Chapter 10

Determinants of Malaria in Sub-Saharan Africa

Jonathan St. H. Cox, Jean Mouchet, and David J. Bradley

The determinants of malaria vary on many scales throughout the world in their effects as well as their occurrence. In many regions, one could argue that there is little justification for considering malaria at a continental scale; often the differences within a continent are too great and diverse. But for Africa, a good case can be made: the vector species are limited in number but widely spread across the continent, and malaria itself has a relatively coherent epidemiology throughout much of sub-Saharan Africa. In particular, because Africa is the home of the most efficient anopheline transmitters of malaria and because transmission reaches much higher levels than elsewhere in the world (with only local exceptions), the characteristics of African malaria are more extreme than observed elsewhere. In addition, the responses to changes in determinants may be different, or more subtle, than may be suspected elsewhere.

The determinants of African malaria and the consequences of changing intensities of those determinants can be understood only in light of the dynamics of African malaria. There often is a quantitative mismatch between the shift in a determinant and the effect produced on malaria, however the latter is measured.

In this chapter, we first analyze how malaria is defined and measured. This explanation is necessary because historically, measurement has focused entirely on transmission. However, recently, other variables have been considered, many of which are more relevant to the populations most affected, in the long or short run. We then address the dynamics of malaria in Africa as the basis for subsequent discussion. Several other general principles of the analysis also are presented.

Malaria and Its Measurement

Malaria must be defined and measured if the effects of possible determinants on it are to be examined. Because the attention of the early researchers and first modelers was on the control of transmission, the first measure of malaria was the basic case reproduction rate (BCRR), as introduced by Ross and developed by Macdonald for malaria. More accurately called the basic case reproduction number, BCRR is very similar to the secondary attack rate that follows one case of malaria in a nonimmune population. It is an excellent measure of malaria at the margins of its occurrence in-space or time (e.g., in situati-
tions where the environment is only marginally suitable for malaria transmission, or where malaria has just begun to spread in its invasion of a nonimmune population or is in the last stages of an eradication program). The target for researchers concerned with systematic climate change has been situations where the environment is only marginally suitable, and the key climate change-malaria models have used the Ross-Macdonald formulation as a starting point. Transmission models have been formulated in terms of $R_0$, which is usually represented in equations as $R_0$.

Researchers more concerned with the risk to nonimmune people introduced into a steady-state endemic situation have instead used the mean number of potentially infective bites per person per night (or per year) as a convenient measure. It is more easily understood but not so appropriate for changing conditions, because it is merely a static description of a dynamic steady state. However, this measure is more easily understood than $R_0$, which has no obvious correlate in the endemic situation.

Both these measures are of infection. But in the African endemic situation, where the majority of children from infancy to adolescence have parasitemia on most days of the year, there may be more concern for the incidence of disease. To define an attack of clinical malaria in the holoendemic situation is profoundly difficult. The parasites are usually present anyway; the fever of malaria under these circumstance is not pathognomonic; and evidence indicates that African children suffer four febrile attacks each per year on average, even in the absence of malaria.

So, how is a clinical attack of malaria to be defined? It may be diagnosed on a combination of fever and a high malaria parasite count in the blood, where “high” is a locally defined age-specific parasite density. Epidemiologically, an “attributable fraction” approach can be used, but this approach requires adequate study populations and substantial effort. Moreover, simple attacks of clinical malaria rarely lead to death. The causes of malaria mortality are profound anemia in the very young and cerebral malaria in all ages from the very young upward. Although the latter point is of immense importance, population-based measurements of the incidence of cerebral malaria are hard to make.

When endpoints are used, the problem is different. Deaths may be recorded or surveyed in various ways, and death is an unequivocal state. In the absence of autopsies in the field, it is hard to reliably ascribe deaths to malaria; however, some limited success has been attained by verbal autopsy. Moreover, measures applied vigorously and successfully to control highly endemic malaria usually reduce the overall death rate by more than the number of deaths ascribed to malaria, so malaria appears to contribute to deaths ascribed to other primary causes. A dynamic model of malaria with disease as the dependent variable has not yet been developed, but it could conceptually be considered relevant for highly endemic situations, even though data are inadequate to construct such a model.

Malaria can be measured in many ways, all with relevance to some situations and all with some drawbacks in operational use. At the edges of transmission, infection and disease become nearly synonymous, because parasitemia is usually accompanied by illness in nonimmune people. In contrast, much of Africa is subject to stable holoendemic malaria, and the effects of environmentally driven changes in transmission cannot be seen as increased prevalence of parasitemia. But there is concern as to whether malaria as a disease may worsen—an outcome that will depend on the shape of the relationship between transmission and disease.

For many decades, this relationship has been viewed as moving to an asymptote at moderately high transmission levels, so that changes in transmission at the top/holoen-
demic) level have been viewed as neutral in their effects on disease. Recently, although several very detailed studies of communities at different levels of endemic transmission in West Africa have supported this orthodox view, queries have been raised from two quarters.

First, the use of insecticide-treated mosquito nets has substantially reduced clinical malaria attacks, even under very high endemicity. Second, data comparing areas with high transmission rates and very high transmission rates have shown a decrease in severe anemia mortality and an increase in cerebral malaria as transmission falls somewhat (Snow et al. 1997). Whether this shift indicates a paradoxical effect of rising mortality with falling transmission at these levels is a more controversial hypothesis, and extensive data related to defined populations are needed to be able to indicate the effects of transmission changes on disease at highly endemic levels. The issue is not irrelevant to consideration of the effects of changing environmental determinants.

**Principles of the Analysis**

**Relationship to Processes**

In considering malaria determinants in Africa, we sought to relate them to the known processes that influence the transmission cycle and the sequence of events that lead to disease and death. This stepwise approach is a relatively cautious one and may miss the sweeping broad assertions of relationship that can come from simple regression of one variable on another. However, the ability to use relationships and to extrapolate wisely to predict the consequences of interventions or of environmental or social changes depends on having insight into the processes concerned. The biological or social plausibility of the relationships of determinants to malaria should not be ignored.

**Inclusion of Control Measures**

The determinants of malaria and its consequences include the measures that are intended to affect transmission or to treat illness. Conventional practice has been to categorize them apart from other determinants. We reject this separation for some purposes and include them in our analysis for several reasons.

First, there is no clear barrier between activities deliberately undertaken to control malaria and activities that are undertaken for different purposes but affect the level of malaria as an infection or a disease. People may buy bed nets for malaria control or to ward off nuisance insects, or even for purposes of privacy or social conformity. The presence of the net and the way it is used will determine its effect on malaria, not the motivation that led to its use. Similarly, the presence of a ceiling in a hut may affect the anopheline biting rate, but ceilings are only very rarely built with this end in mind.

Second, as we emphasize the need to consider health impacts in all aspects of socioeconomic development, the boundaries between deliberate malaria control actions and aspects of environmental planning that have favorable health impacts along with other positive effects become increasingly blurred. The boundary between healthy living and disease control is inevitably unclear.

Third, the population consequences of multiple individual health acts cannot be ignored, especially in relation to genetic change of the pathogen, most notably, the emergence of heritable drug resistance. Chloroquine is given for fever ("clinical malaria") and has been so used throughout Africa for many decades. Much of the fever
is not due to malaria, but over time, the malaria parasites have developed resistance against chloroquine. Misdirected control measures can have major effects on the epidemiology and population genetics of malaria parasites and their anopheline vectors. They are part of the determinants of malaria.

**Historical Dependence of Some Determinants**

Although some malaria determinants can simply be applied as modifiers on the major climatic determinants, others are highly dependent on previous historical processes. An extreme example is the absence of anophelines from some islands of Polynesia and Micronesia, not because they are necessarily geographically unsuitable but because the genus does not seem to have reached them. A far-off, possibly unique event did not happen. One could posit some general rule (e.g., that islands more than a certain distance from others have a lowered risk, or probability of no malaria), but such a method is an unsound way of dealing with rare historical incidents.

A more common situation for which this approach may be appropriate concerns historically determined risks. Drug resistance to chloroquine appears to arise only with great rarity. It can be argued plausibly that chloroquine resistance originally only arose twice—once in the Thai–Vietnam border area, and once in Colombia—and that all subsequent initial chloroquine resistance has been spread genetically from these two sites. In this case, the chance of drug resistance occurring at a given place depends on a set of local patterns of malaria transmission and drug use as well as on the distance from a location where the genes for that kind of resistance are prevalent.

This argument also can be applied to the presence of malaria parasites. If an area of central Asia, far from current transmission, changes environmentally to become highly suitable for malaria transmission, it may take a long while for parasites to be introduced by migrants or to gradually spread from the nearest, but distant, focus of current infection. In contrast, if environmental circumstances become more favorable for malaria transmission at the high altitudes of a tropical mountain whose low slopes abound in uncontrolled holoendemic malaria, parasites will tend to spread rapidly. Thus, models of the impact of climate change on the spread of malaria must account for contagious processes.

**Dynamics of Malaria in Africa**

The key determinant of the dynamics of malaria transmission in Africa is the great efficiency of African vectors relative to those of other continents. This vector system is responsible for very high inoculation rates and is remarkably stable in a wide range of environmental conditions. African vectors also appear to be relatively flexible in exploiting landscape changes brought about by anthropogenic activity (Coluzzi 1984).

Coluzzi (1984) estimates that together, Anopheles funestus, Anopheles gambiae, and Anopheles arabiensis account for 95% of all infective bites in the Afrotropical region. On a broad scale, we would expect the distribution of transmission to mirror that of these species. Other malaria vectors, including Anopheles nili, Anopheles moucheti, and the salt-water breeders Anopheles melas and Anopheles meniscus, are relatively inefficient but may have important effects at the local level. In forested areas of Cameroon, for example, An. moucheti has been as efficient as Anopheles gambiae sensu stricto (s.s.); although its distribution is limited to the slow-running rivers of central Africa.

According to Mouchet et al. (1998), stable malaria has an inertia that tends to absorb environmental changes caused by human activities. However, that buffering
capacity has its limits, even in Africa, and the degree of local environmental changes needed to effect the transition from stable to unstable malaria is uncertain. Some heavily built-up areas near the center of Africa's large cities and mining areas with strictly enforced environmental health regulations have very little transmission. However, experience has shown that in most endemic areas, significant reductions in malaria transmission are difficult to achieve, whether by trying to eliminate breeding sites at the research level in Tanga, Tanzania, or by reducing mosquitoes in West Africa, where less than one mosquito per house maintains endemicity. The findings from bed net studies and Snow et al. (1997) suggest that even under conditions of persistent, stable, highly endemic malaria, environmental changes can change the frequency of febrile attacks or of the prevalent type of severe malaria while having little effect on parasitemia. This area needs much more research attention in terms of determinants, interventions, and clinical research.

The chief determinants of unstable malaria are the factors that vary the level of transmission, whereas the main determinant of stable holoendemic malaria in sub-Saharan Africa is human acquired immunity. It provides a dynamic regulation of malaria levels, producing the "inertia" described by Mouchet et al. (1998).

The extremely efficient African vector mosquitoes, together with a favorably warm climate, lead to very high values of BCRR and of the steady-state entomological inoculation rate (EIR), which is the mean number of mosquito bites infectious for malaria received by the average inhabitant per unit of time (e.g., per year or per night). If transmission is considered in terms of BCRR, a value of 1 means that transmission is just at replacement level; for every individual infected with malaria who recovers or dies, another incident case appears. This situation is very unstable. If transmission decreases, the malaria ceases to renew itself in the human population and tends to die out. However, if the BCRR increases, so will malaria—except as limited by slowly acquired human immunity.

A BCRR value of 10 means that each case will give rise to 10 more, and the resulting exponential increase will lead to a large epidemic until either all the population is infected or the transmission falls as a result of changed environmental circumstances. When the BCRR remains high, the forces of immunity in the affected population will gradually regulate the spread of infection and the level of transmission. This process is seen most clearly in Africa because the BCRR there is so high; it may exceed 1,000 in parts of the savannas of western and eastern Africa. Under these circumstances, the steady-state EIR (i.e., the risk to a nonimmune visitor) may exceed 300 infective bites per year. The features of this very high degree of endemicity must be understood if we are to understand the likely effects of environmental change (including climate change) on the situation.

What leads to this remarkably high transmission level? Three main variables of anopheline ecology determine the BCRR level:

- the density of female mosquitoes,
- the frequency with which each mosquito feeds on human blood, and
- the longevity of the adult mosquito.

Of these variables, density is the least influential, because there is a simple linear relationship between it and transmission. Changes in the human blood-feeding behavior have a greater effect: because one bite is required to infect the mosquito and another bite is required to infect another person, transmission is proportional to the square of the probability of feeding on human blood. Mosquito longevity is even more-crucial because of the exponential survival curve of the adult female mosquitoes; the chance of
surviving through one day is raised to the power of the number of days that elapse between the day the mosquito becomes a carrier of malaria parasites and the first day it becomes infectious to humans.

Therefore, transmission is proportional to the 10th power (or thereabouts) of the chance of surviving through one day, and mosquito longevity is a crucial factor in determining the efficacy of a malaria vector. The three major African vectors are all long-lived. In addition, An. gambiae and An. funestus are intensely anthropophilic—they have a marked preference for feeding on humans rather than other vertebrates, hence the intense transmission.

Very high BCRRs are responsible for the key features of malaria in much of sub-Saharan Africa. Humans tend to become infected at a very early age, so the vast majority of the population is parasitemic in the first year or even the first month of life. Repeated and overlapping infections are usual, so most children have falciparum malaria parasites in their blood on most days from infancy to age 10. Parasite counts in the blood peak in infancy or early childhood and are reduced gradually by progressively acquired immunity to the red cell forms of the infection.

The price of this immunity may be very high; in the absence of chemotherapy, it may lead to a mortality as high as 5% of all births. It also is very difficult to control because up to a 99.9% reduction in transmission may be needed to keep the BCRR below 1 and thus eradicate malaria. In the Nigerian savanna, eradication has proved beyond the capability of spraying homes with residual insecticides combined with the administration of chemotherapy. Changes in the environment related to climate or land and water resource development have a smaller effect and therefore rarely can disturb the stable malaria transmission of the African forest and savanna. Only toward the margins of environmental suitability (e.g., areas of relatively low temperatures associated with high altitudes or latitude, or in desert areas, where mosquito breeding is highly restricted) does the BCRR fall to a level at which malaria becomes unstable and is more readily susceptible to environmental variation.

**Climatic Determinants**

**Temperature**

Environmental temperature affects the development and survival of malaria vectors and, perhaps more significantly, the duration of *Plasmodium* development within the invertebrate host. In simple terms, the duration of sporogony increases hyperbolically with decreasing environmental temperatures to a point at which parasite development ceases altogether. This critical temperature varies by parasite species. For *Plasmodium falciparum*, the most abundant parasite in sub-Saharan Africa, laboratory studies have estimated it to be in the range of 16–19 °C (Macdonald 1957; Detinova 1962). In practice, transmission is commonly assumed to be limited to months in which the average temperature is above this threshold (Molineaux 1988). In Africa, these temperature limits commonly are reached only at high altitudes (discussed below) and at high latitudes.

If a relatively conservative temperature threshold of 18 °C is assumed, then most of tropical Africa experiences temperatures suitable for malaria transmission at least 10 months per year (Plate 10-1*). However, extensive areas in which temperatures are sub-optimal for six months or more are found in the high-latitude fringes of southern Africa (Botswana, Namibia, South Africa, Zambia, and Zimbabwe) and in highland fringe areas

*Color plates for this chapter appear following page 190.
of Madagascar. In these areas, the effects of low average temperatures may be compounded by those of frost. In Zimbabwe, for example, Leeson (1931) found that Anopheles gambiae sensu lato (s.l.) disappeared when minimum air temperatures fell below 5 °C. The limits of vector distributions in South Africa also appear to be determined by those of frost (e.g., de Meillon 1934). In regions near the equator, the effects of low temperatures are likely to be restricted to discrete highlands areas in Burundi, Democratic Republic of the Congo, Ethiopia, Kenya, Rwanda, Tanzania, and Uganda (Plate 10-1). The geographical transition from areas where suitable temperatures persist year-round to areas where temperatures are limiting for significant periods is often sharp.

It is often difficult to compare large-scale and small-scale effects, because environmental changes may be described in different terms. The macroscale effects of climate are usually given in terms of temperature, precipitation, and humidity. Smaller-scale environmental changes include water and land resource changes, such as irrigation and deforestation. Comparability is improved if these changes are also described in terms of their effects on microclimate.

Lindblade et al. (2000) described microclimatic effects in a recent analysis of land use changes in the highlands of southwest Uganda. At 1,500–2,400 meters, the landscape comprises parallel ridges separated by steep-sided valleys, at the foot of which were extensive papyrus swamps half a century ago. To increase food production, some 85% of these swamps have been drained and used to grow crops. There is widespread concern that malaria has increased in the area, most notably in a recent epidemic apparently linked to the El Niño climatic oscillation.

The hypothesis that malaria outbreaks were due to swamp cultivation goes back to the 1940s (e.g., Steyn 1946; Vincke and Jadin 1946). Lindblade et al. (2000) compared measurements of microclimatic and anopheline bionomics from villages beside the valley bottoms, both near the papyrus swamps and near the drained cultivated areas. Eight villages were studied in each category, and indoor-resting mosquitoes were caught for eight months, beginning in the rainy season. Mean indoor resting densities, predominantly of *An. gambiae* s.l., were almost twice as high beside the drained swamps (0.36 mosquitoes/house) as near the papyrus (0.19 mosquitoes/house). However, this difference did not reach statistical significance; one village was responsible for a substantial part of the difference. There also were nonsignificant differences in sporozoite rates and in the EIRs (sevenfold) between the villages. A regression analysis indicated that temperature differences between the villages were a main contributor to the different transmission parameters.

**Rainfall**

Although several studies have demonstrated an association between *An. gambiae* abundance and rainfall (e.g., Charlwood et al. 1995), a direct, predictable relationship does not exist. *An. gambiae* can breed prolifically in temporary, turbid water bodies such as hoof prints or rain puddles, whereas *An. funestus* prefers permanent water bodies. However, both temporary and permanent water bodies depend on adequate rainfall; therefore, there is good reason for using rainfall to indicate the probable presence of vectors, vector survival, and the potential for malaria transmission (Craig, Snow, and Le Sueur 1999).

The geographic pattern of annual rainfall in sub-Saharan Africa is illustrated in Plate 10-2. The highest amounts are found in coastal areas of Cameroon, Liberia, Madagascar, Nigeria, and Sierra Leone, but annual totals in excess of 1,000 millimeters are characteristic of much of the interior of the continent. The driest areas are southwest Africa.
Botswana, Namibia, and South Africa), parts of the African Horn (Somalia and sections of Ethiopia and Kenya), and the northern Sahel. In these regions, the longevity of adult vectors is likely to be negatively affected by low humidity; relative humidity in excess of 60% is generally deemed necessary for effective malaria transmission (Molineaux 1988).

The effects of quite dramatic climatic events on the level of malaria transmission may depend on their timing. Catastrophic flooding in Mozambique consequent to abnormally high rainfall levels in March 2000 clearly illustrates this point. By late April, malaria transmission had not risen unusually, contrary to what had been predicted in the lay media. The heavy rains had washed out anopheline breeding places, and much of the country remained under water; this is not the breeding habitat for the *An. gambiae* complex, nor is it ideal for *An. funestus*. The breeding habitats were likely to be created as the floods receded, but because the flooding was so extensive, breeding would not be very high until after the temperature had fallen to winter levels unsuitable for malaria transmission. Had the timing of the floods been different, the malaria hazard could have been far greater.

Thus, at the limiting temperatures for malaria transmission, the timing of rainfall hazards may be crucial, and the consequences may vary greatly by season. Increased rainfall in the arid zones will have a much greater effect on transmission. Near the equator, even though extra rainfall may augment mosquito breeding and potentially raise malaria transmission, malarial morbidity may be only modestly affected because of the already high levels of transmission and human immunity.

**Climate-Based Models of Malaria Transmission**

The potential effects of geographical variations in climate on continental patterns of malaria transmission risk have been well illustrated by models developed within the Mapping Malaria Risk in Africa project (MARA; Snow, Marsh, and Le Sueur 1996). MARA’s climate-based malaria distribution model has been developed using a simple numerical approach for defining the geographical limits of transmission based on the biological constraints of temperature and rainfall (Craig, Snow, and Le Sueur 1999). This method uses fuzzy logic to represent whether, under average climate conditions, rainfall or temperature is expected to limit malaria transmission at a given site in any given month. The aggregated annual picture (Plate 10-3) is based on the premise that several contiguous months of “suitable” climate conditions are required to constitute a malaria transmission season. The legend in Plate 10-3 therefore corresponds to the maximum model value that can be sustained over a five-month period (or three months in areas above 8°N, where relatively high environmental temperatures at the onset of the rainy season cause vector populations to increase particularly quickly).

It is important to recognize that the MARA model is based on long-term climate averages (Hutchinson et al. 1995) and provides an essentially static picture of malaria transmission potential under expected climatic conditions. The model may, as a result, underestimate the significance of malaria in epidemic-prone areas (where transmission usually depends on unexpected meteorological conditions). Moreover, because it is a purely climate-based model, it does not account for the distribution of human populations or the likely presence of nonclimatic risk factors. Therefore, although the model corresponds well with existing stratification and expert opinion maps on the broad scale, significant anomalies do occur. For example, because the MARA model does not account for the rather patchy population distribution of sub-Saharan Africa (Plate 10-4), it may give a misleading impression of the risk of disease in sparsely populated areas.
Chapter 10: Determinants of Malaria in Sub-Saharan Africa

Climate Change

Given the stability of transmission in many parts of Africa, climate change probably will not yield significant shifts in malaria epidemiology in most areas. The potential impact in fringe transmission areas is likely to be somewhat variable, however. In many areas (particularly desert fringe), the effects of climate change will be limited by very low population densities. In other areas (e.g., Madagascar, South Africa, and Zimbabwe), malaria surveillance and control in fringe localities may be sufficient to mitigate any increases in transmission brought about by climate change. The fringe areas of most concern are the highlands of Madagascar and of eastern and central Africa, which support relatively large human populations (Plate 10-4). Because of the sensitivity of transmission to temperature in these areas, relatively small changes in the climate of highland areas may lead to significant increases in the local altitudinal limits of malaria transmission, thereby putting large numbers of immunologically naive people at risk of infection.

Although the evidence is patchy, data for certain highland localities suggest that malaria has become progressively more serious, especially since the early 1990s (Loevinsohn 1994; Tulu 1996; Malakooti, Biondo, and Shanks 1998; Mouchet et al. 1998; Cox et al. 1999). To what extent these data are a reflection of a more general, regional, or continental trend is unclear. The role of climate change is also uncertain; whereas epidemics have clearly been associated with abnormal weather events, as yet, little evidence indicates that they are a feature of longer-term shifts in climate conditions. In the rare instances where changes in malaria transmission intensity have been correlated with climate change, evaluating the contribution of confounding (nonclimatic) factors has been difficult. For example, recent increases in highland malaria transmission have been observed at a time when, for one reason or another, basic health services and malaria control activities have been in decline. This problem is likely to be compounded by emerging drug resistance and, in certain instances, by uncertain drug supplies. Under such conditions, a rise in observed morbidity and mortality may not necessarily reflect an increase in malaria transmission but nevertheless represents a significant problem for national malaria control programs.

Changes in climate and environment do not always increase malaria transmission. For example, meteorological data from the marshy areas of the Niayes (Senegal) indicate that rainfall in the period 1980-1990 was nearly 30% below the 1931-1960 average and that the rainy season became progressively shorter over the same period (Mouchet et al. 1996). Entomological surveys carried out in 1991-1992 indicated that An. funestus, previously a significant vector, had all but disappeared from the area, and An. gambiae s.s. also had declined—more than the less efficient An. arabiensis (Faye et al. 1995). These changes in vector populations were thought to be responsible for a marked decline in malaria transmission; parasite rates among local children fell from 40-80% in the late 1960s to less than 10% in 1991-1992. Similar trends were observed in the Niger River valley, Zinda, and Dilla areas of Niger, where a 29% decrease in annual rainfall (measured at Niamey) between the periods 1950-1959 and 1981-1990 was considered largely responsible for dramatic decreases in malaria prevalence rates (Mouchet et al. 1996).

Altitude

Although altitude has long been recognized as an important determinant of malaria endemicity (e.g., Hirsch 1883), the transmission factors that are directly or indirectly affected by altitude are actually of more epidemiological significance. The most obvious and important of these factors is environmental temperature, which is negatively corre-
lated with altitude, but rainfall also tends to vary negatively with elevation at high altitudes (e.g., Lauscher 1976). Even though past researchers have been tempted to define altitudinal thresholds for malaria transmission on this basis, for Africa as a whole or for specific regions (e.g., Schwetz 1942; Wilson 1949; Lindsay and Martens 1998), this tendency should be resisted for two reasons.

First, the relationship between altitude and temperature is often oversimplified and in practice may vary substantially over time and space. At the continental scale, the effect of latitude is important, and its significance in the context of malaria has long been recognized (e.g., Gill 1923). In addition to its effect on mean annual temperature, latitude influences the relative importance of seasonal and diurnal variations in climate; the latter tends to predominate in tropical highlands. Highland temperature regimes also are affected by continentality. Specifically, diurnal and annual temperature ranges tend to decrease with increasing proximity to large water bodies, whereas the incidence of cloud and mist increases, significantly reducing temperature.

Second, the assumption that temperature is the sole or principal factor limiting malaria transmission in highland areas may not always be valid. The significance of other transmission factors is suggested by the existence of altitudinal limits of transmission that are far below what would be expected on the basis of temperature alone in many parts of Africa. Large areas of the highlands are too dry; in some areas, local topographical characteristics offer too few breeding sites; in yet other areas, the ecology is not conducive to supporting anopheline populations.

**Land Cover and Land Use Change**

*Surface Water*

The availability of suitable sources of surface water for vector breeding is a prerequisite for malaria transmission. In many parts of Africa, surface water is scarce—either because of the general aridity of the climate or because local topographical characteristics preclude the pooling of water (e.g., de Zulueta et al. 1961). In other cases, existing water sources may be rendered unsuitable as breeding sites for specific species depending on the availability of light and shade and the type of vegetation present.

In fringe transmission areas, the distribution of suitable breeding sites for efficient vectors is likely to have a profound influence on patterns of malaria transmission. A good historical example is provided by parasitological and entomological surveys carried out in highland areas of southwest Uganda. In southern Kigezi (now Kabale district), the surveys of Garnham, Wilson, and Wilson (1948) revealed hyperendemic conditions around Lake Bunyonyi (1,920 meters), where entomological surveys indicated that *An. funestus* was the principal malaria vector present. Away from the lake areas, where *An. gambiae s.l.* was determined to be the main vector, spleen rates dropped off rapidly. Subsequent studies carried out in Kigezi as part of the preeradication effort (de Zulueta et al. 1961, 1964) also showed pockets of endemic malaria around Lakes Bunyonyi, Mutanda (1,800 meters), and Kimbuga (1,600 meters). The absence of permanent malaria foci in highlands beyond these areas was attributed to an “almost complete lack of water collections” in areas above 1,200 meters (de Zulueta et al. 1961).

The anomalous picture created by the presence of hyperendemic sites at high altitudes in sub-Saharan Africa is illustrated in Figure 10-1. Parasite and spleen rates in the vicinity of Lake Buayonyi are atypical of the general trend of decreasing levels of transmission intensity with increasing altitude. However, such pockets of high transmission...
are not unique to Uganda. In Kenya, for example, Roberts (1964) referred to focal swamps in which vectors were perennially present and from which they would spread, given suitable meteorological conditions. Spleen rates in the vicinity of these swamps were typically 50% higher than in the surrounding areas.

The natural distribution of breeding sites may be transformed by the creation of new water sources, such as dams (see later), or by modifications to existing water bodies that render them more suitable to anopheline breeding. In southwest Uganda, for example, the entomological results of Goma (1958) and others indicated that in its natural condition, much of the permanent swamp was unsuitable for vector breeding. From the early 1940s, large areas of swamp were cleared of their natural vegetation for
agriculture, and these operations were accompanied by large increases in both the num­
ber of malaria vectors and malaria incidence (Steyn 1946). A similar phenomenon was
observed in neighboring Rwanda and Burundi (e.g., Vincke and Jadin 1946), where
swamp cultivation was considered to be primarily responsible for the spread of malaria
to higher slopes (Meyus, Lips, and Caubergh 1962).

**Impounded Waters**

The seasonal scarcity of water in savanna areas and the Sahel, together with opportuni­
ties to harness larger rivers to provide hydropower and stores of water to allow dry sea­
son irrigation, have led to extensive dam construction in the semi-arid areas of Africa.

Initially, attention was directed to a series of large dams that created huge lakes,
with significant and often adverse effects on populations from the inundated areas.
Kariba (Zambia and Zimbabwe), Volta (Ghana), Kainingi (Nigeria), and the Aswan High
Dam (Egypt) are notable examples. These dams were the subjects of international con­
cern and financing and, after early health disasters, the objects of research studies and
attempts to mitigate the problems. Advice was not always well founded. In the case of
the Volta Dam, initial advice was based on U.S. experience in the Tennessee valley,
where the periodic abrupt lowering of water levels by siphons or opening sluices had
stranded mosquito larvae and prevented their development. Subsequent better advice
(sought when the original suggestions proved impossible to implement for so vast an
impoundment) drew attention to the likely creation of breeding sites for *An. gambiae*
by lowering the water level and exposing great expanses of muddy shore with puddles.
However, the initial holoendemicity of malaria in the area before dam construction
indicated that although the mosquito population might rise subsequent to dam con­
struction, the level of malaria endemicity was unlikely to change much. This was in fact
the result, and the disease changes mostly affected infections such as schistosomiasis
rather than malaria. The African experience differs vastly from that of India, where dam
construction has been followed by malaria epidemics.

One particular concern was raised concerning the Aswan High Dam and Lake
Nasser, which extends for hundreds of miles south into the Sudan. Twice in the twenti­
eighth century, *An. gambiae* has penetrated north into Egypt from the Sudan. For example,
in the late 1940s, penetration was followed by massive malaria epidemics controlled by
Fred L. Soper, who was able to eradicate *An. gambiae* locally and restore the situation. It
was believed that Lake Nasser would facilitate the northward passage of *An. gambiae*,
with terrible consequences for Egypt. However, these feared consequences have not
materialized.

Greater and more justified concerns have surrounded the construction of small
dams on a huge scale in Africa. One state in Nigeria had more than 550 small dams con­
structed in a few years. International financing is not involved, and health risks are
rarely considered. Dams that are in areas previously too arid for much malaria transmis­
ion or at altitudes at which malaria is unstable may produce adverse results.

Parasitological data have been collected as a part of an ongoing project to assess the
impacts of small-scale irrigation dams in Tigray, Ethiopia, where hundreds of such dams
are planned (Ghebreyesus et al. 1998). Although irrigation dams have increased malaria
transmission in lowland Ethiopia (e.g., Meskal and Kloos 1989), less is known about
their potential impacts in the highlands. Preliminary data from Tigray suggest that para­
site rates in the vicinity of dams are significantly higher than those in outlying areas.
Dam construction has had similar demonstrable effects on local levels of malaria trans-
mission in Kenya (e.g., Khaemba, Mutani, and Bett 1994) as well as in Rwanda and Burundi (e.g., Meyus, Lips, and Caubergh 1962).

Irrigation and Rice

Water resource developments for agriculture in Africa include irrigation schemes on all scales, from the huge area of the Gezira in Sudan, which extends more than 100 kilometers, to small furrows constructed by peasant farmers. Although irrigation is often expected to be followed by malaria outbreaks on other continents, in Africa, many irrigation schemes are constructed in areas of holoendemic malaria, where the addition of mosquitoes may increase the biting nuisance but have little effect on malaria transmission. In highland or extremely arid areas where malaria is unstable or rare, irrigation may indeed facilitate transmission, but this result should not be assumed to be universal.

The Gezira Irrigation Scheme, developed to grow cotton, has increased malaria problems by unintentionally providing mosquito breeding sites in its canals (no drains were built to remove the excess water that would otherwise evaporate, leaving behind salts and eventually salinizing the land; the Blue Nile River water that feeds the scheme has such low salinity that drains were not expected to be needed to protect agricultural interests). Malaria transmission was effectively controlled when cotton was the only crop and discipline over cultivation and water management was very strict. However, with the rise of chloroquine resistance and less rigid management, the problem has increased. In the analogous West African situation at the Office du Niger in Mali, the surrounding area has seasonally transmitted holoendemic malaria. Within the irrigation scheme, malaria transmission is close to perennial, but the actual level of disease is no higher.

In The Gambia, the introduction of irrigated rice into the Middle River region (as distinct from the swamp rice grown throughout the country) has had a complex effect. Irrigation in the dry season causes a second annual peak of mosquito abundance, in addition to that after the rains. But the second peak is not accompanied by any increase in malaria transmission (Lindsay et al. 1991). Whether this difference is due to short mosquito survival in the hot weather, temperatures too high for the malaria parasites to survive in the mosquitoes, or even different mosquito cytotypes is not fully clear.

Therefore, the issue of rice cultivation is perhaps more complex in Africa than elsewhere, and the effects of irrigation on malaria are sometimes counterintuitive. The malaria outcome (in terms of transmission rates and prevalence of the disease) resulting from modification of a transmission factor varies depending on preexisting levels of transmission.

Although rice cultivation has greatly increased populations of An. gambiae in West Africa, patterns of malaria have remained relatively unaffected. In Burkina Faso, for example, sporozoite rates in rice-cultivated areas were one-tenth of those in surrounding savanna areas (where the mopti cytotype is dominant), so although vector densities were 10 times higher, inoculation rates effectively remained unchanged (Robert et al. 1985, Favìa et al. 1997). In Burundi, at intermediate altitudes, rice cultivation has been linked to increases in the population and vectorial capacity of An. arabiensis (but not An. funestus) and to the existence of highly localized, hyperendemic pockets in otherwise unstable transmission areas (Coosemans et al. 1984).

The positive association between rice cultivation and increased risk of malaria transmission has perhaps been demonstrated most strongly in Madagascar, where rice fields have supported relatively high concentrations of An. funestus and An. arabiensis. The rapid development of rice cultivation in the highlands, together with the influx of
workers from malaria-endemic parts of the country, was thought to be responsible for extensive epidemics of malaria in the late nineteenth century. High levels of malaria transmission prevailed until 1949, when control measures (DDT spraying, drug chemoprophylaxis, and the administration of chemotherapy) were introduced (Laventure et al. 1996). By the early 1960s, malaria was widely believed to be eradicated; DDT operations ceased, and malaria treatment centers were later closed down. What followed was described by Mouchet et al. (1997) as a gradual “reconquest” of the highlands by malaria, which culminated in severe epidemics in 1986–1988.

Deforestation

In its natural state, forest vegetation is usually unsuitable for malaria vectors, particularly An. gambiae complex, although An. moucheti is a forest mosquito. However, anophelines may quickly colonize areas that have been disturbed sufficiently to allow direct sunlight on small temporary water collections that are suitable for larval development (Coluzzi 1994). In southern Cameroon, for example, forest clearance for cultivation, village settlements, and road systems has been associated with the invasion of malaria vectors such as An. gambiae s.s. and, to a lesser extent, An. nili and An. moucheti (Livadas et al. 1958).

In Africa, deforestation is usually associated with increases in Plasmodium falciparum transmission, but the scale of this increase depends on the degree of disturbance and the human populations involved. Effects of deforestation are likely to be most extreme when clearance is accompanied by urbanization, as described by Coluzzi et al. (1979). In south Nigeria, An. arabiensis was able to colonize urban areas including Benin City and Sapele to create what Coluzzi et al. called islands of “derived savanna.”

The effects of deforestation on disease will depend on existing levels of malaria endemicity in surrounding areas and the degree of immunity among the new settlers. Where forests are being cleared by local residents in hyperendemic settings, patterns of disease are unlikely to be altered radically, despite local changes in transmission intensity.

Urbanization

The ecological processes associated with urbanization should, in theory, limit malaria transmission by reducing the opportunities for vector breeding and the degree of contact between humans and vectors. Improved access to health care and malaria control measures (e.g., bed nets) also should contribute to a reduced burden of malaria disease. Evidence from the field largely bears out this theory but also suggests that the existence of diverse epidemiological situations in most urban areas makes generalization difficult. In most cases, human settlement initially favors the multiplication of breeding sites and the perennial presence of high densities of An. gambiae. But as urban areas become more established and human and building densities rise, potential vector breeding sites become increasingly scarce. This situation may be compounded by the canalization of streams and other sources of surface water and by the effects of pollution.

The intensity of malaria transmission within an individual city therefore may be quite variable, depending on the degree of development within specific localities. It is illustrated by results of entomological and parasitological surveys carried out in Ouagadougou, Burkina Faso (Sabatinelli et al. 1986), and Brazzaville, Congo (Trape and Zoulani 1987a,b; Trape 1987). In both cases, levels of transmission were generally lower in town areas than in the surrounding countryside, but variation between different urban
sites was considerable. Trape and Zoulani (1987a) demonstrated that although the average Brazzaville inhabitant receives 22.5 infective bites per year, in individual districts, this figure varied from more than 100 infective bites per year to less than 1 bite every three years.

Where larval habitats do exist in urban areas, high transmission rates are likely to be focused on restricted areas, given the limited dispersal of An. gambiae in densely populated areas. In Ouagadougou, for example, malaria prevalence rates were significantly different in groups of children living in houses only 300 meters apart (Sabatinelli et al. 1986).

In cases where the environmental modifications associated with urbanization lead to a change in the composition of local vector species, the effect on levels of malaria transmission may be more difficult to predict. In Cotonou, Benin, transmission rates in many peri-urban sites are reportedly higher than in outlying rural areas because the increased availability of freshwater collections has increased populations of An. gambiae s.s. relative to those of the less efficient An. melas, which is a saltwater breeder (Akogbeto et al. 1988). Urbanization in Accra, Ghana, was allegedly responsible for the complete disappearance of An. funestus while the relatively inefficient An. arabiensis remained widespread in many urban localities because it was better able to adapt to breeding in polluted water (Chinery 1984).

Human, Genetic, and Socioeconomic Determinants

Human Determinants

Human population heterogeneity is another major determinant of malarial consequences, though less so of malarial transmission. In a nonmigrant population under steady levels of malaria transmission, age will be a surrogate for malarial immunity, and the population can be viewed as a whole in its responses to changing environmental determinants of malaria transmission. But the genetic heterogeneity of the human population in genes that affect responses to malaria or a diverse migration history of some elements of the human population may render the effects of malaria and of changes in transmission level more complex.

Migration, always a feature of African malaria (Prothero 1977), is even more evident today. By mixing gene pools and creating populations heterogeneous in their past histories of malaria, migration must be considered part of the determining factors for human malaria.

Genetic Determinants

The picture of the basic science of malaria has become more coherent in the last few years. Malaria can be viewed biomedically as the population genetics of three interacting populations: human hosts, vectors, and malaria parasites. Each is more polymorphic in genetic expression than was previously realized. Although the main human genetic determinant of infection is the Duffy blood group system (which affects susceptibility of red cells to Plasmodium vivax infection), many other polymorphisms affect pathogenesis and the severity of disease, most notably, the hemoglobinopathies (of which sickle-cell anemia is best known). More recently, polymorphisms of the tumor necrosis factor gene and its regulation have been found to affect the risk of severe malaria.

The blood group antigens and hemoglobinopathies have been mapped in some detail for Africa, and they clearly act as a filter on the species of malaria parasite to be
found in a given area and on the frequency of severe and complicated malaria. Because the West African indigenous population is largely Duffy-negative, vivax malaria is very scarce in that part of Africa. P. vivax is rather widely replaced by Plasmodium ovale. Climate and other environmental changes appear unlikely to significantly affect the frequency or geographical distribution of the Duffy antigens. However, one might expect some degree of increase of the sickling gene in areas of Africa (largely hill areas) invaded by P. falciparum as a result of environmental change, so there will be a reciprocal interaction of host genotype and parasite intensity. This process will be slow and imperfect. Therefore, in the short run, host polymorphism should be viewed as modifying the determinants of malaria.

**Socioeconomic Determinants**

Attempts to model climate change effects that also incorporate different socioeconomic development scenarios have been undertaken by the Hadley Climate Centre in the United Kingdom. However, the effect of these socioeconomic variables on malaria is by indirect routes that vary geographically in their effects, depending on the mosquito vector species involved. In particular, economic growth is unlikely to have a major beneficial effect on the distribution of malaria in Africa, although it is likely to reduce mortality by enabling people to afford medicines and seek medical assistance for their children. If incomes rise substantially, the state may be able to run malaria control programs, but programs would be expensive if they were to substantially affect transmission in tropical Africa. In the more temperate climate of Zimbabwe and South Africa, costs of effective transmission control are more modest; consequently, it is feasible to attempt transmission control on a long-term basis, and eradication remains a stated goal in Zimbabwe.

Unlike some tropical infections, the individual and household behavior of people who become more prosperous is not enough to eliminate malaria, even though such people may reduce their individual risk by using bed nets, screening their windows, obtaining prompt treatment, using mosquito repellents, and even taking chemoprophylactic drugs. Even organized control measures by residual insecticide spraying cannot stop transmission in the Sahel, but they can, well do so in highland and other unstable malaria areas and in some urban situations.

The public and private construction works of prosperity may increase risk because building sites may breed mosquitoes in the rainy season, and "borrow pits" along newly constructed roads are a notorious source of anophelines. However, better-constructed houses diminish transmission; the insertion of ceilings tends to reduce vector resting sites, and screens and air conditioning have an even greater effect.

Historically, socioeconomic development has been associated with decreases in malaria morbidity and mortality, particularly when these developments were associated with environmental modifications that limited contact between vectors and humans (Coluzzi 1994). This was the experience in Europe and parts of North Africa, but one probably should be less hopeful for sub-Saharan Africa because of vector characteristics.

**Conclusion**

The chief determinants of unstable malaria in Africa are the factors that vary the level of transmission, whereas the main determinant of stable holoendemic malaria (the disease, not parasitemia) in sub-Saharan Africa is human acquired immunity.
Although the general distribution of endemic malaria in Africa is strongly related to climate, transmission over large parts of the continent is likely to be relatively unaffected by climate change, either because they are already holoendemic for malaria or because current climate conditions are so unsuitable that very extreme shifts in rainfall or temperature would be necessary to create conditions conducive for transmission. Areas where malaria transmission is "sensitive" to long- or short-term climatic variations therefore are likely to be limited to the current edges of the malaria distribution associated with high altitudes, high latitudes, or desert fringes. The precise effect of climate change in these areas will depend on the extent to which malaria surveillance and control can mitigate the effects of increased transmission. At the local level, the influence of nonclimatic risk factors (such as changes in land use or land cover) may dominate over that of climate.

The overall picture of malaria in sub-Saharan Africa that emerges is of a limited number of areas at the limits of altitude or latitude (both surrogates for temperature or rainfall) for malaria transmission where the resulting unstable malaria is highly susceptible to small changes of environmental and other variables. These areas (especially those at higher altitudes) are of greater importance than their relative surface area would suggest because of the population density located there.

The remaining malarious areas—the bulk of the African continent south of the Sahara—are highly endemic stable malaria where the consequences of environmental and social change on transmission will be less apparent because of immunological damping in the heavily infected population. Such changes that might occur are in fact controversial or rather uncertain. However, they should not be ignored.

A truism of epidemiology is that small changes in common diseases make more difference to the public health than large changes in rare diseases. Changes within the uncertainty levels for holoendemic areas might well exceed in mortality and morbidity effects those more apparent and dramatic epidemics that could occur at the edges of transmission. Although much can be predicted and the effects of many variables other than "simple" climate variations and changes can be assessed with some confidence, the areas of our uncertainty in highly endemic malaria need much more analytical attention before reasonable predictions become feasible.

References


Chapter 10: Determinants of Malaria in Sub-Saharan Africa


Cox J.St.H., Mouchet Jean, Bradley D.J. (2002)

Determinants of malaria in Sub-Saharan Africa


Washington: Resources for the Future, 167-186

ISBN 1891853198