this disease to developing countries. In recent years there has been a decided shift in program emphasis to support more research activity, and to give increased attention to the role of PHC in malaria control. The major portion of AID support for field projects in

malaria control has been historically and is presently provided to the Asian area, but with increasing attention being given to the needs of Africa, there may in the future be more support to malaria control efforts in that region.

To a great extent, such support will be extended to malaria control efforts carried out within the orbit of PHC.

REVIEW OF PAST AND CURRENT WHO/PAHO STRATEGIES OF MALARIA CONTROL[1]

A. Evolution of Malaria Control and Eradication Policies in PAHO

The importance of malaria as a public health problem and a serious obstacle to socioeconomic development has been recognized since the concepts of prevention started to dominate those of epidemic control of the eighteenth and nineteenth centuries.

The Pan American Health Organization (PAHO) focused its attention on malaria at the III International Sanitary Conference in 1907, where it recommended to member governments a wide distribution of information on malaria, free distribution of quinine to the poor, the inclusion of malaria in the reports of the Port Health Authorities and exemption from taxation of all products used in the prevention and treatment of the disease. Henceforth, malaria was put on the agenda of all subsequent PAHO Sanitary Conferences.

The VI Conference in 1920 charged PAHO to compile and distribute information on the methodology of malaria control through the Bulletin of the Pan American Union.

The X Pan American Sanitary Conference in 1938 established the Pan American Malaria Commission of the PAHO to conduct studies on the epidemiology of the disease, chemotherapy, vector control, standardization of terminology and malaria legislation. The three reports of the Commission in 1942, 1944 and 1947 provided a thorough coverage of the epidemiology and control of malaria in the Americas; the last of these reports called the attention of the public health services to the very important role that the new insecticide, DDT, should play in malaria control.

The XIII Pan American Sanitary Conference in 1950 considered that the IV Report on Malaria Control in the Americas, prepared by a consultant, was a continuation of the work of the Commission. The report presented a comparative study of the progress achieved and proposed the elaboration of a coordinated plan for the eradication of malaria in the Americas.

[1]Dr. J. A. Najera, Director, Malaria Action Programme, World Health Organization.

The XIV Pan American Sanitary Conference in 1954 launched the continental program of malaria eradication.

Malaria was given a similar importance by the World Health Organization. The Interim Commission in 1946 recognized malaria as a major public health problem and gave a very high priority to its control. The First World Health Assembly (WHA1) in 1948, following the recommendations of the WHO Expert Committee on Malaria of the Interim Commission, decided to assist countries in developing malaria control by setting up demonstration teams on request.

In subsequent meetings the WHO Expert Committee on Malaria analysed the epidemiological situation and provided guidance on malaria control methodologies.

Following the resolution of the XIV Pan American Sanitary Conference in 1954, the Executive Board of UNICEF decided to revise their policy in favor of malaria control, based upon the advice of the UNICEF/WHO Joint Committee on Health Policy which met in 1955 and which recommended supporting malaria eradication. In November 1954, the Second Asian Malaria Conference held in Baguio, Philippines, declared that the ultimate goal of malaria control programs should be the eradication of the disease.

The Eighth WHA, meeting in Mexico in 1955, launched the global malaria eradication program. The Sixth Expert Committee on Malaria defined the strategy of malaria eradication that was further elaborated in subsequent meetings.

B. Malaria Eradication Strategy

Malaria eradication was defined by the Sixth Expert Committee on Malaria as "the ending of the transmission of malaria and the elimination of the reservoir of infective cases in a campaign limited in time and carried to such a degree of perfection that, when it comes to an end, there is no resumption of transmission."

A mechanism was established to coordinate the policies of the international assistance agencies supporting the global malaria eradication program, i.e. WHO, UNICEF, USAID, and USPHS.

WHO provided technical assistance to countries to develop a comprehensive total-coverage plan for the duration of the eradication program. These plans of operations were based on a careful delimitation of malarious areas and a study of the epidemiological situation, an estimation of the needs and identification of resources in terms of personnel, training, supplies and equipment and administrative and financial support.

Training was provided by the Organization at international malaria eradication training centers but most national staff were trained in their own countries, often at special WHO-assisted training centers.

The Organization also developed research programs for the promotion and support of applied and fundamental research necessary as a backup for the eradication program.

Serious problems were identified in the early 1960's and during that decade progress slowed down, so that the Twentieth WHA considered it "necessary and timely to re-examine the global strategy for malaria eradication." As a result of this reexamination, the Twenty-second WHA in 1969 adopted a revised strategy for malaria eradication.

C. Revised Strategy for Malaria Eradication (1969)

This strategy was based on the recognition of:

a) the part played by socioeconomic, financial, administrative and operational factors and the inadequacy of the basic health services in the failures of the programme;

b) the need to justify eradication programmes on economic, as well as health grounds, by demonstrating the reality of the rapid and lasting advantages accruing from them.

The global eradication of malaria was reaffirmed as the long-term goal, but it was recognized that the time and programme schedules as originally planned were, in some instances,unrealistic. Nevertheless, in many of the latter cases malaria represented a very serious health problem and it was necessary to carry out control activities for the protection of the population. It was declared that all antimalaria programmes should be considered as an integral part of the health sector of the national socioeconomic development plans.

The strategy recognized four main groups of countries:

1. Countries with a malaria eradication programme with good prospects of success, where efforts should be intensified to complete eradication and to ensure the development of basic health services, which will ensure the maintenance of the achieved eradication.

2. Countries with less satisfactory malaria eradication programmes, where a multidisciplinary review was recommended in order to identify the factors responsible for the lack of success, and where it should be ascertained whether eradication was feasible in the whole or in a part of the country. Appropriate measures should be taken to rectify the defects and strengthen the programme when eradication was feasible. Adequate control measures should be designed and implemented where eradication was unattainable due to technical or other problems.

As no national programme could be considered independently from the situation in neighbouring countries, WHO was charged with defining, in collaboration with governments, the areas, on an intercountry basis, where eradication was not yet feasible. It was also charged with assisting in the design of adequate control methodologies as interim measures.

3. Countries with areas in maintenance phase, where all efforts should be made to prevent the re-establishment of the disease, by ensuring an appropriate epidemiological vigilance, integrated into the health services or, as a single purpose programme until the services were sufficiently developed to permit such integration.

4. Countries without eradication programmes, where multidisciplinary feasibility studies should be carried out and where the development of plans of operation should be coordinated within the socioeconomic framework in which they will have to operate. Control or eradication programmes should be designed and adapted to local conditions and resources.

In areas where malaria is a major health hazard, malaria control should aim at reducing incidence both as a health measure and as a pre-requisite for economic development.

D. Evolution of the Malaria Situation During the Seventies

Progress towards the goal of malaria eradication continued to slow down during the decade. The strategy reviews that were recommended for countries not making satisfactory progress revealed that many programmes needed to be converted to malaria control. However, it was sometimes not possible to ensure adequate guidance, technical support or administrative adaptability to effect the necessary changes.

Malaria resurgences occurred in several countries in the middle of the decade, particularly in the South East Asia and European Regions and, in the second half of the decade, in the Americas and the Western Pacific Regions. The control of these resurgences was sought through the mobilization of extraordinary resources for the implementation of traditional attack measures.

During the decade the problems of anopheline resistance to insecticides, parasite resistance to drugs and anopheline behaviourial avoidance of contact with insecticides increased in intensity and extent.

The increase in agricultural colonization, construction of large economic development projects such as hydroelectric dams, irrigation schemes, highways, mining and oil prospecting, etc., in tropical areas and the mobilization of large migrant labour forces, increased the risk

of transmission in many areas, often under conditions not easily amenable to control.

At the same time, the increase in the costs of supplies and equipment and, even more, the costs of services and operations, led to a continuous divergence between increasing programme costs and diminishing returns.

At the beginning of the decade several countries had attempted integration of partially effective malaria eradication programmes into poorly developed basic health services, leading to a further deterioration of the malaria situation and, in many cases, to a return to the vertical approach to malaria control.

E. Primary Health Care Strategy

Similar problems affected the programmes for the control of other diseases. It became evident that progress would not be possible unless specific programmes were relieved of the operational costs of control activities which could be carried out by the developing general health infrastructure, by organized community participation and by intersectoral cooperation. The Thirtieth WHA in 1977 recognized this need and called for a concerted effort towards the objective of achieving an even distribution among the population of the available health resources, declaring that the main social target of governments and WHO was the attainment by the year 2000 by all the people of the world of a level of health that will permit then to lead a socially productive life.

The strategy of primary health care (PHC) was defined at the Alma Ata Conference and adopted by all countries and WHO.

F. Malaria Control Strategy

In line with these developments, the Thirty-first WHA adopted a strategy of malaria control aiming at least at the reduction of mortality and of the negative social and economic effects of the disease, the prevention or control of epidemics and the protection of malaria-free areas, with the ultimate objective of eradicating the disease whenever feasible.

Country-specific programmes should be designed in the spirit of PHC, fully adapted to local conditions and resources. The whole spectrum of possible approaches to malaria control were classified into four main tactical variants according to different levels of feasible programmable targets and related programme complexity:

1. Reduction/prevention of mortality due to malaria by administration of antimalaria drugs to all those suffering from the disease;

2. Reduction/prevention of specific mortality and reduction in morbidity by providing antimalaria drugs to all those suffering from the disease and to those in highly vulnerable groups (children, labour aggregations or other population groups);

3. Prevention of mortality and reduction of morbidity and prevalence by administration of antimalaria drugs (as for level 2) and by carrying out vector control measures;

4. Application of control measures on a countrywide basis with the ultimate objective of eradicating the disease.

Any individual country may have areas where any of the above tactical variants can be implemented, provided adequate consideration is given to the ways in which the epidemiological interdependence among them may influence the output of the proposed activities. Equally, the various tactical variants may be taken as different stages of development of a programme.

Antimalaria activities should be planned in adherence to the following principles:

- The national will to control the disease should be clearly expressed through a governmental decision to support antimalaria activities on a long-term basis;

- Malaria control should be an integral part of the country health programme;

- The feasibility and practicability of reducing malaria to a level concordant with the set objectives should be demonstrated;

- The participation of the community should be a condition sine qua non and, since success will greatly depend on its members' understanding of the effects of the different methods of control, emphasis must be put on obtaining the community's appreciation of the importance of all these elements;

- Wherever applicable, permanent measures for control of malaria should be an integral part of relevant physical (e.g. irrigation, drainage, highways) and economic development programms, through the collaboration of the government ministries and agencies concerned.

The selection of control methods should be made following what has been defined as the epidemiological approach in its broadest sense, i.e. taking the fullest possible consideration of the biological, ecological,

social and economic determinants of the malaria problem and those factors which may influence the applicability or effectiveness of individual control measures and their possible combinations.

The first two tactical variants may require only the use of antimalarial drugs through PHC, for which adequate logistic support and training should be developed, as well as a referral system to deal with treatment failures and monitoring of drug-resistance.

Long-term control programmes aiming at the reduction of prevalence should depend on a PHC system which is capable of dealing with the diagnosis and treatment of disease, health education, organized community participation and of responding to abnormal situations. Under these conditions, priority should be given to bio-environmental methods of malaria vector source reduction, wherever they may usefully affect malaria transmission, as well as measures aiming at the interception of man-vector contact. Use of measures requiring regular application at high levels of coverage, such as insecticides or mass drug administration, should be reserved for control programmes with good prospects of achieving and maintaining interruption of transmission or for combating malaria epidemics.

In support of this strategy, it is essential to develop a solid research programme to search for new tools, evaluate their conditions of applicability, improve the knowledge on malaria epidemiology and its variability in space and time, and to improve the methods of programme delivery and evaluation.

Both programme development and research, particularly field research, requires a special effort in manpower development. Training is required not only for malaria specialists but also for the provision of an adequate cadre of health workers and a community well-versed in their role in malaria control.

G. Recent Orientation

The considerable resurgence of malaria during the mid-seventies has been largely controlled. This success has mainly been due to the mobilization of extraordinary resources and the redeployment of traditional control methods. Nevertheless, progress slowed down and, since 1979, resurgences which occurred in some countries counterbalanced the limited progress achieved in others.

The problem of *Plasmodium falciparum* resistance to common antimalaria drugs has spread during the last few years and has become particularly alarming because of its extent into Africa. Collective chemoprophylaxis without controlling malaria transmission poses the serious risk of intensifying and extending the resistance problem. This problem considerably restricts the applicability of the second tactical variant (see Section F-2, above).

With the collaboration of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) a programme for the global monitoring of drug resistance has been developed, including the production of standard test kits and the training of national staff. However, its relevance to malaria control must be seen in perspective, and the degree of resistance and extent must be taken into account for the efficient implementation of antimalaria action. Little progress has been made towards developing effective methods to prevent the development of drug resistance or limit its spread, although considerable knowledge is being accumulated on the mechamisms of drug resistance.

The reorientation of antimalaria action at the country level for the application of the control strategy has started. Nevertheless, many difficulties have yet to be overcome which will require changes in attitudes of malaria specialists and public health personnel and a progressive understanding of the concept and implications of the strategy of primary health care. A flexible and dynamic training programme should contribute to this development.

Three main types of situations must be distinguished in relation to the development of malaria control through PHC.

1. Organized vertical antimalaria programmes which have generally remained separate from basic health services and have rarely been able to make significant contributions to the development of the general health infrastructure. Past failures at integration of services, dismantling the ability to deal with malaria before the development of an ability to deal adequately with health problems within primary health care, has led to some serious malaria outbreaks, forcing the return to vertical approaches and delaying the development of PHC in this area.

   Malaria, therefore, may be considered as an increasing menace to public health, not only by its direct damaging impact on the health of the population but by the potential danger for extensive resurgence which may intefere with the orderly development of a solid health infrastructure. Limited successes were obtained in the broadening of functions of the malaria services to deal with a variety of problems which led, in some countries, to the consolidation of combined health campaigns under a common vertical organization. New approaches aiming at a redistrubtion of resources based on an improved epidemiological definition of the problem, at a decentralization of programme execution and at the progressive incorporation of antimalaria activities into the developing health care system, are beginning to show some success in a number of countries.

2. A few programmes have developed, or are developing, systems of PHC to deal with malaria as a disease and to promote individual and certain kinds of community preventive actions. Subsequent-

ly, or concurrently, attempts are being made to develop resources for organized malaria control activities to deal with special areas of high endemicity or epidemic potential. This approach has its limitations since it presumes the capability of developing an adequate basic health services organization.

3. Tropical Africa was excluded from the planned global malaria eradication programme of the sixties, as existing methodologies had not been shown to be applicable. Africa was, therefore, a field for research for suitable control or eradication methods. The new control strategy recognizes that the prevention of malaria mortality and reduction of suffering are feasible goals which could be achieved through PHC in Africa. Two of the main constraints observed are the shortage of anti-malarial drugs and the absence, or poor development of, logistic systems to ensure continuous availability of diagnostic and treatment facilities.

Various experiences with the above three main types of situation will be analysed by a Study Group on Malaria Control as part of Primary Health Care, which will be convened in November 1983. This group is expected to provide pragmatic policy guidance on what PHC services can do about controlling malaria and what existing malaria services can do about PHC infrastructure development and under what circumstances. The output of this Study Group is expected to be a major input to the Expert Committee on Malaria which will meet in 1985.

As programme development is basically dependent on local conditions, Regional Committees have formulated regional malaria control strategies to provide better guidance and support and to strengthen cooperation through technical cooperation among developing countries (TCDC).

Training requirements for the new control strategy are more demanding than that needed for the application of the standardized eradication methodology. Broader and higher degrees of competence are needed at the planning and formative levels, while an adequate training in malaria is needed by all the echelons of the PHC system and an adequate education in health is needed by the community.

WHO has established an interregional Secretariat for the coordination of malaria training in Asia and the Pacific, set up with support from USAID, which became operational in 1982 and which, during its first year of operation, has been engaged in determining training resources, collaborating with countries in defining their training needs and developing educational materials. The Secretariat aims at engaging all training resources in a collaborative network which could effectively respond to the countries' needs. A training Seminar on Educational Technology took place in April 1983 and a modular training manual is being developed. The Secretariat will collaborate with

training institutions in the organization of specific courses and development of curricula.

A similar coordinated programme is being developed in the Americas where, following a review of resources and needs, a planning meeting was held in September 1982 for the establishment of a collaborative network and a coordinating mechanism.

The WHO Regional Office for Africa is also exploring resources and needs, as well as the collaboration of institutions in developed countries which may be incorporated in a similar programme.

Global coordination is being developed but it will need strengthening as more regional programmes are becoming operational.

Research promotion, coordination and support is being accomplished with the collaboration and support of TDR. Research relevant to malaria control is being supported by three specialized groups in malaria research, i.e. immunology, chemotherapy and field research, as well as the groups on epidemiology, socioeconomic research and biological control of vectors. A very important role is being played by the institution strengthening component of the programme.

TDR-supported research in malaria has been particularly fruitful. In the field of new antimalarial drugs the main results have been the further development of mefloquine and the mefloquine-sulfadoxine-pyrimethamine combination and the coordintion and support of studies on Qinghaosu. WHO evaluation and testing of new insecticides, primarily aimed at new compounds for malaria control, is of vital importance. In the field of immunology, considerable advances have been made towards the development of antimalarial vaccines and in applied field research in the global monitoring of drug resistance.

WHO has also collaborated with countries, through the Regional Offices and Headquarters, in the promotion, planning and evaluation of field studies aiming at problem identification and problem-solving in malaria control as well as in the epidemiological studies needed for the planning or evaluation of control activities.

The Seventh General Programme of Work of WHO, covering the period 1984-1989, calls for the attainment of specific targets by national antimalaria programmes and for the development of WHO-supportive actions in technical collaboration, training, research and the exchange and dissemination of technical and operational information.

COST OF ANTI-MALARIA CAMPAIGNS[1]

A. Introduction

Since 1955 the governments represented at the World Health Assemblies directed the WHO to provide technical advice to implement a global malaria eradication and to support the program through financial contributions for supplies and other essential services. The resources during the period 1955-1967 were provided by: (a) WHO from its regular budget and from the Malaria Eradication Special Account; (b) the UN Expanded Programme of Technical Assistance; (c) UNICEF; (d) The Pan American Health Organization; (d) U.S. Agency for International Development. Most of the resources of the WHO Malaria Eradication Special Account (MESA) were supplied by the United States. Additionally AID (and its predecessors such as the International Cooperation Administration provided technical assistance, local cost support, training and funds for supplies and equipment on a bilateral basis. UNICEF also provided supplies and equipment for malaria projects. According to Pampana, the first director of the WHO Malaria Eradication (1969), the international assistance to malaria eradication totalled during the period 1957-1967 the sum of nearly US$160 million, as indicated in Table I which does not include the direct AID contribution of US $ 407 million.

[1]By: Professor L.J. Bruce-Chwatt, Wellcome Museum of Medical Science, London, England.

Table I

International Assistance to Malaria Eradication during 1957-1967 (after Pampana, 1969)

Year	WHO/PAHO (in 1000 dollars)	UNICEF (in 1000 dollars)	Total (in 1000 dollars)
1957	2,414	7,526	9,940
1958	6,490	8,261	14,751
1959	7,341	8,801	16,142
1960	7,280	8,365	15,645
1961	7,732	5,480	13,202
1962	9,108	4,966	14,074
1963	9,392	5,411	14,803
1964	8,825	7,264	16,089
1965	8,462	5,749	14,211
1966	9,185	4,872	14,057
1967	10,836	4,987	15,823
Total	87,065	71,682	158,747

In 1959 the WHO attempted to produce an estimate of the regional costs of malaria eradication basing its calculation on the average expenditure in each of the six WHO regions of spraying operation and surveillance activity, while assuming that the cost of the latter was 75% of spraying operations alone. The estimated annual average costs of spraying operations alone were shown in relation to the population to be protected in the malarious areas of each WHO region and the resulting figures per capita were given in a WHO report for 1959 (quoted by Pampana, 1969) as follows:

African Region	US$0.80 (0.30-1.28)
American Region	US$0.45
South-East Asia Region	US$0.11 (0.10-0.20)
European Region	US$0.20 (0.10-0.30)
Eastern Mediterranean Region	US$0.20 (0.14-0.42)
Western Pacific Region	US$0.18 (0.10-0.45)

Note: Figures in brackets represent the range

B. More recent estimates of the cost of malaria eradication

Taking into account the additional cost of surveillance activities (for which the national governments are responsible) the conjuctural WHO estimate of the cost of global malaria eradication in 1963 came to the amount of US$1691 million. As admitted by Pampana (1969) this was certainly an underestimate, by at least $186 million, excluding the operations in Africa south of the Sahara, where by 1964 the difficulties of eradication had become fully evident (WHO, 1969).

In 1969 the famous WHO report to the 22nd World Health Assembly stated in unambiguous terms the major obstacles to global malaria eradication while pointing out that developing countries, which for technical, financial and other reasons are unable to reach the goal, will have to content themselves with malaria control.

No specific or total figures for the cost of anti-malaria activities were given but the document indicated that in 1968 the total annual support of external assistance to anti-malaria activities was less than US$50 million of which over one half came from bilateral agreements, especially those of AID (WHO, 1969).

The WHO overall figure for the cost of malaria eradication in 1963 was reassessed by Bruce-Chwatt (1978) in the following way, based on available documentation. Over the year 1957-1967 the WHO (including PAHO) had spent on malaria eradication programs some $87 million (including the funds available under the technical assistance component of the UN Development Program). During the same period UNICEF provided total supplies to the value of $70 million. Assistance provided by AID amounted during that decade to $225 million in dollar grants, $218 million in grants from U.S.-owned local currency and $88 million from low interest loans. The expenses of national governments (at 4 times the assistance of WHO and UNICEF) were estimated at $650 million. Thus the total cost of the first eleven years of malaria eradication were of the order of about $1400 million. However, during the following 8 years from 1968 to 1976 the estimated annual WHO/PAHO expenditure on malaria eradication and control was of the order of $10 million, while the average assistance of AID in grants and loans probably doubled that figure. In other words, during the period 1968-76 the total estimated international assistance to malaria control operations was of the order of $250 million, while the countries concerned spent between three to four times that amount to US$750-1000 million. Thus the cumulative expenditure on global malaria eradication and control over 20 years 1957-1976 was of the order of US$2400-2650 million. Two years earlier, Jeffery had arrived at a somewhat more conservative estimate of US$2000.

A 1978 report of the Director General to the 31st World Health Assembly (A31/19) contained a substantial amount of information on the cost of malaria control. It included expenditure on insecticides, drugs and transport, but stressed the great difficulty of estimating the cost of application, evaluation, and maintenance which vary greatly from one

country to another. It indicated that the worldwide inflation and the increased price of oil were the main factors. However, another important factor was the extension of resistance of mosquito vectors to DDT and the need to use other more expensive insecticides with shorter residual action.

This report quoted the cost of one round of indoor residual spraying with DDT (75% wdp.) of an area with 1 million inhabitants as US$140,000. The comparable cost of one round of malathion (50% wdp.) would be US$345,000.

Noguer (1978) drew attention to the WHO estimate in 1972 of the cost of malaria eradication operations in an area inhabited by a population of 1 million. These calculations were based on the price of one ton of DDT 75% wdp power at US$500; however, by 1977 this price increased to US$950 excluding shipping and insurance. The cost of DDT alone for the protection of the population at two spray rounds per year was US$147,000 in 1972 and rose to US$279,000 in 1977; this meant an increase from US$0.15 to US$0.28 per person per year.

The ratios of increase in cost between 1972 and 1977 were 1:2 for DDT and 1:8 for malathion. Thus if the degree of DDT resistance of mosquitoes is so high that malathion should be used, the cost of this insecticide at 50% wdp four times a year would be US$1,188,000 per annum. The overall cost of malaria control by DDT in an area with 1 million population, which was estimated in 1972 at US$630,000, would be US$1.7 million in 1977, according to Noguer (1978)

Although the costs of application of residual insecticides cannot be estimated with any degree of certainty, the WHO document indicated that the average ratio of such method of control is 30% for insecticides (25%-50% range), 35% for labor and supervision (25%-50% range), 25% for transport (10%-40% range) and 5% for equipment and contingencies (2%-7.5% range).

The estimated yearly global requirement of some main insecticides and drugs for the period 1978-1983 was also tentatively given in the WHO report to the 31st World Health Assembly (of 1978) and quoted for the period 1978-1983 approximate annual requirements as follows: DDT 30,000 tons, malathion 20,000 tons, fenitrothion 750 tons, propoxur 350 tons.

As for drugs, the requirements were: chloroquine 470,000 kg, primaquine 4600 kg, quinine 4100 kg, pyrimethamine 24 kg, long acting sulfonamides 23,400 kg. Naturally the figures for requirements of insecticides (and also some drugs) represent alternatives rather than combined application of specific compounds but the document gave no explanation how the projections were made.

Obviously, in areas of DDT resistance the change to malathion or to other insecticides will be immediately reflected in the cost estimates, since the price of malathion increased between 1972 and 1977 about 4 times faster than the price of DDT.

When it comes to the cost of antimalarial drugs, some estimates were made by the WHO in 1977, when the average single dose treatment using 4.5 tablets of chloroqine (100 mg base per tablet) per person per year would represent the expenditure (for a population of one million) of US$45,000 for the drug alone, or an annual cost per person of US$0.045. This was based on the mean dosage of 10 mg base per kg of body weight and on the cost of US$10 per 1000 tablets.

The latest and probably most reliable estimate of costs of malaria control was prepared for the AID Manual on Malaria control in Primary Health Care in Africa (Washington, 1982). Annex XIII of this manual is a step-by-step primer, designed to guide the non-expert through the several steps of calculating the costs of a malaria control program. It provides illustrative costings for programs of chemotherapy, of chemoprophylaxis and of vector control through the use of a residual spray (malathion). Parallel calculations could of course be made for alternative insecticides, e.g., DDT, fenitrothion, propoxur, etc. The manual describes the process of cost calculation.

For vector control using malathion the calculation is shown in Table 2.

Chemotherapy and chemoprophylaxis are now the most important component of malaria control within the orbit of primary health care. Estimates of cost of this method depend largely on the epidemiological conditions of the relevant area. The most recent estimates were given in the AID Manual on Malaria Control in Primary Health Care in Africa (Washington, 1982) and are tabulated Table 3.

Table 2

Cost of residual vector control by malathion in tropical Africa for a population of 1 million in a rural area

(AID, 1982)

Insecticide, formulation and frequency of spraying at 2g technical product per m^2	Cost of 50% wdp per ton and average sprayable surface per house	Requirement per spraying round of 200,000 houses	Cost of insecticide per year plus reserve and wastage	Spraying equipment including spare parts and nozzles	Transportation		Other supplies (lab. equipment)		Total	
					Initial cost	Annual cost (recurring)	Initial cost	Annual cost recurring	Initial cost approx	Annual cost approx
Malathion 50% wdp. twice per annum each spray round of 6 weeks duration	US$2500 250 m^2	200 metric tons	US$500,000 x 2 = US$1,100,000	750 sprayers at US$100 = US$75,000 plus US$28,000 = US$83,000	US$837000	US$260,000	US$11000	US$2400	US$ 2,036,000	US$ 1,362,0

Note:

The costs of fuel, lubication and maintenance have not been indicated in this table, since they vary greatly in different countries and because the price is subject to fluctuation. A crude calculation based on probable consumption shows that the annual cost of these items would amount to 30%-50% of the annual cost of transportation. Salaries and wages of personnel are not included!

Table 3

Estimated costs of chemotherapy and chemoprophylaxis for an African population of one million of whom 25% are children (10-12 years)

Type and action of Drug	Population composition and other characteristics	Drug formulation and requirements	Estimated costs
Chemotherapy of febrile attack Chloroquine at 600 mg base single dose for adults; half the dose for children	Adults: 750,000 of 60 kg body weight Children: 250,000 of an average 30 kg body weight Fever attacks: adults 1/year; children 3/year	Tablets at 150 mg chloroqine base. 750,000 x 4 tablets = 3,000,000 tablets for adults 250,000 x 2 x 3 = 1,500,000 tablets Total = 4.5 million tablets	Tablets at $15 per 10000 4500 at $15.00 = $67,500 cost per person treated = $0.0675.
Chemoprophylaxis limited to pregnant women and children below the age of 5 years. Chloroquine at 5 mg base per kg of body weight.	Adults: 50,000 (20%) Children 0-5 yrs.: 150,000 with an average body weight of 15 kg. Frequency of prophylaxis: once a week throughout the year.	Tablets at 150 mg chloroquine base. Adults: 50,000 x 2 tablets x 52 = 5,200,000 tablets. Children: 150,000 x 0.5 tablets x 52 = 3,900,000 tablets	5,200 + 3,900,000 = 9,100,000 tablets at $15 per 1000 = 136,500 Cost per person protected $0.6852.

Note: As the Manual points out, these estimates do not include the cost of shipping, customs duties (unless waived), storage, transport and salaries, wages and other charges for the distribution of drugs. It is likely that this will at least double the annual expenditure, but this depends on the structure of the services of primary health care and on the amount of support of community in the form of voluntary workers. It is obvious that the needs for personnel are substantially higher for chemoprophylaxis than for chemotherapy in which essentially static health units are involved.

C. Costs of USAID involvement in malaria eradication and control

Over the past 30 years (1950-1981) AID has been involved in supporting malaria eradication and malaria control activities. According to the GAO report for 1982 (p. 14) the bilateral assistance to 76 various projects involved the cost of US$677.3 millions (of which 79.3% went to Asia, 14.3% to Latin America and the Caribbean, 4.4% to Africa, and about 2% to other projects). Assistance to multilateral projects (these are contributions to WHO, PAHO, UNICEF and UNDP) amounted to US$131 million. The total was US$808.3 million. Of this sum US$114.7 million were disbursed between 1950 and 1956, before the initiation by the WHO of the malaria eradication programme. During that program (1957-1969) AID contributed US$407 million in adition to centrally funded technical assistance (estimated at about US$100 million).

Thus it appears that if the conjectural sum of US$2,000,000,000 spent globally on malaria eradication during that period is acceptable, the AID's proportional assistance to it was of the order of 25%. However, of the total estimated international assistance during that period (about US$180 million) the USA contributed at least 55%-60%.[1]

One should not ignore the fact that in addition to bilateral and multilateral US support of anti-malaria activities (which cumulated during the period 1950-1981 some US$808.3 million) the support to research and development was US$181.2 million. The latter contribution is particularly important as it may produce some new compounds and methods of malaria control at the time when the former insecticides and drugs are of decreasing value, because of the resistance of the pathogens and vectors of malaria.

D. Conclusion

Despite an enormous effort, malaria eradication has not been achieved, although the work of the past 30 years has resulted in many positive achievements. The recent resurgence of the disease in Asia and elsewhere constitutes a setback, attributable in large measure to major reduction of anti-malaria operations despite continued presence of malaria transmission. Unless the world community recognizes the importance and urgency of the problem, many of the gains made so far will be lost. It would be wrong and shortsighted to wait for new weapons against malaria without attempting to stem the tide of malaria in developing countries. The new strategy of WHO consists in identi-

[1]According to AID document DPE-1179-C-00-2013-0 the US assistance to malaria eradication during four years of 1958-1961 amounted to US$122.1 million. This is twice as much as US$59.7 million quoted in Table 1 for WHO/PAHO- and UNICEF-provided assistance during the same period.

fying the weaknesses and setbacks of the antimalaria programmes, co-ordinating all the various efforts, and promoting, organizing and sustaining concerted action at the international level. These activities will be less fruitful unless all the countries strongly support the effort, in order to bring about the success of the new approach.

Problems of cost calculations as a test of feasibility of malaria control in Africa have been well outlined in the AID Manual (1982) and are relevant to other developing countries of the tropical world. The paramount condition, before considering any external support for assistance, is that such aid cannot be granted in the absence of a national commitment to a goal-oriented, well planned, and cost-effective plan of malaria control based on full community participation.

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CONSTRAINTS TO SUCCESSFUL ANTI-MALARIA PROGRAMS[1]

Various identified factors have impeded, and will continue to impede progress in dealing with the problems of malaria. However, mere identification of constraints is of little use unless something can be done about them. Accordingly, these constraints are here listed in a sequence that indicates which factors may be averted or ameliorated by good pre-program preparation, those which the program itself can overcome, and those that represent the hard "facts of life" which planners have to recognize and to which they have to accommodate in program proposals.

To restate: a properly designed malaria program proposal must:

- Identify the problems which the program is designed to overcome or ameliorate.
- Recognize and identify the appropriate role of each participant in the program if program goals are to be attained; and
- Take into account those factors which cannot rationally be expected to change in the short run or be changed by the program itself. Such factors do not militate against initiating a program. By taking them into account, it is possible to avoid the establishment of unattainable goals, comparison with which may cause even remarkable progress to be regarded as failure.

A. Principal Constraints

Among identified constraints to successful malaria control, the following ranked high.

[1]Adapted from The Bureau for Africa's Manual on Malaria Control in Primary Health Care in Africa, December, 1980. Although this list of constraints is drawn from experience in tropical Africa, their application is in virtually every respect world-wide.

1. 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.

2. Inadequate knowledge of cost-effectiveness of control measures.

3. Assignment of anti-malaria responsibilities to a health infrastructure inadequately prepared to assume the burden.

4. Shortages of both trained manpower and essential training capacity; inadequate training facilities at all levels.

5. Poor administrative, managerial and general services support, including coordination of and cooperation among all malaria and related control efforts, agencies and institutions.

6. Structural inadequacy of the anti-malaria effort at the center. A central malaria service within the Ministry of Health is an absolute need to support the "front line" elements of the PHC system.

7. Difficulty of access to malarious areas.

8. Limited resources to cope with the many problems faced (of which malaria is only one).

9. 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, 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.

B. The Role of External Assistance

Of the above-listed constraints (some applicable to one or more national entities; some to all), a number emerge as of particular

interest to sources of external assistance. Recognizing that donor nations and other sources of external assistance will normally concentrate their efforts in areas in which they have a natural competitive advantage, it appears that the following list of "constraints" may be ameliorated in greater or lesser degree by the efforts of one or more of the sources of external assistance.

1. Planning. For those countries where anti-malaria efforts are non-existent, poorly conceived and executed, or being expanded, assistance in the very formulation of a plan will frequently be the most appropriate form of initial external assistance.

2. Operational Research. Both at the outset and subsequently, as program execution progresses, operational research is a valid and essential part of any anti-malaria program. Its purpose is to solve problems, to make better use of available means or to improve available means of dealing with a problem; it may be the device through which a program is formulated or its efficacy demonstrated. As such, to the extent that it lies beyond the capacity of the country to implement, it warrants external support, technical or financial.

3. Basic Research. While some of the developing countries possess basic research capacity, and their use of it (in appropriate cases) may warrant external support, in the main the problems of basic research should continue to be met through the efforts of external sources of assistance. The need for such sources to support basic research is clear cut.

4. Training While expert opinion is unanimous in the view that training should take place as close as possible to the site where the training will be put to use, most developing nations acknowledge that, with few exceptions, they lack the capacity for in-country training of the planners, the evaluators, the managers and the administrators, the trainers of operational level personnel the high-level technical and professional personnel, and the skilled manpower essential to a successful logistics supply system.

No area of activity commends itself more firmly for external assistance.

5. Resource Availability. The criteria to be met by countries seeking external assistance include a long-term country commitment to support the anti-malaria program beyond the termination of external assistance. This is not to suggest that external assistance be given only to those countries which

demonstrate that they can go it alone. Help is needed to initiate an anti-malaria program, and the generally noted constraint of limited resources and cost inflation points clearly to a key area of external assistance: the financing of imported commodities, and the provision of essential technical assistance. Appropriate fields of assistance include:

a. Provision of expertise (short-term and long-term), particularly highly specialized professionals (engineers with public health background, parasitologists, entomologists, irrigation experts, anthropologists) as well as skilled management.

b. Essential supplies. (depending on the tactical variant chosen and the intervention methods selected, this form of assistance could include drugs, insecticides, spray equipment, larvicides, etc.)

c. Transport

d. Support of ancillary but malaria- related activity such as

1. Health education
2. Mass media and public promotion

ANTI-MALARIA METHODOLOGIES: THE TACTICAL VARIANTS

The Seventeenth Report of the WHO Expert Committee on Malaria (WHO, Geneva, 1979: Technical Report Series 640) defines a malaria control program as an organized effort to institute, carry out and evaluate such anti-malaria measures as are appropriate to the prevailing epidemiological and socio-economic conditions, in order to achieve the greatest possible improvement in the health situation of a population subjected to the burden of this disease or exposed to the risk of its resurgence.

The purpose of such a program is to reduce the impact of malaria on the population to the lowest possible level. The control measures selected should be economical and the methods of operation and evaluation must be chosen in relation to the set objectives.

The following sequence of goals and associated anti-malaria methodologies, referred to in the Expert Committee Report as tactical variants, encompasses the major posssibilities of malaria control.

1. Tactical Variant No. 1

   Goal: Reduction and prevention of mortality due to malaria.

   This represents the most elementary form of a malaria control program. For such a program, the only practical measure is the administration of curative doses of an effective schizonticidal drug. For the patient, it will shorten the duration of each episode of malaria fever, reduce absenteeism from school and work, and, in areas where *Plasmodium falciparum* is prevalent, contribute to an improvement in general health.

2. Tactical Variant No. 2

   Goal: Reduction and prevention of mortality and morbidity.

   In this variant, it is necessary not only to provide effective anti-malarial drugs in sufficient quantities for the early treatment of acute malaria cases, but also to pay special attention to certain selected groups (e.g., infants and young children, nursing and expectant mothers, high-priority members of the labor force, etc.). This special attention takes the form of chemoprophylaxis to prevent malaria.

3. Tactical Variant No. 3

Goal: Reduction of prevalence and endemicity of malaria.

Tactical Varients Nos. 1 and 2 are limited "holding operations" which can reduce malaria-related mortality and morbidity but which have relatively little impact on malaria prevalence and endemicity. Tactical Variant No. 3 requires additional measures designed to reduce malaria prevalence. Measures to be taken will be selected on the basis of the epidemiological and environmental situation, fund availability and administrative capacity. They include (in addition to chemotherapy and chemoprophylaxis) such vector control measures as the reduction of mosquito breeding habitats, careful selection of building sites, destruction of adult mosquitoes by residual spraying or space spraying of insecticides, and destruction of mosquito larvae through the use of chemical or biological larvicides. These measures may and usually will vary, not only from country to county, but also among ecological and epidemiological settings within a country. Such a program need not be nationwide in its application; it may be carried out in areas where technical feasibility exists, while Tactical Variant Nos. 1 and 2 are being conducted elsewhere in the country.

4. Tactical Variant No. 4

Goal: Countrywide malaria control, aiming at the ultimate objective of eradication.

This variant requires a long-term malaria control program with specific time targets for attaining the interim objectives described under Variants 1,2 and 3, and leading ultimately to eradication.

AID MALARIA STRATEGY MEETING
Columbia, Maryland 7-10 June 1983

CHEMOTHERAPY OF MALARIA[1]

I. INTRODUCTION

Long before the advent of synthetic antimalarials, quinine was widely used for therapeutic purposes and to a limited extent also for the prophylaxis of malaria. In the suppression (prophylaxis) of malaria quinine was largely replaced in the 1930's by mepacrin and this in turn after the Second World War by the 4-aminoquinolines. Chloroquine and amodiaquine, the most important 4-aminoquinolines, also replaced quinine to a large extent in the area of malaria treatment.

Since the 1950s antimalarial drugs have been used on a very large scale in the general population for therapeutic purposes, namely presumptive and radical treatment in the context of surveillance. Since the attack measures in the malaria eradiction programmes were generally based on the interruption of malaria transmission through vector control, the antimalarial drugs in these programmes had a good measure of protection against the development of parasite resistance. However, in areas where exophilic or insecticide-resistant vectors were responsible for malaria transmission, drugs were increasingly used. These were also the circumstances in which drug resistance occurred. Spread of the resistant parasite isolates was the most rapid where malaria transmission was most intensive.

Chloroquine resistance of Plasmodium falciparum occurred first, and almost simulataneously, in Colombia and Thailand in 1960 and since then it has spread to wide areas of South America and Asia east of New Delhi. Sulfonamides and pyrimethamine were used as alternative therapeutic and prophylactic drugs. However, resistance to these combinations appeared in the late 1970s and a shift to quinine and tetracycline as alternative drugs of the last line became necessary.

In the meantime, research in the area of chemotherapy of malaria has made some progress and it can be expected that mefloquine will soon become available as a drug for the treatment of multiresistant falciparum malaria. Other candidate compounds have been identified and are

[1]by: Dr. W.H. Wernsdorfer, Chief Medical Officer, Research and Technical Intelligence, Malaria Action Programme, World Health Organization.

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already in a phase of preclinical or early clinical development. However, the development of new drugs being an expensive and time consuming undertaking, the drugs which are in hand need to be protected against the development of resistance.

The balance of this document provides an overview of the available antimalarial drugs, of advanced new candidate compounds, of operational drug administration in malaria control and of resistance against antimalarial drugs.

II AVAILABLE ANTIMALARIAL DRUGS

Most of the available antimalarial drugs are blood schizontocides. Primaquine continues to be the only radically curative tissue schizontocide against *Plasmodium vivax* and also the only effective gametocytocidal drug against *P. falciparum*.

A. 4-aminoquinolines

Chloroquine and amodiaquine are the most important representatives of this group. They act as blood schizontocides against all four human pathogenic *Plasmodium* species. In *P. vivax*, *P. ovale* and *P. malariae* they also possess gametocytocidal action. However, they have no tissue schizontocidal and sporontocidal action. Their half-life is much longer than originally thought, namely over one week. These drugs are widely used for the treatment of all forms of malaria and also for suppression. However, drug resistance of *P. falciparum* has seriously limited the usefulness of these drugs, especially of chloroquine, in wide areas of eastern Asia, the western Pacific and South America. Chloroquine is the cheapest antimalarial drug, the cost of one radical treatment (adult dose) representing US $ 0.10 - 0.12. Amodiaquine is apparently slightly more active than chloroquine and may have an advantage in areas with incipient or low-grade chloroquine resistance of *P. falciparum*. However, this drug is significantly more expensive than chloroquine.

B. Dihydrofolate reductase inhibitors
Dihydropteroate synthetase inhibitors

1. Pyrimethamine

This compound has a marked blood schizontocidal effect in all human pathogenic *Plasmodium* species. It also has a causal prophylactic and sporontocidal activity. The drug has a half-life of approximately one week. It has been widely used for the suppression of malaria and in conjunction with the presumptive treatment of malaria as a sporontocide. However, both *P.*

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falciparum and P. vivax have in large areas of the world acquired resistance to pyrimethamine. The effect of pyrimethamine is potentiated by sulfonamides, and moderately pyrimethamine-resistant P. falciparum generally responds therapeutically (with radical cure) to a combination of sulfonamides and pyrimethamine. However, this is less evident in P. vivax. The use of pyrimethamine alone for prophylaxis is considered obsolete.

2. Proguanil

This drug like pyrimethamine is also a dihydrofolate reductase inhibitor. It has a moderate blood schizontocidal action but a very pronounced causal prophylactic and sporontocidal activity. It has been widely employed for the suppression of malaria, requiring daily administration as its half-life is quite short. Proguanil has not been widely used for the treatment of malaria. Cross resistance of P. falciparum and P. vivax to pyrimethamine and proguanil has been reported, but it has not yet been substantiated whether such cross resistance extends also to the causal prophylactic activity of proguanil. Appropriate studies are indicated.

3. Sulfonamides

Sulfonamides are dihydropteroate synthetase inhibitors and are comparatively weak antimalarial drugs when used alone. However, they are potentiators of the activity of dihydrofolate reductase inhibitors such as pyrimethamine. Although sulfonamides with a short half-life act also as potentiators, the use of long acting sulfonamides is preferable so as to match the half-life of pyrimethamine. Thus sulfadoxine has been generally selected as the most suitable partner for combination with pyrimethamine. The formulation of sulfadoxine and pyrimethamine is now available under the trade name of Fansidar. This medicament is used as an alternative drug for the treatment of chloroquine-resistant falciparum malaria. One radically curative dose (1500 mg sulfadozine + 75 mg pyrimethamine) costs US $ 0.25 - 0.30. There is no indication for the use of this combination in the treatment of vivax malaria as P. vivax still generally responds to chloroquine. The prophylactic use of Fansidar is discouraged since this may entail the promotion of drug resistance in P. falciparum.

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4. Sulfones

Sulfones are also dihydropteroate synthetase inhibitors. However, most of these compounds have a short half-life and thus the combination of dapsone and pyrimethamine (Maloprim) is considered to be inadequately matched. Maloprim was developed for malaria prophylaxis and not for the treatment of malaria.

C. Quinine

This drug is the oldest antimalarial available. As a potent and fast acting blood schizontocidal drug, it has retained its place in the treatment of highly acute and complicated malaria. Recently the drug has become very important again as the last line medicament for the treatment of multi-resistant P. falciparum. In this connection it is usually given in association with tetracycline since quinine alone will not always lead to radical cure, especially if quinine is adminstered for less than seven days. Quinine has a very short half-life. When it was used as a suppresive medicament it had to be administered on a daily basis. This and its bitter taste have discouraged its wider application for suppression and the drug has largely stayed limited to therapeutic use. It is relatively expensive.

D. Primaquine

Primaquine is an 8-aminoquinoline. It has tissue schizontocidal activity against P. vivax and P. ovale and gametocytocidal activity against P. falciparum. It is being used for the radical treatment of vivax and ovale malaria (14-day course) and as a gametocytocidal drug (single dose) in association with a blood schizontocide for radical curative treatment of P. falciparum.

Doses and treatment schedules of the above mentioned drugs are shown in Table 1.

III NEW CANDIDATE ANTIMALARIAL COMPOUNDS

A. Mefloquine

This drug, a 4-quinoline methanol, was developed by the Walter Reed Army Institute of Research. Clinical studies were conducted under the auspices of the World Health Organization (UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases and Malaria Action Programme) and industry. The drug is expected to be registered by the end of 1983 as the monocompound;

however, for its use in endemic areas a combination with sulfadoxine and pyrimethamine is being developed, the registration of which may be foreseen for the end of 1984. Mefloquine is a potent blood schizontocidal drug. It has a long half-life of 20-30 days. It can be used both for the treatment and the suppression of malaria. However, experts suggest that its use in endemic countries should be restricted to radical curative treatment.

B. Qinghaosu (artemisinine) and its derivatives

Quinghaosu, a sesquiterpene lactone and active principle of Artemisia annua, was isolated by Chinese scientists and found effective in the treatment of chloroquine-resistant falciparum malaria, using daily doses of 0.3 - 0.4 g in oil suspension administered intramuscularly (i.m.) for three days. The drug is insoluble in water, but is is absorbed when given orally, although it is apparently inactivated for the most part as a result of a first pass effect. Thus, oral doses of 1.5 - 2.0 g per day for three days are required for obtaining the efficacy of the daily i.m. administration of 0.3 - 0.4 g.

Subsequently, derivatives were prepared from artemisinine extracted from plants. Some of these analogues were found to be more active than artemisinine. Two were selected for further development, i.e. artemether and artesunate. The former is soluble in vegetable oils, the latter is soluble in water and can be administered by the intravenous (i.v.) route. Artemether has been used as an i.m. injection (once daily 0.2 g artermether for three days), artesunate as an i.v. injection or drip (0.2 g on the first day, 0.1 g each on the second and third day). The clinical effect, i.e. disappearance of fever and parasitemia, was more rapid with artesunate, which proved to act significantly faster than quinine. However, recrudescences (of the RI type) were more frequent after artesunate as compared to artemether and artemisinine.

Artemisinine and its derivatives have an extremely short half-life and were generally well tolerated at the indicated dose levels. However, a transitory bone marrow depression, and fetotoxicity in animal models indicate the possibility of side-effects which deserve further study. These phenomena may be related to oxidative damage which seems to be also the mechanism of the antimalarial activity of this group of drugs.

Although clinical studies in China of artemisinine, artemether and artesunante (which have included up to now over 2,000 cases of vivax and falciparum, with among the latter a substantial number of patients with cerebral malaria) may suggest that this group of drugs is in a very advanced state of development, the available preclini-

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cal data do not yet comply with internationally accepted standards required for the performance of clinical trials.

WHO's Chemotherapy of Malaria group (CHEMAL), in collaboration with Chinese scientists, is actively promoting the development of artemether and especially artesunate since these drugs hold considerable promise for the treatment of highly acute and complicated forms of falciparum malaria, especially infections with chloroquine-resistant P. falciparum. Current efforts are directed towards the the development of direct drug assay methods, the completion of preclinical toxicological studies, and the investigation of the mechanism of action, with a view to accelerating the clinical development of this drug.

C. Halofantrine

This drug, a 9-phenanthrenemethanol, was developed by the Walter Reed Army Institute of Research, and is now undergoing clinical trials under the auspices of an industrial firm. The drug has been investigated in the classical way, through rodent and simian malaria screens and toxicological studies in various animal models. Observations in volunteers confirmed the blood schizontocidal activity of the compound which was well tolerated in single doses of up to 750 mg and in three doses of 420 mg each in one day. Longer administration at this dose level was associated with epigastric pain, but 250 mg every six hours for three days was well tolerated and uniformly curative against P. falciparum in all cases. The action of halofantrine is independent of chloroquine resistance. The medicament was considered as a replacement drug for mefloquine with which it appeared to share cross resistance, but recent investigations suggest that the sensitivity to mefloquine is independent from that to halofantrine. The present clinical trials aim at determining optimum doses and regimens for a one day treatment. Single dose treatment, even at relatively high doses, was associated with recrudescences, whereas one day treatment with divided doses (e.g. 250 mg every six hours) was radically curative in all cases.

D. Pyronaridine

This hydroxyanilino-benzo-naphthyridine derivative has been synthesized in China and was found to be a very active blood schizontocidal drug. Although the antimalarial activity in simian models (P. inui, P. cynomolgi and P. knowlesi) appeared to be less than in rodent models, its effect in human falciparum malaria is encouraging and obviously independent of resistance against chloroquine. The drug was well tolerated in a variety of animal

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models; the chemotherapeutic index is quite high. There is no evidence of teratogenicity, but induction of mutations was seen in the Salmonella/microsome system with strain TA 1537. The rate of fetal absorption was increased under pyronaridine.

More than 1,000 patients with vivax and falciparum malaria, including a substantial number of cases of cerebral malaria, were treated with pyronaridine in China, using oral administration (6 mg/kg body weight twice on the first day, and once each on the second and third days), i.m. administrtion (two doses of 3 mg/kg body weight at six-hour interval) or i.v. drip (total doses 6 mg/kg body weight). The recrudence rate was highest (8.8%) in the patients having received oral treatment and lowest (0%) in those treated with i.v. drips. In the absence of bioavailability studies after oral and i.v. administration (first pass effect?), it is difficult to explain the different efficacy with the various regimens.

Recent observations suggest that pyronaridine and some of its analogues possess a causal prophylactic activity in rodent models which is superior to that of primaquine.

Pyronaridine and its analogues hold considerable promise, but there is need for completing the preclinical studies and for investigating the pharmacokinetics of these compounds -- also with a view of developing suitable galenic formulations -- before expanding clinical trials.

E. Candidates Among Already Registered Drugs

Besides the registered antimalarial drugs, there exists a variety of antibiotics, antifungal and cytostatic agents, which deserve attention as potential antimalarial compounds, especially as alternative drugs for the treatment of multi-drug resistant malaria. The best example for this group are the tetracyclines which are already being employed in this context, in association with quinine. Similarly, clindamycin has a potent if slow antimalarial effect, but certain side-effects and its high cost preclude its wider use; this drug may therefore be considered as a standby medicament. Although as yet less explored, cyclosporin A and actinomycin D may prove to be useful in this context. Erythromycin deserves special consideration as it has been shown to possess antimalarial activity of its own and to potentiate the activity of chloroquine in chloroquine-resistant malaria parasites to a point at which the curative activity of normal dose levels is re-established. This and other potentiating synergisms are worth further investigation; especially sulfonamides seem to emerge as potentiating agents for a variety of standard antimalarial drugs, an

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observation which may have also practical application in the formulation and use of antimalarials.

A long-forgotten observation on the specific pharmacokinetics of amodiaquine and chloroquine is now of direct interest. If both compounds are given together the blood levels of both drugs are higher than with the monodrugs, and there is also some indication of synergism. Together with the emerging realization that cross-resistance within the 4-aminoquinolines is a heterogenuous phenomenon, this may lead to an improved and more rational use of this group of compounds.

Another question related to antifols has not yet been resolved: although pyrimethamine and proguanil have certainly lost their blood schizontocidal activity against P. falciparum and P. vivax in large parts of the world, it is not known whether proguanil has also lost its causal prophylactic action against P. falciparum. Unconfirmed reports indicate that this is not the case; this is clearly a field for investigation.

Recent studies seem to indicate that quinidine, an optical isomer of quinine normally used as an antiarrythmic drug, is a more active anti-malarial agent than quinine. Again, this is an area meriting further exploration.

IV. METHODS OF DRUG ADMINISTRATION IN MALARIA CONTROL

There are several ways of using antimalarial drugs in the control of malaria. They were, and still are, widely employed, often haphazardly, and today only radical treatment can be taken as a generally acceptable principle.

A. Radical treatment

For radical treatment, antimalarial drugs are given with the objective of achieving complete cure of the malarious infection. In falciparum malaria this is in principle obtained through the administration of an effective blood schizontocidal drug. In areas with low or medium degrees of transmission, primaquine may be added as a single dose treatment for the elimination of gametocytes. In vivax malaria as well as ovale malaria, elimination of latent exoerythrocytic forms (hypnozoites) is required. This is achieved by a course of primaquine (see Table I). When radical treatment is used effectively, there is little risk of selecting resistant parasites. However, to ascertain the efficacy of the drug it is essential to follow up the patient. Radical treatment is today the preferred method of drug administration. If well conducted and properly controlled it can also be administered for mass treatment in compact foci. In areas with a high malaria endemicity, chloro-

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quine or amodiquine used at a dose of 10 mg/kg body weight was recommended up to now as a radically curative drug, presuming that the immunity of the patients would complement the drug effect. However, in the light of present day knowledge on the selection and spread of drug-resistant P. falciparum, this procedure can no longer be universally recommended.

B. Presumptive treatment

This is a method of drug administration which had its justification in malaria eradication programmes sensu stricto. In these programmes doses of 10 mg chloroquine or amodiaquine/kg body weight would be used for the treatment of fever cases on the presumption that these might be malaria infections. Before the administration of the presumptive treatment a blood slide would be taken and would presumably be examined within the next few days. If the case was positive, radical treatment would be given within 7 days from the first blood sampling. However,very few malaria eradication programmes have adhered to that schedule and delays between blood sampling and diagnosis were often substantially longer than 7 days. Thus, presumptive treatment was in many cases equivalent to inadequate treatment and conducive to the selection of drug-resistant P. falciparum. Presumptive treatment has no place in malaria control programmes. Even in malaria eradication programmes, it should be restricted to conditions where delays between initial blood sampling and diagnosis are kept safely below 7 days.

C. Mass drug administration

This is the technical term for any mass administration of antimalarial drugs whether as a single round or in the form of repeated administration. It has been applied in several malaria eradication programmes as a single round right at the beginning of the attack phase in order to drastically lower the malaria reservoir and thus also to reduce residual malaria transmission. Later on mass drug adminstration was increasingly used in areas where insecticide resistance or exophilic behavior of malaria vectors had made malaria control difficult. Thus, mass drug administration has been employed in the place of vector control measures and therefore in the presence of unabated malaria transmission. In this way it exerts considerable selection pressure and is conducive to the occurrence and the spread of drug-resistant P. falciparum. Unless it is carried out in the form of mass radical treatment with the necessary diagnostic and therapeutic follow up and unless it is conducted under the umbrella of highly effective measures against the transmission of malaria, there is no place for mass drug administration in a malaria control or eradication programme.

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D. Suppression (prophylaxis)

Drug prophylaxis except for groups under special risk has rarely been practised within the framework of malaria eradication or control programmes. However, in more affluent countries drug prophylaxis has been widely practised in the private sector, especially in areas where measures directed against the transmission of malaria were not sufficiently effective. Malaria prophylaxis has also been advocated for holo-endemic and hyper-endemic areas as a means of reducing infant mortality in the absence of effective vector control measures. There are clear indications now that this use of drugs increases selection pressure and promotes the occurrence and the spread of drug-resistant P. falciparum. Moreover, it has been asserted that the building up of immunity is hampered as long as the drug prophylaxis remains effective. Mass drug prophylaxis cannot anymore be recommended since it quickly invalidates the drugs at our disposal. Thus, more reliance needs to be placed on radical treatment. However, there are limited indications for prophylaxis also in areas with highly endemic malaria. These exceptions concern pregnant women during the second and third trimester of pregnancy and non-immune temporary visitors to such areas.

V DRUG RESISTANCE

Resistance of human plasmodia to modern synthetic antimalarials was observed soon after these drugs had become widely used. Although pyrimethamine and proguanil resistance was first reported in the early 1950s, this did not present a serious challenge to antimalaria programmes while malaria parasites continued to be highly susceptible to 4-aminoquinolines, especially to chloroquine and amodiaquine, which could be used for both malaria treatment and suppression.

Resistance of P. falciparum to 4-aminoquinolines was reported from Asia and South America in the early 1960s, but the extensive and regular use of effective residual insecticides kept chloroquine-resistant P. falciparum down to a few small and rather isolated foci. However, over the last 10 years, a drastic reduction in the use of residual insecticides because of financial and technical difficulties has led to the spread of malaria. Thus, chloroquine-resistant strains of P. falciparum are now found in many areas where the prevalence of the disease had been greatly reduced and where chemotherapeutic measures had consequently become the main and often the only measures of malaria control.

Autochthonous infections with chloroquine-resistant P. falciparum have since been reported from 23 American and Asian countries, and from six countries in East Africa.

In some countries, resistance has become so widespread and intense that existing drug regimens have had to be changed and chloroquine has

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been replaced by far more expensive alternative drugs. Moreover, resistance to the second line, alternative drug combination of sulfadoxine and pyrimethamine has occurred and is spreading rapidly in eastern Asia and South America, necessitating the use of quinine and tetracycline as last line drugs. These events, and the slow progress in the develoment of new antimalarials, emphasize the importance of the rational use of existing drugs and the deployment of efficient measures against drug-resistant malaria.

A. Factors responsible for the occurrence of drug resistance

The development of resistance to antimalarial drugs has so far always been associated with either the use of these compounds or the deployment of agents with a nontarget action on malaria parasites, in areas with ongoing malaria transmission. This is suggestive of a selective mechanism. The speed with which resistance occurred to individual drugs is obviously related to their specific characteristics and to the mode and the intensity of use, but also to the degree of control of malaria transmission in the area concerned.

1. Mechanism of resistance

None of the available antimalarial drugs is known to induce mutations in the malaria parasite. However, spontaneous mutation with regard to drug sensitivity has been shown to occur in rodent plasmodia with a frequency of approximately 10^{-8} an observation which may also be applicable to P. falciparum. Differences in the sensitivity levels between individual mutations tend to be relatively small with 4-aminoquinolines, but quite marked with dihydrofolate reductase (DHFR) inhibitors. In nature, without drug pressure, these mutants will not be specifically selected. However, under drug pressure such a selection will take place if the less sensitive parts of the parasite population are allowed to survive the drug concentrations to which they are exposed. If the surviving parasites are not numerous, specific immunity may eliminate them in persons with prior substantial malaria experience, but in nonimmunes they are likely to reproduce, giving rise to R responses. This explains the sentinel phenomenon of drug resistance among nonimmune travellers to East Africa in the early 1980s at a time when thre was little sign of in vivo drug resistance among the local population.

Chloroquine-resistant P. falciparum has obviously a biological advantage inasmuch as its viability in vitro and its growth rates are higher than those of the sensitive parasites, and it is known that originally quite sensitive cultures have turned resistant in the course of several years, even in the

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absence of drug pressure. However, in the interpretation of this phenomenon it should be borne in mind that there is little or no immune control of the parasites in the *in vitro* culture.

2. Drug characteristics

High-jump mutations (e.g. resistance to DHFR inhibitors) are selected faster than low-jump mutations. A higher number of serial selections is required for the latter in order to arrive at a level of therapeutic refractoriness. This explains why pyrimethamine resistance occurred much more rapidly than chloroquine resistance.

Pharmacokinetic factors also play a role in the selection process, together with the intensity of malaria transmission. Drugs with a short half-life may select only with regard to the already existing malaria infection if this is inadequately treated, but they do not select in a new infection. In contrast, antimalarials with a long half-life, i.e. prolonged periods of subcritical levels following the therapeutic phase, will lead to selection among parasite populations arriving during the time when subcritical levels prevail. The dimensions of such a selection will depend on the intensity of malaria transmission. Drug prophylaxis and underdosed treatment act, in principle, in the same way. The relative rarity of quinine resistance may be explained by the short half-life of this drug and its very limited use for prophylaxis.

3. Selection pressure

Selection pressure is a function of the survival of parasites exposed to concentrations of the drug which selectively eliminate the more sensitive members of the parasite population. The selected survivors, i.e. parasites with a reduced sensitivity, will be the only ones allowed to reproduce and, in a particular area, largely sensitive populations will gradually be replaced by resistant ones if drug pressure is intensive enough.

From recent observations in Thailand it is known that field isolates of drug-resistant *P. falciparum* consist of a mixture of individuals with very different degrees of drug sensitivity; the specific sensitivity level is being maintained stable after cloning. Other studies indicate that the sensitivity level of *P. falciparum* populations is significantly reduced after unsuccessful treatment with specific drugs. This is a clear indication of selection through inadequate treatment, be it because the drug dose was inadequate, or the chosen

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drug inappropriate. This factor is controllable through correct choice and therapeutic administration of drugs, in keeping with the results of monitoring for drug sensitivity. However, drug pressure emanating from subcritical drug levels associated with the haphazard and prophylactic use of antimalarials in the presence of ongoing malaria transmission is largely uncontrollable as long as these drugs are freely available.

Another source of drug pressure stems from medicaments which have a non-target impact on malaria parasites such as DHFR and dihydropteroate synthetase (DHPS) inhibitors used for the treatment of bacterial infections, e.g. co-trimoxazole. This may render P. falciparum resistant to sulfadoxine/pyrimethamine and account for reports of primary refractoriness to this combination in areas where it has not been used before.

4. Absence of measures directed against malaria transmission

Malaria transmission is a conditio sine qua non for the spread of drug resistance, whether this occurs as a result of inadequate therapeutic use of of a prophylactic deployment of the medicaments. The more intensive the transmission and selection pressure, the faster does resistance spread and its degree increase. These conditions are most marked in areas where drugs were or are being used as a means of controlling malaria in the absence of measures directed against the transmission of the disease, for instance in areas with exophilic or insecticide-resistant vectors (e.g. parts of eastern Asia and South America). The experience in Shirati, Tanzania, has clearly shown that mass prophylaxis with chloroquine in young children, in the absence of measures directed against malaria transmission, is very rapidly reducing drug sensitivity, i.e. from full sensitivity to low grade resistance within 2-2 1/2 years. However, in the case of Shirati, it must be borne in mind that malaria transmission in the area is very intensive and that the large majority of the total local parasite population is being exposed to drug pressure in the course of malaria drug prophylaxis in children under 6 years of age.

B. Distribution of drug resistant malaria (1 January 1983)

Quinine-resistant isolates of P. falciparum were first encountered at the beginning of this century, in Brazil. Sporadic cases of quinine resistance, although rarely substantiated, continued to be reported from various countries until widespread use of this drug was superseded by modern synthetic antimalarials. While

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mepacrine was in use, resistance of P. falciparum to this drug was reported only once, in Papua, New Guinea.

Resistance of P. falciparum to DHFR inhibitors usually appears shortly after starting their use in mass drug distribution schemes, once considerable drug pressure has built up. Parasites resistant to one type of DHFR inhibitor are often resistant to others. It was demonstrated in East Africa that resistant strains were spreading rapidly in areas adjacent to the operational zones, and gradually mixing with the sensitive strains. Today, foci of falciparum malaria resistant to DHFR inhibitors are scattered in most areas where the disease is endemic. Their distribution is patchy and their exact location is often unknown, since systematic monitoring was not attempted at the time when 4-aminoquinolines were the drugs of choice and their efficacy was not threatened by the occurrence of resistance. So far, DHFR and DHPS inhibitors are the only drugs to which resistance has been reported in human plasmodia other than P. falciparum.

The present distribution of chloroquine-resistant P. falciparum is shown in Fig. 1.

The relative prevalence of chloroquine-resistant infections and the degree of resistance are still on the increase in all affected areas. This process is more pronounced in countries of South-East Asia and Africa than in South America where the level of resistance is usually lower. With the exception of a few areas in Brazil and Venezuela, the proportion of resistant cases is still moderate in South America, and RI responses constitute the majority of all resistant cases. However, in the Lao People's Democractic Republic, Thailand, and Viet Nam, RII and RIII responses are more frequent and the majority of falciparum cases are resistant to 4-aminoquinolines. These are also the areas where resistance to sulfadoxine and pyrimethamine is increasing most rapidly, although failures of this combination have also been confirmed in South America and East Africa.

C. Monitoring of drug sensitivity

1. Methods

Sensitivity to blood schizontocidal drugs can be assessed by in vivo and in vitro methods. These have practical limitations, but the evaluation of sensitivity is feasible for the main drugs used by applying one or both techniques.

In the in vivo methods a standard radical cure treatment is given and the response of the plasmodial infection is assessed over a period of seven days when using the WHO Standard

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Field Test, or preferably over 28 days with the WHO Extended Field Test.

The Standard Field Test permits a quick observation of the occurrence of RII and RIII responses, but the Extended Field Test is required to differentiate between S and RI responses. The results of the in vivo tests may be influenced by the immune status of the patients and this should be taken into consideration when conducting this type of test in areas with high malaria endemicity.

In vitro tests permit, in principle, an objective measurement of the sensitivity of P. falciparum to all directly-acting blood schizontocidal drugs. There are three major in vitro field test systems: the macro-technique and the microtechnique in short-term culture.

The macrotechnique is suitable for use with 4-aminoquinolines and mefloquine and is carried out with blood obtained through venipuncture. After defibrination, aliquots of 1 ml of blood are added to vials containing glucose alone (controls) or glucose and different concentrations of the drug. The vials are incubated for 24-28 hours at 38.5°C and thick films are made from the contents of each vial. After straining with saline Giemsa, schizont counts are made on all slides and growth inhibition in the drug vials is calculated in relation to the control readings. Full inhibition of schizont maturation at a concentration of 1 nmol of chloroquine per ml (1×10^{-6} mol/litre) indicates chloroquine sensitivity; schizont growth at 1.5 nmol of chloroquine per ml indicates resistance. The in vitro test results do not permit definite conclusions regarding the degree of resistance, but schizont maturation at 1.5 nmol chloroquine per ml (2.5×10^{-6} mol/litre) is usually a sign of RII or RIII resistance.

The microtechnique employs the same growth medium as the continuous culture and can be used for sensitivity tests with 4-aminoquinolines, mefloquine, and quinine. The test is performed on 8 cm x 12 cm flat-bottom, plastic tissue-culture plates containing samples of different drug concentrations and controls. Blood is taken by means of a heparinized or EDTA-treated capillary and suspended in reconstituted growth medium. Aliquots of 50 µl of the suspension are added to the test wells; the plate is placed in a candle jar and after lighting the candle and closing the jar, the jar is placed in an incubator. Alternatively, a sealed candle water bath can be used. After incubation at 37.5°C for 24-26 hours the plates are taken out and the supernatant removed from the individual wells. Thick films are prepared from the erythrocyte sediment, stained and read for schizont maturation, the findings in the drug wells being expressed on the basis of the controls. In-

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terpretation of the results is similar to that in the macrotechnique, the results being expressed in pmol of drug per µl of blood.

A comparison of the macrotechnique showed nearly identical base values and regression coefficients. The microtechnique will eventually replace the macrotechnique since it has certain advantages, such as the need for a smaller volume of blood, which can be obtained from a fingerprick instead of venipuncture, and a generally higher success rate. Moreover, the application of the technique does not depend on the availability of particular growth stages of trophozoites, nor is it limited by a particular parasite density.

2. Global programme of monitoring

As drug resistance of malaria parasites is a problem of current or potential concern to all malarious countries and to those exposed to the importation of malaria cases, WHO has developed a global monitoring programme. Planning and execution are coordinated at regional level, usually through the regional Advisory Committees on Medical Research and the WHO regional offices. The programme was first implemented in 1977 in the South-East Asia Region. It is now also well advanced in the Western Pacific Region, and is in its early stages in the Region of the Americas as well as in the African and Eastern Mediterranean Regions. Research activities are carried out by the malaria services and collaborating institutes in the countries concerned. Global coordination is effected through the Scientific Working Groups on Applied Field Research and on Chemotherapy of Malaria and their secretariats, as the programme has components of both field and basic research.

The results obtained are collated and evaluated at country, regional, and global levels. Data on baseline assessment and monitoring of parasite sensitivity are published once a year in the Weekly Epidemiological Record. Other results are circulated in the form of WHO documents or published in WHO serial publications.

The global programme has the following objectives in relation to falciparum malaria:

Assessment of the current geographical distribution, prevalence, and degree of resistance to 4-aminoquinolines.

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- Monitoring of sensitivity levels to the spread, relative prevalence, and degree of resistance to 4-aminoquinolines., with the aim of facilitating the implementation of operational countermeasures.

- Assessment of sensitivity to currently used drugs other than 4-aminoquinolines and to candidate antimalarial compounds in order to determine their clinical and operational usefulness and baseline data.

- Methodological research on the determination of drug sensivity.

- Studies on the epidemiology of drug-resistant malaria.

- Elaboration of guidelines on the clinical management of malaria resistant to 4-aminoquinolines.

- Development of operational measures for limiting the spread and eliminating foci of drug-resistant malaria.

While all of these objectives apply to the global programme, individual countries have selected specific sets of objectives and a schedule of implementation which are relevant to the local epidemiological situation.

In view of the importance of P. vivax in many parts of the world, studies related to vivax malaria are being conducted in some countries. However, large-scale testing of drug susceptibility is envisaged only at a later stage of the programme, after improvement of methods, and after major progress has been made in the priority area of drug-resistant falciparum malaria.

D. Protection against drug resistance

The above mentioned factors (see section V-A) responsible for the occurrence and the spread of drug resistance should be a guide to developing the principles for the extension of the usefulness of the drugs in hand and for the protection of new medicaments. The major approaches must be seen in the restricted, yet most effective use, of the antimalarials, in the minimizing of drug pressure and in the curbing of malaria transmission.

1. Correct use of drugs

Antimalarials should as a general rule not be used for malaria control as an alternative to effective measures directed against transmission.

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Antimalarials should, on a general basis, only be employed for the radical treatment of malaria, using adequate dose regimens whose continued efficacy is being monitored on the basis of drug sensitivity tests.

Antimalarials should, generally, not be used for mass drug administration and large-scale suppression (prophylaxis). This does not preclude the administration of well conducted mass radical treatment in specific, limited areas; similarly, nonimmunes staying for limited durations in endemic areas may be protected through drug prophylaxis. Drug prophylaxis may also be given to pregnant women during the second and third trimester of pregnancy.

In areas with intensive malaria transmission it will be more appropriate to bring facilities for the rapid diagnosis and treatment of malaria into the reach of the population in need rather than to promote the suppressive use of drugs which may quickly invalidate the drug in question and ultimately be detrimental to the population.

Wherever possible, the use of drugs with nontarget effects on malaria parasites should be restricted if suitable alternative drugs without such nontarget effects are available for the treatment of the appropriate conditions.

2. Measures against malaria transmission

The intensity of malaria transmission determines the spread of resistant parasites. It is therefore evident that effective measures directed against malaria transmission are the best safeguard against the spread of resistance, while minimizing the drug pressure is the best means of preventing the occurrence of resistance.

Vector control and the reduction of man/vector contact (and where feasible, also favoring the increase of animal/vector contact over man/vector contact) are the most appropriate means of curbing transmission since their action is totally independent for that of drugs.

However, drugs should also play a role in restricting transmission, first and foremost in the radically curative treatment of malaria. In order to avoid transmission for an unsuccessfully treated infection (which has necessarily arrived at a lesser drug sensitivity level as a result of the treatment), the case must be followed up and retreated effectively if there has been a recrudescence. This highlights the need for continuous monitoring of drug sensitivity in order to determine the continued efficacy of specific drug regimens.

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Primaquine is a potent gametocytocidal drug for P. falciparum. However, its routine use in this context, in association with radical curative blood schizontocidal treatment, will be meaningful only if the cases are followed up adequately and recrudescences excluded, since a recurring infection would shed gametocytes again, belonging to a parasite population of lesser drug sensitivity.

3. Limitation of the sale of drugs

Only under exceptional circumstances will it be possible to bring already registered and commercially available drugs under full government control which would be necessary to enforce measures towards minimizing drug pressure. Moreover, government services in some countries, especially in tropical Africa, are not yet in a position to ensure an adequate health care of the population. However, in countries with well developed and efficient curative and preventive health systems covering the whole population, it will be quite feasible to introduce compulsory prescription for the sale of antimalarial drugs and thus to establish an element of control, the impact of which will depend on the comprehension and the cooperation of the medical profession.

The conditions are different with regard to new drugs if governments, industry and the World Health Organization jointly arrive at an understanding which safeguards the rational use of these new medicaments and protects them against resistance. In the approach of this problem, WHO is guided by the recommendations of the meeting on drug resistant malaria, Kuala Lumpur, 10-15 August 1981, which indicate that "any new antimalarial drugs that become available in the future for the treatment of multiple-resistant falciparum malaria, e.g. mefloquine, should be used only under the auspices of the National Health Authorities, and if necessary, legislation should be provided to control the importation and distribution to the public of such compounds.."

It is clear that the implementation of this recommendation requires determination on the part of governments and understanding on the part of industry. With regard to mefloquine, recent negotiations between WHO and a producer indicate the feasibility of limiting the distribution of this new drug in keeping with the above mentioned recommendation, on the condition that government authorities and other future producers will adhere to it as well. Since the marketing of drugs can be controlled through the exercise of their sovereign rights by the governments concerned, it is up to the latter,

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also in their proper interest, to ensure compliance with the recommendation.

In the negotiations between WHO and industry it was also highlighted that the availability of mefloquine - even under government auspices - should remain limited to countries where the chloroquine resistance of P. falciparum is a problem.

4. Suitable drug formulations

It has been shown in laboratory models that the development of mefloquine resistance can be significantly delayed if this drug is given together with sulfadoxine and pyrimethamine. Apart from this effect, mefloquine and sulfadoxine/pyrimethamine proved to have at least additive action and recent observations are strongly suggestive of potentiation. Preliminary clinical findings appear to point in the same direction.

In order to delay the onset of mefloquine resistance it has therefore been envisaged to use this drug generally only in (a fixed) association with sulfadoxine and pyrimethamine. Nevertheless, mefloquine alone would be available for the treatment of pregnant women and persons with hypersensitivity to sulfonamides.

While methods of delaying drug resistance and of obtaining synergism have been investigated with mefloquine, this has not been the case as yet to any significant extent with other available antimalarial drugs. Recent studies with 4-aminoquinolines and DHPS inhibitors and earlier observations on erythromycin and chloroquine indicate that investigations in this field may be conducive to improving and rationalizing the use of existing antimalarials.. This is quite independent from the essential preclinical and clinical development of new antimalarials which must necessarily go through all stages with the monocompounds (except for pure potentiators in the clinical phase) before a clinical exploration of suitable combinations can be considered. On the other hand, highly effective, radically curative monodrugs with a very short half-life may not require a combination partner at all since they exert very little selection pressure.

5. Monitoring drug response

The selection of drugs and regimens for routine treatment should be based on the continuous monitoring of the malaria parasite's response. In vivo and in vitro tests carried out within the framework of the national monitoring activities are

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an indispensible requirement for the general orientation of drug use and the timely implementation of essential modifications imposed by changing drug sensivity. However, it should not be forgotten that the reliable post-treatment follow-up of each individual case is an additional and very sensitive monitoring device and one which, through the prompt administration of alternative medication in the case of failure, will reduce the spread of drug resistance.

VI. OUTLOOK

Drug resistance poses operational and material problems and the ill effects of an over-liberal use of antimalarials have in most of the affected countries quickly outweighed the economy made from reducing effective measures directed against malaria transmission. It is evident that there is a limit to going from one alternative drug to another. This emphasizes the need for protecting the still effective and new drugs through their rational and effective use for radical treatment, the utmost reduction of selection pressure, and the reduction of malaria transmission. These considerations have a bearing on the future policies of drug use and will change some of the traditional concepts of antimalaria strategies in countries with intensive malaria transmission. However, it will be better to recognize and to face up to this challenge than to jeopardize the lives of millions of people whose survival is *inter alia* dependent on the availability of effective antimalarial drugs.

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TABLE 1A

THERAPEUTIC USE OF ANTIMALARIALS

Plasmodium	Area	Drug	Dose of drug (base where applicable) Day 0	Day 1	Day 2	Days 3-6	Days 7-16
Falciparum[1,2]	Chloroquine sensitive	Chloroquine or Amodiaquine	10 mg/kg followed six hours later by 5 mg/kg	5 mg/kg	5 mg/kg	-	-
	Chloroquine resistant	Sulfadoxine and	25 mg/kg	-	-	-	-
		Pyrimethamine	1.25 mg/kg	-	-	-	-
	Multiresistant	Quinine HCL and	3 x 10 mg/kg	3 x 10 mg/kg	3 x 10 mg/kg	3 x 10 mg/kg	-
		Tetracycline	4 x 6 mg/kg	4 x 6 mg/kg	4 x 6 mg/kg	4 x 6 mg/kg	-
		or					
		Mefloquine	12.5 - 16 mg/kg	-	-	-	-
		or					
		Mefloquine plus	12.5 mg/kg	-	-	-	-
		Sulfadoxine plus	25 mg/kg	-	-	-	-
		Pyrimethamine	1.25 mg/kg	-	-	-	-
Malariae		Chloroquine or Amodiaquine	10 mg/kg	10 mg/kg	5 mg/kg	5 mg/kg	-
Vivax[3] and Ovale		Chloroquine or Amodiaquine	10 mg/kg	10 mg/kg	5 mg/kg	-	-
		Primaquine			0.25 mg/kg	0.25 mg/kg	

1 In highly acute and complicated cases of falciparum malaria it will be indicated to commence treatment with an i.v. drip of quinine dihydrochloride 10 mg/kg in isotonic saline or glucose (10 ml fluid/kg) over 1-4 hours according to severity. Repeat at 8-12 hourly intervals until oral standard treatment is possible.

2 In endemic areas with ongoing malaria transmission it is recommended to give a standard single dose of primaquine (0.75 mg/kg) one day after completion of blood schizontocidal treatment (patients of ≥ 4 years only).

3 In acute cases of vivax malaria it is indicated to follow the first dose of 10 mg/kg after six hours by a dose of 5 mg/kg and to give 5 mg/kg each on days 1 and 2.

4 Not in children <4 years.

TABLE 1B

SUPPRESSIVE USE OF ANTIMALARIAL DRUGS*

Plasmodium	Area	Drug	Dose (base if applicable)	Regimen	Remarks
Falciparum	Chloroquine sensitive	Chloroquine or Amodiaquine	5 mg/kg	one a week (repeat first dose on second day)	
	Chloroquine resistant	Sulfadoxine plus Pyrimethamine	10 mg/kg 0.4 mg/kg	Once a week	
	Multiresistant	Mefloquine or	4 mg/kg	Once a week	
		Mefloquine plus Sulfadoxine plus Pyrimethamine	4 mg/kg 8 mg/kg 0.4 mg/kg	Once a week	
Vivax Ovale Malariae		Chloroquine or Amodiaquine	5 mg/kg	Once a week (repeat first dose on second day)	Mefloquine protects also against vivax malariae

* Not recommended as a large scale routine measure in areas with intensive malaria transmission.

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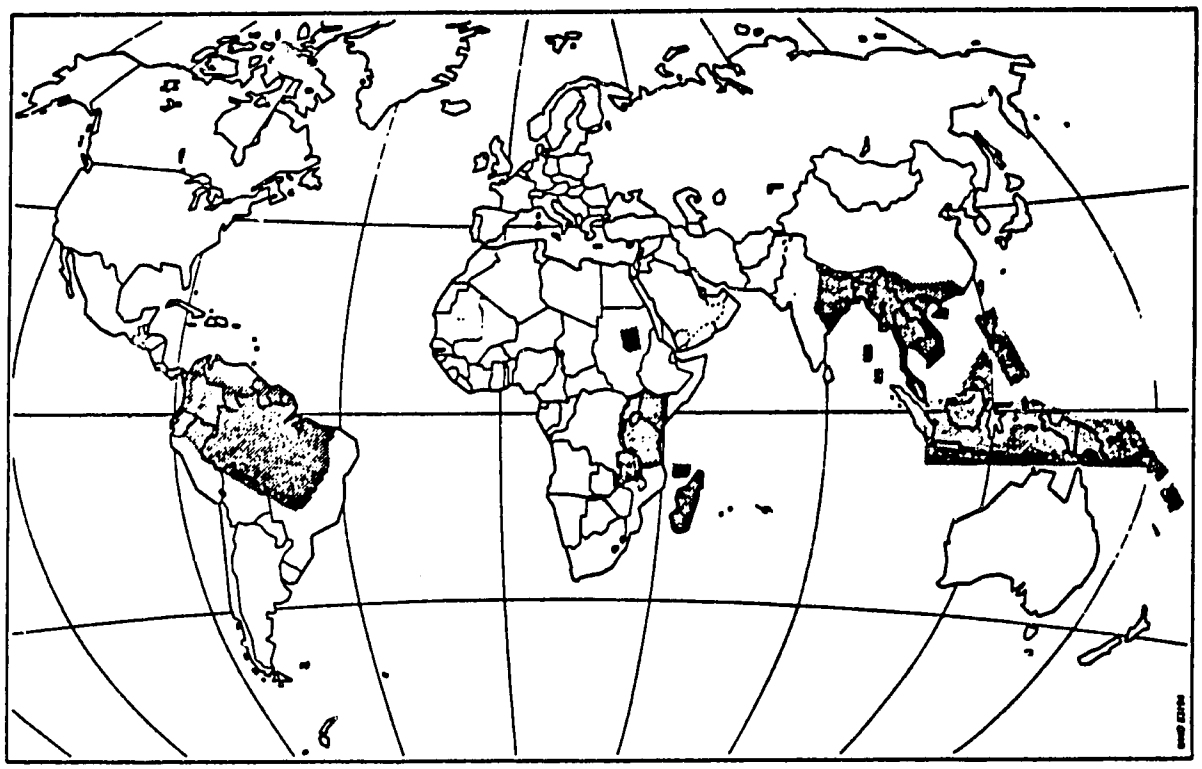
Fig. 1 Distribution of chloroquine resistant *Plasmodium falciparum* (status of February 1983)



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