WHO Expert Committee on Malaria

Eighteenth Report

World Health Organization
Technical Report Series
735

World Health Organization, Geneva 1986
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WHO EXPERT COMMITTEE ON MALARIA

Geneva, 9-17 September 1985

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WHO EXPERT COMMITTEE ON MALARIA

Eighteenth Report

INTRODUCTION

The WHO Expert Committee on Malaria met in Geneva from 9 to 17 September 1985. The meeting was opened on behalf of the Director-General by Dr S. K. Litvinov, Assistant Director-General, who pointed out that during the last 15 years very little progress had been made towards the control of malaria in the world. Therefore, significant and enduring improvements in the global malaria situation were urgently needed.

In 1978, following the resurgence of malaria, the Director-General had proposed a global malaria control strategy, and this was endorsed by the Thirty-first World Health Assembly through the adoption of resolution WHA31.45. This resolution urged Member States to reorient their antimalaria programmes so as to ensure that they form an integral part of their national health programmes, and called upon WHO to provide technical guidance and support. In this respect, the Expert Committee at its seventeenth meeting further developed the strategy of malaria control and its tactical variants (1). Unfortunately, the implementation of this malaria control strategy as part of primary health care has been slow, and the capability of the health services in dealing with the problem is not improving.

The Thirty-eighth World Health Assembly, in 1985, adopted resolution WHA38.24, which recommended that malaria control should be developed as an integral part of the national primary health care system and urged Member States to undertake an immediate review and appraisal of the malaria situation and their existing control strategies in terms of effectiveness, efficiency, and of the prospects of achieving and maintaining the objectives. Such action would form a basis for planning the modifications necessary to maximize the use of resources for the attainment of the objective of health for all by the year 2000, to plan activities utilizing appropriate technologies in order to regain momentum in
controlling malaria, and to mobilize adequate national resources for both malaria control and the conduct of applied research in malaria.

Dr Litvinov stressed that the major consideration was how to control malaria within the primary health care strategy. The malaria control measures chosen should be based on a sound epidemiological understanding in order to develop approaches not only for each country but also for the different ecological areas within each country. These approaches should take into account concurrent control measures for other diseases. Epidemiological appreciation should provide an adequate basis for planning, as well as for monitoring progress, and for evaluating the methods and the results.

It was desirable that the operational responsibilities for antimalaria programmes should be transferred to, and maintained by, the general health services under the expert guidance and supervision of malariologists. This would involve the development of appropriate approaches and techniques for each area, district, and possibly each community within the district, based on a stratification of the malaria problem. During the organization of health care within affected districts it was crucial to include locally appropriate malaria control measures, taking into account not only technical aspects but also social, behavioural, and economic factors as well.

The training of health workers at all levels had to be considered not only in general terms with respect to the epidemiology and control of malaria, but also in very specific terms, particularly at the field level, in relation to the duties to be carried out for malaria control by health workers. These workers should support communities that were attempting community malaria control as well as educate individuals and groups to participate in, and contribute actively to, the control efforts. Research and development studies would be needed to ascertain to what extent non-professional workers, guided and supervised by personnel at the first referral level who, in turn, were advised by experts in malaria, could be trained to cope with these tasks in addition to their other activities.
1. MALARIA CONTROL AND DEVELOPING PRIMARY HEALTH CARE SYSTEMS

1.1 Global and regional analysis of the malaria situation in relation to the development of primary health care

In the last 15 years, the evolution of the malaria problem, as shown by statistical information reported to WHO, was at first dominated by a resurgence of the disease, with a peak in 1976, followed by a decrease in the number of cases, so that by 1982 the number was similar to that reported in 1974 (Table 1). While these figures represent the 5–10 million cases reported, it is estimated that the actual number of new clinical cases may be of the order of 92 million each year. The effects of this huge number of cases are very serious, particularly in rural agricultural areas where the disease predominates. In general there has been very little progress in control in most countries and indeed there has been a slow deterioration during the past 4 or 5 years in many areas.

The epidemiological situation is, however, by no means uniform, as is shown in the following classification:

(a) areas where malaria never existed or disappeared spontaneously following social and economic development (population 1292 million);

(b) previously malarious areas where, as a result of successful control and eradication efforts during this century, of the development of health services, and of changes in social and economic conditions and in the relation of man to the environment, endemic malaria and apparently the risk of infection has been eliminated (population 800 million);

(c) areas where a reduced level of infection is maintained by the continued application of antimalarial measures (population 2117 million)—the majority of the malarious countries of Asia and the Americas are included in this category and in many of these areas the general social and health infrastructure is not sufficiently developed to ensure the maintenance of this reduced level of infection because there is a constant threat of increased transmission as well as an intensification and spread of specific malaria problems that are making the control measures less effective and more costly;

(d) areas where no organized control measures exist (population about 365 million, mainly in Africa south of the Sahara). In these areas malaria transmission has remained unchanged, except in the
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*Taken from World health statistics quarterly, 38, 211 (1985).
*The information provided does not cover the total population at risk in some instances.
*Mainly clinically diagnosed cases.
*Excluding China.
*Provisional.
centre of some cities where transmission has diminished as a result of the elimination of, or high levels of pollution of, surface waters.

1.1.1 Responses to changing epidemiological patterns

(a) The changing patterns. It is generally accepted that malaria disappeared from most developed countries as a result of social and economic improvement. Nevertheless, malaria control activities have rarely been designed on the basis of a serious consideration of different social and economic development patterns.

In the past, specific malaria control activities succeeded in areas where the existing level of social and economic development meant that they could be applied with the required degree of perfection and were accepted by the population. This success was maintained in areas where social and cultural development had changed peoples' lives, and had changed their attitudes to diseases, treatment, and the health services. These changes made effective surveillance possible and, in some cases, actual environmental modifications could be made that prevented the re-establishment of transmission.

In most areas outside tropical Africa, the present malaria problem shows a marked focal distribution that is often quite different from that of the most intense foci existing prior to the beginning of control. Failure to achieve or maintain control has depended not only on the previous intensity of transmission but also on new trends in agricultural exploitation and the distribution of rural populations. These factors have created new conditions of malaria transmission, which is now sometimes more intense than before.

The increasing demands of international trade, together with improved communications, have favoured the change towards extensive agricultural exploitation, which has often replaced subsistence agriculture and sometimes destroyed forested areas. These agricultural developments attract large numbers of temporary workers. The traditional, poor malarious village is being replaced increasingly by a mobile rural population searching for work. The workers are concentrated temporarily in labour camps where inappropriate siting and shelters, lack of care of the immediate environment, and overcrowding create optimal conditions for malaria transmission.

The migration of rural populations from countryside to cities has resulted in the growth of urban and periurban slum areas where
makeshift housing favours malaria transmission. These areas develop a population density far greater than any rural agricultural area, and this intensifies endemicity. The pollution of surface water eventually limits transmission before urbanization occurs. The high birth-rate in these periurban areas and the failure to improve living conditions has created in many countries a counter-migration to the rural areas. Planned or unplanned settlement enterprises, such as prospecting or mining, and large public works such as dams, roads, or railway construction, particularly in forested areas, may establish new foci of intense transmission.

Most malarious areas now have a complex mixture of both new and persistent epidemiological problems, and in those areas current malaria control measures often produce only partial and short-lived relief. Continued application of these measures has contributed to the extension and intensification of specific technical problems, such as the development of vector resistance to, or avoidance of, insecticides and of parasite resistance to drugs.

Chloroquine resistance in *Plasmodium falciparum* has spread throughout large areas of South America and South-East Asia, and in both continents it is increasing in intensity. Resistance to the drug combination sulfadoxine/pyrimethamine is also spreading. There is increasing vector resistance to insecticides, and, in some areas such as the Pacific coast of Central America and south-eastern Anatolia, the main vectors, *Anopheles albimanus* and *A. sacharovi*, respectively, show resistance to several insecticides, including most of the insecticides currently available for indoor spraying. Malaria vectors in many of these areas exhibit evasive behaviour towards insecticides through the phenomena variously described as excito-repellency or deterrent effects.

The impossibility of meeting the high costs of the malaria surveillance (needed for the consolidation or maintenance phases) in the face of other very severe health problems competing for resources was perhaps the main reason why the eradication strategy failed in the majority of developing countries (2). Relaxation of surveillance led to a resurgence of the disease and eventually to the remobilization or re-establishment of the control machinery. The prolonged application of antimalaria measures produced an intense selection pressure for the development of resistance, while the slow change from an eradication to a control strategy often allowed transmission to become epidemic. In some areas, like the Pacific coast of Central America, the existing mesoendemic conditions were
replaced by periodic epidemics as a result of repeated failures to maintain the effective control achieved by the various efforts carried out over the last 20 years (3).

Even in Africa south of the Sahara, the malaria problem is not uniform and there are indications that it is changing in many areas. The malaria problem of Africa on the whole may seem uniform, with very intense uncontrolled transmission leading to a prevalence of infection in young children of nearly 100%, high adult immunity, and high infant mortality. The frequent contact of man with very efficient vectors, conforming with Macdonald's conditions for stable malaria (4), the high parasite rates found in most surveys, the absence of vector control, and the low level of development of health services in most of rural Africa all tend to reinforce this idea of uniformity. However, recent studies indicate that this unchanging pattern may occur less frequently than expected, particularly with regard to malaria as a disease. The prevalence of malaria varies greatly in different localities; morbidity is considerably lower than expected, and mortality due to malaria alone is very low. These findings are in sharp contrast with what would have been expected from the epidemiological observations made 20–30 years ago, and the differences have been attributed principally to the easy availability of antimalarial drugs.

While mortality due to malaria may be declining sharply in many areas of Africa, drug resistance is developing rapidly and spreading throughout the continent. The uncontrolled availability of drugs through commercial channels and the lack of adequate guidance on appropriate doses and treatment schedules favour the use of insufficient doses that relieve clinical symptoms but exert a high selection pressure for drug resistance.

In most areas the poor development of health services and the inadequate logistic support result frequently in the absence of antimalarial drugs from peripheral health posts, creating the impression that the main problem is this absence of antimalarial drugs, which in turn stimulates the development of trade channels of supply.

(b) Antimalaria services and the development of primary health care. In 1978, the World Health Assembly endorsed a malaria control strategy based on the principles of primary health care and on the recognition of the variations in epidemiological situations in different parts of the world, in the status of development of the
health infrastructure in developing countries, and in the financial and manpower resources available. For this purpose, the World Health Assembly proposed four tactical variants ranging from the reduction or prevention of mortality to the interruption of transmission (see section 1.4.1).

Attempts to apply this strategy have run parallel with the countries' efforts to apply the strategy of primary health care for the attainment of the goal of health for all by the year 2000, which they approved unanimously. Even if the malaria control strategy is presented as an integral part of the primary health care strategy, during its actual application there have been problems of interpretation, delays in implementation, and some reluctance to change practices established many years ago as part of a plan for malaria eradication.

Areas or countries can be classified into one of three main categories according to differences in the relative development of their antimalaria services and health infrastructure.

— Areas or countries where the primary health care system has reached a relatively high degree of development and antimalaria measures have been a part of that system's responsibilities. At present, this group is represented mainly by the malarious areas of China. Within the primary health care approach, the implementation of antimalaria measures by community health workers, the provision of opportune diagnosis and treatment, and the improvement of general health conditions through health education can virtually eliminate malaria mortality, considerably reduce the clinical effects of the disease, and even reduce exposure to transmission.

— Areas or countries having a less developed health infrastructure and no organized antimalaria services. This group includes most of Africa south of the Sahara. Previously, national malaria eradication programmes were not fully organized in tropical Africa, except in islands such as Mauritius, Réunion, and Zanzibar. The new strategy offers a way of developing malaria control as part of primary health care; for this it is necessary to study the epidemiology of malaria not only as an infection but also as a disease and cause of death.

— Areas or countries where organized antimalaria services have preceded the development of primary health care at the periphery. In many countries, these antimalaria services are the
only health services that continuously reach the periphery. There have been efforts in the past to integrate these malaria services into slowly developing basic health services. However, these efforts did not contribute significantly to the development of the latter but did lead to a serious deterioration in the level of malaria control and, in several instances, to a resurgence of malaria that in turn led to a reversal of the decision to integrate.

This experience has contributed to a certain degree of resistance to the adoption of primary health care. Nevertheless, the persistence of the malaria problem and the cost of traditional control measures are forcing countries to consider the redeployment of resources.

In several countries vertical health activities or health campaigns, have been combined under a common administration that extends from the centre to the periphery. The establishment of these organizations for health campaigns improved the efficiency of control activities in countries such as Brazil, Colombia, and Venezuela. The campaigns remained highly centralized in all aspects and retained all the functions of searching for, characterizing, and controlling the problems. Continuous health care and all the health problems not dealt with by a direct campaign remained the responsibility of the basic health services.

Some of these countries are preparing plans to transfer the responsibility for the diagnosis and treatment of cases, as well as the collection and analysis of routine epidemiological information, to primary health care services. This will involve the incorporation of the network of malaria voluntary collaborators and their logistic support into the developing primary health care system. At the same time, a decentralization of the executing control organization could permit a more timely and appropriate response to changing needs.

Most countries are experiencing great difficulty in modifying established services. The perpetuation of vertical programmes involving a large labour force results in a constant increase in the proportion of the health budget devoted to maintaining this labour force when budgetary constraints are accompanied by increases in wages and salaries. Increased employment opportunities for professionals and skilled staff both within and outside their country have contributed to their leaving the programme, resulting in a decrease in the operational capability of the programme and a gradual reduction in the number of professional and supervisory staff able to plan and execute its reorientation (Fig. 1).
Fig. 1. Insecticide spraying in the originally malarious areas and numbers of malaria personnel in areas in the attack and consolidation phases in the Region of the Americas, 1972–82
1.1.2 Epidemiological approach to malaria control

The attempt to eradicate malaria from the world has revealed extensive local variations not only in the intensity of the problem but also in the response to control interventions. Most epidemiological situations behave in a similar way to ecological systems, i.e., showing considerable resilience to change and tending to return to the previous state of equilibrium, even after near elimination of the disease. In contrast, in some circumstances, an apparently lesser effort has produced more permanent change. An insight into these anomalies may be gained by extending the conceptual epidemiological model to include a better understanding of the ecological and social processes interacting with the basic elements, such as the transmission chain—parasite, vector, and infected and susceptible host.

Insecticide spraying, mass chemoprophylaxis, and mass drug administration are examples of interventions that are generally very effective; their use can drastically modify both the transmission and prevalence of malaria and, if maintained for a sufficiently long period, may even eliminate the malaria reservoir. However, if the level of perfection of these interventions drops or they are discontinued, the original endemicity is often restored, unless maintenance can be assured by other means. In contrast, less spectacular but more permanent effects are obtained by the elimination of breeding places, improvements in house construction, and particularly (as a result of social development) by making changes in the way of life so that there is an appropriate demand for, and use of, the health services.

(a) Stratification of the malaria problem. The idea of stratifying the malaria problem is derived from the characterization of epidemiological zones in terms of their main determinants, including climate, hydrography, orography, vector biology, anthropology, and social and economic factors. Beklemishev, cited by Lysenko (5), applied Pavlovski's theory of landscape epidemiology to the typing of malaria foci, which were characterized in terms of (i) the landscape that determined the presence of the vector, its ecology and, in a general way, the way of life of the population, and (ii) the social and economic conditions. The concept of stratification has also been used for the study of local variability at the microecological level in order to improve the effectiveness and efficiency of malaria control in difficult problem areas.
The scale of application of stratification may, therefore, vary considerably from the characterization of large homogeneous areas to that of very small epidemiological units, such as a locality. It may also vary considerably in accordance with the nature of the variables used for typification.

(b) Selection of appropriate technologies. The main aim of the epidemiological approach is to identify the appropriate technologies for malaria control as part of the development of primary health care. The concept of an appropriate technology implies that its use is scientifically sound for the solution of the particular problem, and that it is adapted to the society that is considering its application in terms of acceptability and social affordability.

Antimalaria measures differ considerably in the degree of perfection and coverage required during their application in order to obtain an effect. If indoor spraying is to have any effect, then extensive coverage is needed, e.g., if only a few individuals in a community spray their houses with a residual insecticide they will not get any protection whatsoever. In contrast, measures of individual protection (such as the use of mosquito nets, screening of dwellings, demand for prompt treatment of fever) reduce individual risk and have an additive effect in the community.

Another characteristic of antimalaria measures that is particularly important in relation to the strategy of primary health care is their potential for further development into more sophisticated instruments for social progress. Wherever malaria is a serious public health problem, the training of community workers in the diagnosis and treatment of malaria, and their continued support by the health services in terms of supplies and acceptance of referred problem cases, may be the first step in the development of primary health care. Further training and support can then be provided for other major problems as the systems for the provision of supplies and for referral develop. In contrast, vertically organized spraying and mass chemotherapy do not normally engage development processes and often result in conflict, if continued for too long.

In the context of social development, antimalaria measures may be classified according to whether their use can be incorporated into the daily life of the individual or the community as a permanent routine, or whether their use has to be only temporary because of, for instance, cumulative toxic risks, loss of effectiveness by selection
of resistance in the target species, or deterioration of efficiency of application in the long term.

Unless control activities are seen to be effective they may hinder the establishment of primary health care.

(c) Organizational implications. There is no doubt that several antimalaria activities can be carried out by the most peripheral level of the primary health care system. These measures could be introduced at an early stage in the development of the health system when the population is anxious about malaria.

When considering the development or adaptation of structural elements that have an exclusively or predominantly antimalaria function, the main question to be asked is how are they contributing to or complementing the development of the infrastructure for primary health care? The costs of establishing the capability to perform certain activities may be considered an investment in the development of primary health care, while other costs are predominantly for consumption. Of particular importance will be the identification of structural elements that may represent obstacles for primary health care and that will require urgent reorientation or modification.

1.1.3 The malaria control strategy and the research and development approach to its application at country level

Based on considerations of the resilience of epidemiological systems and states of equilibrium, there are two basically different approaches to malaria control:

- the management of malaria without drastically changing the epidemiological equilibrium—this includes the establishment of facilities for diagnosis and treatment as well as health education at the community level that are supported by appropriate referral and epidemiological information systems, allowing the focal management or prevention of abnormal situations such as epidemic outbreaks or drug resistance;
- active intervention to control or interrupt malaria transmission in large areas—this approach is aimed at obtaining an improved malaria epidemiological situation that can be sustained.

The choice between the two approaches should be based, above all, on the feasibility of maintaining the desired results, i.e., the
stability of the improved equilibrium achieved after intervention. If malaria is really a very serious health problem and it can be eradicated in a short time, it may seem logical to do so instead of choosing the slower alternative of management. Nevertheless, the unfortunate experience of many countries shows that in most instances a “malaria-free stable equilibrium” cannot be reached. The choice of active intervention has meant that these countries must continually provide resources for a containment effort that is subject to frequent resurgence of more or less localized transmission that the health services are unable to manage.

Because these two approaches are often not clearly differentiated, and because of the persistence of the value system of the eradication period, there has been some confusion in defining objectives and setting short- and medium-term targets for control programmes.

In applying these approaches to actual local situations, it will be necessary to design “custom-built” strategies by adapting general methodological guidelines to local conditions as outlined below:

(i) In areas with no organized malaria control and no primary health care system, the first decision should be whether the management of fever with antimalarial drugs may be considered as a port of entry for primary health care or whether such a capability should form part of a more sophisticated training activity for community health workers. In many areas, community health workers may be required to give a full course of chloroquine to all infants and young children. In older children and adults the health workers will give a course of the drug to individuals with a fever that they have been unable to identify because of their limited training in the differential diagnosis of common fevers, and they may also give curative treatment and antimalaria chemoprophylaxis to pregnant women. These activities should be supported by a referral system that could deal with individuals who do not respond to treatment by confirming the diagnosis or by identifying and treating resistant infections. An essential function of the referral system should be the treatment of severe cases of malaria. Resources should be used more effectively in developing and strengthening treatment, providing education on the use of the services, and organizing the progressive introduction of individual and communal preventive measures.

(ii) As has been mentioned, in many areas of Africa private channels of distribution of antimalarial drugs reach the periphery
more effectively than do the health services. In such cases the health service should concentrate its efforts on providing adequate information about the use of drugs, improving accessibility to appropriate treatment, and eventually regulating and controlling the drug trade.

(iii) Managing malaria at the periphery is very difficult in the foci of drug-resistant *Plasmodium falciparum* in Asia, South America, and possibly soon in Africa. In these foci, economic exploitation of forested areas means that populations with a low immunity are introduced into areas of intense transmission. In Thailand this problem has led to the establishment of peripheral microscopic diagnostic facilities (malaria clinics).

(iv) Areas with organized malaria control programmes exhibit an extremely wide variety of situations and problems. In most cases it will be necessary to review the malaria problem and the control programme as recommended by the WHO Study Group on Malaria Control as Part of Primary Health Care (6). Some form of redistribution of resources may be necessary, including the decentralization of activities and the replanning of antimalaria activities within primary health care and referral services. Reassignment and reorientation of personnel to meet local needs will be required.

Although action will have to be initiated while there are still uncertainties and some degree of generalization will be unavoidable, the true situation is often more complex than expected and it is at the periphery that real contact can be made and an understanding of what is needed can be established. Planning should be based on as complete a knowledge of local epidemiology as possible and should include not only the control activities to be introduced but should also promote the improvement of knowledge through the setting up of information and evaluation systems. Planned epidemiological, social anthropological studies, or other forms of field research may be required.

(a) *Acquisition and documentation of experience*. The difficulties experienced in trying to reorient malaria control, the variability of malaria epidemiology itself, and the problems associated with its control emphasize the need to improve the understanding of local epidemiological determinants, as well as the conditions of applicability of antimalaria activities.
Seldom will it be appropriate for a country as a whole to follow a single approach to malaria control; in practice, planning will be carried out at the district or provincial level. Guidance should be provided based on well-documented experiences of not only the effects that have followed particular interventions but also the conditions under which similar effects may be expected.

The acquisition of experience should differ essentially from the pilot project approach that was traditionally applied in the health field; the aim is not to test whether a particular technology can achieve certain results under a given set of conditions, but to improve understanding of how these results were obtained and which of the pre-existing or developing characteristics influenced, favourably or unfavourably, the results observed. This understanding may be obtained from a detailed observation of particular experiences, but will more likely result from a comparison of various attempts in different situations.

The experience of the past indicates that what is needed in order to improve malaria control, even more than the development of new and improved technology, is a better understanding of where and how to apply the general knowledge already available. This implies that the acquisition of experience referred to above should concentrate on the following aspects:

— the appropriate definition, or redefinition, of the malaria problem in terms relevant to its control and the feasibility of maintaining this control;
— the criteria for identifying realistic goals in terms of social acceptability and affordability;
— the identification of technologies that are already appropriate for application by the health systems infrastructure;
— the definition of the levels of the primary health care infrastructure at which control, supportive, and referral functions should be established, including the deployment of drugs for first-line treatment and for the management of treatment failures;
— the provision of monitoring and information systems necessary for the appropriate functioning of the control effort and the identification and management of abnormal situations, such as epidemic outbreaks or the development and spread of parasite resistance to drugs or vector resistance to insecticides;
— the definition of the conditions under which complementary services, such as specialized vector control teams, should be
established for the control of epidemics or for the control of malaria transmission in areas where the intensity of the problem and the level of development of the health services require such activities.

(b) The application of experience and technology. It will be necessary to acquire experience not only in areas where malaria control has to be started as part of a developing primary health care system (or as one of the initial activities, perhaps even the first, of primary health care) but also in those areas where malaria control has been an organized activity for many years and, in many instances, the health activity of greatest peripheral penetration.

The evolution of the malaria problem and its intimate links to the modalities of rural development show that the control of malaria in the developing world today cannot mimic the experience of the developed world over the past hundred years. The ways in which available techniques are used and the development of approaches to malaria control have to be based on the appropriate documentation of past experience.

The applicability and relevance of a particular experience will depend on the social, cultural, and ecological conditions influencing it. In many instances, the effect of the application of various methods will depend more on the social and ecological conditions than on the choice of the methods itself. It becomes essential to analyse and document these conditions and their possible influence. Some ecological variables may be isolated for complementary controlled observations but the majority of social variables pertaining to malaria programmes are more appropriately analysed on a comparative basis than under experimental conditions.

The conditions of applicability of positive control experiences become a matter for exploration that can be accomplished by comparative analysis and evaluation.

The Expert Committee believes that WHO can play an important role in this process by:

— collaborating in the planning, execution, evaluation, and documentation of experiences in malaria control as part of the primary health care system, and in the integration of antimalaria programmes into that system;
— facilitating the interchange of experiences among health services trying to solve similar problems, by the exchange of responsible health workers or by joint analysis in a working setting;
promoting more active forms of intercountry collaboration in areas such as joint planning and sharing of technical and material resources between countries with similar problems, or similar social and political structures;
— promoting and facilitating the coordination of international and bilateral agencies that are supporting antimalaria activities at the national or intercountry level;
— consolidating documented experiences and analysing conditions of applicability.

(c) Reorientation of malaria epidemiologists and training for malaria control. The development of new approaches to malaria control will require the training of new cadres of malarialogist who have a broader epidemiological outlook. It will also require the involvement of a variety of skills and the reorientation of the health services to plan, execute, and evaluate antimalaria activities as part of the primary health care strategy.

Training for malaria control will require a capability for ensuring that community health workers and health services personnel are able to meet the needs of the community satisfactorily. To do this, appropriate training will have to be provided for the community health workers and for health services personnel involved in (i) technical and logistic support to the community health workers; (ii) the referral system for treating severe malaria and treatment failures; (iii) epidemiological services; (iv) monitoring of specific problems such as drug resistance; and (v) the control of intense malaria foci or epidemics. Training will also have to be provided for a central core of malaria expertise where needed.

Equally important is the development of appropriate approaches for the education of the population in the use of individual and collective protective measures against malaria, as well as in the appropriate use of the health services. It is vital for the successful implementation of the primary health care strategy that an effective and sustained link be established between the community and the health services.

Health professionals will also have to be trained and guided in the proper treatment of malaria cases, including the detection and management of problems such as drug resistance, as well as in the general development of primary health care. This activity may require the collaboration of university medical departments but
should also involve professional associations since seminars on key subjects may be very productive.

WHO will have an important role to play in strengthening the regional and global coordination of training in order to improve the use of scarce resources. It will be necessary to develop improved methods for practical training in epidemiology and in the use of documented experiences during the planning of locally adapted approaches. The development of essential supporting elements such as training materials, modular courses, and simulation exercises is also important.

(d) Scientific and technological research and its application by health services. The establishment of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases has provided a great stimulus to the support and coordination of research. A classification of research into three categories that cut across the conventional concepts of basic and applied research is proposed:

(i) Research for the development of new tools for control or diagnosis and methods of application; this category itself may be divided by specific purpose into chemotherapy, immunology, and vector control. This research may be considered as motivated by the interests of global knowledge and generated by the scientific community throughout the world. The aim of this type of research is to produce results that are widely applicable; the research activities involved include a very broad range from basic biology, physiology, chemistry, and biochemistry to field testing and evaluation. Field research is included in the form of field trials, the aim of which is to define the specific effects attributable to the particular tool under study as well as the optimal doses and methods and conditions of application.

(ii) Research aimed at the identification and solution of field problems. This research is motivated by the interest of individual countries or areas and is concerned with particular field problems and attempts to solve them. However, problems may be identified that require the collaboration of the laboratory. In addition, specific research of a very basic nature may be required either in epidemiology or in the sciences of entomology, biology, genetics, etc.; these studies may be conducted in the field or in the laboratory. The Expert Committee feels that WHO, through its regional and country structures, should facilitate the integration of this type of
research with the evaluation of control efforts and the
documentation and interchange of experiences in the practice of
malaria control. This integration will require the strengthening of
the relations between the health services and the research institutions
on a country or international basis, as well as the development of
national research policies to induce research workers to address
national goals.

(iii) Research derived from the observation of contrasting results
in the application of control approaches in different areas. This will
be a complement to the validation and documentation of
transferability of experiences described above. It will address aspects
of ecological stability and resilience, and social and cultural factors
in the epidemiology of malaria. This more complete understanding
of the interactions involved may help in predicting future trends.

(e) Application of the strategy at the district level. As operational
responsibilities are being transferred to the general health service,
under the expert guidance and supervision of malarialogists, it will
be necessary to specify what every responsible health officer will need
to know about malaria control in order to organize health care
within his area (6). In summary, this includes:

— the selection of appropriate directives and approaches for each
district and possibly for different communities based on a process
of stratification of the malaria problem;
— the appreciation and management of social, behavioural, and
economic, as well as technical factors, in the design of control
interventions;
— appropriate financial planning, considering the ability and
willingness of people to share in covering costs or alternatively
planning for a more centralized solution to cost coverage.

1.2 Special problems of malaria control

1.2.1 Resistance of *Plasmodium falciparum* to drugs

Resistance of *P. falciparum* to most of the current antimalarial
drugs has emerged as the main technical problem in malaria control.
A knowledge of the extent of the problem in terms of geographical
distribution and degree of resistance is important for the selection
of appropriate control measures and for the development of a policy
for the rational use of antimalarial drugs. The presence of resistant
parasites may necessitate the deployment of other drugs of which there is only a limited range. Curative treatment with 1500 mg of chloroquine base is the least expensive regimen. The cost of the first- or second-line alternative drugs is considerably higher and consequently their use puts a financial strain on individuals and the public economy in general. Compared with chloroquine treatment, the cost of curative treatment with amodiaquine (1500 mg of base) is 2.3 times higher, sulfadoxine/pyrimethamine (1500 mg) 4 times higher, quinine alone for 7 days 15.5 times higher, quinine for 7 days plus tetracycline for 7 days 19.8 times higher, and mefloquine (750 mg) plus sulfadoxine/pyrimethamine (1500 mg) 33.3 times higher.

Some of these alternative drugs produce side-effects and involve lengthy treatment regimens that often result in poor patient compliance—for example, the quinine and tetracycline regimen. Moreover, the development of new antimalarial drugs is a slow process and it is not certain whether this development can keep ahead of the evolution of resistance to the compounds currently in use.

Therefore, the efficacy of the drugs available needs to be maintained for as long as possible and efforts should be made to slow down the occurrence and spread of drug resistance. This may be achieved through the rational and controlled use of the available drugs as well as by the control of malaria transmission, as has recently been recommended by the WHO Scientific Group on Advances in Malaria Chemotherapy (7).

Drug pressure is the major factor responsible for the selection of resistance in malaria parasites and should be reduced to a practical minimum. The use of subcurative doses of drugs contributes most to this selection process and it follows that radical curative treatment, i.e., the administration of drug doses that are more likely to eliminate the parasite completely, is probably the most reliable way of avoiding selective parasite survival. Mass drug administration for suppression, with all its associated problems including the hazard use of drugs, should, therefore, be avoided. One of the safest ways of reducing the spread of resistant parasites is to reduce or interrupt malaria transmission.

In each individual case the decision to alter the malaria treatment may be easy, but when extended to the population or programme as a whole this decision becomes more difficult. Countries will, therefore, need additional and more explicit guidance to assist them
in assessing the epidemiological significance of the drug-resistance problem, and in reaching a decision on the appropriate drugs to be used, as well as on how these drugs can be effectively deployed for as long as possible. In this respect, it is essential to consider the concept of first-, second-, and third-line drug treatment schedules as an important component of an effective referral system, although it should be realized that no ready-made, rigid advice can be given. The frequency and degree of resistance, as indicated by the in vivo response and in vitro confirmation, will have to be taken into account by the national health authorities, in addition to the stage of development of the referral system as part of primary health care, the immediate and long-term programme objectives, the volume and intensity of transmission in a given area, and the availability of resources for the required drugs.

(a) Distribution of drug-resistant *P. falciparum*. Information concerning the changing geographical distribution of malaria due to drug-resistant *P. falciparum* is published by WHO in the *Weekly epidemiological record*.

(i) **Resistance to dihydrofolate reductase inhibitors.** Proguanil, chlorproguanil, and pyrimethamine are examples of dihydrofolate reductase inhibitors, and they have been widely used for chemoprophylaxis. Chloroquine in combination with pyrimethamine has also been used for presumptive treatment in malaria eradication programmes. Resistance of *P. falciparum* to proguanil and pyrimethamine is now apparent in many endemic areas, and it can be expected to occur wherever the drugs have been or will be used on a large scale. It may be focal, however, in any country. Cross-resistance between the drugs in this group has been often found, but not always. When a specific drug pressure ceases, pyrimethamine resistance tends to recede but can quickly reappear if use of the drug is resumed.

(ii) **Resistance to 4-aminoquinolines.** Since its emergence in Colombia and Thailand in the late 1950s, resistance of *P. falciparum* to chloroquine has been reported from the following countries of South and Central America: Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Panama east of the Canal, Peru, Suriname, and Venezuela. In Asia and the Western Pacific, resistance occurs in Bangladesh, Burma, the southern part of China, India, Indonesia, Democratic Kampuchea, Lao People’s Democratic Republic, Malaysia, Papua New Guinea, the Philippines, the Solomon Islands,
Thailand, Vanuatu, Viet Nam, and, most recently, Nepal, Pakistan, and Sri Lanka.

The first well-documented case of chloroquine-resistant *P. falciparum* from Africa was reported in 1979 in a tourist who had contracted the infection in Kenya (8). Since then, cases have increasingly been reported among non-immune visitors to East Africa. From 1981 onwards, resistance has also been reported among indigenous semi-immune inhabitants. By the end of 1983, cases of resistance had been recorded from the following countries: Comoros, Gabon, Kenya, Madagascar, Malawi, Mozambique, Uganda, the United Republic of Tanzania (including Zanzibar), Zaire, and Zambia. Since 1983 cases have occurred in Angola, Burundi, Cameroon, Namibia, Rwanda, and Zimbabwe.

The present geographical distribution of chloroquine-resistant *P. falciparum* is shown in Fig. 2.

The rapid spread of chloroquine-resistant *falciparum* malaria in Africa, when compared to the situation that prevailed in South-East Asia and South America 20 years ago, may be due to the fact that in Africa transmission continues unabated because no vector control operations are in progress and specific drug pressure occurs widely.

Where the degree of resistance is relatively low, chloroquine-resistant *P. falciparum* infections may be more sensitive to amodiaquine. However, amodiaquine might rapidly lose its effectiveness if it were to be used extensively in areas where chloroquine resistance is widespread or of high degree. Nevertheless, the use of amodiaquine may be advantageous for some time in areas where only a low degree of *P. falciparum* resistance to chloroquine has been detected. In combination with tetracycline, amodiaquine has also been shown to be effective in areas where the local strains are highly resistant to chloroquine and also to the combination of sulfadoxine and pyrimethamine (9).

(iii) **Resistance to the combination of sulfadoxine and pyrimethamine.** A synergistic combination of sulfadoxine and pyrimethamine initially proved to be highly effective for the treatment and chemoprophylaxis of chloroquine-resistant *falciparum* malaria, although there were consistently 10–20% of treatment failures attributable to either defective absorption or an anomalous, rapid metabolism of sulfadoxine by the patient.

From 1978 onwards, true resistance of *P. falciparum* to this combination was observed in Thailand among individuals who had
Fig. 2. Areas where resistance of *Plasmodium falciparum* to chloroquine has been reported, 1983∗

*In a few instances this map also contains information relating to 1984.*
contracted the disease there, and this resistance has increased subsequently, such that the cure rates obtained there recently were only 32% in Thai patients living close to the Kampuchean border, 39% in the north-east of the country, and 42% in the western parts of the country (10). Meanwhile, resistance has been reported from Burma, Indonesia, Malaysia, and Papua New Guinea.

In South America, resistance to the combination has been reported from Brazil and Colombia. In 1982, the Pan American Health Organization reported that the efficacy of the combination had diminished by 30–40% (11).

Failures of prophylaxis and treatment with the combination have also occurred in individuals infected with *P. falciparum* in Kenya and the United Republic of Tanzania. Resistance to this drug combination seems to be directly related to pyrimethamine resistance: the higher the degree of the latter, the more likely there is to be resistance to the combination.

(iv) **Resistance to quinine.** Despite wide regional variations in the sensitivity of *P. falciparum* to quinine, many alleged failures of quinine treatment may have resulted from too short a course of treatment with an inadequate dosage. However, studies in eastern Thailand have shown that resistance does occur, usually when the parasite is highly resistant to chloroquine. Evidence of a correlation between the sensitivity of *P. falciparum* to quinine and to mefloquine, two structurally related drugs, has also been obtained in Thailand, and this may indicate that subcurative levels of quinine in the blood of many falciparum malaria cases, resulting from inadequate dosage or treatment compliance, may encourage the development of resistance to mefloquine.

(v) **Resistance to mefloquine.** Clinical trials conducted in South-East Asia, Africa, and South America have not yet provided evidence that mefloquine resistance may be a major operational problem at this stage when the drug, alone and in combination with sulfadoxine/pyrimethamine, is being introduced into malaria control programmes. The cure rates obtained in the dose range of 12.5 mg of mefloquine base per kg body weight (single dose) were consistently higher than 95%. Most of the failures (only RI-type response so far) were associated with drug loss through vomiting that resulted in the blood plasma levels falling below the minimum inhibitory concentration.

However, despite the fact that the drug has not yet been widely used in the field, two cases of mefloquine resistance have been
observed, one in Thailand (12) and one in the United Republic of Tanzania (13). These observations suggest that a potential for mefloquine resistance exists in the gene pool of *P. falciparum*, underlining the need for its rational use in the future and for the monitoring of parasite susceptibility.

(b) Monitoring the response of malaria and malaria parasites to drugs.

(i) Justification. Direct monitoring is justified by two main objectives: to ensure that appropriate drug regimens are used, and to understand the epidemiology of drug resistance in the hope of delaying its selection, or spread, or both. Both objectives are relevant to the control of malaria through primary health care, but they will require different test methods and information systems. Development of these methods and systems has been recommended (7).

(ii) Test methods. *In vitro* and *in vivo* methods have been developed that are both scientifically acceptable and practicable under field conditions. The *in vitro* test, standardized under the auspices of WHO, has been widely used for testing the susceptibility of chloroquine, amodiaquine, quinine, and mefloquine. The appropriate use of this test is strongly recommended to confirm clinically diagnosed resistance and *in vivo* results, with strict adherence to WHO specifications.

(iii) Practical implementation. A number of different agencies are involved in drug response monitoring activities in endemic and non-endemic countries. National activities in endemic countries are of two types: the detection of treatment failures through regular diagnostic and curative health services, and the use of standard WHO test systems by trained specialized teams that are more or less mobile. Such teams exist in many endemic countries, whereas monitoring of drug response through the regular health services may not occur, or only to a limited extent. The two approaches are complementary, and a good monitoring system should include both. Technical guidance is necessary for the coordination of the two approaches and the integration of the first into primary health care. The development of simpler test methods is desirable.

The processing of the data obtained from these tests is carried out by the WHO regional offices and by WHO headquarters. The latter maintains two data banks: a fully computerized system that accepts only results reported on the precoded forms corresponding to the
WHO standard tests, and a more comprehensive system, that is in the process of being computerized, covering, in addition to the above, all other accessible reports and publications. The first system is more standardized and detailed and allows more flexible analyses to be made; the second system is more complete. All of those involved should be encouraged to assist as much as possible in making the two data banks as complete and up-to-date as possible. At the same time, it is important that other kinds of information system concerned with drug response are developed to allow the feedback of relevant information that would facilitate malaria control through primary health care.

1.2.2 Resistance of vectors to insecticides

(a) Present global situation. At present, at least 57 species of Anopheles have been reported to be resistant to one insecticide or more in some parts of their geographical distribution. Six of these species have been reported to have become resistant in the last five years. Although most of the reports are of resistance to organochlorines, there are also instances of resistance to organophosphorus compounds, carbamates, and even pyrethroids (14).

It is significant that most cases of multi-resistance in important malaria vectors—for example A. albimanus in Central America, A. arabiensis in the Sudan, A. culicifacies in India, and A. sacharovi in Turkey—are associated with areas of intensive agriculture where large quantities of pesticides are applied, usually from the air (15). These repeated agricultural applications induce resistance since they contaminate all stages of a mosquito population. Selection pressure is strong since both larval and adult stages are affected, the former by the insecticide in the breeding-sites, such as irrigation and drainage ditches, and the latter by deposits on the vegetation on which both males and females rest.

(b) Factors involved in the epidemiological expression of resistance. Since the first appearance of the phenomenon of resistance in anophelines there has been controversy over its operational and epidemiological significance. In particular, the significance of the results of the WHO test method has been misunderstood, and it has been questioned whether the mortality/survival levels indicated by the test can be related directly to epidemiological impact.

The controversy persists, with claims that, on the one hand, continued use of an insecticide against a "resistant" mosquito
population has a useful epidemiological impact and, on the other hand, that such persistent use is a waste of insecticide. In this context it must be remembered that “resistance” has a variety of aspects—biochemical, genetic, operational, and epidemiological. The objective of vector-borne disease control is to assess the feasibility of gaining and maintaining control of the disease where the vector is showing some degree of resistance to the particular insecticide in question. The actual or potential epidemiological expression of the resistance is governed by a variety of factors, which can be divided into two main groups.

(i) Selection-related factors: these include the selecting chemical or chemicals, which may vary in sequence, being applied separately or together; the intensity of selection pressure and stage of selection (i.e., proportions of resistant heterozygotes and homozygotes), the effect on resistant heterozygotes and the implications of this; the target of selection pressure—larvae, adults, or both; the particular resistance mechanism selected, e.g., enhanced metabolism (which can be due to a variety of enzymes), reduced sensitivity (for example, of the insect nerve acetylcholinesterase), or reduced penetration; the resulting cross-resistance pattern; the proportion of a given population actually under selection pressure (e.g., there may be unselected immigration from untreated areas depending on whether there have been focal or blanket applications of the selecting insecticide); and the fact that the target population may be a species complex, the various components of which have different behaviour patterns and thus different degrees of exposure to the selecting agent.

(ii) Factors not related to selection: these include size of the parasite reservoir in the human population; coverage of the human population achieved by chemotherapy and personal protection; the broad environmental/climatic background and its modification due to, for example, development projects involving irrigation, changes in atmospheric humidity, changes in agricultural pattern (the latter often involving important ecoepidemiological factors such as change in man/animal ratio, migrant labour, resettlement with consequent change in immunity pattern of population), or population growth, (rural or periurban); and the quality of operations in general.

(c) Detection and monitoring. At present, detection and monitoring are based mainly on the application of WHO standard test methods, particularly the exposure of samples of the particular mosquito population to a discriminating dose of insecticide. This
simple test has proved its usefulness at the field level and is adequate for general detection and monitoring as well as demonstrating cross-resistance patterns. Current advances in biochemical test methods promise even greater accuracy in the characterization of resistance mechanisms.

(d) Policy considerations. Although insecticide resistance may have a serious effect on the malaria control strategy in some situations, particularly in areas of intensive agriculture, much appears to depend on the ecoepidemiological conditions prevailing in the area. Resistance has to be considered in relation to the various selection-related and selection-unrelated factors mentioned above before deciding on its actual or potential epidemiological impact. Where the major vector remains susceptible, DDT is still the insecticide of choice for use in indoor residual spraying.

1.3 Information for planning and evaluating antimalaria action

1.3.1 Evaluation indicators

Progress in antimalaria activities must be measured using indicators. These will vary depending on the short- and long-term objectives. The selection of indicators should depend on the local requirements of each programme.

There is an extensive range of variables that influence the malaria problem and of potential interventions for its control, and this means that indicators must be carefully selected, taking into account their relevance to the chosen objectives. One classification of indicators is outlined below:

(a) Indicators for definition of the problem and selection of control approaches. These indicators, which will be the basis for stratification, may have to include broad estimations or even qualitative information of a geographical, ecological, anthropological, social, and economic nature to complement specific demographic, health, and malaria information and, in some cases, even to replace the latter specific information in areas where it is not available.

(b) Indicators for the evaluation of progress in control and/or coincidental natural changes in the prevalence of malaria. Different types of indicator may be used for this purpose; the relative
importance of these will vary in relation to the stage of development of malaria control and of primary health care. They include:

(i) **General indicators of the health status of the population**—these include information concerning infant, childhood, or general mortality, proportion of low birth-weight, and other general attributes, as described in an earlier WHO publication (16).

(ii) **Indicators measuring progress in antimalaria operations**—these provide information concerning programme coverage and activities, the staff at all levels, utilization of tools (including insecticides, drugs, and perhaps in the future vaccines), adequacy of knowledge of the community health workers, and the use of health services by the population. In the early stages, these indicators may provide the only valid estimate of progress, since most indicators directly related to the malaria problem may be greatly influenced by the progressive incorporation of information from areas or population groups that vary significantly in malaria risk.

(iii) **Specific indicators of change in the malaria situation, and its causes**—these include:

— **general malariometric indicators**, such as notification of marked changes in mortality in a malarious area that may or may not be related to the disease, and changes in malaria incidence revealed by the traditional malariometric indices (based on quantitative information about the presence of malaria infection in a population or its more direct manifestations, such as “fever”, “fever and chills”, and splenomegaly). Information may be obtained from regular reports, either from the general health services or specific antimalaria services, or from special malariometric surveys. A traditional malariometric survey will give information suitable for the estimation of point prevalence indices such as parasite rate or spleen rate, which should be interpreted in relation to the representativeness of the sample on which they are based. It will often be difficult to calculate incidence or period prevalence from cases of clinical malaria, or parasitologically confirmed cases notified by the general health services, because of the problem of estimating the denominator. As mentioned above, most antimalaria programmes maintain surveillance systems that carry out active and passive case-detection based on blood examination of fever cases from which indices such as the annual blood examination rate, parasite (or species-specific) incidence rate, and slide-positivity rate are
calculated. Variations in coverage, presence of other causes of fever (such as arbovirus disease or influenza), logistic support for collection and transport of blood slides, and the quality of the laboratory examinations all affect the comparability of these indices; passive case-detection is considerably more efficient than active case-detection as a surveillance mechanism, and as a result consolidated rates calculated from changing proportions of active and passive case-detection and population surveys would lack comparability. Serological indicators of past and recent changes in levels of infection may be used, as may DNA probes and similar newly emerging techniques;

— entomological indicators relating to reduction in prevalence of adult or larval stages of the vector. These may be employed where vector control measures form part of the programme. Where appropriate, insecticide susceptibility tests should also be carried out. Sporozoite rates may be calculated by either microscopic examination of dissected glands or the use of new immunological techniques. This information may be useful as part of the epidemiological investigation or for planning or evaluating malaria control. Possible changes in vector behaviour may be checked by blood-meal analysis;

— social and economic indicators (see also section 1.3.2). These range from indicators assessing broad changes in a population to those affecting individual and household health behaviour. Social indicators that affect malaria interventions include population movements and changes in modes of agricultural production, while indicators affecting health behaviour can be assessed by changes in levels of knowledge and in the use of health services, and an analysis of the use of time by members of a family, particularly that of a wife relative to the extent that she assumes the duties of those who are sick;

— indicators of special technical problems arising during operations. These relate to reduced vector susceptibility to insecticides (for which standardized susceptibility tests are available), resistance of *P. falciparum* to drugs (for which standardized in *vivo* and in *vitro* tests are available), and adverse effects on spraymen following contact with certain pesticides and on patients following treatment with certain drugs (tests are available for both of these);

— indicators of change in the malaria status of particular population groups;
• in children: change in prevalence of fever, change in parasitaemia density and prevalence (assessed by microscopy, serology, DNA probes), behavioural and clinical changes (up to convulsions/coma), anaemia (indicated by haemoglobin levels and packed cell volume), and hepatosplenomegaly.
• in pregnant women: changes in birth weight of infants, rates of abortion, prematurity, perinatal deaths/stillbirths, and anaemia (assessed as in children), and parasitaemia density and prevalence in primiparae (assessed by microscopy, serology, DNA probes).
• in other adults: changes in prevalence of anaemia and hepatosplenomegaly, fever (crude indicator in non-immunes), and change in parasitaemia density and prevalence (assessed by microscopy, serology, DNA probes).

1.3.2 Social and economic determinants and methods for their evaluation

It is increasingly recognized that social and economic factors significantly influence the transmission of malaria and that a better understanding of these factors could lead to more effective and efficient use of the resources available for malaria control. In the past certain customs and behaviours tended to be seen as obstacles, and consequently as factors that must be modified. More recently, it has been recognized that social and economic factors may affect not only certain aspects of the transmission of malaria but also the design of control programmes.

In the development of control strategies, increased attention has been given to the multifactorial aspects of malaria epidemiology. It was within this context that a growing body of research, supported by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, has been undertaken and that work was begun by PAHO/WHO upon development of a conceptual framework of the social factors in the epidemiology and control of malaria.¹

This research is intended to help improve disease control through the inclusion of social, economic, and cultural factors in the planning and implementation of control activities. The two intermediate objectives that guide the promotion of this research are the

¹ Report of the Advisory Committee on Medical Research, Working Group on Social Science Health Research. (Unpublished WHO document PAHO/ACMR/21/5, 1982).
determination of the impact of social, cultural, demographic, and economic conditions on disease transmission and control, and the promotion of the design and use of cost-effective, acceptable disease control programmes and policies.

Among the studies focusing on the transmission of malaria, the main categories of variable identified have included:

— the migration of special population groups
— prevailing methods of production
— concern with the economic consequences of malaria
— attitudes and behaviour affecting transmission and control.

Attention has been given in some of these studies to the social and economic factors that may influence the cost-effectiveness of malaria control. The growing number of variables identified now includes attributes of the population to be served in addition to attributes of the programme to be used. In the former category, cultural values as well as housing and hygienic standards have been identified as factors partially determining the efficacy of antimalaria activities. Some studies have reviewed the contribution of different categories of malaria worker, particularly the community health worker.

(a) Social and economic factors in the malaria planning process. What is needed is a clearer understanding than is now available of the social and economic factors that influence the epidemiology and control of malaria. The requirements include:

— better delineation (stratification) of the malaria problem, including a more precise definition of areas with different levels of endemicity, a more precise definition of populations at risk, and a better understanding of the factors influencing malaria in different situations;
— improved understanding of which antimalaria measures are the most appropriate in different situations as well as the most cost-effective, including their timing and sequencing;
— improved understanding of how technically appropriate measures can be organized and are accepted within different community and local settings;
— improved sensitivity on the part of health workers to factors that can help them perform their jobs better, including recognition of high-risk situations/populations, selection of measures to apply in different social situations, and health education;
— increasing the likelihood of obtaining community participation
and thereby improving the quality of the results obtained from ongoing monitoring and evaluation of measures carried out;
— consideration of malaria control as a priority within the context of national development plans and the concomitant allocation of resources to carry out these activities.

A key concern for planning malaria control would be to optimize the availability of resources and their use in a timely, efficient, and useful manner. This may be difficult given the large number of potentially important factors, the complex way they may interrelate with each other, and, in general, the inability to extrapolate results obtained from one situation to another.

A consideration of the following questions could be used as the first step in the planning process:

(i) Is there any evidence that social and economic factors are significantly affecting epidemiological conditions? If so, in what way? What factors? In what situations? How many people are affected?

(ii) How do social and economic factors contribute to or interfere with the implementation of antimalaria measures? What is known about this relationship? Is it thought to be important? If so, in what way?

In relation to these questions, a number of indicators that may be pertinent to malaria control are being identified through research undertaken in several countries, and include the following:

(i) with respect to health conditions, indicators would include the pattern of seeking health care, access to primary health care and reference centres, and access to and utilization of basic health services;

(ii) with respect to social and cultural conditions, indicators would include awareness and educational level, as well as knowledge of and attitudes to malaria control;

(iii) with respect to living conditions, indicators would include type of dwelling (materials) construction, location in relation to mosquito breeding places, sanitation, and water supply;

(iv) with respect to economic conditions, indicators would include allocation of household time, direct and indirect costs incurred by the family, economic development projects, and income;

(v) with respect to production modes and processes, indicators would include work/ownership relationship, type of produce and size of production unit, employment of labour force, conditions of
labour camps, pattern of activities in relation to seasonality of malaria transmission, mechanization and technologies used, and the use of pesticides;

(vi) with respect to population movement, indicators would include types of movement (migration, mobilization, circulation), their magnitude and organization, characteristics of the migrants, living conditions, and causes for the movement.

Two steps are required to strengthen the work that has been done on social and economic indicators in this field. First, there needs to be a clear specification of the people at high risk for whom control programmes aim to provide protection, in order to determine the social and economic forces that influence the extent of their participation (for example, young children, pregnant women, migratory single labourers). Secondly, in relation to the research that has been undertaken, a systematic and thorough review is required in order to identify what has been learned, what methods have been useful when applied to specific problems, what methodological weaknesses have emerged that require priority attention, and what activities have been carried out and with what results.

1.3.3 Stratification for planning antimalaria action

In many cases, the same degree of reduction of the disease (malaria control) cannot be achieved simultaneously over the whole country because of administrative, operational, technical, and financial constraints. Even if uniform reduction can be achieved, different approaches and means may be needed in the various areas. Hence the requirement for stratification of the country, with the definition of different objectives for each area, and consequently the selection of appropriate control measures.1

Stratification, therefore, is a process that is intended to reduce and simplify a complex problem in order to facilitate its understanding and to formulate solutions. Generally speaking, stratification is the process of uniting strata (areas, populations, situations) that have in common a set of specified characteristics. Many factors that may be stratified contribute to the epidemiology of malaria, such as the distribution and relative prevalence of different species of Plasmodium, the distribution, abundance, and efficiency of vector

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species and their behavioural characteristics, the intensity of transmission, as well as ecological and geographical characteristics of different areas, social and economic conditions of the population, and climatic and meteorological factors that usually are not uniform throughout a country.

Stratification should be dynamic, accommodating both expected or unexpected changes; it should be based initially on whatever information is available. Every situation may be considered as epidemiologically unique given the focal nature of malaria, but the advantage of making the definition of a problem more precise is lost in the difficulties and delays in fitting operations to each “unique” problem.

Within the planning context, stratification is concerned with more than simply distinguishing the epidemiological forms of malaria in districts. Stratification should take into account factors that are frequently considered to be outside the domain of epidemiology, but which may significantly alter the decisions taken as to what should and can be done about the problem. Thus, for example, “strata” may be defined that highlight economically important production activities or economic development projects where malaria control may be a high priority for the country’s economy. Strata may also be defined taking into account the availability of treatment services or the difficulty of organizing epidemiological surveillance activities, i.e., factors that influence the type and extent of antimalaria measures that can be implemented and expected to have a measurable impact on the problem.

(a) Criteria for stratification. In order to delimit operationally homogeneous sub-areas (strata), the following main variables may be considered.

— Epidemiological variables such as the distribution and prevalence of parasite species, drug sensitivity of malaria parasites, distribution and abundance of vector species and their efficiency, insecticide susceptibility of vectors, seasonal patterns of transmission, the current endemicity or intensity of transmission, the potential intensity of transmission in the absence of control (on the basis of past observations).

— Climatic and geographical variables such as areas with similar meteorological conditions, arid zones, irrigated zones, forested zones, areas with or without good logistic facilities depending on the season.
— Socioecological and economic variables such as human ecology (occupation, housing, movement of population), urban areas contrasted with rural areas, agricultural practices (specifying pesticide use, irrigation, livestock), areas with agricultural development schemes or other social and economic development projects, and the distribution of basic health services and other major communicable diseases.

The specific variables to be used for stratification will differ according to the country or area, as well as the perceived nature of the malaria problem. The object of stratification will be to explore the diversity of each selected and relevant variable and to correlate the malaria problem with those considered to be the most relevant.

In carrying out the analysis of the information gathered for stratification, a wide range of procedures is possible, varying from the drawing-up of simple maps and tables to carrying out highly complicated statistical and mathematical analysis.

1.3.4 Surveillance in antimalaria programmes

(a) Existing systems of specific malaria surveillance. In malaria eradication terminology, surveillance has been defined as:

"...that part of the programme aimed at the discovery, investigation and elimination of continuing transmission, the prevention and cure of infections, and the final substantiation of claimed eradication. The individual functions of surveillance are case detection, parasitological examination, antimalarial drug treatment, epidemiological investigation, entomological investigation, elimination of foci by either residual spraying or mass drug administration, case follow-up and community follow-up".¹

In health practice, surveillance means putting a disease or a group of diseases under observation. It is a public health action aimed at collecting knowledge about the disease in the whole community, or in selected localities, in order to plan and implement measures aimed at reducing the effects of that disease on the health of the population. The gathering of information on malaria is normally based on the notification of clinically diagnosed and/or microscopically confirmed cases. Another aspect of surveillance is the epidemiological analysis of data, using a number of parameters on which data have

been collected. The collection of epidemiological data should be proportional to the capacity of the health service (primary health care), and to the intensity of, as well as the risk of increase in, transmission itself.

The surveillance activities carried out in different groups of malarious countries are as follows:

(i) Countries without organized malaria control: activities are limited to notification of the disease problem in urban and periurban areas by health establishments that usually depend on clinical rather than blood-slide diagnosis. The development of peripheral laboratory facilities is an important requirement for improved surveillance, as is the compulsory notification of cases (giving age-group, month of onset, locality) by all levels of the primary health care system. Parasite surveys might be undertaken for epidemiological studies.

(ii) Countries where organized malaria control was implemented after development of the general health infrastructure: multi-disease case-detection and treatment and epidemiological investigation procedures already in use should be improved to keep pace with the progress of the malaria intervention work that is being carried out by the general health services.

(iii) Countries where organized malaria services preceded the development of the primary health care system, and where the latter could be built upon the malaria service: here the original surveillance activities are generally still in use and in most cases should be readjusted according to the control objectives.

(b) Surveillance needs in malaria control programmes. Malaria surveillance as was conceived for the time-limited eradication programmes, has limited usefulness for control programmes. Seasonality and focality of transmission are obscured, while, by assuming responsibility for diagnosis and treatment, this type of surveillance has tended to make the general health services lose touch with, and interest in, the disease. Some aspects of this surveillance remain relevant to control programmes, however, and may be selected to follow locally evolving epidemiological situations.

1.3.5 Information and reporting systems for malaria control

(a) The present situation. In malaria control the design of information and reporting systems must be tailored to meet the
individual needs of each country. In view of the various situations and approaches used in malaria control it is impossible to provide a model that is universally applicable. This may partly explain why the consistency and validity of the information and reporting systems used by malaria control programmes vary considerably from country to country. The necessary improvements can be made using a “learning-by-doing” process so that the systems more appropriately monitor operational and epidemiological malaria control activities.

(b) Development or improvement of the systems. Certain common principles for developing or improving information and reporting systems may be summarized: (i) the information to be reported should be strictly related to the objective(s), activities, and result(s) of the activities; (ii) only data that is essential for the proper monitoring of the activities and that can be adequately processed and analysed at different levels should be collected; (iii) the type of data to be collected and the people responsible for collection should be clearly specified; (iv) if intersectoral collaboration is an integral part of the programme, the type and timing of the information to be provided by or forwarded to the collaborating ministries or agencies should be identified; (v) ad hoc forms, tables, graphs, etc., should be prepared and distributed in advance; (vi) data should be collected on a continuous basis to confirm progress or to identify shortcomings.

(c) Action to be taken prior to adoption of a reporting system for evaluation. This action includes: (i) evaluation of the existing information and reporting systems to assess their adequacy and reliability or to identify deficiencies; (ii) clear identification of the information needed for decision-making at different levels; (iii) assessment of the adequacy of the reporting forms or of the need for improvement.

(d) The content of the reports. At the country level the content of the reports may be divided into three main parts: (i) background information on the programmes; (ii) evaluation of field operations and epidemiological evaluation; and (iii) general appraisal.
1.4 The application of the malaria control strategy

1.4.1 Strategical approaches

(a) The tactical variants. The resurgence of malaria that occurred in many parts of the world, particularly in South-East Asia, between 1966 and 1976 made it necessary to reformulate control strategies. Four general approaches, or tactical variants were devised (in increasing order of complexity), relating to the variety of epidemiological, sociological, managerial, logistic, and financial resources existing in countries of widely differing developmental status. These approaches, were presented to and adopted by the Thirty-first World Health Assembly (1978)\(^1\) and were further developed at the meeting of the seventeenth Expert Committee on Malaria (I).

Tactical variant No. 1. Reduction and prevention of mortality due to malaria. The method envisaged was the treatment of all malaria patients with drugs. This variant is considered to be particularly relevant to those countries or parts of countries where malaria prevalence is high, illness is severe in children, social and economic status is low, and experience in malaria control work is limited. It is felt that the general health services should have the principal responsibility for this approach but that there should also be prompt distribution of the necessary drugs by all types of service and clinic, both public and private, and that community participation should also be encouraged.

Tactical variant No. 2. Reduction and prevention of mortality and morbidity, with special attention to a reduction of morbidity in high-risk groups. This variant calls for the prompt treatment of cases and the distribution of prophylactic antimalarial drugs on a regular basis to special population groups such as infants and young children, expectant mothers, schoolchildren, and special labour groups. In addition, vector control measures might be applied together with other protective measures, either individually or by communities. The technical guidance of the general health services would be necessary.

Tactical variant No. 3. The same as for No. 2, together with a reduction of malaria prevalence. This variant requires the

participation of a specialized antimalaria organization, capable of carrying out epidemiological evaluation and cost-assessment of long-term programmes. It should be aimed at achieving an epidemiologically feasible level of control while still remaining affordable in relation to other health priorities; this control would fall short of eradication.

**Tactical variant No. 4.** Countrywide malaria control with the ultimate objective of eradication. This variant involves keeping countries or areas where eradication has been achieved free from malaria, and vigilance in countries that are naturally malaria-free but are threatened by the introduction of the disease.

The report to the Thirty-first World Health Assembly suggested that these four tactical variants might be used: in the classification of malarious areas according to attainable goals; in the long-term planning of developing programmes starting with the first variant and then changing to other variants as the scope of the programme broadens; and in situations where different variants may be applied in different regions of the same country.

In 1979, in the report of the seventeenth Expert Committee on Malaria, the four tactical variants were discussed (1) as illustrative of the major possibilities of malaria control. It was stressed in the report that no single approach should exclude elements drawn from other approaches, since these four tactical variants should not be considered as the only possibilities. The Expert Committee also considered the variants to be “a sequence of goals and associated antimalaria methodologies” to be used as a framework within which each country may plan a control programme appropriate to its needs.

The present Expert Committee, while reviewing the reported experiences of countries in applying the four tactical variants for the purposes of planning malaria control, noted a number of problems. There had been a tendency to view the variants as mutually exclusive compartments, rather than as a flexible series of steps on which one or more methods might be placed, depending on local requirements as revealed by epidemiological stratification. While the problems in implementing the procedures recommended under each variant had generally been pointed out by national programme directors, the evaluative results and achievements of the procedures had not been adequately analysed or reported. Thus the variants, while serving to highlight the need to view malaria more as a disease problem than
as a parasitic infection, have not inspired countries to develop flexible approaches suitable to their individual needs.

As noted earlier, one of the main lessons drawn from the attempts to eradicate malaria has been the extent of the local variability, not only in the intensity of the problem but in its response to control interventions. The variants have helped to stimulate recognition of the problem of malaria and the multiplicity of approaches available for its control.

(b) Alternative strategic approaches. It is difficult and possibly not even desirable to provide a comprehensive global statement of antimalaria objectives, since these should be developed as part of the planning process relevant to each identified situation. However, it is possible to recognize that methods of attacking the problem can be graded according to their complexity and that these methods require a range of different resources and development activities to ensure the long-term maintenance of any results obtained. One possibility is to begin malaria control with a sophisticated attack on malaria transmission, as was attempted during the eradication programmes, and this has proved to be a successful approach in a few areas.

The tactical variants cannot be considered as a strictly required sequence, but they comprise a hierarchy of objectives, implying that a more complex plan of malaria control should not be adopted unless there is assurance that earlier objectives would be reached.

The application of an epidemiological approach to the selection of the range of objectives must take into account possible limitations imposed by the resources available and the capability of the infrastructure. Two substantially different approaches, aimed at attaining the objectives at both ends of the spectrum, may be identified:

— improvement in the general health services to ensure adequate diagnosis, accessibility to health care, and treatment for malaria cases, as well as to ensure the provision of adequate protection for the population at risk and the promotion of personal and community protection. This includes objectives such as reductions in mortality, in general malaria morbidity, and in duration of sickness;
— establishment of the capability for the long-term control of malaria transmission, this will require the planning of specific antimalaria actions designed to change the epidemiological
equilibrium. This includes the objectives of preventing epidemics, reducing the foci of *P. falciparum* malaria, and transmission control in selected areas or in the entire country.

The first approach would incorporate tactical variants 1 and 2, and the second approach variants 3 and 4. As an absolute minimum, the first approach will need to provide diagnosis and appropriate treatment for the sick, curative treatment and prophylaxis throughout pregnancy, and improved education to the population concerning the better use of health services, the non-tolerance of illness, and the use of personal protective measures. The second approach, involving planned interference in malaria transmission on a large scale, should only be considered if this will effectively change the epidemiological equilibrium and if this change can be sustained.

Intermediate objectives will require the progressive strengthening of the referral system and the development of a meaningful information system, as well as epidemiological surveillance with appropriate recognition of abnormal situations, delimitation of problem areas, and the provision of an adequate response. This will progress from the control of epidemics to their prevention, and to control of the most serious foci. It will include monitoring of problems such as drug resistance and evaluation of the response to control measures.

1.4.2 Development of antimalaria activities and their supporting, referral, and technical guidance systems

To achieve malaria control within the strategy of primary health care requires complete coverage of the population with peripheral care facilities supported by strong referral and technical guidance systems. The type and magnitude of each system depends upon the level of development of primary health care, and the stage of implementation of the malaria control strategy, as well as its relationship with other common health problems, the short-, medium-, and long-term objectives, and finally the availability of resources.

At present, according to the relative development of antimalaria services and health infrastructure, three groups of malarious countries or areas can be distinguished (see also section 1.1.1).

*Group 1* includes countries or areas where malaria is a serious problem but where the health infrastructure is very deficient and there is no organized antimalaria service. This group includes most
of Africa south of the Sahara where the antimalaria strategy should concentrate initially on providing the sick with treatment, particularly those who are in danger of dying.

*Group 2* includes countries or areas where the primary health care system is comparatively highly developed, but where specific antimalaria measures, as part of primary health care, are necessary in at least some areas.

*Group 3* includes countries or areas where organized antimalaria services have preceded the development of primary health care at the periphery. The development of primary health care will require the reorganization of the whole of the health system to support it. The antimalaria services should contribute to this development and in some instances may well form the basis for the development of primary health care, particularly at the periphery where it is often the only health service that is accessible to the whole population.

(a) **Organizational structure in implementing antimalaria activities through primary health care.** A well conceived and effective organizational structure is essential for efficient health service delivery. The types of organizational structure may be considered in relation to the three groups of malarious countries or areas mentioned above.

For countries in *Group 1*, it is necessary to establish a network of diagnosis and treatment facilities at the community level that will provide full courses of an appropriate curative drug to all patients suffering from malaria as well as courses of chemoprophylactic drugs during pregnancy. This network of facilities may be considered as an entry point to primary health care, and the responsibilities of this network could be expanded to recognize, and help in the solution of, other health problems. The antimalaria activities should be backed up by a referral system capable of reviewing the diagnosis in patients who do not respond to treatment and of detecting and treating resistant infections.

For countries in *Group 2*, malaria control activities are implemented as an integral part of the overall activities of the health system. In China, for example, the three-level rural health network is made up of the county hygiene and epidemic prevention stations, the township (commune) health centre, and the village (brigade) health station. With an organizational structure such as this the first contact with the community is at the village level where village health workers carry out antimalaria activities. These workers are

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monitored and supported by the second-line health workers who form part of an epidemic prevention group at the township level. This group is, in turn, supervised and supported by a parasitic disease control unit and epidemic prevention station at the county level. Above this level there may be a parasitic diseases control unit and there may be a provincial institute of parasitic diseases control supported technically by a central institute.

Administratively, the ministry of public health formulates the overall study and guides the provincial department of public health. The latter is the approving body for the plans made by the provincial institute within the framework of the general strategy formulated at the national level. The public health group at the county and township levels execute the plan and adjust the antimalaria activities to the overall health activities.

For countries in Group 3, it is important that malaria is kept at a tolerable level in areas with a high transmission potential. Failure to do this is likely to create an explosive situation. Thus, integration has been taking place rather cautiously. Several countries have consolidated under a common administration all the health activities that are carried out in a specialized (so-called vertical) fashion as far as the periphery. Some are planning to transfer to primary health care the responsibility for the diagnosis and treatment of cases, as well as the collection and analysis of routine epidemiological information. In some other countries, for example Thailand, the national antimalaria programme in areas stratified as high-risk or special-risk remains essentially vertical, whereas in areas stratified as low-risk there is almost complete integration into the general health services.

There seems to be a consensus of opinion on the following three points.

(i) For antimalaria action to be implemented effectively within the framework of a primary health care system it will require a broad network of peripheral facilities, an adequate number of staff possessing the necessary skills, and strong leadership oriented towards primary health care and preventive services. Where these requirements are met, most routine antimalaria activities, including some vector control activities, could be undertaken as an integral part of primary health care.

(ii) Where the health infrastructure is less well developed, or oriented primarily towards curative services, it may be more
appropriate for some vector control operations to be undertaken by a specialized unit until such time as the infrastructure can absorb these activities. If this is the case, then coordination with the health authorities at district and regional levels will be essential.

(iii) Where malaria is a high priority problem and where malaria control skills are available and primary health care very limited, a special project may be the only effective means of implementing antimalaria action. However, there should be a clear plan to incorporate antimalaria activities as part of the development of the primary health care system.

(b) **Supporting system for malaria control within the strategy of primary health care.** In order to develop primary health care programmes in a country, it is crucial to have a good supporting system, and for malaria control specific support is essential. Several aspects of support may be considered, and these are related to different levels of the system.

(i) **Support at the central level.**

--- **Support from the government:** successful primary health care development requires national commitment to this strategy. It needs strong political will and a strong leadership to take and sustain the necessary action. Continual motivation from the central level will be necessary to support the intermediate and local levels. The objectives of malaria control must be clearly defined at the national level according to the relative priority of malaria in relation to other problems as well as to the availability of manpower and other resources.

--- **Support from technical services:** a nucleus of specialized personnel will usually be required at the central level; these will be exclusively concerned with malaria or vector-borne diseases. These personnel should be responsible for planning, monitoring, and evaluating all antimalaria activities in the country; providing training to the intermediate level of health personnel; monitoring drug and insecticide sensitivity; and carrying out special epidemiological and entomological studies as needed. The size and structure of this nucleus of personnel may vary according to local conditions and available resources.

--- **Support from community organizations and from other sectors:** community participation and intersectoral coordination are two key requirements for primary health care as well as for malaria
control. In order to secure support from the community and other sectors, it is necessary to establish a coordinating mechanism at the central level.

Support from health-related sectors: the primary health care strategy clearly identifies intersectoral cooperation for health as one of its major components. The contribution of health-related sectors to antimalaria action is as important now as it was prior to the malaria eradication period. However, the precise roles of other sectors may differ significantly from those previously recognized because the emphasis is now on the adaptation, within the framework of primary health care, of antimalaria activities to the conditions prevailing locally.

It is particularly important that coordination at the central level, involving the main sectors concerned, should lead to coordinated action at the local and intermediate levels. The focal nature of the malaria problem and the emphasis upon seeking solutions based on a sound epidemiological understanding of the local situation underlies this concern. While the central level can establish the basic policies and principles that should govern intersectoral cooperation, the particular action to be taken needs to be worked out at lower levels involving appropriate expertise, and drawing upon, as needed, the higher levels and other special resources wherever available.

(ii) Support at the intermediate level. The important roles of the intermediate level are to identify local needs, to mobilize additional resources, and to stimulate community participation. Often, it is at the intermediate level that intersectoral coordination can be strengthened by establishing horizontal relationships with other agencies and sectors covering the same geographical area.

In a decentralized organization, the intermediate level is also involved in planning activities in addition to day-to-day management. The advantages of planning at this level are that more local situations can be considered and the expertise of the health personnel can be included in the planning process.

(iii) Support at the local level. The first level of contact between the population and the health system in primary health care is usually provided through community health workers acting either individually or as a group. The type of health worker involved will vary in different countries and communities according to the local needs and the resources available. These health workers are entrusted with a variety of duties and it is through them that essential
health care is made accessible to the population. Management at this level is important in order to keep the community health workers active, to secure community participation, and to implement the necessary antimalaria operations.

(c) Referral system. Primary health care activities in the community should be supported by successive levels of referral facilities. At these levels more highly trained staff are involved who are capable of dealing with a progressively wider range of specialized health interventions that require more sophisticated techniques than can be provided at the most peripheral level.

In a primary health care approach, health problems need to be considered more broadly than as just clinical problems of the seriously ill. Consequently, the range of services provided by the referral system must more comprehensive. Community health workers need continuing training, guidance, and supervision; community awareness of health must be promoted and guidance must be provided on appropriate sanitary measures, and on action that the community can take to control local disease problems; and liaison must be maintained with other sectors involved in social and economic development. All these are relevant for malaria control, but the following aspects are particularly important:

— identification of the appropriate level of clinical services for the prompt diagnosis and clinical management of severe, including complicated, malaria, and for the prompt correction of diagnosis and treatment for those who do not respond to the initial medication;

— establishment of a system whereby parasite resistance to antimalarial drugs can be recognized, evaluated, and monitored;

— establishment of a realistic information system and a core group to monitor the epidemiological situation at the periphery;

— establishment of a rapid capability for dealing with emergency situations, such as an outbreak of malaria, development of foci of drug-resistant malaria, and the appearance of *P. falciparum* in new areas or in areas unaffected for many years;

— identification of areas not responding to the malaria control strategy and help in resolving the causes;

— provision of continuous evaluation at the periphery;

— support and guidance for field research.
(d) **Technical guidance system.** Technical guidance is far more important in malaria control than in malaria eradication. The antimalaria measures to be used in a control programme should be selected according to the local epidemiological situation, the objectives determined by the government in relation to its development policy, other health problems, and the availability of health manpower and material resources. Since the measures applied will vary in different places, and in the same place at different times depending upon variation in epidemiological features, a better knowledge is needed to plan malaria control activities and an improved understanding of the plan is needed for its proper implementation.

Accordingly, while the antimalaria measures are carried out by or through community health workers at the periphery, technical guidance should be provided at higher levels by health workers with greater knowledge and skill who are capable of analysing and assessing the existing problems at lower levels. Such guidance may be provided through various activities:

— training and refresher training;
— planning and evaluation of antimalaria measures;
— supervising the antimalaria activities at lower levels;
— assessing the epidemiological situation and carrying out epidemiological research;
— discussing specific technical problems at regular meetings;
— participating in actual field operations in representative areas and analysing the impact of antimalaria measures on the malaria situation;
— analysing information received.

In China, for example, expert technical guidance is provided by technical institutions to the more peripheral levels. At the central level, there is a special committee on malaria research, consisting of leading scientists of various disciplines as well as epidemiologists and malarialogists, that deals with advanced research relevant to malaria.

In order to achieve malaria control within the strategy of primary health care, measures other than those that have a direct impact on malaria transmission are equally important, such as: (i) environmental modification to improve irrigation, and rearrangement of paddy fields and of animal shelters; (ii) improved housing conditions, ventilation, and siting of human settlements; (iii) a
change from sleeping out of doors to sleeping indoors; (iv) popularizing the use of bed-nets and other measures for personal protection; and (v) encouraging the sick to seek medical care.

1.5 Malaria control activities and their implementation as part of primary health care

1.5.1 Diagnosis and treatment

The most basic antimalaria activity is the opportune diagnosis and appropriate treatment of malaria.

(a) There is a need in most malarious areas to institute treatment based on a clinical diagnosis. It is important, therefore, that the clinical diagnosis be defined beyond mere fever (subjective fever or temperature) and that simple fever protocols be established in order to identify, for example, acute respiratory infections, localized infection, and defined epidemic diseases, so that by a process of elimination antimalarial drugs may be administered for fevers of unknown origin (i.e., that do not fit into any defined category). In highly endemic areas, antimalarial drugs should be given to all young children with fever since malaria infection will be a complicating factor.

(b) Such treatment, prescribed on the basis of a very unspecific diagnosis, should be with drugs that are very safe, and in circumstances where severe cases and treatment failures can be treated with second-line drugs or by a parenteral application through the referral system.

(c) The use of these second-line drugs should be based on a specific diagnosis that can be made, at present, by light microscopy, but perhaps in the future by the use of DNA or RNA probes.

(d) In areas where the frequency of RIII-type resistance makes treatment with first-line drugs such as chloroquine or amodiaquine too risky at the periphery, it will be necessary to bring microscopic diagnosis to the periphery. Such a situation has been reached in Thailand and has been solved by the establishment of malaria clinics (17).

(e) Malaria clinics, each staffed with at least one microscopist and serving 50 000–100 000 people, have been established in problem areas throughout the malarious sectors of Thailand. They provide free and immediate blood-smear examination and appropriate treatment according to established drug regimens adapted to local
conditions. These clinics also have a follow-up mechanism for
treated positive cases. The high rate of detection of cases of the
malaria clinics compared with their low cost indicates that they are
very cost-effective.

1.5.2 Antimalaria protection for pregnant women, infants,
and children

(a) Pregnant women. Falciparum malaria in pregnancy frequently
constitutes a grave risk to the mother and the fetus. The risks for the
mother appear to be greatest in areas of unstable transmission.
Pregnant women with falciparum malaria are particularly likely to
develop severe manifestations and complications. In areas of high
endemicity both the clinical symptoms and the levels of parasitaemia
are worse in primigravid compared with multigravid women with
malaria.

(i) Pregnancy and malaria endemicity. The harmful effects of
malaria in pregnant women within a community are determined by
the degree of endemicity of the infection and by age-specific levels
of immunity acquired through exposure to infection (18). In tropical
Africa, where infection is present throughout the year, malaria is
holoendemic and is considered to be stable. In contrast, the Indian
subcontinent, South-East Asia, the western Pacific, and South
America are generally considered to be areas of unstable malaria.
The dominant parasite in regions of stable malaria is P. falciparum,
while this species and P. vivax are important and frequent in areas
with unstable malaria.

Pregnancy increases the risk of malaria in women. However, in
highly endemic areas, the level of risk is moderated by the parity and
immune status of the individual.

(ii) Pregnant women in regions of stable malaria. Indigenous
women in stable malarious areas usually have some immunity to
malaria. Pregnancy is associated with an increased susceptibility to
severe infection. The incidence of infection is highest during the
fourth and fifth month of pregnancy and primigravid women are at
greatest risk. Parasite density is higher in primigravid women than
in multigravidae, and they tend to develop severe anaemia owing to
the destruction of erythrocytes and the depression of erythropoiesis.
The prevalence of parasitaemia appears to be at its peak at 13–16
weeks of gestation, and subsequently falls (19).
The prevalence rates of placental malaria in tropical Africa are commonly between 20 and 34% (18, 20). Heavy infection of the placenta with *P. falciparum* is common in primigravidae. The pathological changes observed indicate that *P. falciparum* malaria damages the placenta and interferes with the nutrition of the fetus. Consequently, malaria in pregnancy leads to intrauterine growth retardation and small-for-gestational-dates infants, the mean singleton birth weight being reduced by 55–310 g in different studies. Mean parasite densities are greater in placental than in peripheral maternal blood. Newborn infants of mothers with parasitaemia do not show parasites in their peripheral blood; this supports the view that congenitally acquired malaria in infants is rare in highly endemic malarious areas.

(iii) *Pregnant women in regions of unstable malaria.* In regions of unstable malaria, pregnant women suffer severe parasitaemia leading to high rates of abortion and fetal death if the disease is acquired in early pregnancy. Stillbirth, premature labour, and maternal death seem more likely to occur if acute malaria occurs during the third trimester. Women of all parities appear to be at risk of infection in areas of unstable malaria, and maternal death has been reported among multiparous women. However, the women at the greatest risk are primigravidae during the second and third trimester. The mortality rate due to cerebral malaria in pregnant women reaches 40% in some areas, while the recurrence of premature labour and placental insufficiency often leads to fetal death (21). Congenital malaria has been reported in the indigenous population of South-East Asia (22).

(iv) *Antimalaria protection for pregnant women.* Antimalarial drugs for chemoprophyaxis should be given to pregnant women in malarious regions. The regular administration of safe and effective drugs will prevent life-threatening attacks of acute malaria in the poorly immune pregnant woman and will protect the fetus from the consequences of maternal fever, anaemia, and placental dysfunction.

On the initial visit, a curative dose of an antimalarial drug should be given since many pregnant women have parasitaemia when they first present at an antenatal clinic. The drug administered should be safe, non-teratogenic, and effective. The combination sulfadoxine/pyrimethamine is not recommended for chemoprophyaxis, and the safety in pregnancy of some of the newer drugs has not yet been established.
It is appreciated that in some malarious areas the provision of chemoprophylaxis to pregnant women may not be feasible. In these situations, it is imperative to provide access to prompt diagnosis and appropriate treatment.

(b) Infants and small children. Falciparum malaria infection of indigenous children during the first 5 years of life can cause severe and potentially fatal illness, particularly in highly endemic areas. In the early months of life the manifestations are usually mild, with low-grade parasitaemia, probably because of passive immunity acquired from the mother. The parasite rate increases with age during the first 3 months of life to 1 year of age, and the rate persists at a high level during early childhood (23). By school age, a considerable degree of immunity has been developed and asymptomatic parasitaemia can be as high as 75% in children of primary school age (24). In areas of low endemicity, however, where the immunity in the indigenous population is low, severe infection occurs in all age groups including adults. Immunity may be reduced by the use of corticosteroids and cytotoxic drugs, and severe malaria may occur in children and other age groups who otherwise would be expected to have mild or asymptomatic infections.

The classical fever pattern seen in non-immune adults is not common in children suffering from malaria. Fever is high (38–40 °C) and continuous, with the result that some susceptible children have febrile convulsions. Rigors may occur in one-third of children infected with P. vivax. Nausea, vomiting, and diarrhoea are common gastrointestinal symptoms. Anaemia (Hb < 100 g/l) is usual, often accompanied by a raised reticulocyte count as a result of haemolysis. Jaundice is detectable in one-third of the children. Hepatomegaly with tenderness of the liver on palpation is a frequent finding. Similarly, the spleen is often enlarged and can be palpated.

In highly endemic, stable malarious areas, children may die of acute general infection or cerebral malaria. Some achieve a relative tolerance to plasmodial infections after several attacks; in these children the clinical manifestations of malaria may be mild.

Mass prophylaxis in children under 5 years old is no longer recommended for the following reasons:

— experience shows that it is impossible to achieve continuous suppression in a significant proportion of the population;
— it may interfere with the development of protective immunity;
— it may accelerate the development of drug resistance;
— it uses scarce resources that may be better used for treatment;
— it might increase the risk of retinopathy occurring during the lifetime of the individual.

In these circumstances, it is preferable to provide curative treatment whenever and wherever it is required, ideally through a primary health care system that provides prompt diagnosis and adequate treatment.

1.5.3 The management of severe and complicated malaria

(a) Diagnosis at various levels of the health service. A parasitological diagnosis of malaria should be carried out whenever diagnostic and clinical facilities allow. However, a practical or operational definition of severe falciparum malaria is required as a basis for treatment. The type of definition that can be established will depend on the competence of the health care personnel and on the laboratory and other facilities available (Table 2).

Table 2. Definition of severe malaria at different grades of clinical competence

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Grade 1*</th>
<th>Grade 2 (first referral)</th>
<th>Grade 3 (second referral)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Too weak to walk (in absence of obvious cause)</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cerebral malaria</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Vomiting after oral treatment; or diarrhoea</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Bleeding and clotting disorders</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Severe anaemia</td>
<td>+/−</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Jaundice</td>
<td>+/−</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Circulatory collapse</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Haemoglobinuria</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Fluid, electrolyte, or acid-base disturbances</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Complicating/associated infections</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Exclusion of other diagnoses</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Parasitological diagnosis</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hyperparasitaemia</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*Reasons for referral include failure to respond to initial treatment.

†Confusion, drowsiness, fits.

‡Exclude meningitis (neck rigidity, photophobia).

§Exclude meningitis (lumbar puncture).

*Defined as parasitaemia >5%. In some areas detection of parasitaemia >2% is possible at the periphery and may be a reason for referral.

1 WHO. MALARIA ACTION PROGRAMME. Severe and complicated malaria. Transactions of the Royal Society of Tropical Medicine and Hygiene, 80 (suppl.): 1–30 (1986).
The extent to which patients may be treated will depend upon the level of medical capability. At least three grades of diagnostic and therapeutic facilities may be distinguished.

Grade 1 (the most peripheral)—Staff receive basic training only; this does not permit them to elicit or interpret complicated medical histories, or to carry out more than a superficial examination (without instruments), or to apply clinical judgement. There are no laboratory facilities. Only oral medication (or suppositories) may be used. Injections cannot be given.

Grade 2 (first referral or intermediate level)—Paramedical staff have received more training than Grade 1 staff. Simple examinations using stethoscope, thermometer, sphygmomanometer, etc., are possible, and some degree of clinical judgement may be applied. Simple laboratory facilities are present that may include microscopic examination, dipstick testing of blood, etc. Parenteral treatment by intramuscular or subcutaneous injection, but not by the intravenous route, is available.

Grade 3 (second referral: hospital or central level)—A trained physician is available and full clinical assessment is possible. Laboratory tests include blood-counts and simple biochemical tests. Radiography is available. Intravenous treatment may be given.

Parasitological examination of blood should be available at the first referral level, and should be incorporated into the diagnostic process as early as possible. The presence of malaria parasites in the blood may be detected by routine thick blood-film examination when the density of parasites is 4 or more per mm$^3$ of blood, provided that 100 fields are examined by a competent microscopist.

The interpretation of parasitaemia as an element of diagnosis of a severely ill patient should take into account the following considerations.

(i) Semi-immune individuals may harbour malaria parasites without presenting any symptoms of disease.

(ii) There is generally a correlation between density of parasitaemia and the severity of malaria (25). Studies have shown that the death rate due to falciparum infections rises steeply as the parasitaemia exceeds 100 000 parasites per mm$^3$ of peripheral blood. There is approximately a 1% mortality rate in patients with a parasite count below this level, and this rises to more than 50% with parasite counts that exceed 500 000 per mm$^3$. Any level of
parasitaemia above 250,000 per mm$^3$ (about 600 parasites per microscopic field, in a thick film, or $>5\%$ of red blood cells in a thin film) should be taken as a sign of severity that requires emergency treatment; in a similar way the presence of schizonts in the blood should be considered a sign for emergency treatment.

(iii) While high parasite densities can be equated with severity, the reverse is not always true, particularly in non-immune individuals. In *P. falciparum* infections, the parasite becomes sequestrated in the internal organs as it matures and, therefore, the density of the peripheral parasitaemia changes cyclically. In infections where *P. falciparum* matures synchronously, parasite densities in peripheral blood may be scanty or even absent during the sequestration period. Thus, it is important to examine serial blood films at intervals of 6–12 hours until parasites are diagnosed or until recovery occurs.

Self-medication or chemosuppression may reduce parasitaemia below the detectable threshold, making it necessary to examine serial blood films for as long as the diagnosis remains in doubt. In all these situations, identification of pigment inside leukocytes is a useful indication of the presence of malaria parasites.

(iv) Microscopic diagnosis of malaria requires a degree of technical precision during the preparation of the blood slide, its handling, and staining, as well as competence and care on the part of the microscopist; the optical quality and illumination of the microscope are also important. In addition, the accuracy, speed, and manner of reporting the laboratory findings may greatly influence the outcome.

(b) *Management at various levels of the health service.* The responsibilities of various levels of the health services in the management of severe and complicated malaria will differ, depending on the degree of training and competence of the personnel as well as on the availability of laboratory diagnosis and parenteral medication.

At the peripheral level (Grade 1) there is usually a health post attendant or a volunteer village worker present. The principal responsibility at the periphery is the prompt diagnosis and adequate treatment of individuals with fever. At this level, management of severe and complicated malaria involves the rapid recognition of severity and the need for referral. The criteria for referral that should be recognized by a community health worker may include (i)
confusion, abnormal sleepiness, coma, seizures; (ii) a patient suspected of having malaria who is too weak to walk; (iii) abnormal bleeding; (iv) jaundice and/or marked anaemia (where these can be recognized); (v) inability to take oral medication; and (vi) failure to respond to initial treatment.

At the intermediate level (Grade 2) The trained paramedical personnel cannot adequately manage extremely severe cases and these must be referred.

There are three major principles for the management of severe and complicated malaria at this level; (i) recognition or confirmation of severe malaria; (ii) rapid referral when necessary; and (iii) intramuscular injection of antimalarials. Appropriate management of seizures and hyperpyrexia, and nursing care, is possible at this level.

At the central level (Grade 3) the most sophisticated medical management of severe and complicated malaria is possible. Parasitological diagnosis is always available.

1.5.4 Guidelines for the use of drugs in malaria control

The use of drugs in malaria control is for the treatment of individual cases and for the prevention of clinical malaria through chemoprophylaxis. Both approaches operate at the primary health care level, the aim being to cover as much of the target population as possible.

(a) Treatment. Use of the drugs currently available for the treatment of suspected or confirmed cases of malaria is summarized below, and in greater detail (together with pharmacokinetics, toxicity, and other aspects) in the report of a recent WHO Scientific Group (7).

(i) Chloroquine. Chloroquine is the drug of choice for the treatment of suspected or confirmed malaria in places where there is no known resistance or even in areas with R1-type resistance. It has been customary in treating semi-immune individuals to use single doses of 10 mg of chloroquine base per kg body weight, but although this may clear the blood of most of the susceptible parasites it may not adequately remove less sensitive parasites. Even in areas where there is, at present, no evidence of overt chloroquine resistance, there appears to be some diminishing sensitivity to the drug (26). In order, therefore, to slow down the appearance of resistance and also to ensure adequate treatment for patients in
whom the parasitological response cannot be monitored, it is advisable to use the full course of treatment consisting of 25 mg of chloroquine base per kg, given over 3 days.

Other drugs in the 4-aminoquinoline group may be used to replace chloroquine. The best known of these is amodiaquine; this has been shown to be somewhat more active than chloroquine against sensitive strains of \textit{P. falciparum} and it also retains activity against some parasites possessing R1- or RII-type resistance to chloroquine (27).

In highly endemic areas where chemotherapy is used only for clinical cure and to reduce mortality with no expectations of influencing transmission, an effective schizontocide alone is given, since there is no need for additional gametocytocidal therapy against \textit{P. falciparum}, or antirelapse therapy against \textit{P. vivax} or \textit{P. ovale}.

(ii) \textit{Sulfadoxine/pyrimethamine}. In areas where there is a high level of resistance to chloroquine, sulfadoxine/pyrimethamine is the drug combination of choice for the second-line treatment of suspected or confirmed malaria if there is either no established resistance to it or the resistance is low-grade or infrequent. Unfortunately, the use of this combination for second-line malaria chemotherapy in areas with widespread resistance of \textit{P. falciparum} to chloroquine has been followed by the appearance of, or increase in the level or frequency of, resistance to the combination. Moreover, \textit{P. vivax} is intrinsically relatively insensitive to sulfonamides and rapidly develops resistance to pyrimethamine: resistance to the combination is therefore common in \textit{P. vivax}. It is desirable, before deploying the combination on a large scale, to determine the sensitivity of the local strains of \textit{Plasmodium} to it.

(iii) \textit{Mefloquine and mefloquine with sulfadoxine/pyrimethamine}. Where there is established resistance to both chloroquine and sulfadoxine/pyrimethamine, recourse may have to be made to mefloquine. Extensive clinical trials of mefloquine in many parts of the world have demonstrated its safety and efficacy against chloroquine-resistant \textit{P. falciparum}.

Field trials of mefloquine have revealed a few instances of resistance or reduced sensitivity to the drug. In some cases, the resistance might be intrinsic and unrelated to exposure to mefloquine. Resistance has also been observed in experimental \textit{P. berghei} infections in mice, and in this model the addition of sulfadoxine/pyrimethamine to mefloquine was found to delay the development of resistance. The combination of mefloquine with
sulfadoxine/pyrimethamine has, accordingly, been subjected to extensive trials in man.

(iv) *Quinine*. Treatment of suspected or confirmed cases of malaria poses a major problem to health authorities in areas where *P. falciparum* is resistant to the 4-aminoquinoline compounds and the sulfadoxine/pyrimethamine combination. In countries where mefloquine has not yet been registered for use, the alternative drug commonly administered is quinine. Unfortunately, treatment with quinine is expensive, the drug is not widely available, and it is relatively toxic. Quinine cannot, therefore generally be distributed at the most peripheral level of the health service.

For uncomplicated infections, quinine is given orally, in 3 divided doses, daily for 7 days. Alternatively, quinine may be given for 3 days in association with tetracycline, the latter to be given for at least 7 consecutive days.

(v) *Primaquine*. Primaquine is a tissue schizontocide and gametocytocide. Gametocytes of *P. falciparum* that are resistant to other drugs remain sensitive to primaquine. Primaquine is used sequentially with a blood schizontocide in *P. falciparum* infections in areas where it is important to reduce the chances of transmission, since following its administration the patient is no longer infective to mosquitoes. This kind of treatment for *P. falciparum* infections may be necessary in areas with seasonal infection, during epidemics, and to prevent the re-establishment of infection in areas from which it has been previously eliminated. In all these instances, chemotherapy is usually combined with vector control activities.

Primaquine is also given as a tissue schizontocide to prevent relapse in *P. vivax* malaria. Such use is indicated only in areas free of malaria or in areas where transmission is considerably reduced.

(b) *Chemoprophylaxis*. Experience has now shown that it is exceptional for the large-scale, prophylactic use of antimalarial drugs in a highly endemic area to have a lasting effect on the level of endemicity or rate of transmission of the disease. On the other hand, such programmes have often diminished the sensitivity of the parasites to the administered drug and resulted in the appearance of drug resistance. Furthermore, in most malarious areas the logistics of covering the entire population present insurmountable problems. Consequently, chemoprophylaxis as a malaria control strategy should aim at reducing morbidity in groups that are at high risk from
severe and complicated malaria, notably pregnant women and non-immune visitors.

Other high-risk groups for which chemoprophylaxis may be desirable are semi-immune or non-immune personnel living temporarily in closed communities in endemic areas, for example, labour forces, police and army units, and refugees in camps. It is always desirable to combine chemoprophylaxis with vector control measures in order to reduce transmission in such communities and delay the establishment of drug resistance.

The drugs currently used for chemoprophylaxis are:

— chloroquine or amodiaquine, in areas where the 4-aminoquinolines are still effective;
— sulfadoxine/pyrimethamine: however, because of evidence of severe toxic reactions associated with the use of this drug combination, it is no longer recommended for prophylaxis (28);
— proguanil: this drug is now being reconsidered for prophylactic use after a long period in which it was thought by some to be of little value because of resistance of \( P. falciparum \) to it. Recent observations have shown that proguanil given alone at a dosage of 200 mg daily or in combination with 300 mg of chloroquine base given once a week (these are the adult doses, to be prorated for children) provides protection in a high proportion of non-immune residents of malarious areas. Proguanil has a weak blood schizontocidal action against all species of plasmodia, but its prophylactic effect on \( P. falciparum \) may be due mainly to activity against the pre-erythrocytic stage of the parasite.

1.5.5 Vector control activities within the context of primary health care

Vector control is still, and will remain for some time, one of the primary weapons to control malaria in many endemic countries. Changes in the strategy of malaria control through primary health care have, of necessity, brought about certain changes in the implementation of vector control measures. Although environmental and biological measures are the ideal methods, the use of insecticides still remains the most practical and widely used method for malaria vector control. However, there is an increasing trend towards the use of self-protection devices, community participation, and integrated methods of vector control. Increasing problems due to the appearance of resistance to insecticides and
behavioural changes exhibited by some anophelines have encouraged the implementation, albeit limited, of biological and environmental methods to reduce dependence on chemical insecticides.

In view of the flexible approaches now required through primary health care, more intensive studies on malaria epidemiology, in general, and vector ecology, in particular, will be required in order to utilize or develop successful integrated control approaches. This means that primary health care workers will need guidance from a central group of experts as has been recommended by the WHO Expert Committee on Vector Biology and Control (29).

Before embarking upon often complex and expensive vector control activities, affected countries should identify priority control areas, consider the local epidemiological situation including social and economic features, and select specific measures based upon the technology available. The latter should be both scientifically appropriate for the solution of the problems and applicable at the primary health care level. The cost should be within the capacity and resources of the health system since it will usually be necessary to sustain and maintain such activities for long periods.

Some vector control activities that are based on currently available techniques, and that can be implemented within the primary health care approach, are given below and in Table 3.

(a) Measures to reduce man–mosquito contact. Measures to reduce man–mosquito contact are important at the household and community levels. Their use is of particular importance in those areas where the vector cannot be effectively controlled by other means.

(i) Individual protection against mosquitoes. The use of bed-nets, preferably impregnated with safe, long-lasting, and repellent insecticides, and various repellents such as mosquito coils, may be considered for protection in all situations, including houses in poorer areas; screening of houses and filling gaps in walls are often only feasible in permanent structures. The impregnation of bed-nets with a knockdown residual insecticide such as permethrin emulsifiable concentrate (0.08–0.2 g of active ingredient per m²) not only provides individual protection, but may also reduce malaria transmission in the village. Promotion of these methods is needed, together with health education, especially through community action. Knowledge about the use of safe and effective products, and
Table 3. Examples of malaria vector control measures for individuals and communities

<table>
<thead>
<tr>
<th>Type of activity</th>
<th>Individual action</th>
<th>Community action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction of man-vector</td>
<td>— Simple or insecticide-impregnated mosquito nets and wall mats</td>
<td>— Site selection of village</td>
</tr>
<tr>
<td>contact</td>
<td>— Screening of houses/bedrooms</td>
<td>— Deforestation and</td>
</tr>
<tr>
<td></td>
<td>— Protective clothing to prevent mosquito bites</td>
<td>— Clearance of undergrowth in the villages and</td>
</tr>
<tr>
<td></td>
<td>— Use of repellents to prevent mosquito bites</td>
<td>— Dwellings (specific to Anopheles balabacensis s.l. and A. punsettii)</td>
</tr>
<tr>
<td></td>
<td>— Use of mosquito coils</td>
<td>— Vector deviation by siting of cattle sheds away from human dwellings (specific</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Zoophilic anophelines)</td>
</tr>
<tr>
<td>Destruction of</td>
<td>— Use of fill-gun or aerosol packs</td>
<td></td>
</tr>
<tr>
<td>adult mosquitoes</td>
<td></td>
<td>Indoor residual spraying of chemical insecticides</td>
</tr>
<tr>
<td></td>
<td></td>
<td>under proper supervision</td>
</tr>
<tr>
<td>Destruction of larvae</td>
<td>— Destruction or removal of small breeding sites</td>
<td>— Larviciding</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Rearing and release of larvivorous fish</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Flushing and cleaning of drains</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Removal of algae and other growth from ponds</td>
</tr>
<tr>
<td>Source reduction and</td>
<td>— Covering water containers</td>
<td>— Community clean-up campaign to remove</td>
</tr>
<tr>
<td>source alteration</td>
<td>— Filling in breeding sites</td>
<td>— Rubbish and water-retaining debris</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Intermittent irrigation of rice fields</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Filling of vacant plots and pumping out of water</td>
</tr>
<tr>
<td></td>
<td></td>
<td>— Land reclamation</td>
</tr>
</tbody>
</table>

assurance that they are locally available, can be promoted through health services personnel, community shops, and through government distribution channels.

(ii) Site selection. The setting and design of new settlements and villages should receive special consideration. This applies to communities displaced from areas to be flooded by new dams, and to the resettlement of populations in newly irrigated areas and those moved from drought-stricken areas. In addition, consideration should be given to the siting of camps for immigrant labourers, nomadic refugees, and tourists. Whenever feasible, new settlements should be sited as far as possible from actual and potential mosquito breeding sites. The flight-range of vectors and potential biological or geographical barriers are among the factors to be considered. Such considerations are difficult in those countries
where the government policy is to develop jungle areas or to resettle populations for demographic reasons.

(iii) Deviation of vectors to animals. Provision for the deviation of vectors to animals should be incorporated in the design of new agricultural settlements and development projects. It should be part of the duties of primary health care workers and their supervisors to advise the population on the selection of sites for herds of cattle to rest overnight. The areas chosen should be on the periphery of the village or camp, situated between the settlement and mosquito breeding sites to allow the greatest possible opportunity for mosquitos to take their blood-meal on the cattle in preference to man.

(b) Insecticide spraying. The methods used include house spraying with residual insecticides to reduce vector longevity and outdoor space-spraying to reduce vector populations quickly (30). Special consideration should be given to:

— the safety of the measures, considering hazards both to the population and the environment;
— the acceptability of the measures under local conditions; and
— the long-term cost of the programme and the prospects of being able to maintain it.

House spraying with a residual insecticide could be considered by national health authorities where the health infrastructure is relatively well developed and resources are available. It may also be used in localized areas where there is either a particularly high endemicity, or the risk of, or an actual outbreak of, an epidemic (as is often the case when imported labour is used for development projects such as hydroelectric dams, irrigation, resettlement projects, etc.). Residual spraying should not usually be carried out in urban areas, other methods being more appropriate. Some countries (for example, Ethiopia, Sudan, Thailand, Viet Nam) have been able to mobilize communities to participate in spraying activities using appropriately trained community workers or volunteers. The use of community members as spraymen has increased the efficiency of spraying operations in some countries but has led to failure in others. Community spraying also reduces the individual worker’s contact with insecticides and therefore the incidence of toxic effects. Such an approach is not necessarily cheaper and requires a high level of motivation on the part of the community, as well as good supervision and support from the health services.

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Outdoor space-spraying may be necessary for a rapid reduction in the prevalence of infected mosquitoes. To achieve maximum benefit from this expensive measure, it must be carried out at the appropriate time and frequency; these will depend on the habits of the vector and on the insecticides used. These operations must be undertaken by a highly specialized unit, which many countries will be able to afford only for periurban areas, national development projects, pilgrimage or disaster areas, and for the temporary protection of organized groups of non-immune migrants residing in highly malarious districts.

(c) Control of mosquito breeding. Control of mosquito breeding is only useful and effective in certain cases, such as urban areas, irrigation schemes, and some arid rural areas. The measures used include larviciding with chemical larvicides, the use of biological agents and environmental manipulations, and modifications using appropriate engineering methods (such as drainage).

The WHO Manual on environmental management for mosquito control (31) lists techniques that may be used. The choice of method depends on the character, number, and size of the breeding places. Some of these activities require a considerable initial investment as well as specialized services to maintain them. In towns and large irrigation schemes, they should be implemented as an integral part of the development process. Provision should be made for the creation of specialized bodies under the technical supervision and guidance of the town council or project authorities for their follow-up, and to encourage the active involvement of communities.

Although a reduction in vector breeding generally requires considerable resources and technical competence, this does not apply to relatively simple measures such as peridomestic sanitation, filling of small water collections and ditches in and around villages, removal of unwanted water by simple drainage, and the proper management of small-scale irrigation systems. These activities, if carried out continuously through the coordinated efforts of members of the community, may result in a permanent reduction in malaria transmission and facilitate the involvement of the community in other antimalaria actions.

(d) Integrated vector control measures. Integrated vector control has an important place within the primary health care strategy (29). It involves the use of all appropriate scientific and management techniques to bring about an effective degree of vector suppression
that is cost-effective. It is also very important that the effectiveness of all the methods in reducing malaria morbidity should be carefully assessed to avoid wasting valuable resources.

(e) Intersectoral coordination. Effective malaria vector control within the primary health care system requires a high level of coordination between public and private sectors of the community including construction industries, health departments, universities, public works departments, railways, new media, and voluntary services. The formulation of such organizational and intersectoral approaches, which provide a framework for environmental management so that development projects and the associated ecological changes do not favour increased malaria transmission, is important and is one of the terms of reference of the Panel of Experts on Environmental Management (PEEM).

1.5.6 The use of epidemiological information in malaria control

At the most peripheral level, only essential epidemiological information should be collected. The decision to ask community health workers or dispensary or health centre staff to collect specific information should be made with due consideration of their other responsibilities and with the knowledge that the resources exist to analyse the information and to respond appropriately.

There are two main problems concerning which epidemiological information should be collected at the periphery and analysed on a regular basis: a change in the response of malaria infections to the antimalarial drugs being used; and the occurrence of an epidemic.

(a) Monitoring the response of malaria to drugs. The first evidence of resistance will be reports of individuals who fail to respond to drug treatment. Since the principal responsibility of the health services in areas where malaria is a public health problem is to provide prompt diagnosis and adequate treatment, it is important to develop ways of detecting treatment failures (for example, persistence of fever 3 days after treatment), and then to take appropriate action.

At the intermediate level of the health services, information is required to perform the referral and supervisory activities associated with malaria control. For patients who have been referred because of treatment failure, the action taken would include investigation of the failure and recording of the findings. The first referral level can
maintain records and report results regularly to the central level. This information could contribute to the planning of national drug policies.

The information needs at the central level differ from those at the periphery since at this level there is more emphasis on planning and evaluation. Resources for collecting specialized information can be mobilized at the central level.

One approach to monitoring the response of *P. falciparum* to antimalarial drugs is to employ one or more trained teams whose responsibility it is to visit different parts of the country, investigate reports of treatment failure, and perform confirmatory *in vivo*, and perhaps *in vitro*, tests according to the established WHO procedures.

(b) Early detection, investigation, and prediction of epidemics. Epidemiological information is needed to investigate reported malaria epidemics and select epidemiologically sound control measures; to identify areas and populations subject to periodic epidemics, and the conditions triggering these, in order to prevent them by the early application of appropriate control measures; and where possible to identify the causal factors that lead to the epidemic. For malaria control through primary health care, the term epidemic implies an abnormal increase in malaria mortality and/or morbidity.

(i) Collection and analysis of information. The methods applied will vary from place to place. At the periphery a mechanism should exist to ensure that an abnormal increase in cases, illnesses, and/or deaths is reported to the first supervisory level. This information should be analysed regularly by supervisors so that trends and abnormal situations requiring action can be detected.

A central unit can plan for epidemics by identifying areas where problems are likely to occur, marshalling the resources necessary to respond quickly when the abnormal situations appear, and carrying out routine monitoring so that an epidemic may be detected at an early stage. During monitoring it is often possible to identify the causal factors such as population movement, increased vector density, emergence of vector resistance or reduced vector contact with insecticides, or parasite resistance to drugs. This information can be used to prevent future epidemics in the same area or to prepare guidelines for other similar situations.
(ii) *Forecasting potential epidemics.* In some instances, potential epidemics can be predicted and control measures prepared in advance. Examples of changes that may lead to epidemics are large-scale population movements and the migration of labourers during agricultural, irrigation, mining, and construction projects. Some epidemics are seasonal and may be geographically fixed. Control measures can be introduced to prevent the expected increase in malaria mortality and morbidity, or surveillance can be intensified to provide warning of possible epidemic situations.

In most countries, the intermediate level of the health service will be responsible for managing patients referred from the periphery and for supervising community health workers, and this level will often play the most important role in preparing for, detecting, and responding to epidemics.

2. EDUCATION AND TRAINING OF HEALTH MANPOWER FOR MALARIA CONTROL

2.1 Manpower development strategies

2.1.1 *Health education of communities*

Health education in this context may be regarded as any effort that enhances general awareness of both the malaria problem and the need for action. Included in health education are efforts to make the public aware of the problem and the measures they can undertake individually and collectively, and also efforts to obtain support from high-level decision-makers outside the health field (32).

Health education of individuals and communities for malaria control may be particularly difficult in view of the fact that many of the areas where the population is at the greatest risk from malaria are areas characterized by weak community organization (for example, newly developed agricultural lands that are attracting the jobless from various geographical areas and cultural backgrounds).

2.1.2 *Reorientation and training at all levels*

In contrast to time-limited eradication programmes for which mostly single-purpose, skill-oriented training was required, malaria control requires more complex training covering functional tasks at
all levels of the primary health care system. There is a clear and important need to make health service personnel at all levels aware of the significance of the problem of malaria and of the strategy of control through primary health care. This orientation will be carried out using different formats and mechanisms, depending upon the particular target group involved.

Unfortunately, the required changes in manpower development strategy and training have not taken place in most countries, although there have been some modifications in training in some malaria programmes to incorporate control as well as eradication concepts and procedures.

In the case of decision-makers and programme administrators, there is a need to ensure that they participate actively in the development of the strategy for malaria control through primary health care. Without the involvement of this key group of individuals, the implementation of the revised malaria strategy will be difficult, if not impossible.

At other levels of the health services system, reorientation towards the primary health care approach will be more task- and skills-oriented (33). Health workers will need to be trained and oriented to perform specific tasks of malaria control. At all levels, it is necessary to develop epidemiological competency. At the periphery this might be limited to the routine acquisition of information and recognition of certain abnormal situations requiring assistance from a higher level. At the higher levels, it will be necessary to develop the capability to undertake epidemiological analysis for remedial action, programme development, and replanning. Epidemiological concepts should be integrated into training programmes, since malaria control activities are dependent upon epidemiological analysis for programme planning and implementation.

At all levels, it is important to provide training in community development skills. The increasing recognition of the community as the main partner for the achievement of improved malaria control has re-emphasized the need for all health workers to have a better understanding of the communities in which they are working and to gain the confidence of, and acceptance by, the community. This will in turn enhance the cooperation and involvement of the community in malaria control activities, while the inclusion of the community in the planning of malaria services will help ensure that these services are appropriate to the community's needs. The development of
training to provide community involvement and interaction will require specialized knowledge from the disciplines of anthropology, sociology, and health education; experts from these fields should be involved in the training process.

2.1.3 Role of specialized knowledge

The existence of appropriate malariological skills at each organizational level is fundamental to the effective functioning of antimalaria activities within the primary health care system. At the central level, a group of professionals with the appropriate skills will be required to plan and organize the programme, carry out training and evaluation, and deal with the various technical aspects of the programme. Most of the necessary specialized knowledge will be at the central level. The number of individuals and the professional disciplines represented will depend on the magnitude of the malaria problem and the nature of the control activities. Training for this type of specialist will, in most instances, take place through international courses or in selected institutions.

Specialized knowledge at the regional or district level will also be required, although in some instances it will not be necessary to employ full-time specialists. Special training in malaria control activities for district or regional staff should be sufficient in most instances, provided that they are also conversant with the antimalaria strategy, the general epidemiological characteristics of malaria locally, and in the major problem areas. It is very important for malaria control activities that the required expertise is available promptly when required.

In addition to the usual professional disciplines required, such as malarologist and medical entomologist (vector control specialist), competent advice in the area of social sciences should also be made available to the health professionals to assist in understanding the interaction between the community, control activities, and the epidemiology of the disease.

Another group that will need orientation on the malaria problem is the medical community. This orientation can be initiated by involving the schools of medicine and public health. These schools should assure the development of teaching materials on malaria and its control for the education of students. In addition, it is desirable to develop continuing educational activities for the medical profession so that they are kept up to date on any advances in the
diagnosis and treatment of malaria. This continuing education could be developed jointly by the local medical associations and the universities, with the assistance of the core group of malaria specialists from the health services.

2.2 Education and training

2.2.1 Review of national and international training programmes

In the past five years numerous training activities at national, regional, and international levels have been carried out in order to respond to the needs expressed by national health authorities. A number of deficiencies have been identified at the regional level that have interfered with the training and orientation process required in many countries. These include job insecurity, limited potential for promotion, and the perception that working in malaria results in overspecialization, which creates difficulties in moving into other areas of health work. Another major problem that has been observed in many countries is the shortage of trained personnel to staff the national training centres and training courses.

In order to cope with the changing requirements of specialized training in malaria control that is adapted to the needs of current strategy, several international training courses in malariology and entomology have recently been introduced.

2.2.2 Role of training at various levels of the health care system

At the central level of the health system, the role of training is to assist in the development of the necessary technical knowledge and expertise including that required for epidemiological (including social and economic aspects), parasitological, entomological, and vector control guidance to the intermediate and peripheral levels of the health services. Intersectoral cooperation and coordination with other training institutes occurs at this level.

At the intermediate level, the major role of training is to develop the capacity to support the periphery in areas such as planning, response to problems and abnormal situations (such as drug-resistant parasites, vector resistance to insecticides, and epidemic control), training of peripheral workers, evaluation, epidemiological support of control activities, analysis of information, laboratory diagnosis, and management of severe cases of malaria.
The community health worker will be the main person to implement malaria control through primary health care. Training of community health workers must take into account the fact that they will function as multipurpose workers and will need to develop the appropriate skills in order to deal with all of their duties. Since their training will focus on the accomplishment of specific tasks, the development of skills through supervised on-the-job activities (learning by doing) should be emphasized. In-service and continual training of these workers is also important. Training and support may also provide motivation and impetus for communities to maintain health workers even in the absence of direct financial remuneration from the health services.

2.2.3 **Requirements of training methods and materials**

There is an urgent need for the development of the specialized methods and materials that are essential for the training of primary health care staff and the reorientation of malaria staff. Innovative methods will be required to enable staff at the central and intermediate levels of the health system to develop the necessary skills in malaria control. Training for their many responsibilities (which precludes their receiving highly specialized instruction in malaria) can be most suitably achieved by an initial course of briefing and orientation followed by on-the-job training periodically supplemented by relevant and necessary formal instruction. In this regard, one approach that the Expert Committee believes needs further development is the use of case studies drawn from actual situations that illustrate the essential features of malaria control integrated with primary health care. This type of training could be complemented by selected simulation exercises that may provide more detailed concepts than can be derived from the case studies, and scenarios that would broaden their scope.

2.2.4 **Training of trainers**

One of the major problems being encountered by countries that are attempting to upgrade their training capabilities is the scarcity of people who can provide the requisite training. One approach to the solution of this difficult problem has been the development of the training-for-trainers programmes, in which individuals with teaching responsibilities are brought together in a workshop to learn
the rudiments of competency-based, systematic curriculum design and development. Through this process, several health service personnel can acquire the skills necessary to enable them to become more capable teachers, and they in turn can teach these skills to other individuals who have teaching responsibilities in the health service. This multiplier effect would help ensure that a significant number of people with teaching skills will become available to implement the necessary malaria training.

In this connection the Expert Committee took note of the valuable work being undertaken in organizing the training of trainers in malaria control, including trainers in entomology and vector control, and considered that this approach particularly merits international support.

2.2.5 Global coordination of malaria training

The global coordination of malaria training activities is regarded as being of particular importance. A major step towards establishing this has been the development of the WHO Secretariat for the Coordination of Malaria Training in Asia and the Pacific that is based in Kuala Lumpur, Malaysia, and was inaugurated in 1982. The mandate of this Secretariat is:

— to strengthen national expertise in malaria and its control by developing and expanding national capabilities in malaria training to the level needed for effective implementation of malaria control activities, including implementation through primary health care;
— to develop and/or organize support in the form of technical materials, training manuals, and guides that will eventually be produced as a comprehensive modular training system in malaria;
— to identify and facilitate the development of a network of training institutions that will collaborate on a regional, interregional, and eventually a global basis in fulfilling the needs of the countries.

Coordinated efforts are being pursued in other regions along similar lines.
3. TECHNOLOGICAL ADVANCES AND THEIR APPLICATION TO MALARIA CONTROL

3.1 New approaches to malaria diagnosis

The microscopic examination of blood-films has been the mainstay of parasite detection in infected mosquitoes and in man, but this method has serious shortcomings in that it is time-consuming and often not practicable at the peripheral levels of primary health care. In addition, epidemiological assessment could be improved if better and more widely applicable serological tests were available that could reflect present or past contact between the parasite and man, distinguish primary infections from relapses and recrudescences, and measure immunological status and protection.

Thus, it is necessary to develop simpler and better diagnostic tests for use in well-equipped central laboratories, intermediate and peripheral health reference laboratories, and under peripheral field conditions. This subject has recently been reviewed in detail (34).

There are operational and economic advantages in introducing, at all levels, techniques that use the same principles and equipment for antigen and antibody detection. The various categories are discussed in the following sections.

3.1.1 Tests reflecting the presence of plasmodia in the arthropod host

These tests include immunoradiometric assay (IRMA) and enzyme-linked immunosorbent assay (ELISA), both based on the use of monoclonal antibodies to the circumsporozoite (CS) proteins of *P. falciparum* and *P. vivax* (35). Their purpose is to determine the prevalence of naturally-infected mosquitoes, their sporozoite load, and the species of *Plasmodium* present. Similar tests for other stages of *Plasmodium* in mosquitoes, namely oocysts, ookinetes, and gametes are at the research or developmental stage.

3.1.2 Tests reflecting the presence of plasmodia in the human host

Solid-phase immunoassays have been developed for the detection of malaria antigens in lysed erythrocytes, using radio- or enzyme-labelled antimalaria antibodies (36, 37). Soluble malaria antigens have been detected using gel precipitation and countercurrent
immunoelectrophoresis. The use of DNA probes is promising and may have advantages for diagnosis as an alternative to blood-film examination. The sensitivity and specificity of tests based on DNA and RNA probes compare well with those obtained by light microscopy (38).

3.1.3 Antibody detection tests

These tests include the circumsporozoite precipitation (CSP) test, which is based on the capacity of antispzrozoite antibodies to bind to antigenic components on the sporozoite surface, and the immunofluorescence test, which detects conjugated ant-immunoglobulins of antibodies bound to sporozoites that have been fixed (39). Several techniques have been used as serodiagnostic tests for malaria, but their wider application has been impeded largely by the lack of standardized reagents, in particular antigens, and by their high cost. The use of recently identified and purified specific blood antigens could provide new serodiagnostic tests. Gene-cloning techniques may also provide alternative sources of antigen at relatively low cost.

3.1.4 Tests with potential relevance to protective immunity

These tests include methods for quantifying the effect of immune sera on the invasion of erythrocytes by merozoites of P. falciparum, for detecting inhibition of binding of infected erythrocytes to endothelial cells, for detecting surface antigens on infected erythrocytes by means of immunofluorescence, for identifying cell-mediated immunological processes, and for demonstrating inhibition of sporozoite invasiveness.

At present, probably as a result of the interaction of these factors, a single test for protective immunity to malaria does not exist. Nevertheless, several in vitro tests are available that give important information on the potential function of malaria antibodies and of host cells, some of which may be relevant to protection.
3.2 Recent advances in chemotherapy of malaria

3.2.1 Mefloquine alone and in combination with sulfadoxine/pyrimethamine

Mefloquine, a quinoline methanol, is the most important drug that has been produced by the antimalarial drug development programme of the United States Army. It has received extensive testing and been found to be safe, well tolerated, and effective against 4-aminoquinoline-resistant *P. falciparum*. It is very potent against the blood forms of all the malarias affecting man, and is particularly useful in the field because it is administered as a single oral dose. Mefloquine is rapidly absorbed and very slowly eliminated (the elimination half-life is between 15 and 33 days, with a mean of 21.4 days). The advantage of single-dose administration is particularly striking when compared with the regimen required with the only reliable alternative for the treatment of multiresistant *P. falciparum* infections. The alternative regimen consists of quinine administered for at least 3 days, together with tetracycline administered for at least 7 days. In practice in the field, the failure rate of this regimen is as high as one-third of cases because of problems of compliance, and not yet because of parasite resistance (7).

In field trials conducted in Thailand, mefloquine was shown to be a highly effective chemosuppressive agent against *P. falciparum* and *P. vivax* infections (40). The drug is currently under evaluation in Thailand for the treatment of pregnant women, and in Thailand and Zambia for the treatment of young children.

In order to delay, for as long as possible, the selection of parasites that are resistant to mefloquine, its combination with sulfadoxine/pyrimethamine has been studied and found appropriate for operational use. In Thailand, the largest field trial ever conducted with an antimalarial drug has recently been completed. During this trial the triple drug combination was administered to more than 40,000 patients who had slide-diagnosed *P. falciparum* infection. More than 3000 individuals were followed-up for as long as 3 months after treatment. The triple combination was found to be radically curative in nearly 97% of infections and tolerance was good, side-effects being mild, of short duration, and self-limiting.

A recent WHO Scientific Group on the Chemotherapy of Malaria recommended several precautions that should be taken to prevent the misuse of mefloquine (7). These include strict governmental
control of the importation and distribution of the drug alone or in combination, limitation of its use to areas where it is precisely indicated, in vitro and in vivo monitoring of sensitivity of *P. falciparum* to the drug, and deployment of mefloquine or its combination with sulfadoxine/pyrimethamine as part of an integrated approach to malaria control. These recommendations were endorsed in 1985 at a meeting between WHO and malaria directors from South-East Asian countries. The recommendations of the Scientific Group were extended to the effect that governments should apply or develop legislation to control the importation, manufacture, distribution, and use of mefloquine, that the drug should not be made available for over-the-counter sale, and that the responsible malaria authorities should advise each government concerning its deployment. It was stressed that the drug alone or in combination should not be used for prophylaxis in populations in endemic areas except when absolutely necessary and always under strict supervision.

3.2.2 Other new drugs under development

The current status of other new drugs under development has also been reviewed recently (7). Qinghaosu (artemisinine), a Chinese herbal preparation, and some of its derivatives have been found to be extremely quick acting when given parenterally; these substances may have a potential as important therapeutic agents for the treatment of severe and complicated malaria. Certain preclinical tests, including toxicological studies, are being undertaken; studies in animals have suggested that fetal toxicity may be a side-effect, and it may not be possible to use the drug during pregnancy. Two other drugs, halofantrine and enpyroline, are currently under clinical trial under the auspices of the United States Walter Reed Army Institute of Research. Halofantrine, a phenanthrene methanol, has been shown to be safe and active, but bioavailability problems will require refinements of its formulation. Enpyroline, a pyridine methanol, also shows promise and is undergoing Phase III tests.

3.3 Recent developments in malaria vector control

The Committee noted that this subject has recently been reviewed in detail (29).
3.3.1 Vector control activities

Vector control is an integral part of the prevention of malaria, and until now has mainly been organized at the central or regional levels and has been based on a vertical administrative approach. In recent years, within the primary health care system, there has been a gradual shift of emphasis from a strictly vertical approach to a more flexible one, involving well-motivated community participation.

3.3.2 Residual insecticides

The number of new compounds produced by industry has decreased in recent years, as a result of several factors, including the high cost of developing new compounds that are biologically active but that are also safe for man and his environment (30). The WHO Pesticides Evaluation Scheme (WHOPES), which involves industry and WHO collaborating centres in many countries, is stimulating the development of new compounds and their testing for efficacy and safety. These compounds include bendiocarb, pirimiphos-methyl, chlorphoxim, and synthetic pyrethroids. In the field, it has been found that selective spraying of residual insecticides (lower parts of house walls, or only cattle shelters) is both effective and economical and is less hazardous for the spraymen.

3.3.3 Antilarval measures

Pirimiphos-methyl, and controlled-release formulations using polymers impregnated with fenthion or temephos, have been successfully tested in the field. Laboratory studies with two new synthetic pyrethroid larvicides, alphamethrin and cyfluthrin, have been promising, as have studies on a new insect development inhibitor, fenoxycarb. Formulations of the insect growth regulator triflumuron (a benzoylurea compound) were tested against an anopheline species and resulted in complete control that lasted for 7 days.

3.3.4 Biological control measures

This developing field (41) includes the investigation of (a) pathogens and parasites, such as the larvicial bacteria *Bacillus thuringiensis* serotype H-14 and *B. sphaericus*, fungi, protozoa, and
nematodes particularly merthithids such as Romanomermis culicivorax; and (b) larvivorous fish of several genera in addition to Gambusia.

3.3.5 Integrated approaches and community development

Developments are taking place in integrated approaches and community involvement in malaria vector control (29, 42). Through health education and community awareness and involvement, such simple measures as source reduction, rearing and release of larvivorous fish, and prawn and carp rearing are being undertaken by villagers. In India, the feasibility of using economic incentives to improve community involvement is being studied, for example, the harvesting of algae for paper production, conversion of lagoons to prawn culture, and various types of environmental modification. In this way, vector control has become integrated with social and economic development. The rearing of larvivorous fish in Indonesia (where the digging of pits along the slanting edge of rice fields has allowed fish to survive and at the same time provides food for the farmers) and the introduction of indigenous fish in barkits (earth or cement water tanks) to reduce the vector density and malaria in semi-arid areas of northern Somalia, are both examples of an integrated approach.

3.3.6 Community-based approaches against adult vectors

Among the measures available for self-protection and the avoidance of man-mosquito contact, the use of untreated and permethrin- or deltamethrin-treated bed-nets is proving significant. This treatment allows the effective use of these nets even when they are damaged.¹ Bed-net treatment by pyrethroids that remains effective for several months can be safely and economically carried out by the community. Mosquito repellents applied to the skin, and repellent-impregnated clothing are also useful in special situations. Mosquito coils (generally containing synthetic pyrethroids) are


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widely used by householders, and their effectiveness is being evaluated.

3.4 Malaria vaccine development and testing

The Expert Committee noted that this subject has recently been reviewed in detail.¹

Malaria vaccines will be based on pure parasite antigens that stimulate specific protective immune responses. “Protective” antigens are present in several of the developmental forms of the parasite and future vaccines may contain antigens from one or more of these. At present, most of the relevant research concerns *P. falciparum*.

The strategy for malaria vaccine development involves identification and characterization of “protective” parasite antigens, cloning of the corresponding genes and their expression in bacteria, analysis of their nucleotide sequence, and deduction of the amino acid sequence of the encoded molecule. The “protective” epitope (the immunogenic portion of the antigen molecule) may then be produced by genetic engineering methods or by chemical synthesis.

In attempting to identify “protective” plasmodial antigens, attention has been focused on those antigens that are exposed to the immune system, either on the surface of the parasite or on the membrane of the infected erythrocyte. Vaccine targets currently envisaged are sporozoites, asexual erythrocytic stages, and gametes and other forms developing in the mosquito midgut. It is likely that these types of vaccine will become available for testing in the field, each type having its own functional characteristics. Protective immunity in malaria is species-specific and largely stage-specific, so that each vaccine will protect only against the life-cycle stage or stages on which it is based.

A *sporozoite vaccine* should prevent the establishment of plasmodia in the host and thus induce sterile immunity; in such a case parasitaemia, asexual or sexual, would not occur, clinical illness would not supervene, and the subject would remain incapable of infecting mosquitoes. A vaccine of this type if applied to human populations sufficiently widely would interrupt natural transmission

of malaria irrespective of the prevalent endemic level. The operational indications of the sporozoite vaccine will largely depend on the duration of protection. In considering the indications for operational use, it will be important to assess the role of natural challenge as a potential booster of protective immunity.

An asexual erythrocytic-stage vaccine is expected to induce immunity that operates by restricting the replication of asexual blood-stage parasites without necessarily inducing sterile immunity. Consequently, its function will be to reduce the morbidity and mortality due to malaria. Such vaccines would be used in highly susceptible groups in endemic areas to induce a level of immunity that would prevent serious illness following infection. The objective would be to confer a degree of protection equivalent to that which develops only after several infections in endemic areas. Infection might serve to boost the vaccine-induced immune response. Asexual blood-stage vaccines seem unlikely, if used alone, to interrupt transmission in any endemic area.

Transmission-blocking vaccines will operate by inducing serum antibodies in the human host that block the fertilization of female gametes by male gametes within the mosquito gut, or inactivate the fertilized zygote or ookinete. Such vaccines seem capable of interrupting malaria transmission at the mosquito level, but will neither protect the human host against sporozoites, hepatic forms, and asexual blood-stages, nor prevent the development of gametocytæmia. However, their use may reduce the overall rate of transmission in endemic areas and thereby play a role in malaria control. These vaccines would probably be used in combination with protective vaccines against sporozoites and/or asexual erythrocytic stages.

The effect of vaccines on transmission will be influenced by the extent of population coverage and this is related to acceptability of the vaccine, including the population's perception of its value, their social customs, the movement of individuals within the community, and the extent to which such movements are known to the health system. Special attention should be given to the development of methods for the rapid appraisal of social and economic changes so that relevant information can be used effectively.

Vaccines of the three types described above are currently being developed. The development of sporozoite vaccines, a natural precursor of which was first successfully tested in man more than 10 years ago (43), is at a more advanced stage than that of the other
vaccines. Sporozoite vaccines of two types representing the immunodominant epitope, a synthetic peptide and a gene insert into *Escherichia coli*, are now entering Phase I trials in man. Studies will include preclinical, clinical, and field trials in Phases I (tolerance and immune response), II (protective efficacy), III (efficacy under natural challenge), and IV (safety, efficacy, and epidemiological effects) (44).

4. RESEARCH RELEVANT TO MALARIA CONTROL: FIELD AND LABORATORY

The reorientation of the global antimalaria effort, the identification of appropriate strategies, and the necessity of making antimalaria action an integral part of primary health care have given impetus and direction to malaria research.

The Committee noted that malaria research covers not only the traditional areas of chemotherapy, epidemiology, and vector control but also includes largely innovative or formerly neglected fields such as the development of vaccines and new diagnostic tools, and the elucidation of social, economic, ecological, and behavioural determinants of malaria and its control. Current research aims primarily at the development of relatively simple tools for diminishing mortality and suffering from malaria and for controlling the disease.

4.1 Parasite biology and control

4.1.1 Parasite biology

The Committee noted that progress in research in this area has recently been described in detail (34).

Two important recent advances are the finding that (i) malaria relapses originate from the persistence of uninucleate latent stages of the parasite, namely hypnozoites, in the liver, and (ii) the development of techniques for the cultivation of the erythrocytic stages of *P. falciparum*. The latter achievement has enabled studies to be undertaken that form the basis for many recent advances in malaria biochemistry, parasitology, immunology, and chemotherapy. Subsequently, methods have been developed for drug-screening and for testing the susceptibility of *P. falciparum* isolates in the field to antimalarial drugs.
Culture techniques have also permitted important studies to be made on the invasion of the erythrocyte by the parasite and the subsequent changes that occur in the infected cells. Such studies have not only proved to be important for a better understanding of the host–parasite relationship, but have also led to the identification of antigens that may be potentially useful for antimalaria vaccine development and as targets for chemotherapy. Methods that allow the development of infective gametocytes in cultures of *P. falciparum* have also been developed, and these have permitted the identification of gamete-specific antigens for use in a potential transmission-blocking vaccine and have led to the development of methods for the screening of potential gametocytocidal drugs.

The recent development of techniques for the *in vitro* cultivation of the exoerythrocytic stages of malaria parasites has already had a major impact on immunological research concerning the sporozoite and exoerythrocytic stages, and may be applicable to the screening of tissue schizontocides.

Significant advances have been made in the understanding of the biochemistry of the malaria parasite that may provide a basis for the rational development of new antimalarial compounds with novel modes of action.

*P. falciparum* constitutes a single worldwide population of organisms potentially capable of interbreeding. However, the frequent observation of multiple enzyme types and clones with differing drug susceptibilities in a single isolate suggests the common occurrence, in individual patients, of multiple infections with genetically distinct parasite clones. Of these clones, chloroquine-resistant parasites appear to have a biological advantage over chloroquine-sensitive ones, whereas pyrimethamine- and mefloquine-resistant parasites appear to be at a biological disadvantage. These factors are pertinent to an understanding of the reasons for the spread of drug-resistant malaria.

4.1.2 *Chemotherapy*

The Expert Committee noted that research into the chemotherapy of malaria has recently been reviewed in detail (7). There continues to be a need for the development of new antimalarial compounds with novel modes of action, and for improvements in the use of existing drugs. The establishment of screens for blood and tissue schizontocidal, gametocytocidal, and
sporontocidal drugs has led to the identification of several promising compounds. However, it must be appreciated that it usually takes more than a decade to develop a compound from this point to its clinical use. Such development cannot take place without the involvement of the pharmaceutical industry, and it is encouraging that several companies remain actively involved in this work.

Primaquine is the only tissue schizontocidal drug currently available for the radical treatment of *P. vivax* and *P. ovale* infections; it also has a gametocytocidal action. Recently the use of sophisticated assay methods has provided notable advances in our understanding of the metabolism, pharmacokinetics, and mode of action of this drug, and has led to the identification of other 8-aminoquinolines that are currently being studied.

The successful though limited deployment of the triple combination of mefloquine, sulfadoxine, and pyrimethamine in areas where multidrug resistant *P. falciparum* exists has been an incentive for the study of the applicability of other drug combinations. The combination of artemisinine (Qinghaosu) and mefloquine has been shown to be synergistic and to enhance considerably the suppression of a mefloquine-resistant isolate of *P. falciparum* in *vitro*.

Microtest kits for testing the susceptibility of *P. falciparum* to chloroquine, amodiaquine, mefloquine, and quinine are now widely used for field studies. This test system, in its present form, cannot be used to test the susceptibility of sulfa drug and antifolate drug combinations, but a modified growth medium has been developed for this purpose and a standard test kit for such combinations is being produced. For *in vitro* tests and other appropriate field applications, an incubator operated by an electronic battery (or solar cell) has been developed.

Such susceptibility testing depends also on the availability of methods for determining drug levels in those being tested. At present these methods still require the use of expensive sophisticated equipment, but alternative simpler techniques for use at the primary health care level are under development.

4.1.3 Immunology

The Committee noted that research in this area has recently been reviewed in detail (44). The impetus provided by the introduction of cell fusion (hybridoma) techniques for the production of monoclonal
antibodies has been particularly valuable. This has led to the identification of candidate antigens of all stages of the parasite that are capable of inducing a protective immune response. Modern techniques of protein analysis and synthesis, gene isolation, and genetic engineering have provided the means by which these antigens can be produced for inclusion both as potential vaccines and diagnostic tests.

4.2 Vector biology and control

4.2.1 Application of mosquito genetics to epidemiology

Sibling Anopheles species, although morphologically indistinguishable, may differ in biological features such as larval habitat, feeding, and other traits that have an important bearing on their vectorial competence and amenability to control strategies. Separation of sibling species may depend on the detection of genetic divergences by methods based on chromosome characteristics, biochemical differences, and crossing experiments; relevant research in the field and laboratory has recently been described.1

4.2.2 Studies on vector control

New insecticides and larvicides are tested as they become available from industry (30). Those recently examined and found to be potentially valuable are bendiocarb, pirimiphos-methyl, and several synthetic pyrethroids. New methods of application, such as selective spraying of houses and cattle shelters, based on the resting preferences of the vectors, and spraying of bed-nets with synthetic pyrethroids, are being tested in an effort to reduce both costs and the selection pressure for anopheline resistance. These methods may be employed by the community with little associated hazard; this is an important factor with some of the newer insecticides (45).

Among the new products tested against mosquito larvae are some synthetic pyrethroids, insect development inhibitors, bacterial pathogens, fungi, and nematodes. Useful larvivorous fish are being identified, cultivated, and released. The introduction of well-known genera such as Gambusia into new areas may have adverse ecological

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1 UNDP/World Bank/WHO. Malaria vector species complexes and intraspecific variations: relevance for malaria control and orientation for future research. (Unpublished WHO document TDR/FIELDMAL-SWG(3)/84.3).
effects; therefore the emphasis is now on using local species. The advantages of these and other methods that may be community based or provide protection for individuals have already been discussed (section 3.3).

4.3 Field research

The current work includes studies of the parasite and of the biology and control of the vector, use of existing and new tools, and epidemiological situations and problems. The proposed direction of field research, and some conclusions drawn from existing studies, are discussed in the following sections.

4.3.1 Assessment of the malaria situation

In the future, the principal lines of research into malaria will include (a) the epidemiology of the disease and its local manifestations; (b) the social and economic factors that have an important bearing on malaria transmission and control; (c) the development and/or evaluation of stratification methods; (d) the epidemiology of drug resistance; and (e) vector susceptibility to insecticides, including genetic aspects.

4.3.2 Use of existing tools

The value of serological methods in epidemiological studies is an important subject for continuing research. Among the conclusions that have been drawn from studies of existing tools and approaches (those involving community participation in malaria control have a particular relevance to delivery of the service through primary health care) are (a) that the services provided should be polyvalent and as comprehensive as possible; (b) that the community must have strong leadership; (c) that traditional health providers, for example village birth attendants, should be used after suitable training; (d) that drugs should be provided for treatment rather than prophylaxis; (e) that diagnostic services should be extended, when feasible, to the periphery, and (f) that community-based services need recognition and support from, and regular contact with, government authorities. These conclusions form the basis for further studies on the diversity of customs and habits of the innumerable communities affected by malaria.
Other related research priorities include (a) identification of predators of mosquito larvae and pathogens that can be used as components of an integrated control programme; (b) use of biological control agents; (c) development of monitoring systems that can forecast the build up of epidemics; (d) remote sensing that provides advanced information on the increase in mosquito population densities; (e) integrated control activities to deal with exophilic and/or exophagic vectors; and (f) deployment of in vitro methods of testing and monitoring parasite resistance to drugs, and of methods for evaluating vector susceptibility to insecticides.

4.3.3 Evaluation and adaptation of new tools

As regards new parasitological tools, further field research will concentrate particularly on the use of DNA diagnostic probes for the detection of human plasmodia in infected blood, and the assessment of current methods for the characterization of P. falciparum isolates in relation to malaria epidemiology. Important entomological subjects that will require field research include the development of new techniques for the identification of anophelines, particularly sibling species, and the detection of sporozoites in mosquito salivary glands.

5. REVIEW OF THE PRESENT STATUS OF REGISTRATION OF MALARIA ERADICATION

The Expert Committee reviewed the present status of registration of malaria eradication, and took note of the revised procedure for registering countries or areas which have met the necessary requirements in the intervening period between meetings of the Expert Committee. These procedures consist of circulating the assessment report of the inspection team to members of the previous Expert Committee instead of holding it for submission to the next Expert Committee. On the basis of their recommendations, the Chairman submits the final recommendation to the Director-General for approval. This procedure has been exercised in the interim period between the meetings of the seventeenth and eighteenth Expert Committees, when Australia and Singapore were added to the list of countries so registered.
6. AWARD OF THE DARLING MEDAL AND PRIZE

The Expert Committee examined the various nominations submitted for the award of the Darling Medal and Prize in conformity with Article 5 of the regulations concerned.

Having discussed in private session the relative merits of the candidates nominated, the Expert Committee, in conformity with Article 7, sent its recommendations by letter to the Director-General of WHO, who is the Secretary of the Darling Foundation Committee.

7. CONCLUSIONS AND RECOMMENDATIONS

1. Countries should review their antimalaria activities in the light of the policy of health for all and the principles of primary health care and their state of development. The planning of malaria control as a component of primary health care should take into account concurrent activities for health promotion and for the control of other diseases.

2. Malaria control should be based on an epidemiological approach, recognizing local variability in the distribution and evolution of problems. This will permit the design of appropriate strategies, the selection of suitable control measures, the training of all levels of staff, the monitoring of progress, and the evaluation of results, not only at the country level but also within different ecological areas.

3. The planning of antimalaria activities or the transformation of existing ones should take into account, particularly:

   (a) the relevance of current or proposed objectives and approaches, in terms of their feasibility, and the appropriateness with which the basic objectives, in particular the prevention of mortality, are to be attained;

   (b) the adequacy of the infrastructure to ensure total coverage of the population with timely diagnosis and treatment, and malaria prophylaxis during pregnancy, supported by an appropriate referral system capable of treating severe cases and managing the problem of drug resistance—this infrastructure should include the epidemiological services necessary for the detection and control of
high-risk areas or population groups, epidemic outbreaks, and the monitoring of special problems:

(c) the need for all health services dealing with malarious areas to develop and maintain a nucleus of expertise to give guidance in the study of the malaria problem and the planning and implementation of its control, and the development of effective links to complement this core of experts with other technical resources available in the country or through intercountry or international collaboration;

(d) the use of appropriate evaluation and surveillance mechanisms for the effective monitoring of progress in malaria control in the context of primary health care;

(e) the development of methods of integrated vector control, particularly source reduction and personal protection measures, that can be carried out, sustained, and afforded by the community and that are less dependent on chemical pesticides.

4. As operational responsibilities are being transferred to the general health services, under the expert guidance and supervision of malariaologists, it will be necessary to specify what every member of the service will need to know about malaria control. In order to organize health care within each district, it is particularly important that the district medical officer be fully capable of:

(a) selecting appropriate directives, approaches, and technologies for each district, and possibly for different communities, based on a process of stratification of the malaria problem;

(b) appreciating and using knowledge of social, behavioural, economic as well as technical factors in the design of control interventions;

(c) appropriate financial planning, considering the ability and willingness of people to share in covering costs or alternatively planning for a more centralized solution to cost coverage.

5. The required reorientation of malaria control will not be possible without some redistribution of manpower, material, and financial resources. In particular, resources from the central level should be concentrated according to the intensity of the problem and local capabilities for controlling it.

6. The need to guide the health services in the implementation of the malaria control strategy makes it necessary to support and expand training at all levels, and to coordinate it globally. Training capabilities should be developed further, particularly as regards
instruction related to the application of the epidemiological approach to control. Other important aspects of training are:

(a) definition of the role and type of training necessary at different levels of the health services system, assessment of the national training needs and resources, and incorporation of these two aspects into a national manpower development plan—such a plan should allow for the appropriate coordination of malaria training with that of other communicable diseases;

(b) emphasis on the need for primary health care workers to work effectively in the communities towards the common objective of a reduction in the malaria problem;

(c) the development of curricula to reflect the epidemiological approach to malaria control through primary health care, appropriate training modules that have general applicability, and a mechanism for implementing intercountry exchange of educational materials, such as prototype intervention case studies;

(d) the desirability of developing and expanding intercountry training courses, workshops, and seminars on malaria and its control to provide the opportunity to discuss and analyse individual country experiences in malaria control;

(e) the desirability of updating curricula in medical schools and schools of public health to include the new approaches to malaria control as a part of primary health care and the latest information on the diagnosis and treatment of malaria.

7. The diagnosis, prevention, and treatment of malaria are of major importance at the primary health care level, as regards both the individual and the community, and the following elements should be carefully considered:

(a) facilities for microscopic diagnosis should be made available as close to the periphery as is feasible according to local resources and the nature and extent of the malaria situation;

(b) simple, specific, and sensitive methods of diagnosis of infection should be developed that are appropriate for use at all levels of the primary health care system, but especially at the periphery, and, in particular, methods that provide both clinical and epidemiological information;

(c) the protection of children aged under 5 years living in malarious areas should not be based on a policy of chemoprophylaxis, but, instead, should be based on access to prompt diagnosis and appropriate treatment;
(d) antimalaria chemoprophylaxis should be made available where possible on a regular basis to pregnant women, together with curative treatment at the initial visit—other members of the community should receive chemoprophylaxis only in exceptional circumstances;

(e) training and guidance of health services personnel at all levels in the recognition and management of severe and complicated malaria should be vigorously pursued, and encouragement given to efforts to document experiences regarding the treatment of severe and complicated malaria;

(f) national health authorities should pay particular attention to the problem of drug-resistant malaria, its detection by an appropriate monitoring system, and its management through the rational use of drugs and other antimalaria measures;

(g) drugs should be deployed for the treatment of malaria on the basis of known susceptibility of the local parasite species, bearing in mind that the detection of resistance per se does not necessarily rule out the usefulness of a particular drug for treatment or prophylaxis;

(h) the capacity at the periphery to detect, and respond to, drug resistance should be developed and supported by the regular monitoring of parasite susceptibility by competent trained personnel using standard in vivo and in vitro techniques;

(i) the problem of chemoprophylaxis should be given particular attention in areas where P. falciparum resistance to chloroquine is high, in order to identify alternative safe and effective compounds in the light of current observations related to the toxicity of the combination of sulfadoxine and pyrimethamine—efforts to detect such adverse effects should be intensified to define the role of this drug combination in chemotherapy and chemoprophylaxis;

(j) epidemiological studies of primaquine as a gametocytocidal drug in areas highly endemic for P. falciparum should be undertaken to determine what influence this drug has on transmission;

(k) (i) governments of countries where malaria is endemic should endeavour to develop effective measures to control the importation, manufacture, and distribution of mefloquine and its combinations, in order to delay, for as long as possible, the selection of resistant parasite populations through inappropriate use of the drug(s);

(ii) in malaria-endemic countries, mefloquine and its combinations should be used only for the treatment of
slide-positive *P. falciparum* infections that are likely to be resistant to other standard antimalarials—initially, such use will be at the referral level of the health care system but as resistance to other drugs progresses to the extent that it becomes necessary to use mefloquine or its combinations at the primary levels, the diagnostic facilities should be expanded to reach these more peripheral units;

(iii) mefloquine or its combinations should not be considered for prophylaxis except for well-defined special groups temporarily at high risk of infection with multidrug-resistant *P. falciparum* and even then under strict supervision.

8. Plans to control malaria or to modify existing malaria control programmes should be based on the best available information and experience. However, in most instances this will require the acquisition of complementary knowledge and well-documented learning-by-doing experience to be fed back into the management process. This constitutes the main component of a “research and development” approach. The range of subjects for research and development studies include:

(a) improving the general and local understanding of the epidemiology of problems such as resistance to drugs and insecticides;

(b) the influence of social, cultural, behavioural, and economic processes on the epidemiology and control of malaria, including the problems associated with the disestablishment of vertical programmes;

(c) approaches to training non-professional workers to cope with antimalaria activities in addition to their other activities;

(d) factors influencing community participation and intersectoral cooperation;

(e) ways of providing guidance and supervision by the health services, and ultimately, by malaria experts;

(f) appropriate implementation at the community level of malaria control, control of other priority diseases, and other primary health care activities, including studies of whether (or where) such activities could be carried out by a multipurpose community health worker, or whether the malaria control activities should be divided among a number of categories of worker, such as those dealing with disease
control and those dealing with other promotional and preventive activities, i.e., those dealing with people and those dealing with the environment;

(g) ways of developing and promoting the popular, habitual use of simple, safe, cheap, and effective methods that could be used by individuals and communities for their own protection against disease vectors.

9. Further research into a variety of matters affecting the malaria control programme is essential to facilitate the introduction of new approaches and methods.

(a) The pursuit of basic research on malaria should be continued in view of its importance in the development of new approaches to, and tools for, malaria control.

(b) The elucidation of the epidemiological background and the solution of operational problems requires that appropriate field research activities be developed through relevant mechanisms as an integral part of the national malaria strategy, that research in the context of primary health care be conducted especially in areas where malaria control was hitherto not feasible or did not yield the desired results, and that the relation between epidemiological features of malaria and social, economic, and ecological factors and their dynamics be studied thoroughly and systematically, including:

— further development of a comprehensive conceptual framework, and related guidelines, relating to the social and economic factors that may affect malaria transmission and control programmes,
— compilation and assessment of the principal research studies undertaken in the field,
— establishment of a data bank of social and economic indicators,
— preparation of research protocols to stimulate emerging research interests,
— development of case studies documenting the social, economic, and policy dimensions of malaria control programmes.

(c) The urgent development of new antimalarial drugs that have novel modes of action, particularly those possessing the following characteristics: blood schizontocidal, tissue schizontocidal, hypnozoitocidal, sporozoitocidal, and gametocytocidal/sporontocidal activities, safety, low cost, stability for long periods under sub-optimal storage conditions, and if possible, and where appropriate, long-lasting action.

(d) In view of the importance of chemotherapeutic agents in
reducing the mortality and suffering from malaria, there is an urgent
need to develop:
— suitable, simple drug assay methods to monitor drug compliance,
that can be applied at the peripheral levels of primary health care.
— a reliable, simple test method to monitor the early drug response
in falciparum malaria that could provide guidance for the
management of severe and complicated falciparum malaria at all
levels of primary health care;
— safe medicaments and/or drug formulations, and guidelines for
their use, for the emergency management at peripheral primary
health care levels of patients with severe or complicated
falciparum malaria who cannot be treated orally;
— monitoring systems for the detection and documentation of
adverse reactions to all antimalarial drugs, and in particular
studies of the interactions between these and other drugs to
facilitate the development of guidelines for the safe and rational
use of antimalarials.

(e) There is a need for further development of in vivo and in vitro
tests for accurate monitoring of the prevalence of drug-resistant
falciparum malaria, these tests being based on standardized,
recognized procedures and materials—reporting systems must also
be established to facilitate the use and dissemination of the
information obtained.

(f) Collaboration between WHO and its Member States is
essential to expedite and coordinate the development and field
testing of malaria vaccines.

(g) Concerning the vectors of malaria, the principal areas needing
increased research are the identification and determination of their
status and ecology wherever indicated, the impact of vector
resistance to insecticides on malaria control, and the testing and
evaluation of imagicides, larvicides, biological agents, and
environmental methods of vector control.

10. The role of WHO in the required reorientation of the malaria
control strategy and practice will be vital. As part of its promotional,
collaborative, and supportive functions, WHO could make
important contributions:
(a) at the country level
— by focusing its activities on epidemiological support, on research
and development activities, and on bringing to the attention of
national health workers the experience obtained from similar
situations elsewhere;
— by collecting, analysing, and documenting experiences gained and using them for training within and outside the country;
— by collaborating in the reorientation of existing malariologists and health personnel and in the education of new cadres of malariologists/epidemiologists.

(b) at the regional and global levels

— by emphasizing cooperation with countries, in line with the new approach, and by agreeing to provide support only to activities following this approach;
— by training and reorienting WHO and national staff;
— by organizing country, intercountry, and regional seminars, when needed, using available experience, and establishing collaborative mechanisms for the acquisition of the necessary knowledge and the progressive introduction of that knowledge into control programmes;
— by preparing documentation and learning materials (including prototype scenarios) on national, district, and community control approaches (together with their tactical variants);
— by preparing reviews of the use of epidemiology in malaria control in actual situations, including the development of appropriate simulation exercises;
— by supporting the preparation of protocols for research and development studies and collaborating in the actual conduct of these studies as required;
— by supporting country, intercountry, and regional seminars as well as the direct operational activities in countries as required;
— by collecting and analysing experiences and establishing an appropriate information system for dissemination of the results and, when appropriate, preparing training materials based upon them;
— by encouraging coordination with other programmes to ensure that a common strategy is followed towards primary health care;
— by monitoring and evaluating the progress of malaria control and suggesting what modifications may be required;
— by integrating the new approach to malaria control into the curricula of medical schools and schools of public health throughout the world;
— by promoting and coordinating additional research for the development of simple diagnostic methods for use by non-professional primary health care workers and field testing them;
— by promoting research and development on the basis of country experiences; and
— by providing in-service training on the above.

ACKNOWLEDGEMENTS

The Expert Committee wishes to acknowledge the special contributions made during its deliberations by the following: Dr J. Cohen, Director-General's Office and Secretary of the Global Programme Committee, WHO, Geneva, Switzerland; Dr E. B. Doberstein, Research and Technical Intelligence, Malaria Action Programme, WHO, Geneva, Switzerland; Mr J. Hempel, Epidemiological Methodology and Evaluation, Malaria Action Programme, WHO, Geneva, Switzerland; Dr S. Goriup, Epidemiological Methodology and Evaluation, Malaria Action Programme, WHO, Geneva, Switzerland; Dr N. Gratz, Director, Division of Vector Biology and Control, WHO, Geneva, Switzerland; Dr R. Guidotti, Maternal and Child Health, Division of Family Health, WHO, Geneva, Switzerland; Dr C. W. Hays, Programming and Training, Malaria Action Programme, WHO, Geneva, Switzerland; Dr V. Ivorra Cano, Programming and Training, Malaria Action Programme, WHO, Geneva, Switzerland; Dr R. Kouznetsov, Programming and Training, Malaria Action Programme, WHO, Geneva, Switzerland; Dr K. Lassen, Regional Officer for Malaria, WHO Regional Office for Europe, Copenhagen, Denmark; Dr S. Litsios, Programming and Training, Malaria Action Programme, WHO, Geneva, Switzerland; Dr F. Lopez-Antuñano, Programme Coordinator, Tropical Diseases, WHO Regional Office for the Americas/Pan American Sanitary Bureau, Washington, DC, USA; Dr L. Martinez, Research and Technical Intelligence, Malaria Action Programme, WHO, Geneva, Switzerland; Dr L. Molinaux, Epidemiological Methodology and Evaluation, Malaria Action Programme, WHO, Geneva, Switzerland; Dr D. Muir, Malaria Action Programme, WHO, Geneva, Switzerland; Dr E. Onori, Chief, Epidemiological Methodology and Evaluation, Malaria Action Programme, WHO, Geneva, Switzerland; Dr C. P. Pant, Chief, Ecology and Control of Vectors, Division of Vector Biology and Control, WHO, Geneva, Switzerland; Mr D. Payne, Research and Technical Intelligence, Malaria Action Programme, WHO, Geneva, Switzerland; Dr K. M. Rashid, Malaria Adviser, WHO Regional Office for South-East Asia, New Delhi, India; Dr N. Rishikesh, Ecology and Control of Vectors, Division of Vector Biology and Control, WHO, Geneva, Switzerland; Dr P. Rosenfield, UNDP/World Bank WHO Special Programme for Research and Training in Tropical Diseases, WHO, Geneva, Switzerland; Dr A. Smith, Ecology and Control of Vectors, Division of Vector Biology and Control, Geneva, Switzerland; Dr H. Spencer, Programming and Training, Malaria Action Programme, WHO, Geneva, Switzerland; Dr P. I. Trigg, Research and Technical Intelligence, Malaria Action Programme, WHO, Geneva, Switzerland; Dr W. H. Wernsdorfer, Chief, Research and Technical Intelligence, Malaria Action Programme, WHO, Geneva, Switzerland.
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