Malaria Redux:

The History and Ethics of Malaria Eradication and Control Campaigns in Tropical Africa

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During the 1950s, colonial malariologists, in conjunction with experts from the World Health Organization (WHO), set up malaria eradication pilot projects across tropical Africa. They deployed new synthetic insecticides such as DLD, HCH, and DDT, and new antimalarials, such as chloroquine and pyrimethamine, in an effort to establish protocols for eradication. These efforts 'protected' some fourteen million Africans. Yet by the early 1960s, the experts concluded that malaria eradication was not feasible, and the pilot projects were disbanded. The projects had achieved extremely low levels of infection for years at a time, but the experts had to accept with regret that their interventions were unable to reduce malaria transmission to zero. The projects had high recurrent costs, and it was understood that they were financially unsustainable. The pilot projects were allowed to lapse.

The malaria eradication pilot projects had reduced the rates of infection to levels so low that the 'protected' populations lost their acquired immunities to malaria during the years of the projects. In the immediate aftermath of the projects, the Africans were subject to severe malaria, which sometimes afflicted entire communities in epidemic form, until they regained their immunities.

How Should We Understand the Ethics of the Early Eradication Efforts?

The ethics of malaria control in the 1950s and 1960s seemed self-evident to the interventionists. Malaria was a major killer of children under the age of five, and it was one of a cluster of infections that could produce severe co-morbidities when it did not kill. Any intervention that reduced mortality and morbidity would be a boon to the afflicted populations, and any such effort would likely produce a general improvement in the economic health as well as the physical health of the population. Bouts of malaria among adults reduced productivity and inhibited economic progress.

This rather straightforward ethical underpinning was never explicitly articulated during the era of the search for an eradication protocol. It was, in a sense, too obvious and uncontestable to require elaboration. And because the interventions were carried out on a population level---rather than an individual level---there was no felt need to acquire the consent of the populations who lived in the regions that were slated for the malaria eradication projects.

From the vantage point of the malariologists, the WHO antimalaria programs in tropical Africa seem to have been considered as a logical extension of the colonial-era campaigns to control disease. The interventionists, whether working directly for the colonial governments or the WHO, viewed their work as virtuous and as beneficial to the African populations.

Earlier population level disease control programs had produced highly varied results. Historians have described in detail the sleeping sickness campaigns of the early decades of the twentieth century and the devastating consequences including blindness and death that resulted from the use of atoxyl to destroy the trypanosome in the human body.[1] Other interventions produced strongly positive results, although not always without some unwanted medical consequences. For example, medical personnel in the yellow fever vaccination campaigns discovered that the FNV vaccine used in Nigeria produced encephalitis in 0.3-0.4% of vaccinated children and that 40 percent of those with encephalitis had died.[2] In 1956, the WHO recommended that the use of the vaccine be restricted to those over the age of 14. Thereafter the numbers with serious reactions to the vaccine were deemed to be low enough to not provoke concern, and the French Neurotropic

Vaccine (FNV) continued to be used in francophone Africa into the 1960s. Production of the FNV was ended only in 1980.

The yellow fever campaigns, and indeed the sleeping sickness campaigns, continued to be prosecuted only as long as the interventionists judged that the benefits outweighed the costs. The benefits, even if never explicitly described, appear to have been considered as a matter of morbidity and mortality costs foregone: lives saved and sickness prevented. The health costs of interventions were in some circumstances roughly quantifiable. The death rates and rates of blindness caused by atoxyl poisoning could be counted. Similarly, the expected savings in human lives from the suppression of yellow fever epidemics could be roughly estimated.

When alternate therapeutic interventions were available, a different calculus was necessary. Both the Rockefeller Foundation and the Institut Pasteur in the 1930s developed anti-yellow fever vaccines. The Rockefeller vaccine, known as 17D, was safer than the FNV vaccines, made by the Institut Pasteur in Dakar, but 17D was more expensive to administer. It required a syringe, whereas the FNV was administered with a 'scratch' technique.

The switch from FNV to the Rockefeller 17D vaccine was slow to occur in French Africa, perhaps owing to a national pride in the French vaccine. Yet because it was administered by a scratch technique rather than by injection, it was extremely inexpensive and often given in combination with a smallpox vaccination. Thus one implicit justification for its continued use was that protection against yellow fever could be extended and broader coverage achieved than would have been the case with the Rockfeller 17D.

The early malaria eradication pilot projects were built on the same ground of virtue. The ethical choices were among the effective antimalarials and among the effective synthetic insecticides. The choices among the effective synthetic insecticides were initially determined by the perceived 'knock-down rate', the length of residual effectiveness, and price. Later, when resistance emerged, yet another variable---the extent of resistance---had to be factored into the considerations. The issue of toxicity was raised only with regard to the sprayers. There seemed to be no problem with DDT. By contrast, with DLD (Dieldrin), in particular, some sprayers received toxic doses, and the WHO made recommendations for better protection for sprayers, although apparently these were rarely implemented.[3]

Antimalarial Drugs in Tropical Africa, 1945-1965

By the mid 1950s, as the evidence began to accumulate from the first cluster of pilot projects that indoor residual spraying (IRS) with synthetic insecticides alone would not be able to interrupt transmission, malariologists designed a second cluster of projects that combined IRS with a chemoprophylactic or chemotherapeutic component or both.[4] At a WHO technical meeting on African malaria held in Brazzaville in 1957, the malaria experts unanimously recommended the initiation of large-scale experiments with the mass administration of antimalarials. The recommendation was to employ different drugs and dosage schedules, in order to determine the efficacy of the interventions.[5]

The mass administration of antimalarial drugs had a long and checkered history into the mid-twentieth century. The Italians had undertaken the first national mass drug administration

program, with mixed success. In a mixed malarial zone of vivax, falciparum, and malariae infections, the mass administration of quinine had dramatically reduced malarial deaths, but not morbidity.[6]

In tropical Africa before the Second World War, there had been no comparable experience with the mass drug administration of quinine. The British and French colonial powers had set up cinchona plantations during the interwar years, but the quantities of cinchona alkaloids produced had been small. Some Africans, particularly those living in urban areas, acquired quinine through post office sales of single doses, but the number of individuals who availed themselves of this chemical therapy was relatively small. From a public health point of view, the limited local supplies and the high cost of quinine on the international market had excluded the option of mass campaigns.

After the end of the Second World War, cinchona plantations might have been revived in the African colonies, but there seemed little need to do so. In the immediate postwar period, the availability of synthetic drugs opened up a new world of possibilities for malaria interventions. The synthetic drugs pyrimethamine and chloroquine seemed to have fewer side effects than quinine.[7] Both could serve either as a malaria prophylaxis or a cure. As the price of the synthetic drugs dropped, their sheer inexpensiveness allowed malariologists to consider deploying the drugs in new roles. They might limit the damage from outbreaks of epidemic malaria in highland areas in which African populations had little or no immunity; interrupt transmission before or during an IRS campaign; protect the young in the absence of other efforts to control malaria; and/or reduce malaria during the transmission season, whether or not other control efforts were on-going. If IRS alone could greatly reduce but not completely interrupt transmission, the drugs might be able to clean up the 'human reservoir' of parasites and perhaps reach the goal of zero transmission. In the event that zero transmission could not be achieved, it might be possible to adopt an alternate strategy of regular, ongoing mass chemoprophylaxis.[8]

A major challenge was how to get drugs to rural populations within a project zone. One option was to mix antimalarial medicines into sodium chloride, on the theory that everybody consumed salt. Moderately large-scale distributions of chloroquine-medicated salt were introduced into a zone of 30,000 people in northern Ghana and into communities of laborers with a total population of over 23,000 who worked on two sugar estates in Uganda. Both programs ran into insurmountable difficulties, including the rejection (or non-use) of the medicated salt.[9] A trial in Tanzania, in a region in which the supply of salt could be completely controlled, in conjunction with a successful health propaganda campaign, produced a short-term medical success.[10]

In Bobo-Dioulasso in Upper Volta and at Bernin Kebbi in northern Nigeria, project managers oversaw the direct distribution of antimalarial tablets to the Africans in the project zones. This proved time-consuming and thus expensive, and an alternate approach, known as unmonitored direct distribution—which meant providing drugs to village heads or other local authorities that in turn distributed them—was tried. The risks were that the intended users would not understand when to take the drug or in what dosage. Underdosage would hasten the emergence of parasite resistance to the drug and overdosage could produce unknown, toxic reactions. In Uganda and in northern Cameroon, the project authorities tried a monitored distribution of a single-dose of antimalarial drug during the spraying cycle, and this approach succeeded in further reducing the

parasite prevalence. Monitored distribution, however, proved too costly to be 'scaled-up.' In Madagascar, Ghana, and Senegal, there were programs of unmonitored direct distribution of antimalarials for long-term prophylaxis. Costs were lower, but the effectiveness of distribution diminished quickly, and the programs ran the risks of inadvertent underdosing or overdosing.

Researchers judged the overall results of the chemotherapeutic interventions to be unimpressive. In monitored distribution schemes in Upper Volta, northern Cameroon, Ghana, and northern Nigeria, pyrimethamine was initially highly efficacious, but it produced resistance in the falciparum parasite within a few months. Chloroquine alone or in combination with primaquine also cleared infections, but the prospects for long-term prophylaxis were poor. The major impediment—deemed nearly insuperable—was the establishment of a regular rhythm of distribution and use. Moreover, the utility of mass drug distribution schemes was called into question by their apparent inability to achieve project goals. In combination with IRS, antimalarial drugs could drive rates of infection extremely low, but not to the point of fully interrupting transmission.[11]

The withdrawal of the malaria eradication projects unleashed severe malaria in the once-protected communities. This was known at the WHO, but the general feeling seems to have been that while this was terribly unfortunate, there was little that could be done to counter it, and in any event, the situation---conceptualized as a return to the status quo--was not worse than it would have been without any intervention at all. The question of compromised immunity was an extremely difficult one to have investigated; and it was politically infeasible at the WHO at the time. In the midst of the malaria eradication program, the setbacks experienced in tropical Africa had to be interpreted as partial successes that for a variety of financial and political reasons could not be pursued all the way to eradication. They were then buried in the archives. This is the reason that the scientific literature is replete with the notion that the malaria eradication program was not undertaken in sub-Saharan Africa.

An Infectious Confidence in the Protective Nature of African Immunity

The lack of interest in the health consequences of re-infection after the loss of acquired immunities was rooted in a long-standing belief that Africans, after passing through a period of immunological challenge in early childhood, acquired immunity to malarial infections that stood them in good stead for the rest of their lives. Those with an acquired immunity might have bouts of malaria, but these bouts would be passing phenomena and would not compromise their general health.

This belief took root in the early twentieth century, based on observations that Africans were generally untouched by malaria while whites were struck down. There was, however, no agreement on whether or not the loss of immunity would entail severe consequences. Expert opinions differed.

At the Kampala conference, the unresolved question of the health consequences of the loss of acquired immunities in populations living in areas of heavy endemic transmission as a result of malaria interventions had been explosive.[12] Childhood morbidity and mortality were conceptualized as "costs" that were paid to acquire adult and adolescent immunity. How high were the "costs" of the acquisition of immunity? What was the extent of childhood morbidity

and mortality that was attributable to malaria? The advocates for greater caution buttressed their arguments with the assumption that childhood mortality costs in areas of heavy endemic transmission were relatively low. The implication—contested by their opponents—was that these putatively low childhood mortality costs might be an acceptable price for fully functional adult immunity.

In the aftermath of Kampala, in the early 1950s the medical community moved closer to a consensus on the high costs of childhood mortality. An estimate of 25 percent of childhood mortality directly attributable to malaria came to be more widely accepted, and thus, for those who accepted this estimate, one of the reasons for caution in malaria intervention dissipated. By virtue of the good that could be conveyed to those in the early years of life through the prevention of malaria transmission, the concern over the harm that might be done to adults in areas of heavy transmission whose acquired immunities had been compromised through malaria interventions seemed to pale by comparison. The issue disappeared into the shadows of the medical curriculum.

This issue of acquired immunities to falciparum malaria had greatest salience in tropical Africa. It was not a major issue in the broader global campaign to eradicate malaria (1955-1969) because on no other subcontinent region was principally falciparum transmission maintained at such high levels. In malarial environments with a mix of P. faliciparum, P. vivax, and P. malariae infections, it was virtually impossible to sort out which parasite brought on a bout of malaria without time- and money-consuming microscopy, and thus the issue of the loss of acquired immunity to falciparum was broadly ignored, because of the belief held by malariologists at the forefront of the Malaria Eradication Program (MEP) that malaria was on its way to extinction as a human infection. Any infections that might resurge would be ephemeral and ultimately inconsequential in the larger scheme of things.

Thus, with enthusiasm for the prospects for full success, malariologists were not drawn to an exploration of the consequences of partial success or of the lapsing of control measures. This was a significant oversight, because in some instances in tropical Africa when malaria control or eradication projects in areas of heavy endemic transmission lapsed—which was nearly invariably the case—those whose acquired immunities had been compromised bore a suddenly *increased* burden of death and disease. The 'rebound' malaria epidemics that followed on the heels of the malaria interventions in Africa produced an increase in human suffering in a different age cohort from those who benefited from the interventions. Absent the infectious belief in the protection afforded by acquired immunity, a moral conundrum would have surfaced. It was noble to save the life of a child. What was the moral accounting when the rebound epidemic malaria from a lapsed intervention struck down the father, mother, or grandparent? This moral conundrum lay inchoate, veiled by the belief that epidemic malaria in African communities could only produce conditions of temporary morbidity that would be resolved by the reestablishment of an *a priori* equilibrium.

There was, in fact, very little known about the natural course of malaria infections in tropical Africa. How long did it take for acquired immunities to degrade? Did they degrade fully or only partially? Some small-scale clinical studies advanced evidence that individuals reinfected after having been resident in an antimalaria pilot project zone might be free of malaria symptoms; yet

the fact of asymptomatism suggested to other malariologists that the interventions had not continued long enough to cause a fuller degradation of immune status.[13]

In some of the project zones, the evidence of epidemic malaria was straightforward. According to L. Bruce-Chwatt, one of the outstanding malariologists of the twentieth century, in the aftermath of the pilot project near Yaoundé, epidemic malaria produced symptoms of acute malaria that had only exceptionally been previously recorded.[14] In the aftermath of the pilot project in the Kpain region of central Liberia, epidemic malaria surged through the once protected communities.[15] The extent of the problem remained in dispute, however, because when 'rebound' epidemic malaria struck, the disease consequences went unmeasured. Although the Kampala conference had recommended that malaria control services be established to allow for effective intervention in the case of rebound malaria, this recommendation had not been implemented. The malaria control projects had not been charged to create a malaria service or any other type of public health infrastructure, and the institutional capacities for medical surveillance in tropical Africa in the 1950s were rudimentary at best.

Ironically, following the collapse of the malaria eradication campaign, malaria deaths in tropical Africa declined markedly during the 1960s and 1970s. This was in part because of the increasing availability of chloroquine that allowed sufferers to medicate themselves and their children during acute attacks of the disease. The decline in malaria deaths was likely also a function of a broad improvement in per capita incomes, particularly during the 1960s, in African regions that exported agricultural goods on global markets.

Malaria and The New Economic Orthodoxy

In the U.S., the electorate voted Ronald Reagan as president in 1982, and a new political discourse gained wind. The poor economic performance of the U.S. economy in the late 1970s, rocked by rapid increases in the energy prices, was blamed on excessive government interference with the economy, and in the U.S. it became accepted fact in Republican political circles that the federal government was to blame for unemployment, inflation, and other economic ills. This vision of the dysfunctionality and superfluousness of government was disseminated from the World Bank and International Monetary Fund through calls to reform African governments by shrinking the public sector and promoting private enterprise. These calls became strident when the Soviet Union slid into severe financial and political crisis, and that the Cold War concerns no longer had pride of place in policy-making.

By the mid 1980s, the demands for structural reforms were translated into requirements for African governments to reduce public spending in order to continue to receive funds from the IMF to forestall bankruptcy. The result was dramatic. In many public sectors, African government jobs and services were reduced. This was not, however, the case in the health sector. Expenditures in health remained steady or, in some cases, increased. But new requirements to impose user fees to acquire healthcare produced some of the same results. The spindly infrastructure of rural clinics came under financial pressure. Some clinics closed and in others key medicines disappeared from the shelves and were not replaced. In some urban hospitals, the provision of services was similarly constricted. In Conakry, the staff of the hospitals were paid less than a living wage and had to raise funds from those who needed services. Many in need were turned away because they were desperately poor.

The decade of the 1980s also saw a major increase in donor funding for public health. The WHO, dependent upon contributions from the member states, continued to issue advisory opinions, but the World Bank assumed a position as the preeminent arbiter of global health policy. In 1985, it made monies available for investments in the health sectors of developing African nations, with the goal of institutionalizing a market model of health care in tropical Africa. A few African states--Botswana, Nigeria, and Zimbabwe--produced detailed health planning documents. Across most of tropical Africa, the efforts to reorient the allocation of health resources to reach rural populations faced severe economic constraints. Zimbabwe succeeded in effecting a modest reorientation from medical care programs to preventive programs and services with its scant resources. Botswana, bolstered by robust economic growth, succeeded in reaching most of its rural populations. But in general, the African government commitments to the principles of Alma Ata remained largely symbolic.[16] The United Nations Development Report 1991 estimated that more than half of all sub-Saharan Africans had no access to modern medicine.[17]

What were the implications for malaria control? The US Agency for International Development (USAID) commissioned a "Manual on Malaria Control in Primary Health Care in Africa," from the American Public Health Association in 1982. The document adopted from the recommendations of the WHO four possible combinations, conceptualized as "tactical variants."[18] The most basic, "Tactical Variant I," aimed to reduce mortality through the broader use of choloroquine. The other three variants were more ambitious, combining mortality and morbidity reduction in Tactical Variant II, and moving to progressively more ambitious comprehensive malaria control in Tactical Variants III and IV.[19] In tropical Africa, the best that could be hoped for was Tactical Variant II. This placed the principal emphasis on the chemotherapeutic use of antimalarial drugs, at a time when the threat of resistance to the drugs was on the rise. At least in principle, the expansion of primary health care networks would provide increased access to the antimalarials, but the constraints to the successful implementation of such networks were considerable. In addition to those at the national/central/provincial levels such as a low level of economic development, lack of a clear national health policy and a sound health manpower policy, and lack of suitable planning, there was a raft of other constraints at the level of the primary health care unit.[20]

The US moved forward with a broad new program called the Africa Child Survival Initiative--Combating Childhood Communicable Diseases (CCCD). It concentrated on reductions in childhood mortality due to malaria, diarrhea, and vaccine-preventable diseases. The Tactical Variant I was the heart of the malaria initiative. Its control strategy relied on the use of drugs, and the CCCD encouraged the creation of national malaria control units, and in eleven of the twelve countries that were endemic for malaria, new units were created to work within the primary health care systems.[21] But the African commitment to the malaria control programs was not robust, and over the course of the 1980s, some programs unraveled.

A Lagged Cataclysm in Madagascar

On the island of Madagascar, the control program collapsed with disastrous results. In 1949 the French had launched a program to enroll the school-age children in the highlands in a malarial prophylaxis program using quinine. In combination with indoor residual spraying (IRS) with

synthetic insecticides, the antimalaria program achieved very good success. It did not achieve the full interruption of malaria transmission, but the number of infections dropped to a small number. By 1957, malaria transmission had been reduced to such a low level that it was no longer a significant public health problem.

Control efforts slackened and were cut back progressively in the early 1960s. There was little malarial disease to prevent. In 1975, however, there was a significant uptick in infections. Nearly thirteen thousand cases of clinical malaria were recorded, and the following year, in the central province of Antananarivo, there were thirty deaths. At first, the outbreaks remained localized. They blossomed slowly, among a population that had grown up immunologically naïve.

In 1977, in Antananarivo province, there were 37,750 clinical cases and 140 deaths. Thereafter the epidemic spiraled upward, reaching more than 1,600 deaths in 1984 and again in 1985, doubling to more than three thousand deaths in 1985, and doubling again to more than 6,500 in 1986, and reaching a peak of 9,584 deaths in 1988. When the data from Fianarantsoa province were added, some researchers estimated the death tolls at 15,000 per year during the four worst years of the epidemic.[22]

The "cause" of the epidemic was undoubtedly complex. The government of Madagascar had embarked on a socialist program of development during the 1970s and had established health clinics and hospitals in rural regions. The international economic downturn of the 1970s, however, had hit the island hard. Incomes had dropped by approximately 40 percent. The government of Madagascar had borrowed heavily in order to finance its program of nationalizing industry. By 1980, the IMF had imposed an austerity program and price reforms. When the epidemic struck, there was a dearth of antimalaria drugs to treat the critically ill.

Yet beneath the swirl of complex and countervailing forces that complicate the analysis of the epidemic are two fundamental epidemiological facts. The first was that the late colonial-era programs had transformed the mix of malaria parasites. Chloroquine is differentially more effective against vivax than falciparum, and the campaign of chloroquine prophylaxis had all but eliminated vivax from the highlands. The second fact was that this chloroquinization program, in combination with the dramatic reduction in malaria transmission that had been achieved through vector control, had created a population nakedly vulnerable to malaria. By the mid 1970s when the increase in infections started, the people living in the highlands of Madagascar were non-immunes. By the late 1980s, when the epidemic had been brought under control, the gravesites of the tens of thousands of victims marked the public health tragedy of malaria control-and-lapse.

A Nearly Immediate Control-and-Lapse Epidemic in the Gulf of Guinea

The creation of non-immune populations was, however, one of the unavoidable and integral consequences of successful malaria control, and it was not one that was restricted to the highlands. From 1980 to 1981, a malaria eradication project took place on the islands of São Tomé and Principé in the Gulf of Guinea. As had been the case on other small islands, local transmission could be fully interrupted by using synthetic insecticides. The interventionists believed that eradication was at hand. In 1983, however, migrant fishermen reintroduced

falciparum malaria to the islands, and in 1986, an epidemic broke out. It took more lives during its ten-month reign than had died from malaria in the seven years before 'eradication.'[23]

Resistance to Chloroquine Comes to Tropical Africa

Early in the era of the global malaria eradication campaign, resistance to chloroquine developed. In 1957, researchers noted the first cluster of falciparum parasites resistant to the wonder drug along the Thai-Cambodian border, and the resistance spread quickly into Thailand. A few years later, in 1960, two separate clusters emerged in South America, in Venezuela and Columbia. Yet another focus of resistance was reported in Papua New Guinea, in 1976.

In tropical Africa, chloroquine-resistant falciparum malaria first appeared in 1978 in nonimmune travelers who had visited Kenya and Tanzania, and within a few years there were more reports of resistance in Madagascar, Tanzania, and Kenya. By 1983, the resistance had spread from the East African coastal areas into Sudan, Uganda, Zambia, and Malawi. Genetic studies indicated that the resistance had been introduced from Southeast Asia.[24] By 1988, chloroquine resistance had reached every country in tropical Africa.[25]

The problem emerged slowly. At first, chloroquine remained fully effective against most faliciparum infections, and thus remained the front-line drug of treatment. Gradually, however, the number of treatment failures grew, and the tragedies from clinical malaria began to climb. The first longitudinal study took place in Senegal. There, malaria researchers had studied three rural populations in different ecological zones---the sahel, savanna, and forest---before the emergence of chloroquine resistance in 1990. They continued their observations for another five years, to 1995. Deaths had increased dramatically among children, ranging from a two-fold to eleven-fold increase.[26] It was a harbinger of things to come.

Deaths from malaria soared to levels not seen since the 1930s. Medical personnel after agonizing delays succeeded in convincing African governments that new treatment protocols were necessary. In 1993, Malawi became the first African country to switch from chloroquine to a combination of sulfadoxine-pyrimethamine (SP). Clinicians in other countries also tried SP. It proved to be a useful stopgap measure. But by 1994, researchers in Tanzania discovered a high level of falciparum resistance to SP.[27] And once unleashed the genie of resistance ripped a destructive path through the populations of small children across the continent. The era of inexpensive and efficacious drug treatment for clinical malaria was shuddering to a halt.

And there were complications. When children with clinical malaria are treated with a failing drug, there is an increased risk of severe anemia. In a hospital setting, this condition can be treated with blood transfusions. But by the early 1990s, some of the blood supplies were tainted with the HIV virus, and in some countries, tainted blood supplies accounted for approximately one-quarter of HIV infections in children.[28]

The failure of chloroquine sparked a surge of interest in African plant products that might be useful as mosquito repellents. In Guinea Bissau, for example, Western researchers discovered that Africans burned both outdoors and indoors a number of different plants to reduce mosquito biting activity and that all but one had a significant impact on mosquito activity. Some of the same plants produced oils that could be applied to the skin; these, too, reduced the number of

mosquito bites that the users endured.[29] Yet these were "traditional" practices that, although they might have reduced nuisance mosquito bites and the number of bites from infected anopheline mosquitoes, did not seem to have any discernible impact on various malariometric indices.[30]

Another surge of interest was directed toward plants thought to have antimalarial properties that Africans used to reduce the suffering from malaria. One of the most promising was the neem tree (*Azadirachta indica*), native to South and Southeast Asia.[31] The National Academy Press published a volume entitled *Neem: A Tree For Solving Global Problems* in 1992, and a number of international conferences were held to explore the prospects for a range of useful neem products. But little came of these initiatives as far as malaria control was concerned. The versatility of neem made it appropriate for home treatment, and in Nigeria, neem tea infusions were used to treat malaria. Neem seed and leaf extracts were shown effective against malaria parasites, including those that were resistant to chloroquine and those that were sensitive to it, and some researchers called for a drug-development program.[32]

Yet Africans continued to use chloroquine throughout most of the sub-continent. Chloroquine was very inexpensive and readily available in small commercial shops, and thus the small shops were the principal point of access to malaria treatment. Indeed, in the early 1980s, only twenty percent of rural Africans were estimated to have easy access to any kind of medical facilities. Study of the utilization of antimalarials outside of the formal health system was not extensive. A study of communities along the coast of Kenya found that most mothers whose children suffered from malaria sought out antimalarials from commercial shops. A course of treatment of three pills of chloroquine cost the equivalent of nine cents U.S., and spared the mother the costs of travel to and the long waits in line at a medical clinic.[33]

The recourse to chloroquine was part of a larger, changing pattern of treatment seeking for malaria symptoms. A survey of the sparse evidence on treatment seeking from eastern, western, central, and southern Africa suggested that most cases of presumed malaria were treated either at home ("self-treatment") or at a clinic. Only a few sought recourse to local healers. And most efforts to cure began with self-treatment, using either medicines bought in shops or local plant-based medicines. Yet few used the local remedies as the sole treatment. A major shift in African therapeutic practice had taken place in the decades since independence.[34]

Malaria Control in Regions Suffering from Political Violence and Political Chaos

During the first wave of the struggle for African independence from European rule, political violence in most colonies had been limited. The French and British colonies in which there were no large European settler communities achieved self-rule without convulsive disruption. In part, this was because the British and the French, weakened during the devastation of the Second World War, had come to the conclusion that African independence would not threaten their spheres of influence in Africa. Indeed, in their view, African independence might even be something of a boon, in that it would free them from the burden of governance at the same time that the economic relations of empire could continue undisturbed. The British and the French negotiated their ways toward African independence.

In British colonies with settler populations, the process was marked by political violence. In Kenya, whose Mau Mau rebellion over land and freedom had burst into violence in the early

1950s, the brutal government suppression of Mau Mau broadened the base of the independence movement. After the declaration of a state of emergency and the mass detention of Kikuyu who might be somehow associated with the Mau Mau movement, the British realized that a political transition to African independence was inevitable and they took steps toward a graduated transition of responsibility for governance.

In the Belgian Congo, the Belgians hastily prepared for a hand-off of power, and this precipitated an internal struggle for power among ethnically based political parties. The winner of the national election, Patrice Lumumba, was an African nationalist who preached independence tinged with a hard-line anti-imperialist rhetoric, and Western powers with economic interests in the rich mineral reserves of the internal Katanga province financed a war to overthrow Lumumba and to establish an independent Katanga that would facilitate their access to the reserves. The US assassinated Lumumba, and in the chaos that followed, the US backed Joseph Mobutu, who presided over an impoverished state known as Zaire until his death in 1997.

During the 1970s, the struggles for independence in the Portuguese colonies of tropical Africa---Guinea-Bissau, Angola, and Mozambique---reached a conclusion after long years of guerilla warfare. The military dictatorship of Portugal was overthrown in 1974, and the civilian government that replaced it moved quickly to extricate itself from its African quagmire. The guerilla fighters had outlasted their colonial rulers, and in 1975, Guinea-Bissau, Angola, and Mozambique joined the ranks of independent African states. They were soon followed by Zimbabwe in 1980. By the beginning of the 1980s, the white-ruled apartheid regime in South Africa with its quasi-colony of South West Africa (Namibia) was the last standing of the colonial era regimes. The apartheid regime of South Africa was committed to the savage repression of the anti-apartheid movement, in an all-out effort to forestall the emergence of African rule.

The political transitions in Guinea-Bissau and Mozambique were relatively peaceful. This was not the case in Angola. It devolved into civil war at the end of Portuguese rule and war continued until 2002. Like the other states that had achieved political independence in Southern Africa, Mozambique joined a loose political alliance in opposition to the apartheid regime in South Africa, providing a haven for anti-apartheid fighters. In retaliation, South Africa attempted to destabilize the anti-apartheid alliance states, and in Mozambique, South Africa funded a rebel army known by the acroymn RENAMO that wreaked destruction.

These conflicts rendered it all but impossible to initiate or maintain malaria control programs in the states that were embroiled in war. They created zones of intense malaria transmission. Southern Africa seemed to be the region the most cursed by conflict, and this was true during the 1970s. But during the course of the 1980s, chaos reached new areas of the continent.

In 1980, a military coup overthrew the Americo-Liberian government and within a few years Liberia was embroiled in war. The civil conflicts continued until a peace agreement was reached in 2003. Approximately 250,000 people died during the conflict. Sierra Leone was embroiled in civil war from 1991 to 2002, and approximately 75,000 people lost their lives, and two million fled to neighboring countries. A military coup in Sudan in 1989 ushered in a series of wars in the south and west of the country. Hundreds of thousands of people lost their lives, and millions were turned into refugees.

But by far the largest, longest, and most destructive conflict took place in the heart of central Africa. The murderous, episodic ethnic pogroms launched between Tutsi and Hutu communities in Rwanda and Burundi since the 1960s crossed into large-scale genocide in 1994, when approximately 800,000, mostly Tutsi, were hacked to death with machetes in Rwanda. When an invading Tutsi military force then ousted the Hutu government, a massive exodus of Rwandans who were mostly Hutu flooded into Zaire (now, the Democratic Republic of Congo). This further destabilized the eastern Congo, and when neighboring states became involved in the chaos in an effort to unseat Mobutu, the central African region descended into a nightmare of political violence. To date, some five million have lost their lives.[35]

The overall significance of these conflicts for malaria control was straightforward. Malaria control was not possible in the war zones. The conflict zones were incubators of infections, because refugees were exposed to a wide range of health threats and often had to sleep in makeshift shelters or fully exposed.

Malaria Between the Blue and White Nile Rivers

Many of the conflicts took place in zones had never had any effective malaria control, and thus there is no way to measure the increase in infections wrought by the migrations and increased human suffering. In Sudan, by contrast, the Gezira-Managil irrigation scheme in the region between the Blue and White Nile Rivers had been a focus of long-standing malaria control because of the region's economic importance as the center of cotton production for export and the principal source of state revenues. Following an epidemic in 1971, project managers launched a program of emergency house spraying, and malaria was brought under control for several years. Another epidemic broke out in the mid-1970s that was again countered with IRS. The result was that the synthetic biocides, in the cotton fields and in the sprayed houses, produced anopheline resistance to HCH, DLD, DDT, and Malathion.

In 1979, a new health initiative, the Blue Nile Health Project (BNHP), was launched in response of a broad health crisis that included a range of infectious diseases, of which the snail-borne bilharzia (schistosomiasis) and malaria were the most dangerous. The project oversaw the extension of IRS into villages at risk, and undertook environmental modifications to eliminate vector-breeding areas. Other interventions followed, such as canal weeding, the use of fish to consume mosquito larvae, and improved drainage systems. Political turmoil wracked the administration of the project, beginning in 1984, and many of the senior staff members were jailed. Some fled the country. Even so, by 1989, the health initiatives had been implemented in about half of the entire Gezira-Managil System, reaching about one million people.

And then in 1989, malaria rates quadrupled in the study zone, just as the BNHP project was winding down. In 1990, heavy rains flooded the drainage systems, and increased the density of the vectors that transmitted malaria. No drugs or insecticides were available. Donor funding had come to an end. The ten years of work of the BNHP shuddered to a halt. Malaria ripped through the populations.[36]

Like the initiative in the highlands of Madagascar, the control of malaria had been a double-edged sword. Protection had been purchased at the expense of immunity. And when protection

failed, owing to political change, donor fatigue, or the failure of control technologies, the "protected" populations became suddenly vulnerable to the ravages of malaria.

The experiences in the highlands of Madagascar and in the lowlands of Sudan were on the periphery of tropical Africa. They offered cautionary signals, however, that had wider applicability. In Madagascar, mass prophylaxis with chloroquine and mosquito control with synthetic insecticides had proved dramatically successful in reducing malaria to a minor public health problem for more than thirty years, from 1949 until the mid 1980s. The mass prophylaxis had also transformed the parasite mosaic from a roughly 50-50 mix of vivax and falciparum to 100 percent falciparum. The resurgence of malaria was enmeshed in international financial policy, internal political change, and the view, by the early 1980s, that malaria was no longer a problem. The slow response to the epidemic allowed it to gain deadly momentum.

In the Sudan, the success in malaria control had been briefer. There had been no mass prophylaxis program and no transformation of the parasite mosaic. There had been deft and innovative use of environmental engineering, after the use of pesticides had provided only short-term successes. A broad program of malaria control had reduced infections to a relatively low level. And then the program had ended, at the end of a cycle of donor funding and in the midst of political turmoil and regime change. Severe malaria became reestablished in the vast project area.

For malariologists who watched in horror at the unraveling of successful control, the lessons were difficult to digest. What were the key variables to maintaining control? Was successful control dependent upon internal political stability? If so, this boded poorly for the control of malaria across much of tropical Africa. The entirety of the central African region was in turmoil, and it was unclear when or how political order would be reestablished. Major conflicts continued in the Sudan, and in West Africa, some states were failing, and warlordism was the rubric for western understanding of the political chaos that ensued. From this perspective, malaria control programs could not possibly be undertaken on a sub-continent-wide basis. They would necessarily have to be national programs, centered on urban areas and economic centers of importance to the state.

On the highland frontiers of mainland tropical Africa, during the 1980s and 1990s epidemic malaria continued to afflict some of the upland communities. The populations living in these areas of unstable infection made up a small percentage of the total population of sub-Saharan Africa, but their vulnerabilities made them epidemiologically significant, and researchers began to investigate the association between increased rainfall and other variables of weather and changes in the density and longevity of the vector mosquitoes. Research linked some of the epidemics to global weather events such as El Niño, yet it was clear that other weather variables such as temperature fluctuations and local rainfall events were deeply implicated. Indeed, local conditions and local epidemiology could often be determinant.[37] The impact of the epidemics varied. Some were intensely destructive. Between 1995-2000, epidemic malaria in the highlands of western Uganda caused a large increase in under-five mortality, at the same time that decreases in under-five mortality were registered in other parts of the country. The increase was large enough that when combined in the national data, the western data produced an overall

national increase in under-five mortality. Researchers judged that this was likely the result of a highland epidemic in 1997-1998.[38]

Were ongoing financial commitments from external donors necessary for successful malaria control? If so, during the 1980s and early 1990s, this question was moot. There were no protocols for successful control that could be "scaled-up," and thus there were no calls for massive and continuing financial commitments.

In the mid 1990s, however, USAID launched a new initiative to improve the survival rates of African children. Two of its constituent parts were a set of guidelines for the treatment of malaria that focused on the recognition and management of acute and chronic malaria and another for the treatment and management of malaria in pregnant women. It also pointed the way forward, toward an era of insecticide-treated bednets to reduce transmission.[39]

USAID undertook clinical studies of the impact of treatment and management of malaria in pregnant women in Malawi. The issue was of high importance, because even women who lived in holoendemic areas and who had a robust acquired immunity to malaria infections were likely to lose their immunities during pregnancies. They regained their pre-pregnancy immune status at about the time of delivery. Their vulnerabilities were greatest during first pregnancies, but even during successive pregnancies, more than half of the western Kenyan women studied had high levels of parasitaemia and placental infections.[40] The USAID findings underscored the medically efficaciousness of using antimalarial drugs to reduce malarial infections in the pregnant woman, her placenta, and the umbilical cord. Children born from treated women had improved birth-weight and a lower risk of neonatal and infant mortality. It became obvious that antimalarial interventions for high-risk pregnancies should be a part of a malaria control or antenatal care program.[41]

This was the first significant advance in therapeutic interventions in the twentieth century. It was the harbinger of an approach known as Intermittent Preventive Therapy (IPT). It first hinged on the administration of antimalarials to pregnant women (IPTp), and later was extended to infants (IPTi) and children (IPTc). The intermittent treatment of infants and children was found to reduce significantly mortality and morbidity and to improve their general health. The empirical findings of the physicians in the Belgian Congo in the 1930s had been discovered sixty years later.

Building Capacity for Malaria Control

In response to the unfolding malaria disaster, the WHO in 1992 convened a Ministerial Malaria Conference in Amsterdam. The conference adopted a Global Malaria Control Strategy whose four basic elements called for disease control through early diagnosis and treatment, selective and sustainable preventive measures, detection and intervention to contain or prevent epidemics, and the strengthening of capacities to regularly assess the national malaria situation.[42] It was a giant step away from the eradication era. The goals for the new control strategy were lofty: to reduce malaria mortality in the year 2000 by 20 percent compared to 1995. And by the end of 1996, more than ten thousand individuals were in training at the district and community levels, and by mid-1997, some 47 of 49 countries in sub-Saharan Africa had produced national malaria control plans.[43] In 1998, the WHO launched a new program, Roll Back Malaria (RBM), in a

effort to coordinate national efforts to reduce malaria morbidity and mortality. And in the year 2000, at a WHO conference in Abuja, Nigeria, African heads of state pledged their support for the goal of reducing malaria deaths by 50 percent by 2010.

This was not a new model of malaria control, but an old one with new emphases and with new resources committed to it. It aimed high, and like many of targets for global health, it was meant to be inspirational, to encourage greater effort. There were significant problems with the "roll-out" of the RBM program. African states were slow to develop national malaria control programs that were in line with RBM requirements, and donor monies were slow to reach the national programs.[44]

An even larger problem was rooted in the weak, underfunded, and understaffed national health systems. The number of doctors and nurses trained to staff the health systems were inadequate to the tasks, and large numbers of African doctors and nurses found employment overseas, where compensation was higher. Overall, sub-Saharan Africa was short hundreds of thousands of physicians and hundreds of thousands of nurses. The training capacity was low, and the ability to retain staff was weak.[45] The impact of health policy reforms under structural adjustment in Africa was surprising and somewhat paradoxical. The structural adjustment programs did not reduce public health expenditures. In fact, many countries spent more on these programs. Many African governments introduced user charges for health services, a policy advocated by the World Bank. The results were quite mixed. On one hand, the user fees reduced the affordability of health services for the poor. On the other hand, some of the fees were used to cover non-salary items and to maintain facilities for urban populations.[46] The overall picture was that, with few exceptions, the prior bias toward urban, curative, hospital-based services continued, and the health status of rural African populations deteriorated. Mozambique and Zimbabwe were exceptions, taking significant steps to reorient their budget spending to increase primary and preventive activities.[47]

With the establishment of the Global Fund in 2002, the President's Malaria Initiative in 2005, and the Bill and Melinda Gates Foundation's call in 2007 for a new campaign of global malaria eradication, a new chapter in the history of African malaria eradication and control opened. The campaign has deployed some well-established malaria control tools, such as IRS, and increased the availability of a new generation of antimalarials (ACTs, artemisinin combination therapies). It has also distributed insecticide-treated bednets (ITNs) on a large scale. It has funded research on new vaccines, medicines, anti-parasitic fungi, and transgenic mosquitoes, all of which hold promise but are far from ready for large-scale use in tropical Africa.

To date, the new campaign has forged ahead without an endgame in sight. The funders trust that technological advances will ultimately defeat malaria. The campaign, however, is already confronted with the spread of mosquito resistance to the synthetic insecticides for IRS and on ITNs. Parasite resistance to artemisinin-based drugs has emerged in Southeast Asia, where falciparum resistance to chloroquine began decades ago, and there is no new line of drugs that can replace the ACTs. The danger is of a resurgence of the severe malaria that followed on the lapses of the malaria eradication and control programs of the second half of the twentieth century.

Rolling out malaria control programs using the same basic tools that were employed in previous campaigns without taking account of the consequences of the lapsed interventions in those programs is a serious ethical shortcoming. The historical records of these campaigns demonstrate that they have failed for a variety of different economic, political, and technical reasons, and that when the malaria control interventions have lapsed, epidemiological disaster has been visited upon the 'protected' populations. Public health specialists' ignorance of the historical epidemiology of past campaigns constitutes a significant public health risk that is borne by Africans.

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[1] Maryinez Lyons, The Colonial Disease: A Social History of Sleeping Sickness in Northern Zaire, 1900-1940 (Cambridge: Cambridge University Press, 2002).

[2] Alan D. T. Barrett, "Yellow Fever Vaccines," Biologicals, vol. 25, no. 1 (1997), 17.

[3] Dieldrin also exacted a human cost: On some malaria control projects, the spraymen suffered dieldrin poisoning. The problem was documented as early as 1955 in Nigeria; the use of dieldrin continued for several years across tropical Africa. [Wayland J. Hayes, Jr., "Dieldrin Poisoning in Man," Public Health Reports, vol. 72, no. 12 (1957), 1087-1091. The Nigerian experience was documented in J. Haworth, "Observations on the Possible Toxic Effects of Dieldrin," WHO/Insecticides/60, 1955, cited by Hayes, "Dieldrin Poisoning," 1088; see also Wayland J. Hayes, Jr., "Report on the Toxicity of Dieldrin to Man," WHO/MAL/215, 5 January 1959.] Studies at the malaria control project at Taveta-Pare in Tanganyika, where spraymen adhered closely to guidelines to limit contamination, found no evidence of clinical symptoms of dieldrin poisoning. [T.E. Fletcher, J.M. Press, and D. Bagster Wilson, "Exposure of Spray-men to Dieldrin in Residual Spraying," Bulletin of the World Health Organization, vol. 20, no. 1 (1959), 15-25.]

[4] Max J. Miller, "Chemotherapy in Malaria Control," 20 September 1955, WHO/MAL/137; I.H. Vincke, "Place of Chemotherapy in Modern Malaria Control Programs," 27 October 1955, WHO/MAL/147; L.J. Bruce-Chwatt, "Chemotherapy in Relation to Possibilities of Malaria Eradication in Tropical Africa," 21 May 1956, WHO/MAL/175.

[5] M.A.C. Dowling, "The Use of Mass Drug Administration in Malaria Projects in the African Region," [n.d.; circa 1961], AFR/MAL/39, 1.

[6] Snowden, The Conquest of Malaria, 53-114.

[7] As M. Robert, M. le Médecin Général Inspecteur, Directeur Général de la Santé Publique en A.O.F., put it: "Certains essais de chimio-prophylaxie de mass par la quinine et même dans certains cas par les synthétiques, ont fait apparaître la fièvre bilieuse hémoglobinurique avec une grande fréquence chez les africains, alors que cetter affection était extrêmement rare chex eux avant l'introduction des anti-malariques et était réservée à l'européen non immunisé par les infections de l'enfance et soumis a une prophylaxie quinuinique mal appliquée…."

"Il est remarkable, et ceci est démontré par les statistiques, comme par l'expérience des médecins des hôpitaux d'A.O.F., que la fièvre bilieuse hémoglobinurique est en voie de disparition depuis l'utilisation de la chimio-prophylaxie individuelle des produits synthéthiques.

"Appliquer à l'africain une chimio-prophylaxie quininque généralisée serait, dans les conditions actuelles, aboutir, non à l'éradication du paludisme—puisque les conditions de transmission persisteraient—mais à une dimunition dangereuse de son remarkable pouvoir de résistance vis-à-vis des complications sévères du paludisme." [IMTSSA, Box 232. Dossier

Antipaludiques. M. Robert, M. le Médecin Général Inspecteur, Directeur Général de la Santé Publique en A.O.F., "Note au sujet de: La Quinine dans la lutte anti-palustre en A.O.F.," 3.]

[8] The French had a different view of the prospects for mass antimalarial prophylaxis than did the British. In 1949, the French launched an extensive program of malaria control on the island of Madagascar that used mass chemoprophylaxis, and this interest was extended to their antimalaria projects on the mainland. The French medical legacy continued after independence: Cameroon and Senegal developed national antimalaria chemoprophylaxis programs. [A.B.G. Laing, "The Impact of Malaria Chemoprophylaxis in Africa with Special Reference to Madagascar, Cameroon, and Senegal," Bulletin of the World Health Organization, vol. 62, supplement (1984), 41-48.]

The British never developed such programs in their African colonies, and neither did any of the independent African states that gained their independence from the British. British view was that regular prophylaxis did not make much sense in tropical Africa because the high rate of malaria transmission (in conjunction with a concern about compromising the immunological status of Africans) meant that a regime of prophylaxis would demand high levels of compliance, and this was deemed unachievable.

[9] S.A. Hall and N.E. Wilks, "A Trial of Chloroquine-Medicated Salt For Malaria Suppression in Uganda," American Journal of Tropical Medicine and Hygiene, vol. 16, no. 4 (1967), 429-442; [n.a.], "Assessment Report on the Ghana-18 Medicated Salt Pilot Project," 2, SJ 5, JKT 1, Ghana, WHO7.0017, WHO Archives, Geneva.

[10] D.F. Clyde, "Suppression of Malaria in Tanzania with the Use of Medicated Salt," Bulletin of the World Health Organization, vol. 35, no. 6 (1966), 962-968.

[11] J. Hamon, J. Mouchet, and G. Chauvet. "Bilan de quatorze années de lutte contre le paludisme dans les pays francophones d'Afrique tropicale et à Madagascar. Considérations sur la persistence de la transmission et perspectives d'avenir," Bulletin de la Société de Pathologie exotique, t. 56, no. 5 (septembre-octobre 1963), 945-946.

[12] At the Kampala conference, new definitions were agreed to distinguish between levels of heavy endemic transmission in which there were different percentages of the population with distended spleens. The areas in which the spleen rate in children of 2-10 years of age was constantly over 50 percent and in which the spleen rate in adults was "high" were to be classified as *hyperendemic*; those areas in which the spleen rate in children of 2-10 years of age was constantly over 75 percent and in which the spleen rate in adults was "low" were to be classified as *holoendemic*. The "strongest adult tolerance" to malaria was said to be found in holoendemic regions. [Report on the Malaria Conference in Equatorial Africa. World Health Organization Technical Report Series, no. 38 (Geneva: World Health Organization, 1951), 45.] Malariologists later discovered regions of heavy endemic malaria transmission in which the spleen rates of the populations did not accord well with these definitional criteria.

[13] L.J. Bruce-Chwatt investigated the state of knowledge of this issue in his 1962 report "A Longitudinal Survey of Natural Malaria Infection in a Group of West African Adults," 17 December 1962, WHO/MAL/369. This work was also published as "A Longitudinal Survey of Natural Malaria Infection in a Group of West African Adults. I," West African Medical Journal, vol. 12 (1963), 141-173 and "A Longitudinal Survey of Natural Malaria Infection in a Group of West African Adults. II," West African Medical Journal, vol. 12 (1963), 199-217.

Bruce-Chwatt was a well-known advocate for the expansion of indoor residual spraying in tropical Africa, and at the Kampala conference he had championed the interventionist

position. In his 1962 report, he found that the evidence about the medical consequences of lapsed intervention was mixed and difficult to interpret.

[14] Bruce-Chwatt, "A Longitudinal Survey," WHO/MAL/369, 62.

[15] J.L.A.Webb, Jr., "The First Large-Scale Use of Synthetic Insecticides to Control Malaria in Tropical Africa: Lessons From Liberia," Journal of the History of Medicine and Allied Sciences, vol. 66, no. 3 (2011), 347-376.

[16] Kwesi Dugbatey, "National Health Policies: Sub-Saharan African Case Studies (1980-1990)," Social Science & Medicine, vol. 49, no. 2 (1999), 224-226. Dugbatey chose four states (Botswana, Ivory Coast, Ghana, and Zimbabwe) for his comparative study. Forty of the forty-seven sub-Saharan African states did not have health policy documents with enough substance to allow for analysis.

[17] United Nations Development Program, Human Development Report 1991 (New York: Oxford University Press, 1991), 36.

[18] WHO, Technical Report Series, no. 640. Seventeenth Report of the WHO Expert Committee on Malaria (Geneva, 1979).

[19] [American Public Health Association], Manual on Malaria Control in Primary Health Care in Africa (Washington, DC: Bureau for Africa, USAID, 1982).

[20] Geoffrey M. Jeffrey, "The Role of Chemotherapy in Malaria Control Through Primary Health Care: Constraints and Future Prospects," Bulletin of the World Health Organization, vol. 62, supplement (1984), 49-53.

[21] J.G. Bremen and C.C. Campbell, "Combating Severe Malaria in African Children," Bulletin of the World Health Organization, vol. 66, no. 5 (1988), 611-620.

[22] Sixte Blanchy, A. Rakotonjanabelo, G. Ranaivoson, and E. Rajaonarivelo. "Epidémiologie du paludisme sur les hautes terres malgaches depuis 1878," Cahiers Santé, vol. 3 (1993), 155-161.

[23] J.G. Viegas de Ceita, "Malaria in Sao Tome and Principe," in A.A. Buck (ed.), Proceedings of the Conference on Malaria in Africa, Practical Considerations on Malaria Vaccines and Clinical Trials, Washington, DC, December 1-4, 1986 (Washington, DC: American Institute of Biological Sciences, 1987), 142-155.

[24] A.O. Talisuna, P. Bloland, and U. D'Alessandro. "History, Dynamics, and Public Health Importance of Malaria Parasite Resistance," Clinical Microbiology Reviews, vol. 17, no. 1 (2004), 236-237.

[25] Jean-François Trape, "The Public Health Impact of Chloroquine Resistance in Africa," American Journal of Tropical Medicine and Hygiene, vol. 64, nos. 1-2 (2001), 12-17.

[26] Jean-François Trape, Gilles Pison, Marie-Pierre Preziosi, Catherine Enel, Annabel Desgrées du Loû, Valérie Delaunay, Badara Samb, Emmanuel Lagarde, Jean-François Molez, François Simondon. "Impact of Chloroquine Resistance on Malaria Mortality," Comptes rendus de l'Académie des Sciences, vol. 321, no. 8 (1998), 689-697.

[27] A.M. Rønn, H.A. Msangeni, J. Mhina, W.H. Wernsdorfer, and I.C. Bygbjerg, "High Level of Resistance of Plasmodium Falciparum to Sulfadoxine-Pyrimethamine in Children in Tanzania," Transactions of the Royal Society of Tropical Medicine and Hygiene, vol. 90, no. 2 (1996), 179-181.

[28] Talisuna et al., "History, Dynamics, and Public Health Importance," 247.

[29] Katinka Pålsson and Thomas G.T. Jaenson, "Plant Products Used as Mosquito Repellents in Guinea Bissau, West Africa," Acta Tropica, vol. 72, no. 1 (1999), 39-52.

[30] R.W. Snow, A.K. Bradley, R. Hayes, P. Byass, and B.M. Greenwood. "Does Woodsmoke Protect Against Malaria?," Annals of Tropical Medicine and Parasitology, vol. 81, no. 4 (1987), 449-451.

[31] Many specialists accept that Indian immigrants in the late nineteenth century introduced the neem tree into eastern Africa because of its well known and widely appreciated medical properties, although I have not found any historical documentation that explicitly supports this claim. In the early twentieth century, the British introduced neem into their colonies in West Africa, in order to supplement the indigenous species with exotics that might have economic uses. [Edward Ayensu, "Plant and Bat Interactions in West Africa," Annals of the Missouri Botanical Garden, vol. 61, no. 3 (1974), 713.] By the late twentieth century, the neem tree was found throughout sub-Saharan Africa, its dryland range limited by its modest requirement of rainfall or shallow groundwater.

[32] Kausik Biswas, Ishita Chattopadhyay, Ranajit K. Banerjee, and Uday Bandyopadhyay. "Biological Activities and Medicinal Properties of Neem (*Azadirachta indica*)," Current Science, vol. 82, no. 11 (2002), 1336-1345.

In more recent years, researchers have explored the efficacy of neem as a larvicide that might be used by villagers to suppress mosquito density. See, for example, Rebecca L. Gianotti, Arne Bomblies, Mustafa Dafalla, Ibrahim Issa-Arzika, Jean-Bernard Duchemin, and Elfatih A.B. Eltahir. "Efficacy of Local Neem Extracts for Sustainable Malaria Vector Control in an African Village," Malaria Journal, vol. 7 (2008). Doi:10.1186/1475-2875-7-138.

[33] R.W. Snow, N. Peshu, D. Forster, H. Mwenesi, and K. Marsh. "The Role of Shops in the Treatment and Prevention of Childhood Malaria on the Coast of Kenya," Transactions of the Royal Society of Tropical Medicine and Hygiene, vol. 86, no. 3 (1992), 237-239.

[34] S.C. McCombie, "Treatment Seeking for Malaria: A Review of Recent Research," Social Science and Medicine, vol. 43, no. 6 (1996), 933-945. Another literature survey found that more than three-quarters of the population in many countries took recourse to self-treatment. [U. Brinkmann and A. Brinkman, "Malaria and Health in Africa: The Present Situation and Epidemiological Trends," Tropical Medicine and Parasitology, vol. 42 (1991), 207-208.]

[35] For an introduction to the conflicts, see Jason K. Stearns, Dancing in the Glory of Monsters: The Collapse of the Congo and the Great War of Africa (New York: Public Affairs, 2011).

[36] William R. Jobin, Dams and Disease: Ecological Design and Health Impacts of Large Dams, Canals, and Irrigation Systems (London: E & FN Spon Press, 1999), 335-353.

[37] J. Mouchet, S. Manguin, J. Sircoulon, S. Laventure, O. Faye, A.W. Onapa, P. Carnevale, J. Julvez, and D. Fontenille. "Evolution of Malaria in Africa for the Past 40 Years: Impact of Climatic and Human Factors," Journal of the American Mosquito Control Association, vol. 14, no. 2 (1998), 121-130; Kim A. Lindblade, Edward D. Walker, Ambrose W. Onapa, Justus Katungu, Mark L. Wilson. "Highland Malaria in Uganda: Prospective Analysis of an Epidemic Associated with El Niño," Transactions of the Royal Society of Tropical Medicine and Hygiene, vol. 93 (1999), 480-487.

[38] Fred Nuwaha, Juliet Babirye, and Natal Ayiga, "Why the Increase in Under Five Mortality in Uganda from 1995 to 2000? A Retrospective Analysis," BMC Public Health, vol. 11:725. Accessed at http://www.biomedcentral.com/1471-2458/11/725.

[39] [U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, International Health Programme Office], "Addressing the Challenges of Malaria

Control in Africa" (Washington, DC: USAID, Africa Regional Project (698-0421), n.d., [c. 1993]).

[40] B.J. Brabin, "An Analysis of Malaria in Pregnancy in Africa," Bulletin of the World Health Organization, vol. 61, no. 6 (1983), 1005-1016.

[41] [U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, International Health Programme Office], "Malaria Prevention in Pregnancy: The Mangochi Malaria Research Project" (Washington, DC: USAID, Africa Regional Project (698-0421), n.d., [c. 1993]).

[42] The World Health Assembly in 1993, the Forty-Ninth Session of the United Nations General Assembly and the Thirty-third Ordinary Session of the Assembly of Heads of State in 1994, and the Government of the Organization of African Unity in 1997 confirmed the Global Malaria Control Strategy. [P.I. Trigg and A.V. Kondrachine. "Commentary: Malaria Control in the 1990s," Bulletin of the World Health Organization, vol. 76, no. 1 (1998), 13.]

[43] Trigg and Kondrachine, "Commentary: Malaria Control in the 1990s," 14.

[44] Randall M. Packard, The Making of a Tropical Disease: A Short History of Malaria (Baltimore: Johns Hopkins University Press, 2007), 220-227.

[45] Charles Hongoro and Barbara McPake, "How to Bridge the Gap in Human Resources for Health," Lancet, vol. 364, 16 October 2004, 1451-1456.

[46] For studies of the impact of user fees in Ghana, see C.J. Waddington and K.A. Enyimayew. "A Price to Pay: The Impact of User Charges in Ashanti-Akim District, Ghana," International Journal of Health Planning and Management, vol. 4 (1989), 17-47; Catriona Waddington, and K.A. Enyimayew. "A Price to Pay, Part 2: The Impact of User Charges in the Volta Region of Ghana," International Journal of Health Planning and Management, vol. 5 (1990), 287-312.

[47] David Sahn and Rene Bernier. "Have Structural Adjustments Led to Health Sector Reform in Africa?," Health Policy, vol. 32, nos. 1-3 (1995), 193-214; Lucy Gilson and Anne Mills, "Health Sector Reforms in Sub-Saharan Africa: Lessons of the Last 10 Years," Health Policy, vol. 32, nos. 1-3 (1995), 215-243.