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Malaria

New Patterns and Perspectives

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Jose A. Nájera, Bernhard H. Liese, and Jeffrey Hammer

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Jose A. Nájera is director of Tropical Disease Control for the World Health Organization. Bernhard H. Liese is director of the Health Services Department of the World Bank. Jeffrey Hammer is senior health economist in the Population, Health, and Nutrition Division of the World Bank.

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Introduction

Malaria is a collective name for different diseases that may result from infection of any parasites of the genus *Plasmodium*. Four species of malaria parasites naturally infect humans: *Plasmodium falciparum, P. vivax, P. malariae,* and *P. ovale.* The characteristics of the disease vary with the intensity of the infection, the host's level of immunity, the adequacy of and opportunity for treatment, and the parasite's susceptibility to it.

Transmission between humans occurs through the bites of certain species of mosquitoes of the genus *Anopheles*. In this cycle, the parasite matures and reproduces sexually in the anopheline mosquito (the vector), which is, strictly speaking, the parasite's definitive host, and man is its intermediate host.

A natural history: parasite and vector

The life cycle of the parasite follows a general pattern. The infecting parasite, an actively motile form called a sporozoite, is inoculated into the blood with the saliva of the biting mosquito. After about half an hour, the sporozoites invade liver tissue cells, where they develop and multiply. Small parasite forms called merozoites, capable of invading the red blood cells, burst into the blood — as many as 20,000 per successful sporozoite. The time needed to multiply in the liver, the preerythrocytic stage, varies with the parasite species: 6 to 7 days for *P. falciparum,* 14 to 16 days for *P. malariae,* and 7 to 8 days for *P. vivax,* although some *P. vivax* parasites remain dormant in the liver for months, even a few years, in a form called hypnozoite.

Once the parasites invade the red blood cells they initiate the cycle of development and multiplication that causes clinical manifestations of the disease. Disease symptoms are caused only by parasites in the blood, so the late development of hypnozoites gives the disease a long incubation period, or a pattern of cure alternating with repeated relapses, since common antimalarial drugs that may clear the blood of parasites are not effective against parasites in the liver. Merozoites invade red blood cells where they grow and multiply to produce 8 to 24 merozoites (depending on the parasite species), which rapidly invade new red blood cells. This development is accomplished in 48 hours for the so-called tertian malarias (benign, if from *P.vivax* and*P.ovale;* malignant if from*P.falciparum*) and 72 hours for the quartan (from *P. malariae*). This development takes place in the peripheral blood, for *P. vivax, P. malariae* and *P. ovale.* But with *P. falciparum,* only red blood cells infected with very young parasites (called ring forms) are found in the peripheral blood; those infected with developing or dividing parasites are sequestered in the capillaries of such internal organs as the brain, and cause the severe manifestations typical of *P. falciparum.*

Some individual parasites do not follow the cycle of asexual reproduction just described. Instead, they differentiate into male and female gametocytes, which are eventually taken up by an *Anopheles* mosquito, in which they can mature, achieve fertilization, and multiply in the stomach wall — producing about 1,000 sporozoites, which burst into the mosquito's body cavity and finally invade the salivary glands. This sexual cycle takes

between 9 and 30 days or more depending on the temperature and the parasite species.

Not all species of anophelines are vectors of malaria and those that are vary greatly in their ability to transmit the disease. General or specific refractoriness may be due to many causes, e.g., the plasmodia is unable to develop or to invade the salivary glands, or the mosquito cannot live long enough to complete the parasite's extrinsic cycle, or the mosquito has so little contact with humans that it is unlikely to bite a human after becoming infected. Of the roughly 400 species of *Anopheles*, only about 60 are vectors of malaria under natural conditions — some 30 of them of major importance.

As for all mosquitoes, the habitat of the immature *Anopheles* is in water. Eggs are all laid on the water or at its edge and hatch in 2 to 3 days to produce larvae (wrigglers). Larvae develop through five aquatic stages — four larval and one pupal — to produce adult flying mosquitoes. Only the female mosquito bites, as it needs blood for its eggs to mature — the male feeds on vegetable juices. Mating occurs only once soon after the adult female emerges. The female stores the spermatozoa in a deposit called a spermatheca. The aquatic stages commonly last 7 to 20 days, depending on the temperature. The adult female may live from a few days to well over a month, going through several cycles of blood feeds and egg-laying (some 100-200 per batch) every 2 to 4 days. Survival and egg development depend mainly on temperature and relative humidity. In temperate climates, mosquitoes may go into hibernation, which allows some of them to survive the winter.

Larval habitats vary enormously, reflecting mosquitoes' evolutionary adaptability. Different species will breed in different water habitats — from permanent to transient bodies of water, from fresh to brackish water, from standing water to flowing canals and open streams, from open sun to deep shade, from shallow pools to deep wells, from clean drinking water to water highly polluted with organic matter, from large open marshes to the tiny pools of water that collect between the leaves of bromeliads, in plant axils, in trees, in rock or crab holes, in cattle footprints or in discarded artificial containers. But the characteristics of breeding places are rather narrowly defined for each species, so larval habitats can be modified for control of a particular mosquito species.

The seasonal availability of breeding places and the great influence of weather conditions on mosquito activity and survival are largely responsible for the marked seasonal cycles in mosquito population densities and malaria transmission in most areas outside of permanently humid tropical areas.

Specific behavioral characteristics of mosquitoes may also affect their vectorial ability. Mosquitoes' preferences for feeding on human or animals and their frequency of feeding are important determinants of the probability of their transmitting malaria. Human dwellings and domestic animal shelters — particularly those with thatched roofs, dark corners, and many cracks in the walls — are good resting places where mosquitoes can digest the blood they've consumed, while their eggs mature. Such areas favor mosquito survival, but are also vulnerable to insecticidal spraying.

Malaria as a disease

The chief symptom of malaria is fever, periodic bouts of which tend to alternate with days of less or no fever. The classical paroxysm of fever lasts 8 to 12 hours, typically in three stages: *cold* shivering rigor, *burning dry* skin, and *drenching sweat* that lowers the temperature. This pattern is more typical of *P. vivax* (tertian periodicity) and *P. malariae* (quartan) than of *P. falciparum*, which typically involves prostrating fever, with brief and incomplete remissions, more often irregular than clearly periodic. Untreated, the acute attack is shorter than that of *P. vivax*; in fatal cases, death often occurs in 2 to 3 weeks, and sometimes as soon as 2 to 3 days after the onset of symptoms. Repeated infections give rise to an immune response in the host which eventually controls the infection and the disease. Untreated or incompletely treated infections will produce several recrudescences, after long symptomless periods, from parasites surviving in the blood. By this mechanism alone, *P. falciparum* may persist for one or two years, while *P. malariae* has been reported to recrudesce up to 52 years after last exposure to infection. With *P. vivax*, true relapses may occur, as latent hypnozoites will mature in the liver and invade the blood after other parasites have been completely eliminated from it. Without reinfection, *P. vivax* may persist for 3 to 4 years.

In the absence of other complicating factors, acute severity and mortality occur almost exclusively in *P. falciparum* infections. This parasite causes the surface of infected red blood cells to become adhesive and to be sequestered in the capillaries of internal organs, leading to pathological changes and the main severe forms of ma-

laria: cerebral, renal, pulmonary (oedema), and gastrointestinal. Other severe forms — such as severe anaemia and hemoglobinuria (or blackwater fever) — are the results of more complex mechanisms.

P. falciparum malaria can lead rapidly to death so it is important to recognize signs of severity early and refer the patient immediately for medical care. These signs include shock, anaemia, convulsions, jaundice, hyperpyrexia, renal failure, impaired consciousness, spontaneous bleeding, macroscopic hemoglobinuria, and pulmonary oedema or respiratory distress. Health services that suspect severe malaria should treat it as a medical emergency, providing immediate treatment and, whenever possible, laboratory monitoring of such signs of severity as hypoglycemia, parasite density, and an imbalance of fluids and electrolytes.

The risk of severe malaria is almost exclusively limited to nonimmunes. In highly endemic areas this risk affects children older than 3-6 months, who have lost the immunity transferred from their mother, up to the age of about 5 years, when surviving children have developed their own immunity. African health authorities report that in the last few years cerebral malaria is being seen increasingly in older children and young adults. It has been suggested that this may be the result of urbanization and personal protection, which reduce the risk of infection and delay the development of immunity. Severity in adults is seen in areas of low endemicity, where people may reach adulthood without immunity. Equally at risk are immigrants and travellers from nonendemic areas — particularly laborers, who are often concentrated in camps, where nonimmunes and the infected live side by side in overcrowded conditions where the risk of transmission is high. Also at risk are pregnant women, possibly because natural immunity is depressed during pregnancy.

Most deaths from malaria occur in young children living in highly endemic areas of tropical Africa and the Western Pacific islands. The most common causes of death are cerebral malaria and severe anaemia. Malaria may also contribute seriously to the severity of other childhood diseases.

In pregnancy, *P. falciparum* malaria in the nonimmune may lead to death, abortion, prematurity or low birthweight. In the semi-immune inhabitants of highly endemic areas, malaria represents a serious risk in a first and second pregnancy. Pregnant women are susceptible to anaemia, hypoglycemia, and other complications. Malaria is also an important cause of low birthweight and high neonatal mortality in first and second born children of semi-immune mothers even in the absence of symptoms and parasitaemia.

2

The public health significance of malaria

Roughly 110 million clinical cases of malaria occur annually. Some 270 million people are infected, carrying malaria parasites, although not necessarily developing symptoms. Indigenous malaria still exists in some 100 countries or areas. Accurate estimates are impossible because the accuracy of reporting varies considerably. Reporting from tropical Africa — where more than 80 percent of the clinical cases and 90 percent of the parasite carriers may be found — is especially irregular and fragmentary. Reported cases are believed to represent about 2 to 8 percent of the actual cases.

Geographical distribution

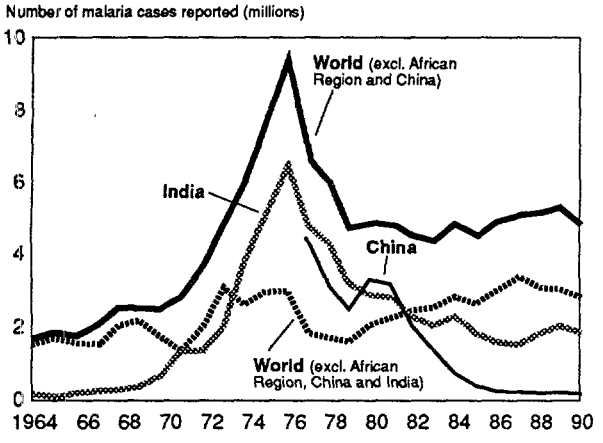
Every year, in the *World Health Statistics Quarterly*, the World Health Organization (WHO) publishes an overview of the world malaria situation (see map 2.1). The overview for 1988 (WHO, 1990) indicates that the world population (about 4,991 million people) can be classified according to people's experience with malaria and their residence in areas where:

- Malaria never existed or disappeared without specific antimalarial interventions (1,371 million people or 27 percent of the world population).
- Endemic malaria disappeared after a specific campaign to control it was implemented and the area has remained malaria-free (1,617 million people or 32 percent).
- Endemic malaria was reduced or even eliminated after control measures were implemented, but the disease was reinstated and the situation is unstable or deteriorating (1,599 million people or 32 percent). This category includes zones (which include about 1 percent of the world population) where the most severe resurgence of malaria has recently developed due to major ecological or social changes, such as sociopolitical unrest and agricultural or other exploitation of jungle areas.
- Endemic malaria remains basically unchanged and no national antimalaria program was ever implemented, because of the enormous difficulties of achieving control. Malaria is most endemic in these areas, which contain 85 percent or more of the malaria cases in the world, affecting 474 million people or 9 percent of the world population. These areas are mainly in tropical Africa; in some of them — including forested and medium-altitude areas — pilot projects were reportedly successful in interrupting malaria transmission, but in low savannah areas, particularly in the Sahel, no pilot projects ever reported full success.

Trends

The evolution of the malaria problem is traditionally described in terms of the number of registered cases reported to WHO by member states. Figure 2.1 (taken from WHO, 1990) — which excludes information on tropical Africa because of inadequate, irregular reporting from that area — shows the impact of the massive resurgence of malaria transmission in India in 1976 and its subsequent control. Changes in China are shown separately, as the Chinese started officially reporting to WHO only in 1977. China did not implement a national malaria control program until it had de-

Figure 2.1 Number of Malaria Cases Reported, 1964-90



Source: WHO Wkly Epidem. Rec., numbers 22 and 23, 1991.

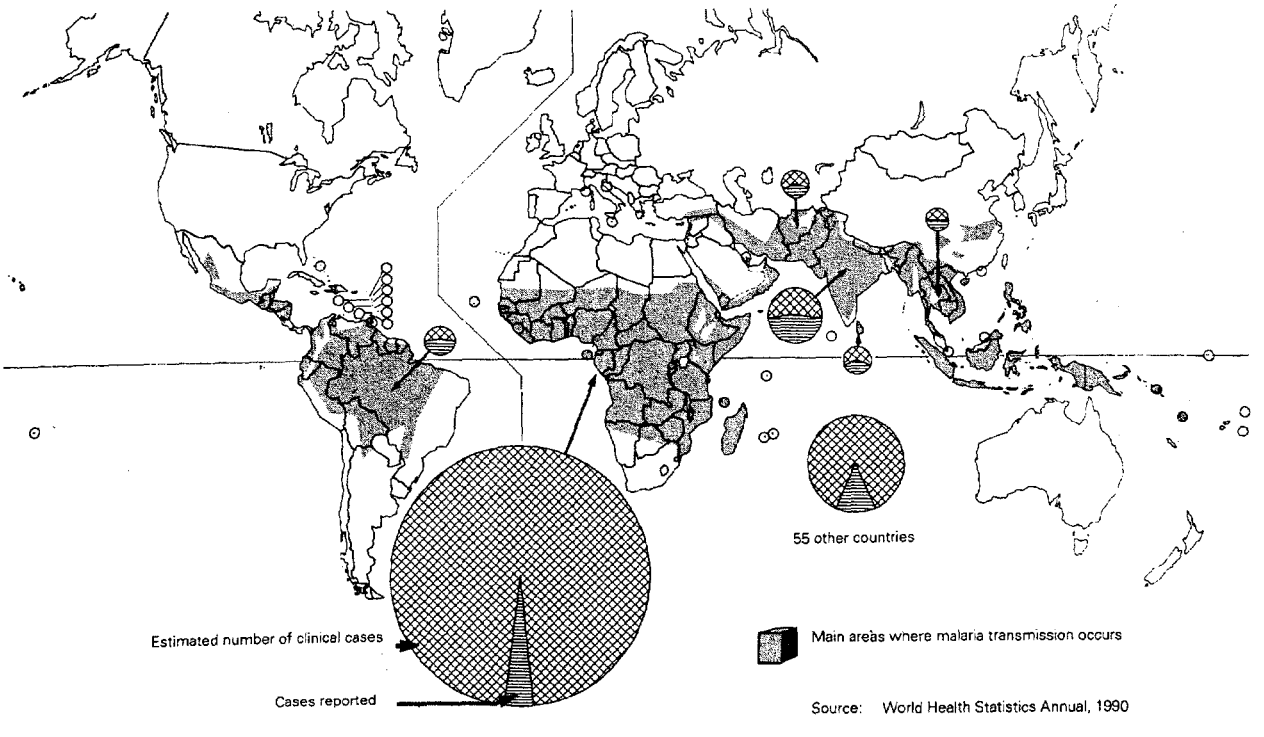
veloped a health infrastructure that has been considered a precursor of primary health care; the malaria incidence is similar to the pattern in countries that eradicated malaria. Figure 2.1 also shows that, if India and China are excluded, the rest of the world has stagnated since the late 1960s, with a slow but steady deterioration in the last 15 years. Data from India indicate that, after recovery from the 1976 epidemic, improvement slowed down and the situation seems to be stagnating.

The general pattern described here masks great local differences, not only in the intensity of the problem, but also in the pattern of its evolution over time. The geographical distribution of malaria is far from uniform; it can be seen that malaria clearly thrives in certain areas and it may be said that it occupies definable socioecological niches. The limits of malaria foci are much more diffused than those for contagious diseases such as smallpox, however, so it is more difficult to target their control.

Morbidity in tropical Africa

In the last decade African countries south of the Sahara have reported between 2 and 7 million cases a year to WHO but, extrapolating from fever and parasite surveys, it is estimated that 100 million clinical malaria cases may occur every year, and 210 million may carry malaria parasites. The levels of endemic malaria are among the highest in the world. Extensive forest or savannah areas up to about 1,000 meters high, with rainfall over 2,000 millimeters (mm) a year, often present the highest endemicity, classified as holoendemic. Areas between 1,000 and 1,500 meters high or lowland areas with between 1,000 and 2,000 mm/

Map 2.1 Malaria incidence



year of rainfall are characterized as hyperendemic. As altitude increases above 1,500 meters or rainfall decreases below 1,000 mm/year, malaria becomes less endemic and is concentrated in progressively smaller valleys, where favorable microclimatic conditions and mosquito breeding places exist or are created by such human activities as irrigation, dam construction, and the establishment of fish ponds. Of course, altitude and rainfall are only rough indicators of malaria's endemicity; other factors, such as temperature, humidity, the distribution of rains, and the slope and permeability of the soil also play important roles.

As endemicity decreases, the potential for epidemic outbreaks increases because fewer people have a chance to develop immunity. Equally, in areas of marked seasonality — as in the dry savannah of the Sahel — the transmission season, even if it occurs every year, takes on the characteristics of seasonal epidemics, at least as it affects younger age groups. Severe large-scale epidemics occur in areas that have been free from transmission for several years in a row, and exhibit a secular periodicity determined by the semicyclic occurrence of prolonged heavy rains or other climatological determinants. Such epidemics have been historically reported in high-altitude areas following abnormally warm and rainy summers. Such was the dramatic epidemic in the highlands of Ethiopia in 1958, which caused more than 3 million cases and claimed an estimated 150,000 lives. Epidemics also occur in dry areas after abnormally heavy and prolonged rains — as in the epidemic of 1975 in Gezira and Central Sudan and the 1988 epidemic in Khartoum and Northern and Eastern Sudan. In 1988-90 a number of epidemics, or serious exacerbations of endemicity, occurred in several highland areas of Africa, particularly in Botswana, Madagascar, Rwanda, Swaziland and Zambia.

In the high plateau of central Madagascar increasingly extensive and severe epidemics occurred between 1986 and 1988, reaching dramatic proportions in the first four months of 1988, when tens of thousands of people died. One of the main causes of this series of epidemics was that the DDT spraying campaign of the 1960s and early 1970s seems to have eliminated the main vectors of malaria *An funestus* and *An gambiae s.s.* so that malaria transmission was practically interrupted for about 20 years. But after spraying was discontinued and because of other opportunistic circumstances, both species progressively spread in the high plateau.

Smaller and more localized malaria epidemics have occurred when colonization efforts or agricultural or other economic development projects in endemic areas have attracted nonimmune populations from nonmalarious areas. This happened in the late 1950s, for example, when the lowlands of Kigezi (Uganda) began to be colonized by people from the overpopulated highlands, resulting in a tragic malaria epidemic with an extremely high mortality rate. This led to the establishment in 1959 of one of the few successful malaria eradication pilot projects in Africa (de Zulueta and others, 1961). In the last few years malaria endemicity has reportedly spread in the highlands of Amani in Tanzania. This intensified transmission has been attributed to the active colonization of those areas and the subsequent intensification of agriculture with terracing and leveling of the land in and around human settlements which increased potential anopheline breeding places (Matola and others, 1987).

Another possible factor in the apparent increase of epidemic potential in the last few years in the highland areas of Africa is the so-called greenhouse effect — in which accumulated carbon dioxide and other gases in the atmosphere may retain heat. In Madagascar the average temperature in the coastal areas was 0.5°C warmer than in the previous 30 years; in the high plateau the difference was about 1°C. These figures may not be fully comparable because data for the high plateau may be influenced by local ecological changes, such as the growth of Antanarivo — but an increase of even 0.5°C could increase the potential transmission period in marginal areas, which might change a normally nonmalarious area into one subject to seasonal epidemics (de Zulueta, 1988).

Morbidity in other malarious areas

Outside of tropical Africa, most malarious countries have similar reporting systems that permit some degree of comparison. As for the intensity of the problem, 81 percent of the 5.09 million cases reported to WHO in 1988 (not including tropical Africa) are concentrated in 10 countries (India, Brazil, Sri Lanka, Afghanistan, Thailand, the Philippines, Viet Nam, China, Mexico and Colombia — in decreasing order of total number of reported cases). These countries represent 63 percent of the population living in the world's malarious areas, excluding tropical Africa. India and Brazil, with only 26 percent of the population, report 46 percent of the cases. With only 30 percent of the popu-

lation, the first seven countries report 74 percent of the cases. And within these countries, malaria is focused in certain areas. In India, for example, six states (Orissa, Uttar Pradesh, Punjab, Madhya Pradesh, Gujahrat and Assam) have 66 percent of the cases. In Brazil, 97 percent of the cases are in Amazonia, which has only 15 percent of the country's population; two states (Rondonia and Para) report 70 percent of the cases, and four municipalities in Rondonia and four in Para report more than 60 percent of the cases in those states.

Countries and areas show great variability not only in the intensity of the problem, but also in its evolution over time. Cases reported annually to WHO since the mid-1960s show distinct patterns:

- *Group A.* Malaria declined and the situation has remained favorable in Algeria, China, Costa Rica, Cuba, Egypt, Hong Kong, Korea, Morocco, Panama, Paraguay and Tunisia.
- *Group B.* Malaria increased markedly in certain areas in Afghanistan, Bangladesh, Belize, Bhutan, Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guatemala, Guyana, Madagascar, Mexico, Myanmar, Nepal, Papua New Guinea, Peru, the Philippines, Saudi Arabia, Thailand, Vanuatu and Vietnam.
- *Group C.* The incidence of malaria has oscillated — at relatively short cycles and with a quasihorizontal general trend, at least since the early 1960s — in Argentina, Democratic Yemen, El Salvador, Honduras, Indonesia, (the Outer Islands, reporting since 1970), Iran, Malaysia (Sabah), Nicaragua and Surinam.
- *Group D.* In the last 20 years, one or two relatively short major epidemics have occurred in the Dominican Republic, India, Indonesia, (Java and Bali), Iraq, Libya, Malaysia (Sarawak), Mauritius, Oman, Pakistan, Somalia, Sri Lanka, Sudan, Syria, Turkey, Venezuela, Yemen and the Solomon Islands.

The only purpose of this preliminary classification is to stimulate analysis of the patterns of change. Groupings are based on total numbers of reported cases, and the fact that two countries appear in the same group does not indicate similarities in other epidemiological characteristics.

Except for India and China (which are major producers of cases because of their great size) and Sri Lanka (which may be changing from a pattern of periodic epidemics to one of progressive deterioration because of sociopolitical unrest); most major producers of cases are in group B. These countries are characterized by recent efforts to increase the exploitation of natural resources (through agricultural colonization of forest or jungle areas) or by civil war or sociopolitical conflict (including illegal drug trade) and large movements of refugees or other mass migrations. Eight of the ten main producers of cases have been on that list since at least 1986.

All of the countries in group A (where malaria has declined) have shared a degree of social stability and socioeconomic development, including health services easily accessible to the public.

Group C countries have suffered periodic bouts of malaria, followed by remobilized control efforts, after which the situation improved but could not be maintained, so malaria recurred. This pattern of "fire fighting" may progressively improve matters in the more developed areas, as people become less tolerant of epidemics and health services become more responsive. In marginal areas, the response is nearly always late and possibly ineffective as it often comes when the epidemic is naturally declining.

Drug-resistance and proportion of *P. falciparum*

The proportion of *P. falciparum* in endemic areas outside of tropical Africa — where *P. falciparum* remains the predominant species — was 36 percent in 1988 (compared with 15 percent in the early 1970s). In the last few years there has been an increased selection and progressive dispersal of *P. falciparum* parasites resistant to antimalarial drugs, as these drugs are used increasingly as prophylactics and for automedication, usually in insufficient doses (see map 2.2). The problem of drug resistance has been particularly alarming in Africa; in recent years it has spread across the continent and is now developing rapidly in West African countries. Its continual intensification hampers efforts to provide adequate treatment in rural areas. It is difficult to assess how much to attribute this phenomenon to the migration of resistant parasites and how much to local selection, as both mobility and drug consumption have increased considerably. For some time the widespread use of chloroquine was advocated as the most effective way to reduce deaths from malaria in Africa; chloroquine, it was said, should be treated as a commodity, and not as a drug. In many places in Africa people use chloroquine more often than aspirin for minor fevers and aches. Chloroquine has no doubt helped reduce deaths

from malaria, but maintaining this gain will require targeting antimalarial drugs to those actually suffering from malaria, particularly where more toxic and less affordable drugs are needed.

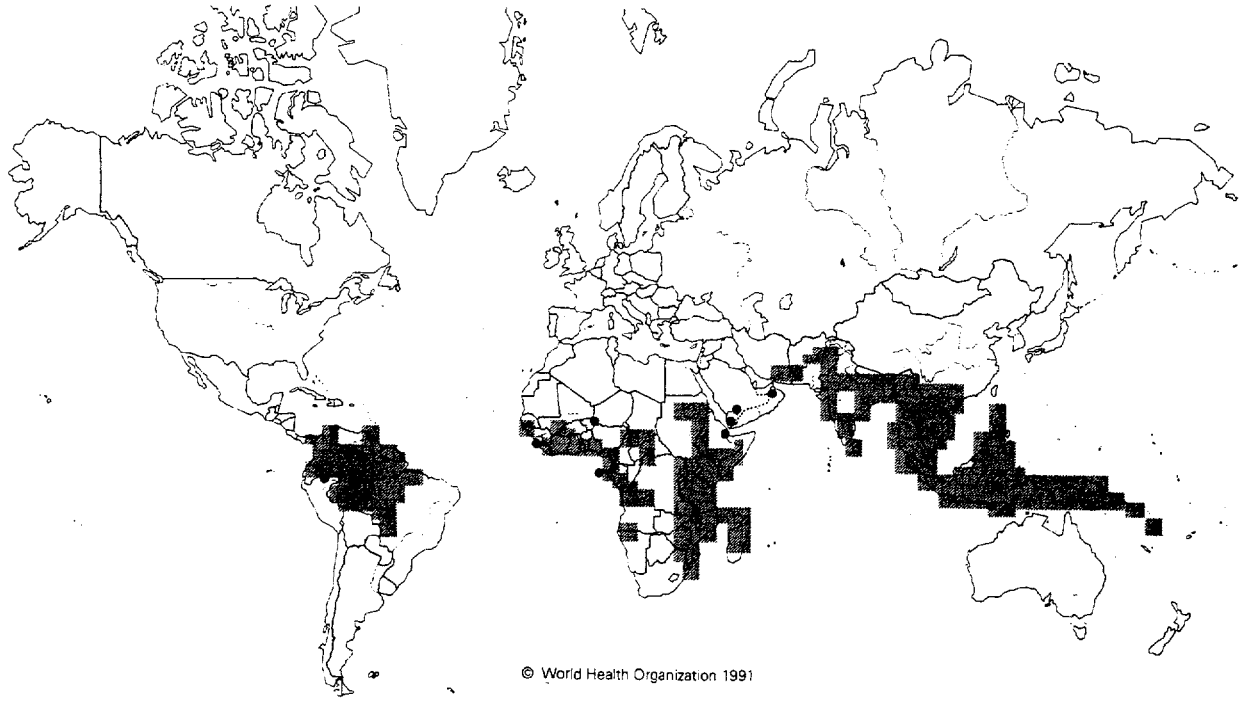
Mortality

Most deaths from malaria occur in tropical Africa. As in all highly endemic areas, deaths occur most among the young. Maternal immunity transmitted to infants may reduce mortality in the first 3 to 6 months of life, but this effect may be masked in areas of marked seasonality. Past studies indicated mortality rates between 10 and 30 per thousand in infants and between about 7 and 11 per thousand in children 1 to 4 years old. In 1962 the WHO Regional Office for Africa estimated that every year between 200,000 and 500,000 African children die from malaria (Pampana, 1969). In 1969 Bruce-Chwatt put that figure at about 1 million, a figure extensively quoted ever since. Molineaux (1985), reviewing the impact on infant mortality of some malaria control projects, especially in Kisumu (Kenya) and Garki (Nigeria), concluded that malaria was responsible for about 20 to 30 percent of infant deaths. Greenwood and others (1987), studying deaths from malaria in the Gambia, concluded that the mortality rate from malaria was 6.3 per 1,000 for infants and 10.7 per 1,000 for children 1 to 4 years old representing 10 percent of the deaths of children less than a year old and 25 percent of deaths for children 1 to 4.

There are signs that in some parts of Africa general infant and malaria-specific mortality may be declining, often independently of specific interventions, reflecting social development and general education. Studies in the Congo and Burkina Faso in the late 1970s indicated that malaria-specific mortality might be lower than expected in areas where, some decades ago, malaria was a major cause of infant mortality. The authors (Vaisse and others, 1981) attributed their findings to the widespread, albeit indiscriminate, use of antimalarial drugs, often in doses inadequate to eliminate parasites but effective enough to produce a clinical cure and prevent death, even if collectively it increased drug pressure on the parasite population and could thus be contributing to the selection of drug-resistant parasites.

The wide availability of antimalarial and other active drugs has also been identified as possibly contributing to the general decline in infant mortality observed in the Kisumu area of Kenya. There, between 1972 and 1976, infant mortality reportedly declined from 157/1,000 to 93/1,000 during an effective malaria control program (spraying

Map 2.2 Areas where chloroquine-resistant *Plasmodium falciparum* has been reported



● Reported after 1988

fenitrothion inside houses). Between 1981 and 1983, a slight decline in postneonatal mortality (from 73 to 67 per 1,000) and a marked drop in the mortality of children 1 to 4 years (from 25 to 18 per 1,000) were recorded after implementation of a program of community-based antimalaria treatment. But most of that decline was attributed to a measles epidemic in 1981-82; malaria-specific mortality, being relatively low, did not change significantly in the year of intervention. This study (by Spencer and others, 1987) confirmed in a small rural area the general observation that child mortality differentials can be explained largely by differences in maternal education, which no doubt influences the amount of drug use but, more important, improves hygiene and general living standards. Differences in infant mortality between districts in Kenya, as reported in the 1979 census, ranged from 38 to 153 per 1,000. When spraying in Kisumu ended in 1976, the area did not return to the previous infant mortality rates. Infant mortality rates for the district in which this area is located declined from 220 in 1959 to 181 in 1969, and 147 in 1979 (Spencer and others, 1987).

Deaths from malaria outside tropical Africa occur mainly among nonimmunes who become infected by *P. falciparum* in areas where appropriate diagnosis and treatment are unavailable. This happens especially to newcomers to endemic areas, such as agricultural workers, laborers, gold and gem miners, prospectors and other settlers in recently colonized or other frontier areas of economic development. Most affected are young adults, although whole families of settlers may be affected — for example, in the tropical jungles of South America (especially the basins of the Amazon and the Orinoco), in the outer islands of Indonesia, Sabah, Kalimantan and, on a smaller scale, throughout the tropics. In the Brazilian Amazon, an estimated 6,000 to 10,000 people a year die from malaria (Fiusa Lima, 1990).

Possible future patterns of morbidity and mortality in 2000 and 2015

Malaria transmission is focal and depends on the dynamics between man, vector, parasite and environment. More importantly, it depends on the effectiveness of control efforts, socioeconomic development, and political stability. It is thus quite risky to generalize about future patterns of morbidity and mortality. However, given the increasing resistance of the parasite to antimalarial drugs, treatment of malaria in the future will be more difficult and less effective thereby increasing the risk of both morbidity and mortality. Although new drugs are being investigated, and work is progressing on various potential malaria vaccines, alternative first or second line drugs or a vaccine are several years away, even under optimistic circumstances.

Furthermore, population instability in areas where there is the potential for malaria transmission is usually associated with an increasing burden of illness including mortality due to malaria. This instability might result from political conflicts, natural disasters, economic development or relocation schemes, or migration due to population pressure. Examples from Brazil, Thailand, Indonesia and Sri Lanka may illustrate different facets of this problem. To the extent that development projects ignore health impacts or that political conflicts create large refugee populations, malaria is likely to increase in each such local situation. On the other hand adequate socioeconomic development and political stability will facilitate effective and sustainable malaria control.

In terms of predicting patterns of morbidity and mortality in the future, it is safe to predict that there will be more morbidity and possibly mortality due to malaria in several areas, but how much more and, more specifically, which regions will bear most of the burden is less obvious. Well-documented case studies could serve as examples of potentially devastating impacts given similar scenarios in other areas of the world (i.e., Brazil, Madagascar, Sudan, Indonesia, Afghanistan, Sri Lanka, etc.)

But most importantly in view of the presently deteriorating worldwide malaria situation referred to earlier, a forceful effort to rehabilitate, activate or develop new malaria control activities in those countries most affected is crucial. Without such an effort malaria patterns in the year 2000 will be entirely different and substantively worse than the ones predicted.

Economic costs of malaria

The economic costs of malaria theoretically would include its impact on the economy and economic development, and on the local community, the household and the individual.

Costs of mortality and morbidity

There have been few community-based approaches to evaluate the economic impact of ma-

laria. The study by Conly (1975) highlights the problems encountered in attempting to quantify the impact of malaria on economic development — because of the difficulty of collecting and processing data on a sufficiently large population and the complexity of the interactions of the parameters measured.

Malaria imposes high costs in increased mortality and high morbidity rates. The impact of mortality varies with the age distribution of deaths, which in turn varies by ecological zone. In Africa, where most deaths are among infants and young children, the impact of and the perception of mortality will be different from other areas where the mortality is among the main breadwinner or primary caretaker of the family. Mortality and morbidity among adults is high in areas of low to moderate endemicity. (See Over and others, 1989, on the consequence of adult deaths.)

Malaria and productivity

Public health activities have been justified as improving productivity ever since debates about the "laziness disease" at the beginning of this century (Garcia, 1981). Malaria is a classic example of a debilitating disease that impairs productivity. As the most prevalent disease in the poorest rural areas, malaria produces recurrent infections with attacks or fever in the warm and rainy seasons, when most workers are needed to collect crops. Often, affected people also suffer from malnutrition and other infections and lack of medical care. In areas subject to epidemics, these also tend to strike at times of peak demand for agricultural work.

The focus of much of the research has been on attempting to measure the effects of bouts of illness on lost output of workers due to lower productivity. This research has been reviewed in Barlow and Grobar (1986). Research on the physical impact of the disease can be found in Conly (1975), Malik (1966), Russell and Menon (1942) and Van Dine (1916). Disability per case of malaria is estimated in these studies to range from 5 to 20 days. Other physical measures include effects on output or land cleared. Values for the former vary from zero to 1.5 for the elasticity of output of rice with respect to malaria prevalence (Audibert, 1984), while the effect on cropped area was a reduction by 60 percent in families with malaria (Bhombore and others, 1952). Conly (1975) traces a variety of adjustments in farm families in Paraguay, including increases in labor input per unit output as well as reallocations of land and hired labor. The reallocations of land entailed substitution of relatively low-value crops whose crop season was not malaria-prone in lieu of higher-value crops whose were. De Castro (1985) finds that such reallocations may include an increase in the work load of healthy family members. While this may be seen as an ameliorative factor which reduces the net impact of the disease, it may simply mean that some costs of the disease are borne by others besides those who are ill. In Southern Rhodesia, Hanlon (1955) estimated that the loss of manpower to malaria was from 5 to 10 percent of the labor force, with the heaviest incidence at the peak of agricultural production.

Estimates are much lower in highly endemic areas, where anyone who survives childhood can generally tolerate a malaria infection showing only minor symptoms at most, although malaria is an important contributing factor in severe anaemia. A study in Liberia (Brohult and others, 1981) showed no detectable loss of physical ability in people with malaria parasites in their blood, but a marked correlation between anaemia and loss of physical ability.

A common convention in the literature has been to use seven days of work lost to disability per bout of malaria whenever this parameter is needed to assess a program but is not independently estimated (see studies by Niazi, 1969; Quo, 1959; San Pedro, 1967; and Sinton, 1938); when independently estimated the parameter varied between 5 and 15 days. A further issue, raised by Wernsdorfer and Wernsdorfer (1988), is the undermining of the effectiveness of investment in education. In highly endemic areas, where adults normally have acquired sufficient immunity to make the symptoms less severe, school children are more severely affected. Judging the degree of impairment caused by illness would be hard to do and one can only wonder at the cost. However, Macdonald (1950) estimated that the learning of 35 to 60 percent of children may be impaired by malaria.

Other studies emphasize direct financial benefits from activities made possible by eradication or control. These are also surveyed in Wernsdorfer and Wernsdorfer (1988). Malaria has hurt economic development projects as well as armies at war and police forces or border patrols in endemic areas. Malaria had to be overcome for the successful construction of the Panama Canal and most roads and railways in tropical countries, for the agricultural development of the Roman Campagna and the Venezuelan *llanos*, for the build-

ing of railways and roads in tropical areas, and for the protection of armies from World War I through Viet Nam. Agricultural development and mining in tropical jungle areas, attracting workers from densely populated, often nonmalarious, areas is one of the particular problems associated with malaria. An example of research into the benefits of malaria control in this situation is found in Griffith and others (1971) who estimate the increased profits derived from allowing workers to enter new areas for mining. Forgone profits are the measure of the cost of disease. Sinton (1938) documents many cases in India where malarious regions prevented an expansion into new territories with substantial losses in forgone earnings. Demographic changes since then, however, have probably made such opportunities much rarer in the subcontinent.

Distribution of cost

Litsios (1990) highlights the uneven distribution of malaria risk across a population. Data from Adana, Turkey (Yumer, 1980), for example, show that anopheline bites per person were five times more frequent in the tents of migrant workers than in the houses of village residents. Malaria has been concentrated among migrant laborers in most areas were there is extensive cultivation of cotton and sugar cane and in some areas where coffee, bananas and rice are cultivated. Litsios concludes that "as malaria becomes a problem to be primarily found in marginal or fringe areas, it becomes a problem that is identified with marginal people." This can be seen by the tendency in some countries to associate malaria with "foreigners" or minority migrant groups who are then accused of being responsible for carrying the parasites into areas that might otherwise be malaria-free. In endemic areas the burden of malaria is also borne disproportionately by the poor.

Problems in measuring cost

The focus on days lost from work or output forgone is oddly narrow. In welfare terms, two alternate measures would be preferable. The first is the compensating variation in income, that is, the amount one would be willing to pay to avoid having the disease altogether. The second is the equivalent variation for the willingness to accept the disease, that is, the amount one would need to be paid to accept having the disease. In many contexts, these two measures are similar, but in cases where possible mortality is involved the latter measure could be considerably greater than the former. Willingness to pay is bounded by ability to pay, or lifetime earnings. In practical application, it would be limited by borrowing constraints as well. Willingness to accept is under no such limitation. Either of these measures would capture the subjective, even psychological, impact of the disease. In any case, using a measure which respects personal preferences would be more inclusive than simply including the instrumental effects of the disease on the productive capacity of the worker.

There are a number of objections to using these alternative concepts. They require defining which set of preferences (before or after falling ill) are relevant for the comparison. The most important criticism, though, is that obtaining this number practically requires a major research effort. Such calculations have been made in the environmental impact literature but are not widely used. It is possible to infer a lower bound, though, by calculating the total costs required to obtain treatment. The total costs borne by families and individuals include payments for treatment, time and transport costs in seeking treatment, time costs for family members who look after the patient, and time and money costs of preventive action taken by households and the community. These costs vary greatly with variables such as access to primary health care, national drug distribution policies, the presence of chloroquine resistance, the level of malaria endemicity, the behavior and bionomics of the local vector(s), and whether or not malaria is perceived as a serious health problem by the local community.

There are two main sources of cost underestimation. First, this calculation misses costs before treatment is sought. Second, there are those (inherently hard to measure) who have decided that the costs of seeking treatment are too high relative to the costs of letting the disease run its course. For them, there is still a relevant cost and degree of necessary compensation. For people in remote areas, or those afflicted at peak agricultural seasons (when implicit wages are high, both for the person falling ill or, in the case of children especially, for those needing to accompany the person), or — more difficult to evaluate — those who are uninformed about treatment prospects, these costs can be high.

A careful study of Thailand (Kaewsonthi and others, 1986) has attempted, among other things, to measure the costs borne by patients in seeking

care. These were dubbed "external costs," that is, external to the malaria control organization. They amounted to $20 per positive case or nine times the minimum daily wage. This estimate is for people who come to the malaria clinic and therefore does not include those who have handled the disease in other ways. This study includes costs entailed in seeking local treatment before travel to the clinic. Costs for local treatment amounted to 15 percent of the costs per positive case and is a component of the full cost to those who do not seek formal treatment. The degree of underestimation of the cost to sufferers is probably quite high. Time lost before and after seeking treatment can be considerable and varies with the quality (primarily speed) of service provided. This varies substantially within Thailand, let alone across countries.

Since the costs of malaria are borne disproportionately by the poor, there are further issues of aggregating individual costs into social costs. Whether disease averted should be weighted by the income of the sufferer (due to social welfare consideration or to the possibility of successfully seeking treatment) is an ethical issue to be appraised by policymakers.

In summary, Andreano and Helminiak (1988) state that "despite the many studies and the excellent work by Barlow and Conly, which represent methodological advances in the study of tropical diseases, we remain woefully ignorant of the social and economic effect of malaria in those countries of the world where it is prevalent." They also emphasize that findings in many of these studies cannot be easily generalized from one area to another.

3

Malaria control

History of control efforts

The idea of eradicating malaria, postulated as early as 1916, gained currency after World War II. Malaria epidemics had devastated parts of Southern Europe, and DDT had been extremely effective in controlling not only those epidemics but also endemic malaria in both temperate and tropical areas, including Venezuela, British Guiana and Taiwan. The Expert Committee on Malaria of the newly created World Health Organization, in its first five reports, adopted a cautious attitude, expressing concern about increasing reports of technical problems and of some disappointing results in the use of DDT, particularly in Africa. But the goal of eradicating malaria became irresistible, and the impending resistance to DDT was seen as a reason for racing to eradicate malaria before resistance developed. In 1954 the Pan American Sanitary Conference adopted a continental plan to eradicate malaria from the Americas. In 1955 this plan was extended to the world by the World Health Assembly (WHA). In 1956, the Sixth Expert Committee formulated a strategy for eradicating malaria (WHO, 1957).

Soon after the WHA resolution and the report of the Expert Committee, most countries of the Americas, Europe, North Africa, Asia and the Pacific officially declared that their antimalaria programs were eradication campaigns. In retrospect we can see that many of these programs were short on epidemiological knowledge and administrative organization. These deficiencies were overlooked because of the program's humanitarian appeal, the sense of urgency, and the feeling, shared by many, that peer pressure could shake the chronic apathy of the health services.

As anticipated, tropical Africa and some parts of Southeast Asia posed problems, because of their high endemicity, primitive state of development and lack of human and economic resources. Successes elsewhere, although slower than expected, were still remarkable. But as more and more areas advanced into the program's consolidation phase, the expectation that a surveillance mechanism would maintain areas malaria-free, after spraying was interrupted, was not fulfilled. Resurgences occurred increasingly often in the consolidation and maintenance phase, particularly in Central America and Southeast Asia. And at the end of the decade a massive epidemic broke out in Sri Lanka, where malaria had been almost eradicated. Evidence began to accumulate that although it was possible to reduce and even interrupt malaria transmission by spraying insecticide in large areas, it was difficult if not impossible to establish effective surveillance without a solid health infrastructure.

Finally in 1969, after reexamining the global strategy of eradicating malaria, the World Health Assembly reaffirmed that eradication was the ultimate goal but stated that, in regions where eradication is not yet feasible, control of malaria with the means available should be encouraged and may be a necessary and valid step toward that goal (WHO, 1969).

Unfortunately, after 15 years of strictly regimented antimalaria action, health authorities — even malariologists — were reluctant to introduce the necessary changes in the programs, while the

concept of malaria control, and an acceptable global strategy for it, remained undefined. The Expert Committee provided only sketchy guidance on how to transform an ineffective malaria eradication program into a control program, emphasizing that "the objectives in these areas would be to consolidate the gains so far achieved, to extend the programme to areas where protection would give maximum socioeconomic benefit and to protect high risk groups" (WHO, 1974). Unfortunately, most countries thought that the only way to consolidate gains achieved was to maintain as many routine activities as they could afford, without making the necessary investment to evaluate their local effectiveness.

WHO's formulation in 1978 of a strategy to develop health care infrastructure included malaria control among its essential elements (WHO, 1978). In line with these developments, the 31st WHA adopted a strategy of malaria control aimed at least at reducing mortality and the negative social and economic effects of the disease, preventing or controlling epidemics and protecting malaria-free areas, with the ultimate objective of eradicating the disease whenever feasible.

Malaria control measures

The most common antimalarial measures are: (i) chemical control through residual intradomiciliary spraying with DDT or other insecticides, in selected instances aerial spraying or local fogging (U.L.V.), and (ii) the treatment of fever cases with antimalarials. These activities are sometimes supported by limited environmental management measures mostly in urban areas where such measures can be easier to implement than in rural ones. They involve drainage or filling of water bodies. Water level fluctuations or intermittent irrigation are used in some large development schemes. Biological control measures are presently for all practical purposes not relevant. In addition to these active intervention measures, all control programs undertake active or passive malaria surveillance.

Specific antimalarial measures can be classified according to their mode of action and the scope and scale of their utilization (table 3.1).

Two substantially different approaches may be pursued in malaria control.

- Improving general health services to ensure adequate diagnosis, access to health care, and treatment for individual malaria cases, as well as promoting personal and community protection. This approach aims to eliminate deaths from malaria and to reduce the severity and duration of illness associated with it.
- Establishing the capability for long-term control of malaria transmission, control and prevention of epidemics, and progressive reduction of malaria endemicity (particularly in areas affected by *P. falciparum*).

The two approaches are in no way mutually exclusive and ideally should be complementary, but they differ greatly in their requirements for specialized services. While the former is a basic requirement in all malarious areas, the second would developed progressively, according to the intensity of the problem and resources available.

New perspectives for control

In 1985, the 38th World Health Assembly expressed its continuing concern about resurgent malaria and, in particular, about the apparent inadequacies of existing malaria control strategies. Consequently, the WHO Expert Committee on Malaria (WHO, 1986) reviewed the global malaria situation and attempted to further develop the

Table 3.1 Malaria control measures

Action envisaged	*For individual and family protection*	*For community protection*
Reduction of man-mosquito contact	Bednets, repellents, protective clothing, screening of houses	Site selection, zooprophylaxis
Destruction of adult mosquitoes	Use of domestic space spraying (aerosols)	Residual indoor insecticides, space spraying, ultra-low volume sprays
Destruction of mosquito larvae	Peridomestic sanitation, intermittent drying of water containers	Larviciding of water surfaces, intermittent irrigation, sluicing, biological control
Source reduction	Peridomestic sanitation, small-scale drainage	Environmental sanitation, water management, drainage
Destruction of malaria parasites	Early diagnosis and treatment, chemoprophylaxis	Establishment of diagnosis and treatment facilities, chemoprophylaxis for pregnant women, mass treatment
Social participation	Motivation for personal and family protection	Health education, community participation

Source: Adapted from Bruce-Chwatt (1985).

epidemiological approach to malaria control, which had been proposed by the Expert Committee in 1979, giving particular emphasis to socio-economic factors. This epidemiological approach recognizes that variability among diverse malaria situations is due to a multitude of factors that will also affect the effectiveness of control measures. Mapping the distribution of these determining factors would constitute a "stratification" of the local malaria problem and would provide a useful framework for selecting and testing appropriate sets of control interventions.

Identification of malaria patterns

In practice, the identification of all relevant epidemiological factors has not come easily to control program managers. They are often not equipped to analyze and interpret the massive quantities of epidemiological, parasitological, and entomological information that need to be collected — or to use this information to define appropriate control actions. In particular, control programs have generally lacked the ability to see specific malaria situations in their economic and social context, that is, to analyze the relationships between patterns of human occupation and exploitation of the environment and trends in malaria transmission.

Nevertheless, accumulated experience and some specific studies of major problem areas showed that there are identifiable ecological and social situations where malaria is not only more frequent and serious but also more difficult to control. In the Brazilian Amazon, for example, economic, social, environmental and political factors have converged to produce three epidemiological patterns (sometimes referred to as "prototypes" or "paradigms"), collectively referred to as "frontier malaria" (Marques, 1988; Sawyer and Sawyer, 1987; Wilson and Alicbusan-Schwab, 1991). These patterns are found in the now famous *garimpos* (gold mining areas), in areas of new agricultural settlement and in the rapidly expanding peri-urban areas of the region. Although found in less than one in ten municipalities, they account for more than 80 percent of all malaria cases reported. Similarly, most malaria situations throughout the world, when viewed in their social and economic context, fall into a few major types.

It has been suggested (Nájera 1981, 1989) that it is possible to recognize and describe a limited number of prototypes, synthesizing, from a global perspective, those observations in different countries, complemented with summaries of control experiences in such situations. These descriptions, which have been referred to as "malaria paradigms," could help health planners in the important task of designing and implementing appropriate sets of control measures, either to develop new programs or to adapt existing ones. Some patterns this far identified are outlined below:

Malaria patterns associated with specific ecological conditions

African savannah

Characteristics. African savannah represents the highest malaria endemicity in the world. The factors responsible for high levels of continuous transmission include propitious climatic conditions for vector breeding and the presence of highly efficient vectors such as *An. gambiae* and *An. funestus.* This pattern is characterized by high frequency of illness among young children and pregnant women, high childhood mortality and high frequency of asymptomatic infections in older children and adults. Transmission may become seasonal in areas with less rainfall and at higher altitudes. Recently, the malaria problem has been aggravated further by the rapid spread of drug resistance across the African continent.

Control. In the African savanna context, the most important aspect of malaria control is to reduce the impact of the disease by providing effective treatment to all people suffering from malaria, which would require extension of services and health education to improve their use by the population. Pilot projects, aimed at the interruption of transmission in savanna areas, have been only partially successful, and institutional problems have constrained expansion of vector control programs (Sokoto: Bruce-Chwatt and Archibald, 1959; Bruce-Chwatt, 1979) (Pare Taveta: Wilson 1960) (Kankiya: Foll and others, 1965; Nájera and others, 1973). However, there are some areas or population groups where vector control may be feasible; in particular it may be possible to introduce effective insecticide-impregnated bednets or curtains.

Plains and valleys outside Africa

Characteristics. These areas correspond to the classical descriptions of malaria as a rural disease, being more intense in the poorest areas and in periods of economic depression. As in the Af-

rican savanna, transmission may be from continuous to seasonal, depending on latitude, altitude and aridity. The risk of transmission tends to increase with the introduction or extension of irrigation but considerably decreases with good water management and the improvement of farming techniques, houses, and animal shelters. In most of these areas malaria was brought under control by the early eradication campaigns and vector control has continued over the last three decades. Unless disturbed by civil unrest, insurgence or war, which would not permit the functioning of health services, these areas today show low endemicity.

Control. In most instances, it will be possible to maintain this favorable situation by continuing the development of their health and epidemiological services and their ability to detect and control increased risk situations.

Forest and forest fringe areas

Characteristics. These areas, which are extensive in Africa, South America, and Southeast Asia, have increased in importance for malaria transmission with intensified exploitation of forest resources. Malaria risks are associated with the type of human activity which modifies the microenvironment and man's and vectors' relations to it. Nomadic and semi-nomadic tribal populations of forest areas, engaged in gathering and hunting, are generally too dispersed and mobile to sustain intense transmission. In the fringe of the forest or deforested areas, sedentary populations tend to be engaged mainly in agriculture but also utilize the forest to collect firewood and hunt. In Africa, the main malaria vectors, *An. gambiae* and *An. funestus*, follow man into the forest and, although they are more easily controlled than in the savanna, they are able to maintain the same levels of very high endemicity. In Asia and the Americas, settled population groups, engaged in regular agricultural activities in deforested areas, have a different malaria experience than those engaged in forest activities. The former suffer mostly from *P. vivax* infection and tend to have much lower malaria incidence, easily controllable with residual insecticides. However, activities at the edge or inside the forest are associated with a high risk of acquiring *P. falciparum* malaria.

Control. Residual insecticides are practically ineffective against the highly exophylic forest vectors. Protection has been traditionally dependent on the use of drugs, often excessive and irregular, due to the absence of organized curative services. When international borders run across these areas, as is common in South America and Southeast Asia, there may be a concentration of illegal activities, which make areas even less accessible to programmed control. Chloroquine-resistant *P. falciparum* originated in areas of this type, both in the Colombian-Venezuelan and the Thai-Kampuchean border (Field, 1967). Today more effective means of personal protection, such as pyrethroid-impregnated bednets and repellents, offer a possibility of complementing the partial effect of currently available antimalarial drugs and eventually reducing the dependence on chemoprophylaxis.

Highland fringe and desert fringe

Characteristics. Altitude, drainage and temperature are limiting factors in both mosquito breeding and in parasite development in the mosquito. Therefore, these factors have an important impact on the potential for malaria transmission along the *fringes of highland areas*. The highlands themselves, which tend to have less malaria, often are characterized by high population density and pendular migration between the highlands and neighboring valleys. These neighboring areas, which offer economic opportunities on plantations or in other development projects, often tend to have more malaria. Unusually warm rainy seasons may cause serious epidemics in highland areas of low endemicity, resulting in high mortality (e.g., East Africa and Madagascar in 1987-90). In Southeast Asia, vectors that breed in foothill streams (e.g., *An. minimus* and *An. fluviatilis*) are more efficient vectors than those in the plains. Therefore, the foothills in such areas tend to be more malarious than the plains. In transitional zones adjoining deserts, the lengthy dry season also limits vector proliferation and malaria. Also, the populations of such areas tend to be dispersed and nomadic; epidemics may occur in years of exceptional rainfall or with the introduction of irrigation.

Control. As everywhere, effective disease treatment is fundamental in both highland and desert fringe areas. In addition, surveillance for the monitoring of epidemic risk indicators, and for the early detection of epidemics, is crucial. In different areas, different responses may be feasible. These responses may include a combination of preven-

tive vector control, strengthening of treatment facilities, and mass fever treatment.

Seashore and coastal malaria

Characteristics. The most typical situation is found where the mosquito vector breeds in brackish waters. Such mosquitos are generally less efficient as vectors than those of neighboring inland areas, as is the case in Africa with *An. melas* and *An. merus* and in South America with *An. aquasalis*. However, in Southeast Asia and the Pacific, *An. sundaicus* and *An. farauti* are responsible for very serious malaria transmission. In some coastal areas, as in Central America and Mexico, fresh water breeding mosquitos may cause intense seasonal transmission by breeding profusely in estuaries closed by a sand bar during the dry season. A frequent form of economic development in coastal areas is the establishment of tourist resorts, which often make important investments, not only in malaria control, but also in pest mosquito control, for the protection of the installations. The development of tourism often attracts more people than those that can make a living from the existence of the tourist resort, creating situations similar to those of peri-urban slums (see below).

Control. Disease control in tourist resorts is similar to urban areas (see below). In the case of rural coastal populations, whether engaged in agriculture or fishery, the basic measure should be case management and engineering methods, such as opening or flushing estuaries, land reclamation for agriculture or tree plantation, regulation of water courses, and so forth.

Urban malaria

Characteristics. Except for some cities in Southern Asia, where *An. stephensi* is fully adapted to the urban environment, malaria transmission does not occur in well-established, densely populated urban areas. Nevertheless, many tropical cities are surrounded by rapidly growing slums, which are basically a high concentration of shelters in what is still a basically rural environment. This leads to increased malaria transmission. Eventually a high contamination of surface waters may prevent anopheline breeding before urbanization reaches the slum areas. Malaria transmission in urban areas varies considerably in space and time, but in certain situations may be very high.

Control. Malaria control in urban areas relies on environmental sanitation in order to eliminate existing mosquito breeding sites and prevent the creation of new ones. In addition, man-vector contact can be reduced through improved house construction and personal protection.

Malaria patterns associated with specific occupations or social conditions

Agricultural colonization of jungle areas

Characteristics. Areas of new colonization attract low-income people either from cities or from densely populated areas, with low malaria endemicity. Many people thus have little or no acquired immunity and suffer severely from malaria when exposed to the high transmission risk in the jungle environment. The effectiveness of vector control based on intradomiciliary spraying is limited in these areas because shelters are generally precarious and the vector does not always feed or rest indoors. Social services in these areas are weak or absent. Over time, the situation tends to improve as these settlements become more developed. This pattern is found in Brazil, parts of India, and the Outer Islands of Indonesia (Marques, 1988; Binol, 1983). The agricultural settlement of large new areas is usually accompanied by the rapid growth of supporting urban centers as well. These centers attract large numbers of poor, often unemployed or underemployed migrants, who settle in precarious conditions on the urban periphery. This explosive peri-urban growth is also associated with high levels of malaria transmission (Sawyer, 1986; Sawyer and Sawyer, 1987).

Control. Traditionally, protection has been dependent on the use of drugs, especially during the initial phases of settlement. However, use of drugs has often been excessive and irregular due to the absence of health services in these remote areas. Residual insecticides have proven less effective against highly exophylic forest vectors. In some areas traditional vector control activities may be possible. Furthermore, measures for personal protection, such as pyrethroid-impregnated bednets and repellents, may be introduced in combination with appropriate information and health education.

Gold and gem mining

Characteristics. Malaria is usually serious in remote forest areas among populations of miners

who migrate frequently between existing mining areas, new mining areas, and urban and rural areas (e.g., Brazil and Venezuela). Occupation of these areas is often temporary and investments in basic infrastructure and services is rare, especially in countries where small-scale mining is illegal. *P. falciparum* drug resistance is frequent (e.g., Thai-Kampuchea border, Colombia-Venezuela border, Brazilian Amazon). Because they have tended to penetrate deeply into frontier areas, these gold and gem miners have often exposed highly vulnerable indigenous peoples to malaria and other diseases, with disastrous consequences.

Control. In these areas malaria control activities are exceedingly difficult. Case management is clearly a priority. Recently, attempts have been made to introduce insecticide-impregnated curtains and bednets. In high-risk areas lacking any health facilities, it may sometimes be appropriate to establish specialized malaria clinics.

Migrant agricultural labor

Characteristics. Cotton, sugar, and large-scale rice cultivation often require large contingents of temporary labor for planting and harvesting. The workers generally live in crowded, unsanitary camps where mosquitos abound and precarious shelters offer little protection against the malaria vector. Because of heavy pesticide use for agriculture, often sprayed by airplanes (especially in cotton farming), vector resistance to a broad spectrum of insecticides is common.

Control. Disease control requires case management and the application of residual pesticides, where possible. In some cases aerial pesticide application is very effective. In addition, personal protection measures, such as the use of impregnated bednets, can sometimes be applied. If irrigation practices allow, drainage, biological control and other source reduction measures may be indicated.

Displaced populations

Characteristics. Sociopolitical disturbances (such as wars, unrest, famines) often create situations where the civilian population suffers from a lack of basic supplies, the destruction of houses, and forced displacement; people may even be temporarily or permanently housed in refugee camps. These factors, combined with the disruption of health services, may cause epidemic outbreaks even in areas previously well under control. Such outbreaks particularly affect the civilian population while the military and police contingents are likely to benefit from organized control in their camps and chemoprophylaxis while in action.

Control. In these areas control depends on the size and organization of the refugee population and the intensity of the problem. It may be possible to consider mass fever treatment, temporary chemoprophylaxis, and even spraying of shelters. Sometimes relocation of camps and some sanitation measures are possible.

Patterns and measures for control

The matrix in table 3.2 relates the patterns identified above with control measures that have or have not proven effective in malaria control programs. This table is neither comprehensive nor prescriptive; its intent is to help operationalize the concept of epidemiological stratification.

It must be noted that the diagnosis and treatment of cases — including the management of drug resistance — applies equally to all patterns. Case management and drug treatment, which in most cases represents the care of fever, without specific diagnosis, are dependent on the structure of the general health care system. Diagnosis and treatment should be undertaken by the general health services; in areas where such services are very weak or nonexistent — such as in forest fringe areas/frontier areas — special fever treatment posts or malaria clinics may be needed. Transmission control interventions must be used more selectively as shown, wherever they are affordable and can achieve sustainable results.

Vector control operations have relied overwhelmingly on spraying of residual insecticides. The effectiveness of residual spraying varies substantially with the biting and resting behavior of the mosquito vector, the type of housing and the habits of the people. A control measure which is receiving increasing attention is the use of insecticide-impregnated bednets or curtains.

Other techniques of vector control play a more restricted role but, where indicated, may be highly effective. Space or aerial spraying is seldom used — and is rarely justified. Larvicides are feasible only with easily identifiable breeding places. Source reduction techniques such as drainage and water management techniques, can be the measures of choice in urban and peri-urban areas and

Table 3.2 Patterns associated with ecological and social conditions

	Major ecological conditions							Specific occupations/ social conditions		
Control intervention	*African savannah*	*Plains and valleys outside Africa*	*Forest and forest fringe*	*Highland and desert fringe*	*Seashore and coastal*	*Urban*	*Agricultural colonization of forest*	*Gold mining*	*Migrant agriculture labor*	*Displaced populations*
Management of clinical malaria										
Diagnosis and treatment	+	+	+	+	+	+	+	+	+	+
Care of treatment failures	+	+	+	+	+	+	+	+	+	+
Protection of pregnant women										
Chemoprophylaxis	+	-	+	-	-	-	+	-	-	-
Bednets and personal protection	+	+	+	+	+	+	+	+	+	+
Vector control										
Residual spraying	-	Selective	Selective	Epidemic control	Selective	Limited	Selective	-	Limited	Epidemic control
Fogging ULV	-	-	-	-	+	Limited	-	-	Limited	+
Impregnated bednets or curtains	+	+	+	-	+	-	+	+	-	-
Environmental control										
Drainage and source reduction	-	-	-	-	+	+	-	-	+	-
Larviciding	-	-	-	-	+	+	-	-	+	-
Biological control	-	-	-	-	Limited	+	-	-	+	-
Surveillance										
Epidemiological surveillance	+	+	+	+	+	+	+	+	+	+
Monitoring epidemic risk	-	+	+	+	-	-	-	+	+	+
Health education	+	+	+	+	+	+	+	-	-	-

economic development projects. However, they are normally too costly for widespread use.

Residual practices from malaria eradication programs

Many malaria control programs continue to depend on practices that have been held over from the eradication era and that require adjustment. Indoor spraying of residual insecticides, the main control activity of eradication programs, consumes a large part of present program budgets. In principle, coverage with residual insecticides should be complete and regular to achieve significant reduction or interruption of transmission. Today's spraying is seldom regular, as most budgets do not provide enough insecticide to cover all cycles; they are rarely complete as people often refuse to allow continuous routine spraying. Therefore, more selective, targeted, and cost-effective use of pesticides is needed.

Many malaria control programs continue the practice of case detection as the main mechanism to diagnose and treat malaria. This procedure, devised to confirm the disappearance of malaria during the consolidation phase of a malaria eradication program, aims at the collection of a blood slide from every fever case in the population by a system of periodic house visits and the collaboration of all outpatient clinics of the health services. All fever cases are given a single-dose (presumptive) treatment; if the blood slide is positive, a full (radical) treatment follows (now, in most cases, weeks or months later, when the result from the laboratory becomes available).

The consequence of insisting on a thick blood film for every fever case are that malaria microscopists are overwhelmed with negative slides, the examination of which not only takes most of their time but could also distract them and cause them to miss positives. The diagnosis is often late, so that it cannot help in the differential diagnosis of nonmalarious fevers, and the radical treatment, when offered, may no longer be needed. Reports to WHO indicate that 150 million slides are collected each year, with an average positive result rate of 3 to 5 percent. Some malaria programs make great efforts to maintain a network of laboratories staffed by reasonably trained microscopists, engaged most of the time in the diagnosis of ambulatory fevers. But they do not feel responsible for making competent microscopy available in the medical care establishments for the diagnosis and monitoring of treatment of suspected severe malaria cases; case detection continues to serve mainly an epidemiological purpose and does

not contribute to improving the quality of care of the health services.

The epidemiological services of the malaria programs were designed to confirm that malaria had been eradicated and insisted on confirming directly that the parasite reservoir had been eliminated. These services overlooked indirect indicators of risk. As a result, malaria programs have a poor record for early detection, let alone prediction, of malaria epidemics. A number of epidemics reported in the literature were detected by poorly organized general health services reporting abnormal increases of fever cases, while the malaria program case detection mechanisms operating in the area detected no abnormality until months later, when slides had been examined, results reported, and reported cases consolidated and analyzed. This mechanism often is unable to detect abnormal situations until they become large enough to overcome the dilution effect of consolidated reporting, as practiced by centralized malaria programs. General health services and local authorities are more sensitive and more likely to demand action in response to peripheral complaints, if encouraged to do so.

4

Costs of malaria control

Patterns, cost effectiveness, and the choice of interventions

The nature of the different scenarios has a strong impact on the choice of appropriate policies to combat malaria. Calculations of cost effectiveness need to be made in each specific circumstance. The value of calculating cost effectiveness of interventions is to help policymakers make decisions about competing uses of resources. The steps in any such analysis are the following: 1) identify the policy instrument which is actually under the control of the decisionmaker, 2) determine the relation between the policy instrument and the measure of outcome desired, and 3) pursue the activity until the marginal effectiveness per unit of marginal cost falls to a level comparable to other uses of funds. Each of these components is problematic and each is sensitively related to the epidemiological pattern the decisionmaker encounters.

Interventions

Often, the set of available policy options is clear. However, there is sometimes confusion over what is actually controlled by the government. For example, chemoprophylaxis for pregnant women and the use of insecticide-impregnated bednets are included as control interventions. This is merely shorthand for policies that promote the use of these techniques of control: for example, Information, Education, and Communication activities (IEC) for prenatal care (in conjunction with a protocol for drug prescriptions); and either a subsidy on the sale of bednets or free distribution of materials, and an IEC campaign on their appropriate use. Strictly speaking, it is these latter policies that should be evaluated on the basis of cost and effectiveness.

Organizational, political and social factors implicit in some of the patterns define or impose limits on the appropriate policies. For example, the policies involved with management of clinical malaria are specific to the structure of the general health care system. Costs associated with malaria are sensitive to the organization of the health system. Mills (1987) compares the costs of provision in vertical programs versus integrated programs in Nepal and finds that the higher the volume of cases, the more similar the costs of the two organizational approaches. In areas where case loads are low, integrated programs can have substantial cost savings since personnel can switch to other health needs as appropriate.

One decision concerning provision of treatment (for all complaints, not just malaria) would be the density of location of health centers or, more realistically, the location of new centers. The difficulty in separating care for malaria from care for anyone who presents with fever is sharply defined in this case. While probably the most important factor in the care of malaria in endemic areas, such decisions cannot possibly be made with regard to malaria alone. To the extent that malaria generates a large proportion of visits to health centers, however, this could argue for shorter distances to clinics in new areas of agricultural development (relative to more stable communities) because of the greater severity of the disease in these areas

(even though the set of appropriate interventions is the same for the two settings). Again, this is part of a much larger problem. In general, the interventions involved with case management are not specific to malaria and include protocols for the public health facilities; protocols for the regulation, taxation or subsidization of drugs and/or private health care providers; and recommendations on care for these providers. Benefits accrue to the system from any of these interventions but attributing them to malaria is misleading.

Returns to scale

Costs per measure of outcome (deaths averted, discounted healthy life years gained) vary substantially with the level of activity of the intervention. Certain features of intervention programs are relatively fixed and therefore independent of scale of operation (facilities, staff salaries in the short run), others are variable and proportional to output, and still others rise more than proportionately with output. Assessing the (marginal) cost per unit of outcome achieved needs to be assessed in each context. At a global level, Molineaux speculates (1988) that there may be "decreasing returns" as many early programs of malaria reduction were recognized as having very strong effects while recent efforts have been more disappointing.

Portfolio of interventions

For a number of alternative policy options in malaria control, there are good reasons to expect diminishing returns to most single activities; effective policies should therefore comprise several instruments. Costs to vector control activities will rise with decreasing densities of vectors and people. Costs to case management operations will rise also with decreasing frequency of cases and the eventual need for costly public information or IEC campaigns. Barlow and Grobar (1986) suggest that the great uncertainty surrounding cost estimates argues that a combination of policies needs to be used in parasitic disease control programs. An analogy to financial management can be made, that is, a "portfolio" of instruments should be used to reduce the risk of the entire program resulting in failure. Here, we argue that for malaria, at least, a combination of policies would be desirable (even with accurate information) because of diminishing returns to any one instrument.

Vector control

The cost effectiveness of residual spraying varies substantially with the endemicity of the disease in the locale and the degree of intensity of use. In regions of low to medium endemicity, where either the elimination of the disease or substantial reductions in prevalence in humans due to vector capacity reductions are possibilities, the effectiveness of vector control may be high. It may also have thresholds or regions of "increasing returns" near levels where eradication is possible. Generally though, there are good reasons to expect rising marginal costs associated with increasing workers hired for spraying. However, with decreasing density of housing units and increased distance from facilities in urban or regional centers, costs per house protected will rise as more man-hours will be needed for more remote areas. Similarly, small regions with high densities of the vector will be cheap to reach while expansion to wider areas will become costly. Within a region, the cost per house protected will rise due to decreasing chemical effectiveness on the vector pool. Refusal of populations to have dwellings sprayed also makes improvements on the margin more difficult.

Other techniques of vector control play a much more restricted role. Space or aerial spraying is seldom used, with possible exceptions for urban epidemics or to interrupt short transmission seasons, and is rarely justified on cost grounds. Larvicides are feasible only with easily identifiable breeding places and are thus of limited use. Other source reduction techniques, such as drainage and land management, can have significant effects in mainly urban areas, planned human settlements or economic development projects, but cannot be a major part of widespread control operations.

Clinical management

The cost of chemotherapy depends on both the cost of treatment itself as well as the cost (both to the health care system and to the individual) of getting the patient to seek treatment. For self-diagnosis (for over-the-counter purchases of chloroquine), or for spontaneous presentation at a health care facility, these costs are generally quite modest though they depend on the availability of drugs and distances to facilities. For a target population of malaria sufferers who do *not* seek help in either of these forms, expansion of chemotherapy requires the use of information campaigns de-

signed to encourage people to seek timely care or the use of active case detection methods, which are usually very expensive.

As to the effectiveness of drug treatment, to date, the use of chloroquine has been a remarkably effective and cheap method of dealing with the disease. People have been able to obtain the drug easily and much treatment has taken place outside of the formal health care system. One consequence of this may well have been speeding the progress of chloroquine resistance. The spread of chloroquine-resistant malaria has changed the picture substantially. Not only are the costs of other drugs higher, they also require more professional supervision and some of them run into more serious problems of compliance with drug regimens. At 1987 prices one adult course of drug treatment with chloroquine costs $0.23 per person; with sulfadiazine / pyrimethamine, $0.50; with mefloquine / sulfadiazine / pyrimethamine, $1.20; and with quinine and tetracycline, $3.00. Drug treatment is likely to continue to be the principal antimalaria weapon. However, the possibility of multiple resistance and the difficulty of extending suitable health care to more remote rural areas are two reasons the costs of malaria control will continue to increase if based on the indiscriminate use of antimalarial drugs.

Personal protection

To some degree, the government can rely on public information messages to increase people's use of protective measures or to influence their use of drugs. The protective measures include bednets, perhaps impregnated with insecticides, and modification of evening activities and clothing. For bednets, a subsidy on their sale is also a possibility. Although bednets have been shown to reduce disease, the prospect for increasing their use is unknown. Some people (more educated or concerned) may be quite easy to reach, but increasing usage to any great extent would probably be expensive. To the extent that behavior does change, however, it can increase the effectiveness of antivector campaigns.

More rational use of antimalarial drugs should help slow the spread of resistance that has been encouraged by excessive and inappropriate use. To the extent that behavior can be changed by public information campaigns, this effect can be ameliorated. What this might cost and how much it might be worth require research geared to helping operations.

Cost analysis for decisionmaking

Most countries with malarious regions have in place some institutions designed to address the problem. The activities which are undertaken by these institutions depend partly on the local needs but also on history, cultural acceptability and political concerns. The most practical use of cost information is to assist managers of the local malaria public health facilities in making better incremental decisions in a constrained environment. When specific activities are proposed for a specific area, costs can be gauged relatively easily as changes in scale are not at issue. Incremental benefits can also be appraised in terms of the local epidemiology and institutional and administrative conditions. Costing exercises in these cases can greatly improve allocation decisions by managers. Good examples of this use is the work done by Kaewsonthi and Harding (1986) in Thailand and by Mills (1987) in Nepal. In these studies, comparisons between techniques of vector control and between vector control and therapy are made clearer by careful costing procedure at local levels; based on comparison results, practical recommendations for improvements are made. Mills, for example, was able to suggest a reduction in active case detection methods and an increase in malaria clinics or other treatment-based facilities (and further suggested that either of these methods would be preferable to spraying).

Estimates of cost effectiveness

From the review paper by Barlow and Grobar (1986) mentioned above and Mills (1987), the costs per year of life saved and benefit-cost ratios are calculated for a variety of countries. These results are presented in tables 4.1 and 4.2, respectively.

The most striking feature of these numbers is their variability. Indeed, the differences between the studies are so marked that it would be hard to make any generalizations about them. The costs per case prevented ranged from $2.10 to $259 (in 1987 U.S. dollars) and the benefit-cost ratios from 2.4 to 146. The higher benefit-cost figures make malaria control seem of utmost importance. The lower figures bring it into competition with many other government programs as well as with many estimates of the marginal deadweight loss from tax collection (the systematic undervaluation of costs of government sources). Part of the explanation of the wide range of variation is not very illuminating. Differences in data quality, in as-

Table 4.1 Cost effectiveness ratios
(1987 U.S. dollars)

Author	Country	Method	Cost per case prevented	Cost per death averted	Cost per discounted QALY saved by case fatality rate[a]			
					2%	1%	0.5%	Observed
Barlow (1968)	Sri Lanka	Insecticide	..	78	..	..	..	2.8
Cohn (1973)	India	Insecticide	2.10		3.6	7	14	
Gandahusada and others (1984)	Indonesia	Insecticide	83-102		142-174	284-349	564-693	
Hedman and others (1979)	Liberia	Vector control and chemotherapy	14		24	48	95	
Kaewsonthi and Harding (1984)	Thailand	Vector control and chemotherapy	27-74		46-127	92-253	183-502	
Mills (1987)	Nepal	Vector control and chemotherapy	1.30-172					2.8-255
Molineaux and Gramiccia (1980)	Nigeria	Vector control and chemotherapy	259		443	886	1759	
Ortiz (1968)	Paraguay	Insecticide	60		103	205	407	
Walsh and Warren (1979)	LDCs	Vector control		990				34

a. QALY is quality-adjusted life year.
Source: Barlow and Grobar, 1986; Mills, 1987; authors' calculations.

sumptions used in the analyses (e.g., the estimation of mortality avoided), in the definition of the relevant costs, in the length of time studied, in the discount rate applied, and in the coverage and purpose of the original intervention all account for much of this variation. As one example, in the Garki Project study (Molineaux and Gramiccia, 1980), which generated the figure of $259 per case averted per year, the costs of the extensive research and monitoring exercise that accompanied the intervention are included in the program costs. Similarly, some of the studies included administrative costs while others used only the cost of materials. Some costs were calculated on the basis of small pilot projects (Indonesia: Gandahusada and others, 1984) and others on the basis of national efforts (Sri Lanka: Barlow, 1968).

The last four columns of table 4.1 calculate the cost per discounted, quality-adjusted life year (QALY) saved for differing assumptions concerning the case fatality rate for cases where the study does not explicitly present that value. The numbers are very sensitive to this assumption, much more so than to any other parameter in the QALY calculation. Any attempt to calculate "cost per discounted quality-adjusted life years" saved by the program requires locally relevant estimates of case fatality rates.[1]

However, as discussed above, there are more important, systematic reasons to expect average costs per unit of output to vary substantially between studies: 1) differences in the ecological/epidemiological/social characteristics between areas, 2) wide variations, within areas over time, of the incidence and severity of malaria, 3) variations in the organizational structure of control programs, and 4) differences in the intensity of application of the interventions being appraised.

Table 4.2 Benefit-cost ratios in malaria control

Author	Country	Method	Cost
Barlow (1968)	Sri Lanka	Insecticide	146.0
Griffith and others (1971)	Thailand	Chemoprophylaxis	6.5
Khahn (1966)	Pakistan	Eradication prog.	4.9
Livadas and Athanassatos (1963)	Greece	Eradication prog.	17.3
Niazi (1969)	Iraq	Eradication prog.	6.0
Ortiz (1968)	Paraguay	Insecticide	3.6
San Pedro (1967)	Philippines	Eradication prog.	2.4
Dem. Rep. of Sudan (1975)	Sudan	Control program	4.6

Source: Barlow and Grobar, 1986.

1. For purposes of presentation, the other parameters in the QALY calculation were assumed to be: 29 discounted years gained per death averted, 8 days of illness and a 10 percent quality of life adjustment for nonfatal cases. Except at very low case fatality rates, the calculations are quite insensitive to large ranges in the assumed values of these three parameters.

5

Priorities

Our perception of malaria has been changing rapidly over the past decades. Malaria is not, as once was thought, evenly spread over the geographic areas in which it is prevalent. Instead, it is highly focal, primarily affecting the hardest areas to reach, and it is intimately linked to development efforts such as agricultural development, road building, fiscal incentives, and colonization projects. Furthermore, malaria, which once was easily treatable with chloroquine, has reemerged as a new disease called drug-resistant malaria. Drug-resistant malaria has been spreading and serious problems in treatment are becoming more and more common. Finally, parasite distribution has not remained stable, but there is a general increase and a general shift from the more benign tertian malaria caused by *P. vivax* to the often fatal tropical malaria caused by *P. falciparum*.

Taking into account the epidemiological situation of malaria at present, the trends in the past 15 to 20 years and the prevailing level of endemicity in tropical Africa, it is reasonable to believe that a considerable deterioration of the situation is to be expected before the end of this century, unless a more serious control effort is made. Even if vaccines, new drugs, or new insecticides are developed, in view of the time required for their final testing in the field, it is difficult to expect a significant impact on malaria in the 1990s. The most critical activities that could accelerate the progress in malaria control can be summarized as follows:

- In countries of Asia, the Americas and North Africa, in which organized malaria control activities have been carried out for nearly three decades, the priority should be on reassessment of activities. Replanning of programs must be based on epidemiological analysis, implementing, at the same time, necessary changes in the organization and administration of these programs.
- In Africa south of the Sahara, priority should be given to the extension of coverage by the health care system. At the same time, a nucleus of malaria specialists should be trained and selective control programs started. This should enable realistic planning and implementation of malaria control activities bearing in mind the public health importance of other endemic diseases prevailing in given areas. The implementation of any control activity on a larger scale should be preceded by an epidemiological field study that would contribute to the better understanding of the local epidemiology of malaria.

Human resources development

At the beginning of the malaria eradication program a major effort was made to train the personnel needed for the program, but, as programs became staffed and because malaria was expected to disappear soon, manpower resources — especially young professionals and technical staff — became increasingly scarce. It has been said that the global malaria eradication program did not eradicate malaria, but did eradicate malariologists. Moreover, training for eradication was definitely oriented toward the execution of the highly standardized program tasks and operations. The training of malariologists did not give them the epidemiological background needed to

adapt to changing situations, to solve problems, to manage uncertainty or to adapt or change control approaches and strategy.

To meet current needs and achieve sustainable control, it is essential to create the manpower needed and to reorient human resources not only to apply standard solutions to recognized problems, but also to identify and find a solution to future problems. In that way we may be able to avoid repeating the cycle described in 1927, in the Second Report of the Malaria Commission of the League of Nations: "The history of special antimalarial campaigns is chiefly a record of exaggerated expectations followed sooner or later by disappointment and abandonment of work."

National training programs should be supported and coordinated to ensure, through technical collaboration between countries, that all countries are able to:

- Maintain a corps of adequately trained professionals with the necessary epidemiological expertise to understand the malaria problem and to adapt control strategies and programs to new situations.
- Train and orient general health services staff in the clinical management of malaria, recognition and treatment of severe and complicated malaria, monitoring of drug resistance, and collection and management of epidemiological information.
- Develop appropriate training approaches for nonprofessional workers and community health workers so they can better manage fever and promote personal protection and an improved environment.
- Promote the development of curricula in schools of medicine and schools of public health, to include new approaches to malaria control and to develop their capability for staying abreast of the latest information on the diagnosis and treatment of malaria.

Drug and vaccine development

The development of new or improved methods or materials for malaria control — in particular, antimalarial drugs and potential vaccines — should continue to receive the highest priority. This view, which is widely supported and, to an important extent, has shaped the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases' (TDR) research priorities, was recently reconfirmed by the National Academy of Sciences/Institute of Medicine report on malaria.

6

Research

The most damaging effect of the malaria eradication years was probably the neglect of malaria research and malariology's lack of appeal as a career for young scientists and epidemiologists. In the words of McGregor (1982), "throughout the world support for further research into malaria, even that concerned with insecticides and chemotherapeutics, contracted swiftly. Worse still, the apparently imminent demise of a once important disease removed the necessity for training scientists in malariology. It took 10 more years and a war to halt this tragic trend."

The reawakening of interest in malaria research showed a marked bias toward new technological developments through laboratory-based research, mostly in chemotherapy, immunology, genetics and the genetic control of vectors, and the possible use of mosquito pathogens.

In particular, since 1976 the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) has assumed a key role in coordinating and funding malaria research. It has made malaria its first priority and continues to provide technical drive toward development of new tools for control.

Actually, most available antimalaria interventions are far from ideal, not only in effectiveness but in their suitability for incorporation into long-term policies or the everyday practices of peoples and communities. Moreover, many of them have lost much of their original effectiveness because resistant strains of parasites or anophelines have developed. We must improve our understanding of the epidemiology of malaria and of problems such as parasite and vector resistance. We must improve the tools of epidemiological investigation so we can identify problems in the field, plan and evaluate potential solutions, and more effectively target interventions to problems. We must understand and monitor social and economic processes that may influence the epidemiology of malaria and facilitate or hamper the effectiveness of potential control measures. And we must come to understand how these processes may facilitate the incorporation of malaria control in developing health infrastructure.

Funding for malaria control programs shrank when people began to recognize that malaria could not be eradicated, when the "basic health services" approach to developing a health infrastructure did not succeed, and when no successful models developed for incorporating malaria control into the primary health care strategy. Malaria and general public health services exhibited a nearly universal reluctance to redefine their responsibilities toward the malaria problem.

Research may provide new and improved technologies needed to extend the feasibility of control, may provide epidemiological tools that improve efficiency of control, and may show better ways to combine interventions in more effective and efficient strategies. But it is also necessary that any new tool be validated in the field and field tested to determine its applicability in disease control. It is important that operational research search for better ways to integrate new and old tools for control. It is important to use health systems research to find the best ways to incorporate new control approaches into the health infrastructure and deliver them to individuals and com-

munities. And as part of the strategy of primary health care, we must test ways to control malaria through a process of research and development.

Malaria control and malaria research have drifted apart over the years. While malaria control programs continued their fight using an established set of tools, research institutions moved off in search of new technological solutions — both under increasing financial constraints.

In some parts of the world, control programs and research institutions have developed a curious rivalry: programs are almost defensively entrenched in the use of established methods such as residual spraying, while researchers uncritically proclaim as alternatives what should be seen as complementary techniques. On the whole, researchers have undertaken projects that are of little relevance to ongoing control operations and the specific problems of control institutions. At the same time, control programs, which often collect massive amounts of valuable information, have lacked the capacity to select research priorities and carry out research projects.

Given the present status of malaria and malaria control programs, we recommend that priority be given to research in the following areas:

- *Epidemiology.* Research is needed to improve our epidemiological tools and understanding and thereby improve our ability to identify problem areas and better target control interventions. In particular, we must understand and monitor social and economic processes that may influence the epidemiology of malaria and facilitate or hamper the effectiveness of potential control measures.
- *Technology.* Research is needed to develop and field test new control technologies and new combinations of old interventions in order to increase efficiency and cost effectiveness of control programs.
- *Organization and management.* Research is needed on the organization and management of control programs in order to develop more effective and efficient organizational structures and management processes.
- *Health infrastructure.* Research is needed on health systems to examine the potential and means for effective participation of the general health services in malaria control, in particular, in epidemiological surveillance, diagnosis and treatment, and community mobilization. Many countries have embarked on a process of decentralization of health services that could impact negatively on the efficacy of vertical malaria control programs. These countries, in particular, will need to move cautiously and study carefully the alternatives for enhancing the general health services' capacity to assume new responsibilities in disease control.

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