Cover photos

Top row, left to right:
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There is no single method of attack against malaria. Spraying equipment has to be constantly maintained and repaired. World Health Organization, PRINT-EURO-MALARIA, Photo No. 17939. © World Health Organization. Used by permission.

Second row, left to right:
A young patient being checked for possible enlargement of the spleen caused by malaria. Over much of Africa, there is so much malaria that present methods of vector control are inadequate to check the disease. World Health Organization, PRINT-AFRO-MALARIA, Photo No. 4931. © World Health Organization. Used by permission.

Anopheles mosquito by James Gathany.

A routine malaria survey on the island of Grande Comore to obtain the seasonal malaria parasite rate among schoolchildren. Under the eye of the schoolmaster, the children line up to have a blood slide taken. World Health Organization, PRINT-AFRO-MALARIA, Photo No. 180[illegible] © World Health Organization. Used by permission.

Bottom row, left to right:
DDT spray operations by an antimalaria team in a village of M[illegible] World Health Organization, PRINT-SEARO-MALARIA, Photo No. [illegible] © World Health Organization. Used by permissio[illegible]

Child showing scars that resulted after local[illegible] d to eli[illegible] the congestion caused by malaria. World H[illegible] AFRO-MALARIA, Photo No. 11888. © [illegible] Organ Used by permission.

Humanity's Burden

A Global History of Malaria

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Africa Redux

In the spring of 1944, the Allied Control Commission in Italy invited a Rockefeller Foundation team to determine what could be done to cope with the malaria epidemics that the Nazis had unleashed. Their answer was surprisingly simple and effective: In two trials on flooded lands, the Rockefeller group showed that a single spraying of a new insecticide known by its initials DDT could stop the spread of malaria for an entire season. DDT worked so well that by 1945 the Health Division of the UN relief organization decided to undertake a comprehensive DDT campaign to drive malaria out of Italy. In the immediate postwar period, DDT campaigns were also launched in Greece, Venezuela, and Ceylon. In 1946, the Rockefeller Foundation, inspired by its successful participation in the eradication of *A. gambiae* in Brazil, decided on an experimental program on Sardinia to eradicate the sole mosquito vector, *A. labranchiae* – and thus malaria – from the island.[1]

DDT seemed like a miracle. The venerable Paris Green worked well as a larvicide, but it could not kill adult mosquitoes. The natural insecticide pyrethrum made from the dried flower heads of the chrysanthemum plants (*Chrysanthemum cinerariaefolium* and *Chrysanthemum coccineum)* was effective against adult mosquitoes, but it was highly unstable and quickly lost its potency. DDT killed adult mosquitoes, *and* it was a residual killer. It could stop mosquito transmission dead. In most areas of seasonal malaria transmission, two applications per year were enough. Where DDT was laid down, the number of new malarial infections plummeted toward zero. Here was an approach that had broad appeal. DDT sprayers reduced mosquito populations vastly more effectively than had Ross's

[1] Gordon Harrison, *Mosquitoes, Malaria and Man: A History of the Hostilities since 1880* (New York: E.P. Dutton, 1978), 223–224.

mosquito brigades, and DDT cost far less than chemical therapy. Because DDT got rid of other nuisance insects and crop pests, it initially had a broad popular constituency.

In the midst of these early momentous victories, however, distressing news began to filter in from the killing fields. In Greece, in 1947, common houseflies began to show a surprising resistance to the killer insecticide. Then, on the island of Sardinia, houseflies also demonstrated resistance to DDT. By 1951, some anopheline mosquitoes in the Greek islands had become impervious to the insecticide treatments, alighting on DDT-treated walls and flying off again to bite.

The early successes with DDT inspired malaria specialists to think more broadly than ever before about the control of malaria – not only in Europe, the European colonies in Asia, and the Americas but also in Africa. The conclusion of World War II heralded not only the victory of the Allies over the German, Italian, and Japanese fascists, but it also precipitated the great movement for decolonization of European empires in Asia. As India, Ceylon, and Burma began to move toward independence in the immediate postwar period, it was clear that the continuing claim of the European empires to rule other tropical peoples would have to include greater provisions for the health and welfare of colonial subjects, particularly if they were to be inoculated from the revolutionary rhetoric of Marxist-Leninism that championed the movements for national self-determination of colonized peoples. What could be done about African malaria?

THE CONUNDRUM OF ACQUIRED IMMUNITY IN TROPICAL AFRICA

In 1948, the newly created WHO took over the work of the Malaria Commission of the now-defunct League of Nations. The first major conference on African malaria took place in Kampala, the capital of the British protectorate of Uganda, in 1950. There expert malariologists clashed over the issue of tropical Africans' acquired immunity to falciparum malaria. What could and should be done to combat malaria in tropical Africa? Was it financially practical and morally sound to bring chemical insecticides to bear on African malaria? The debates at Kampala reprised issues that the League of Nations had grappled with two decades earlier.

During the interwar years, the daunting realities of malarial infections in the imperial tropics had impressed themselves on the European colonizers. It was clear that most Africans suffered from malaria, and that the death rates, particularly for children, were very high. It also seemed to

be the case that many tropical Africans were functionally immune to falciparum malaria. The core paradox was that the rates of malarial infection – as measured by the spleen index and the presence of blood parasites – remained high in adults, although most adults appeared to suffer few, if any, ill effects from malaria.[2] Given this acquired immunity, what types of treatment were appropriate? How should scarce resources be spent? During the early 1930s, the League of Nations Malaria Commission had suggested a strategy aimed to promote the acquisition of "relative immunity" through a "nonradical" treatment of severe symptoms that did not attempt a full and complete "cure" of infected peoples living in highly endemic areas. Critics attacked this position as heartless, and it was abandoned as an official strategy.[3] The shift in official strategy, however, had limited practical significance for African colonial subjects because, with the exception of laborers who worked on colonial plantations or in mines and were treated by hired doctors and of those within the orbit of Christian medical missions, most Africans had little or no access to Western antimalarial medicine in the period before 1950.

The issue of mosquito control in tropical Africa was largely moot: The near ubiquity of breeding sites and the fact of year-round transmission in regions of high rainfall seemed to rule out environmental engineering interventions. Malaria specialists had long recognized that the tropical African malarial situation was more difficult than in other regions. Until the immediate postwar years, mosquito control had been practiced principally outside of tropical Africa, and the body of knowledge about mosquito control was based principally on experiences outside the continent. Most regional programs had been in the United States, Central America, South America, and Western Europe, where the infections were primarily vivax. Sickness, rather than death, was the principal hazard. Drawing on the successes of the Rockefeller Foundation programs and the regional malaria control efforts in the vivax and mixed infections zones, and now armed with the miracle insecticide DDT, many malariologists endorsed the accepted wisdom that any degree of endemic malaria was harmful. How could this be reconciled with the broad experience of acquired immunity in tropical Africa?

In 1950 at Kampala, the experts discussed for the first time the possibility of a full-scale assault on malaria. The sheer inexpensiveness and residual

[2] D. Bagster Wilson, "Implications of Malarial Endemicity in East Africa," *Transactions of the Royal Society of Tropical Medicine and Hygiene*, vol. 32, no. 4 (January 1939), 435–465.

[3] G. Corbellini, "Acquired Immunity against Malaria as a Tool for the Control of the Disease: The Strategy Proposed by the Malaria Commission of the League of Nations in 1933," *Parassitologia*, vol. 40 (1998), 109–115.

killing power of DDT suggested the new possibility of attacking mosquito transmission in tropical Africa. The conference chairman, Dr. N.H. Swellengrebel, had conducted malariological research in the Dutch East Indies, traveled widely in Africa, and published seminal work on levels of immunity to falciparum malaria. He raised strong cautions about the idea of eradication and was deeply concerned that incomplete or unsuccessful epidemiological interventions could compromise individual or collective immunities and leave entire communities worse off than they had been before.[4] This was far from a purely theoretical position. The British antimalarial campaign in Bombay in the early twentieth century, for example, had been curtailed as soon as the incidence of malaria began to fall. This had paved the way for a disastrous recrudescence of the disease.[5] What would be the health impact of the loss of immunity to falciparum malaria?[6]

The question of acquired immunity was so difficult to address because the scientific understandings were so incomplete. Moral certainties about the need to protect human populations collided with realistic assessments of the possibilities for intervention. There were two extremely thorny issues. First, the "costs" – in terms of sickness and death – for parasitized adults to acquire "relative immunity" were extremely high. If large-scale mosquito control or eradication efforts failed, the acquired immunities might deteriorate and populations might be at greater risk than before. The maintenance of relative immunity appeared to depend on continuous infection. Second, the carriers who had achieved an acquired immunity remained infectious and thus were a health threat to nonimmunes. Relative immunity referred to absence of malaria symptoms, not to the absence of malaria parasites, which remained in the blood.[7]

The experts also grappled with the fact that there were different degrees of acquired immunity. Those who had a fully functional acquired immunity lived in what were termed areas of *holo-endemicity*. These

[4] J.P. Verhave, "Malaria: Epidemiology and Immunity in the Malay Archipelago," in ed. G.M. van Heteren, A. de Knecht-van Eekelen, and M.J.D. Poulissen, *Dutch Medicine in the Malay Archipelago* (Amsterdam: Rodopi, 1989), 98–100.

[5] Gordon Covell, *Malaria Control by Anti-Mosquito Measures*, 2nd ed. (Calcutta and London, 1941), 119–120; Gordon Covell, *Malaria in Bombay* (Bombay: Government Press, 1928).

[6] World Health Organization, Afr/Mal/Conf/25, Geneva, February 27, 1953; Malaria Conference in Equatorial Africa, November 27–December 9, 1950; Town Hall, Kampala, Uganda, Summary Records of the Meetings, 48.

[7] The fact that quinine did not destroy the gametocytes of falciparum was recognized as early as 1900 (Harrison, *Mosquitoes, Malaria, and Man*, 173).

populations, however, were interspersed with others whose immunities were less complete because they lived in areas of *meso-endemicity* in which transmission was less intense, and who were thus at greater risk as adults from additional infective bites. Populations in both epidemiological environments were thought of as isolated from one another.[8]

At the Kampala conference, Swellengrebel posed the moral challenge that cut to the heart of the "eradicationist" activities under discussion for tropical Africa. Did Europeans have the moral right to take away the immunological status of Africans? Did they have the right to bring workers from less endemic regions into more endemic regions, if this represented greater risk to those workers? Should the imported workers be protected if this meant compromising the immunological status of others?[9] There were no easy answers.

The eradicationists argued that the idea of allowing Africans to suffer infections in order to acquire a functional immunity was a repudiation of the pretensions of the scientific community in general and the malariologists in particular. In their view, malaria should be considered in the same light as other communicable diseases, and African populations should be relieved of this pressure. There was no higher morality in allowing poorer and less technologically sophisticated peoples to suffer.

At the Kampala conference, the divisions among experts were protracted and bitter. The eradicationist school of thought prevailed and established malaria as a health problem in Africa to be tackled with the modern weapons of DDT and chloroquine.[10] The acquired immunity school of thought argued for a pilot study to test the efficacy of mosquito control interventions and to monitor the health of the populations. The Kampala participants threw a sop to the losers and agreed that a long-term study of the impact of the antimalarial campaigns should be undertaken, and in the event that the antimalarial campaign was shown to have not brought about an improvement (or had brought about a decline) in the health of the populations, the study would continue to track these results over time.

[8] N.H. Swellengrebel, "Reflections à propos de la Conference sur le paludisme de Kampala (1950)," *Annales de la Société Belge de Médicine Tropicale*, vol. 31 (1950), 113.
[9] Ibid., 114.
[10] M.J. Dobson, M. Malowany, and R.W. Snow, "Malaria Control in East Africa: The Kampala Conference and the Pare-Taveta Scheme: A Meeting of Common and High Ground," *Parassitologia*, vol. 42 (2000), 149–166; World Health Organization, Afr/Mal/67, February 19, 1965, "The Malaria Eradication Programme in the African Region," 1.

One of the malariologists most concerned about the health consequences of the potential loss of immunity, D. Bagster Wilson, along with his wife Margaret, a parasitologist, undertook a longitudinal study to track the health impacts of malaria control measures in the highlands of East Africa. This study at Pare-Taveta in northeastern Tanganyika and southeastern Kenya (1954–1966) produced frustratingly ambiguous data. The use of insecticides and larvicides, in combination with medical treatments, reduced the incidence of malaria, particularly among infants under the age of one and small children between the ages of one and four. At the end of the project, mortality among small children returned to preproject levels, but mortality among infants did not, for reasons that were not understood then and are not understood now.[11]

While the Pare-Taveta study was in progress, government authorities and malaria experts began to back away from the commitment to push for aggressive malaria control in Africa. The costs of these interventions – owing to the pervasiveness of the infections and the near-ubiquity and efficiency of the vectors – seemed prohibitively high and unable to be funded. Some pilot projects in some regions of tropical Africa enjoyed small-scale successes, seeming to block the transmission of malaria in high-plateau regions in southwestern Uganda and in forest areas of Liberia and southern Cameroon. In the southern Cameroonian city of Yaoundé, in 1958, the interventions completely interrupted malaria transmission.[12] However, in other regions the results were disappointing. The pilot projects in the savannah areas of northern Cameroon, Upper Volta, Senegal, Ghana, Nigeria, and southern Dahomey failed to interrupt transmission.

Then a malaria disaster struck populations in the northeastern highland frontier of tropical Africa. An epidemic of falciparum malaria broke out in the Ethiopian highlands between June and December of 1958. Unusually wet conditions, along with abnormally high temperatures and humidity pushed the *A. gambiae* vector into elevations above 1,600 meters, where the communal immunity of the population was very low. Food shortages, owing to crop failures the previous year, eroded the health status of the highlanders. Some three million people came down with malaria during the epidemic, and more than 150,000 are thought to have lost their lives.[13]

[11] Ibid., 160–166.
[12] Jean-Paul Bado, "La lutte contre le paludisme au Cameroun des années 1950 aux années 1960," in *Colloques internationaux. Milieux de vie et santé. Quelques pratiques interdisciplinaires* (Aix-en-Provence, France: Edisud, 2008), forthcoming.
[13] Russell E. Fontaine, Abdallah E. Najjar, and Julius S. Prince, "The 1958 Malaria Epidemic in Ethiopia," *American Journal of Tropical Medicine and Hygiene*, vol. 10, no. 1 (1961), 803.

The epidemic underscored the vastness of the challenge in controlling malaria in Africa.

The upshot was that the great "global" eradication program was never cleared for takeoff in tropical Africa. The paradigm of the global eradication campaign focused on the interruption of transmission,[14] and the African project reports took the same approach, highlighting the efficient vector (*A. gambiae*), the long transmission season, the extremely high levels of endemicity, the poor communications infrastructure, and the weak administrative structures. The issue of acquired immunity to falciparum lay dormant.

By 1960, the malaria problems of tropical Africa began to slip quietly off the global health agenda.[15] During the 1960s, the WHO and the United Nations Children's Fund helped to fund a few pilot projects in tropical Africa. Considerable tension arose over whether or not public health monies should be poured into basic health services or into a program to build a public health infrastructure to support a malaria eradication program.[16] The initiatives threw into bold relief the differential impacts of malaria on different age cohorts. Outside of tropical Africa, in the zone of mixed infections, malaria imposed high costs in suffering and death across the generations. In tropical Africa, malaria principally killed and sickened children under the age of five. Was the model designed for the zones of vivax and mixed infections appropriate for tropical Africa? Was there only one model of global public health? What was the proper use of scarce public health monies? Who should decide?

THE GLOBAL ERADICATION CAMPAIGN, 1955–1969

During the late 1940s and early 1950s, the antimosquito campaigns to interrupt the transmission of malaria achieved important successes outside of tropical Africa. The aggressive interventions in Venezuela, Ceylon, Greece, and Italy and the many other national programs of DDT use in their early stages spurred the optimism of eradicationists in the early 1950s,

[14] The Sixth Session of the Expert Committee defined *malaria eradication* as "the ending of the transmission of malaria and the elimination of the reservoir of infective cases in a campaign limited in time and carried to such a degree of perfection that when it comes to an end, there is no resumption of transmission." Cited by J.A. Nájera, "Malaria Control: Achievements, Problems and Strategies," *Parassitologia*, vol. 43, no. 1–2 (2001), 35.

[15] Tropical Africa's exclusion from the global eradication campaign went unmentioned in the WHO resolution that started the campaign or in subsequent assemblies (ibid., 35).

[16] World Health Organization, Afr/Mal/67, February 19, 1965, "The Malaria Eradication Programme in the African Region," 6.

even as the problem of DDT resistance spread. The eradicationists' argument was simple: It was logical, necessary, and prudent to move toward total eradication before mosquito resistance to DDT became more widespread and before parasite resistance to chloroquine began to emerge. The core questions about the potential loss of acquired immunity in tropical Africa were sidelined.

The enthusiasms of the eradicationists proved infectious. The Eighth World Health Assembly of the WHO in 1955 endorsed a global campaign to eradicate malaria. The global eradication program would be organized by national campaigns. The campaigns would progress in successive phases – preparation, attack, consolidation, and maintenance. Each national eradication campaign would be a building block, and phase-by-phase this building block approach would yield a stable architecture of global public health.

There were significant problems with the model. It largely ignored the realities of transnational labor migration. This was an important issue within the tropics of Southeast Asia and between Southeast Asia and China. If Burma could achieve eradication within its national borders, this condition would be difficult to maintain, given the flows of parasitized migrants from the wider region. It was an even larger issue in tropical Africa. During the era of the eradication campaigns, it was conservatively estimated that five million people were involved in migrant labor movements within Africa south of the Sahara. The model also overlooked the importance of religious pilgrimage to Mecca for Africa's Muslim populations. The Sudan, for example, embarked on an eradication campaign in 1962, even though it was the region through which most Sub-Saharan Muslim pilgrims traveled on their way to Mecca.[17]

Even apart from nonparticipation of most of tropical Africa, there was another potentially enormous lacuna in the global program: mainland China. The People's Republic of China was not a member of the United Nations, and it was one of the great malarial expanses of Eurasia. In 1956, the Chinese Communist Party launched a national program for agricultural development and convened a special antimalarial conference with a goal of eliminating malaria within seven years. At the beginning of this campaign, some thirty million Chinese were sick with malaria.[18]

[17] R. Mansell Prothero, *Migrants and Malaria* (London: Longmans, 1965), 41.

[18] The Chinese antimalarial campaign did not have to start from scratch. During the 1930s, the Nationalists, with the assistance of the Rockefeller Foundation, had carried out some antimalarial work in the southern falciparum zone. The Chinese Communists integrated the malariological findings of the Nationalists into a vertically organized system.

Little detail is available on the Chinese campaign from the mid-1950s until the late 1970s, a period in which the successive calamities of the Great Leap Forward (1958–1960) and the Cultural Revolution (1966–1976) severely disrupted the health care system. It is clear, however, the Chinese program was two-pronged and involved extensive destruction of mosquito breeding habitat – as part of the national campaign to eliminate the "four pests" of rodents, flies, mosquitoes, and bedbugs – and the mass treatment of patients with modern antimalarial drugs, herbal remedies, and even acupuncture. By the late 1970s, China reported that it had made enormous strides against malaria, and the infection rate had been cut by almost 97 percent. The Chinese government had succeeded in mobilizing the masses of the Chinese peasantry and in constructing a rural primary health care infrastructure staffed by barefoot doctors. At the same time, the top-down system created regional antimalarial alliances with strategies tailored to regional conditions.[19]

From a geographical perspective, the major successes in China were in the zones of what had been vivax infections. The Chinese medical interventions made less progress in the zone of mixed infections in the south, where falciparum malaria remained a major problem. In part, this was owed to the large-scale movement of populations across the Chinese border in Yunnan province with Burma, Vietnam, and Laos. Even today, the south of China retains its epidemiological affinities with the larger malarial zone of Southeast Asian mixed infections.[20]

The other Eurasian behemoth, the Soviet Union, had also suffered an enormous expansion of malarial infection in addition to the vast human losses of World War II. The Soviet Union had developed an expert antimalaria service during the 1930s, and in the postwar period (1945–1960) it undertook its own, self-styled program of malaria control, based on Soviet scientists' concepts of "landscape epidemiology." Soviet scientists developed new synthetic antimalarial medicines and revived their network of research institutes and treatment facilities. A major focus was on the destruction of mosquitoes through the large-scale use of DDT and hexachlorane. In 1950 and 1951, 236 million square kilometers were doused with these insecticides. Before the emergence of resistance, the Soviet Union was able to reduce the number of infected persons to less than two per

[19] K. Yip, "Antimalarial Work in China: A Historical Perspective," *Parassitologia*, vol. 40 (1998), 35–37.

[20] In the 1990s, these population movements were estimated at ten to twenty million person crossings per year. C. Kidson and K. Indaratna, "Ecology, Economics and Political Will: The Vicissitudes of Malaria Strategies in Asia," *Parassitologia*, vol. 40 (1998), 41–43.

ten million. But by the mid-1960s, malaria was breaking out in pockets once again, this time fueled by imported infections and by massive deforestation, large irrigation projects, and the creation of massive reservoirs for hydropower production that provided new habitats for the mosquito vectors.[21]

The global eradication campaign was launched during the height of a global cultural movement known to historians of science as "scientific modernism." The core belief was that there was to be great progress in the resolution of old problems through the application of science. The science was to be universal. The model of malaria eradication by successive stages seems remarkably naïve in retrospect, an analog to the models of development that were going to allow for universal economic progress in the 1960s. It was blind to the social and political landscapes on which the malaria eradication programs would have to work and overly optimistic in its estimates of the time and money that would be required.

It also proved unexpectedly costly to the field of malariology. Until the immediate post–World War II years, the sheer diversity of malarial ecologies had earlier argued for the importance of local epidemiological studies – the need to understand the local topography, the species composition of the local mosquito populations, the behaviors of those species, and the types and distributions of malarial infections. This was time-consuming and expensive. The complexities of the local ecologies were sidelined by this belief in universal science, in particular by the delivery of a brilliant, unitary mathematical model of malarial dynamics by George MacDonald, a professor of tropical hygiene at the University of London and director of the Ross Institute.[22] During the course of the global eradication campaign, local epidemiological studies fell out of favor, and the prestige of malaria specialists was significantly downgraded. They were no longer considered necessary.[23] The universal model of antimalarial activities foreclosed the role of local epidemiological studies in favor of a broad antimosquito focus. The ironic result was that the field of malariology dried up. As the retiring malariologists would later joke bitterly, the global campaign had succeeded in eradicating malariologists rather than malaria.

The belief that one approach fit all circumstances soon ran into difficulties. Problem areas began to be reported – particularly in areas of extensive agriculture with large temporary work forces. The fields were

[21] L. Tchesnova, "Socio-Economic and Scientific Premises for Forming the Strategies against Malaria in Russia under Soviet Power," *Parassitologia*, vol. 40 (1998), 103–108.

[22] George MacDonald, *The Epidemiology and Control of Malaria* (London: Oxford University Press, 1957).

[23] Nájera, "Malaria Control: Achievements, Problems, and Strategies," 42–43.

larded with huge doses of DDT and other pesticides to reduce agricultural losses, and this multiplied the evolution of mosquito resistance to these chemicals. Moreover, the in- and out-migrations meant that workers could contract malaria *in situ* and then return to their sending communities. Other problem areas were those of new colonization – such as new mines in "jungle" areas and slash-and-burn agriculture or charcoal-making pits in forest areas. Others were in regions with dispersed populations or in zones of conflict that prevented the operation of antimalarial services.[24] The realities of malaria were more complicated than had been suggested by MacDonald's model. The conceptual chessboard on which the global eradication campaign was played had been artificially simplified. Other problems were encountered with the "maintenance" part of the plan. The continued surveillance of infections required a health service that in some countries simply did not exist. Should malaria eradication properly wait for the development of basic health services?

Despite all of these problems, in many areas outside of tropical Africa the early eradication campaigns made large initial strides. This was true in India, Taiwan, the Philippines, and Ceylon. These strides were so large that as early as 1959, the directors of these national programs moved to implement the general policy of the global eradication campaign, to pass from the attack phase that focused on the mosquito to the consolidation phase that identified and treated the sick. From the point of view of the entomologists, this spelled a potential catastrophe. The redoubtable Fred Soper visited the national programs and sounded the alarm. In his view, the costs and logistical difficulties of surveillance of the populations for evidence of infection were impractical, and the shift of resources away from mosquito destruction could be disastrous.[25]

One full success was achieved in Asia. Taiwan followed the WHO guidelines for malaria eradication closely and developed a program that progressed from the preparatory stage through the attack, consolidation, and maintenance stages. In 1965, the WHO certified Taiwan as free of malaria – a status that it has maintained up to the present day. It was by any measure a grand achievement in a region that had been plagued by malaria at least since its colonization by settlers from mainland China in the seventeenth century.[26] In the Mediterranean basin, the eradication

[24] Ibid., 45.

[25] Socrates Litsios, "Criticism of WHO's Revised Malaria Eradication Strategy," *Parassitologia*, vol. 42 (2000), 167–172.

[26] The successes of the Taiwanese nationalist government built on the antimalarial program of the colonial Japanese administration (1895–1945). By the late 1930s, more than three million people underwent routine blood examinations for parasites every year, and the Japanese succeeded in preventing any large-scale epidemics during their rule. The Chinese nationalist government had received assistance from the Rockefeller Foundation as early as the 1930s, and after the transfer of the nationalist government to the island in 1949, the foundation supported a malarial laboratory that undertook entomological and epidemiological studies that were crucial to the planning of the eradication campaign. Confounding our ability to understand the cause-and-effect relationships that led to success in malaria eradication was the fact that Taiwan was under martial law, received financial and technical backing from international agencies, and was in the midst of carrying out other public health initiatives, all the while undergoing a process of economic growth in both agricultural and industrial sectors (K. Yip, "Malaria Eradication in Taiwan," *Parassitologia*, vol. 42 [2000], 117–126).

[27] John Mason and Phillipe Cavalie, "Malaria Epidemic in Haiti Following a Hurricane," *American Journal of Tropical Medicine and Hygiene*, vol. 14, no. 4 (1965), 533–539.

campaigns scored additional full successes in Portugal, Spain, France, Italy, and Greece. In the Americas, malarial infections were extinguished in Chile and on five small islands in the Lesser Antilles of the Caribbean. Measured on a national scale, these were highly impressive victories. Measured by the ambitious goals of the global eradication campaign, the full victories appeared few.

There were also indications that the partial successes might not be permanent. On one of the larger islands in the Caribbean, for example, the ongoing work of eradication proved highly vulnerable to uncontrollable acts of nature. In October 1963, Hurricane Flora smashed ashore in Haiti and undid the gains from two years of DDT spraying. The massive storm destroyed housing, driving most of the population either out into the open or, at best, into temporary shelters, where mosquitoes feasted on them. The heavy rainfall and extensive flooding brought about an explosive increase in mosquito breeding. Two or three months later, a malaria epidemic swept through Haiti, causing seventy-five thousand cases, and the malaria eradication program there was set back to the beginning.[27]

Elsewhere, the best that could be achieved was a substantial reduction in infections. In South Asia, the Indian antimalarial program had to deal with a bewildering complexity of environments and a vast landscape. The problems had been daunting, and some of the efforts had been plagued by incompetence at various levels. The antimosquito DDT teams cleared out malaria from rural and urban areas. The areas where malaria had been endemic were in the zone of mixed infections, where general immunities to falciparum had not been achieved. The overall result of the Indian campaigns was a substantial improvement in health. Even when the vector

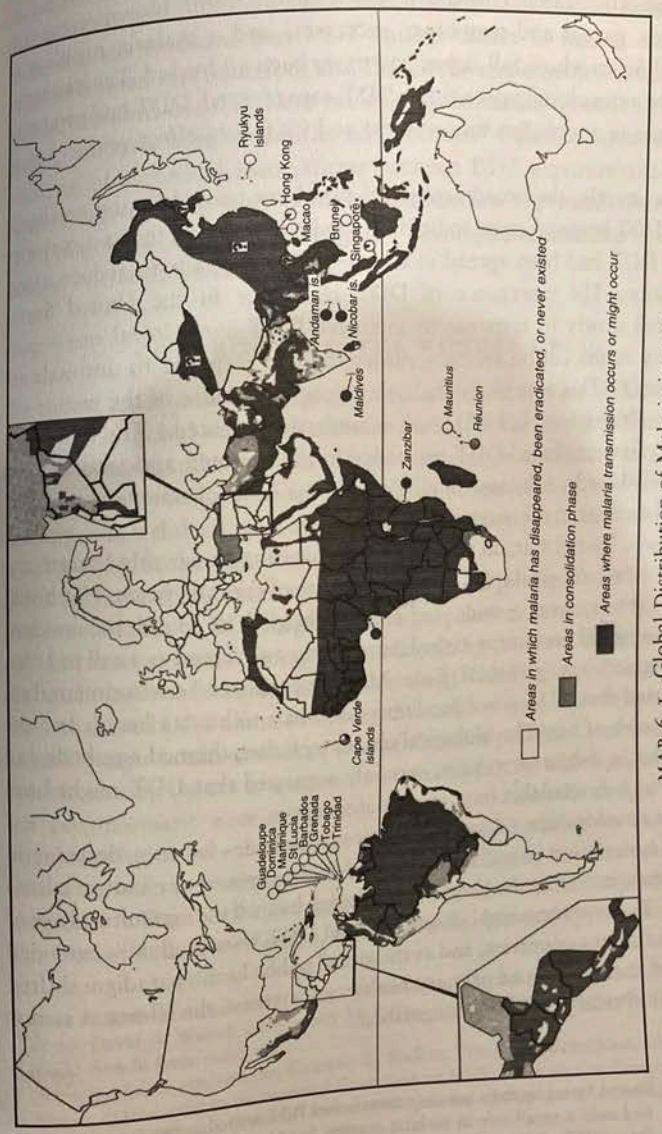
rebuilt its strength and malaria returned at lower levels, the new infections were principally of vivax.

Malaria cases declined dramatically. In a mere decade, India reduced its malarial burden by several orders of magnitude – from perhaps seventy-five million cases in 1951 to some fifty thousand by 1961. In the early 1960s, India seemed on the verge of slamming the door shut on malaria. Then, the number of malaria cases started to rise, to 350,000 by the end of the 1960s and then precipitously from 1973 to 1976 when 6.5 million cases were reported. Vigorous attack then brought the number of cases down to 1.5 to 2 million per year. Sri Lanka had edged even closer to full eradication, reducing the number of malaria cases to a mere handful by 1954 and verging on complete eradication in the early 1960s. The final steps proved illusive (Map 6.1).[28]

In retrospect, the campaign for the global eradication of malaria had serious conceptual shortcomings, and it was also grossly underfunded. The major donor, the United States, had initially committed funds to global eradication, predicated on the notion that global eradication could be accomplished in three to five years. In 1960, the International Cooperation Administration of the United States projected the need for a tenfold increase in funding, but none was forthcoming, and the U.S. Congress closed off any further appropriations for malaria eradication after 1961. In 1963, the flow of antimalaria funds to the WHO Malaria Special Account (but not to the Pan-American Health Organization or selected country programs) stopped cold. Of the forty-four countries that had made some financial contribution between 1956 and 1963, the United States had contributed 86.1 percent. Without U.S. support, the costs of the eradication effort were shunted to the governments of developing nations. When the malaria eradication funds dried up, the WHO emphasized the need to expand basic health services globally as a prerequisite for malaria eradication.[29]

Although the global eradication campaign fell far short of its goals, it had a profound effect on the global distribution of malaria. By the 1970s, in the Americas and in Asia, endemic malaria had been driven out of most urban areas and largely restricted to frontier areas and regions of political instability. In tropical Africa, malaria continued to exact an enormous toll in human sickness and death, although the expanding use of chloroquine and other synthetic antimalarial drugs reduced the extent of the suffering.

[28] Harrison, *Mosquitoes, Malaria and Man*, 253–255.
[29] J.A. Nájera, "Tropical Diseases and Socioeconomic Development," *Parassitologia*, vol. 36 (1994), 17–33.



MAP 6.1. Global Distribution of Malaria in 1970
Source: World Health Organization.

THE VEXED CAREER OF DDT

The eradication campaigns ended with an array of full-blown permanent successes, partial and temporary successes, and a malaria problem in tropical Africa whose full extent had never been addressed. The banner of the great antimalarial insecticide – DDT – was frayed. DDT had produced resistance in anopheline mosquitoes, and its future effectiveness was in doubt.

Concurrently, the broad ecological problems caused by the profligate use of DDT began to come to light. In the United States, the vast majority of the DDT had been spread in the agricultural sector to reduce insect infestation. The emergence of DDT resistance in the United States appeared slowly in response to intensive DDT agricultural use – particularly in the cotton sector – rather than in response to antimalarial activities.[30] (This was likely the case throughout most of the rest of the world, although global DDT use is underdocumented.) The wholesale applications produced DDT resistance in the targeted agricultural pests and killed birds, fish, and small animals – a kind of unanticipated collateral damage in the war against insects.

In 1962, Rachel Carson published a devastating and highly literate critique of the biological costs of large-scale use of the insecticide. Her book, *Silent Spring*, won a wide audience. It helped to found the modern environmental movement in the United States and served as a call to arms, rallying activists against DDT use. Many scientists and environmentalists suspected that DDT posed fundamental threats to human health and the broad web of life. The biological chaos, including thinned eggshells and dead birds, fish, and rodents, certainly suggested that DDT might have grave and incalculable long-term consequences.

The development of new alternative insecticides led to a decrease in DDT agricultural use in the 1960s, and in the 1970s, many industrialized countries, including the United States (1972), banned the agricultural use of DDT. The environmental concerns about DDT were gradually extended into malarious countries, and as the global public health paradigm shifted toward the creation of primary health care systems, the efforts at vector control in many countries languished.

[30] In the United States, malaria was in retreat before DDT arrived in the chemical arsenal, and it had only a small role in malaria control. See Margaret Humphreys, "Kicking a Dying Dog: DDT and the Demise of Malaria in the American South, 1942–1950," *Isis*, vol. 87, no. 1 (1996), 1–17.

The deleterious impact of DDT use on birds, fish, and small animals raised alarms about the consequences for human health of the use of DDT for malaria control. A sizeable body of scientific literature argued that there was no evidence that DDT caused cancer in human beings or affected human reproduction, and that in the communities in which the highest amounts of DDT have been found in human tissues and human milk, there have been no confirmed ill effects.[31] Other researchers found evidence of statistical associations between DDT exposure and breast cancer, and, in recent years, some researchers have expressed concern that DDT may be an endocrine disrupter – a compound that interferes with normal hormone functioning.[32]

CHLOROQUINE: THE WONDER DRUG

The other great arm of the global eradication campaign was chemical therapy. The grand success of atebrine during World War II was followed by the even grander success of chloroquine in the postwar period. Chloroquine promised the prospect of inexpensive and safe chemical therapy, and it did not have atebrine's undesirable side effect of producing a yellow cast to the skin.

Initially, the eradication campaigns were based principally on DDT use, but as resistance to DDT began to emerge, planners envisioned a greater role for mass chemical therapy administered by the state. Some projects that included mass drug administration along with DDT fared better than those that used DDT alone. However, the results were not positive enough to justify their broad extension. One of the main problems – as had been the case during the era of quinine use – was that those who were infected but asymptomatic were notoriously reluctant to take the drugs.[33] One possible solution was to distribute medicated cooking salt that was laced with synthetic antimalarial medicines. Malariologists had launched an early trial in Brazil in the late 1940s and subsequent small-scale projects in The Netherlands, New Guinea, and Cambodia, but soon pyrimethamine

[31] Peter F. Beales and Herbert M. Gilles, "Rationale and Technique of Malaria Control," in ed. David A. Warrell and Herbert M. Gilles, *Essential Malariology*, 4th ed. (New York: Arnold Press, 2002), 170.

[32] For other health concerns, see Kathleen R. Walker, Marie D. Ricciardone, and Janice Jensen, "Developing an International Consensus on DDT: A Balance of Environmental Protection and Disease Control," *International Journal of Hygiene and Environmental Health*, vol. 206 (2003), 425–426.

[33] World Health Organization, Afr/Mal/67, February 19, 1965, "The Malaria Eradication Programme in the African Region," 20–21.

resistance was reported. Chloroquine-medicated salts were also tried, including a large-scale trial in Guyana that had the most success, but this method of mass drug administration produced wide variations in the levels of the ingested drug.[34] In the 1970s, the WHO shifted its focus back to control of the mosquito vector. The official view was that mosquito control was the only way to effectively reduce endemic levels of malaria.[35]

Chloroquine, however, remained the drug of choice for malaria treatment. Chloroquine allowed for many of the tropical African poor to self-medicate, just as North American pioneers had done with quinine and other cinchona alkaloids in the nineteenth century. The difference was one of scale. The sheer inexpensiveness of chloroquine saved many millions of lives. In tropical Africa, sufferers could purchase chloroquine by the pill in the local market. This pattern of incomplete treatment probably sped up the evolution of parasite resistance, although the exact details of this process will likely never be known.[36]

Chloroquine was effective throughout the 1960s and much of the 1970s and 1980s. Resistance, though, began to be reported as early as 1960 in Colombia, Venezuela, and Brazil; in the early 1960s in Southeast Asia; and, during the 1970s, more widely in South America and Eastern and Central Africa. By 1988, chloroquine-resistant parasites had been reported all across tropical Africa. Even so, chloroquine continued to be used as the frontline treatment for malaria into the mid-1990s.[37]

In tropical Africa and in parts of Asia, choloroquine had a major impact on the health of the populations. In tropical Africa, the rapid expansion of basic health services to some large sectors of the population also made a significant contribution, but it is likely that choloroquine was probably most responsible for the marked trend toward fewer malaria deaths and

[34] U. D'Allesandro and H. Buttiëns, "History and Importance of Antimalarial Drug Resistance," *Tropical Medicine and International Health*, vol. 6, no. 11 (2001), 846.

[35] World Health Organization, Afr/RC25/7, June 9, 1975, "Development of the Antimalarial Programme in Africa," 18.

[36] In 1993, Malawi became the first African state to replace chloroquine with sulfadoxine and pyrimethamine for the treatment of malaria. In 2005, randomized clinical trials in Blantyre of 210 children with uncomplicated falciparum infections who were treated with chloroquine indicated that chloroquine had regained its efficacy. Miriam K. Laufer et al., "Return of Chloroquine Antimalarial Efficacy in Malawi," *New England Journal of Medicine*, vol. 355, no. 19 (November 9, 2006), 1959–1966.

For early and promising research on the reversal of chloroquine resistance, see Maud Henry et al., "Chloroquine Resistance Reversal Agents as Promising Antimalarial Drugs," *Current Drug Targets*, vol. 7 (2006), 935–948.

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

lower morbidity from the 1960s until the mid-1980s, when the efficacy of chloroquine broadly declined. From the early 1980s, the International Monetary Fund and the World Bank imposed "structural adjustment" programs in exchange for new loans, in an effort to shrink the public sector of African economies. By the 1990s, all of the antimalarial gains from chloroquine use and the expansion in basic health services had been lost, and malaria reaped a toll in childhood mortality comparable to that in the 1930s, in the era before effective interventions for colonial subjects.[38]

During the global deployment of both DDT and chloroquine, malarial infections had been greatly reduced. In some regions, where DDT agricultural uses had been heavy, the mosquito vectors had outsmarted DDT and developed resistance. In some regions where chloroquine use had been pervasive and incomplete, the malaria parasites had outsmarted the antimalarial drug and developed resistance. In the process, a major shift in the geography of malarial infections had taken place: Malaria was all but eliminated from the Western nations and the wealthier Asian tiger economies and was greatly reduced in India, China, Latin America, and the Caribbean. Africa became indisputably the center of global malaria. Early in the twenty-first century, an estimated 80 to 90 percent of contemporary infections and 90 percent of malaria deaths occur in tropical Africa.[39]

THE REDISCOVERY OF NATURAL THERAPIES

By the 1990s, the prospects for reliable chemical therapy were tenuous. The emergence of chloroquine resistance, and then resistance to the next generation of antimalarial drugs including sulfadoxine-pyrimethamine, suggested a potential crisis.

Help came from an unexpected quarter. During the Chinese cultural revolution, the Chinese rediscovered the efficacy of an ancient antimalarial drug, an alkaloid that could be extracted from a common plant known as sweet wormwood (*Artemisia annua*). The drug, known as artemisinin, extended a new lease on life to the chemical therapy approach. Artemisinin-based drugs could be produced in quantity, but

[38] Robert W. Snow, Jean-François Trape, and Kevin Marsh, "The Past, Present, and Future of Childhood Malaria Mortality in Africa," *Trends in Parasitology*, vol. 17, no. 12 (2001), 593–597.

[39] Nájera, "Malaria Control: Achievements, Problems, and Strategies," 52.

they cost much more to produce than chloroquine, even if the annuals were grown on plantations in Africa, close to their markets and using local labor. Would the higher price of artemisinin put it beyond the means of the very poor?

There was trouble, too, on the biological front. Experts agreed that it was only a matter of time before artemisinin-based drugs provoked parasite resistance. As of the early twenty-first century, quinine – the venerable alkaloid from the nineteenth century that was never used in large enough quantities to provoke significant resistance – remained the drug of last resort for the treatment of multi-drug-resistant falciparum malaria.

The fact that another natural alkaloid was effective against malaria, though, provoked a broad and ongoing reassessment of other natural antimalarial remedies. There were, however, literally thousands of possibilities, and the early findings were positive if not overly hopeful. Those natural remedies that did have antimalarial properties (and this was a small fraction of the total investigated) were less efficacious than the cinchona alkaloids or the artemisinin-based drugs. The acceptance of the (partial) efficacy of these natural remedies, however, was a retrenchment and part of the growing acceptance that the complex realities of malarial infection would have to be addressed through a multitude of means.

In the early twenty-first century, more than 1,200 plant species from 160 plant families are used to treat malaria and fever. Perhaps one-fifth of all patients use traditional herbal remedies for malaria in endemic countries. There are few data, however, on safety and efficacy. Even among traditional healers, there is no consensus on the plants, preparations, and dosages that are the most effective; and the concentrations of active ingredients in a plant species varies considerably.[40] The positive side is that the lack of standardization impedes the evolution of parasite resistance.

Another hopeful development is the reevaluation of the ancient techniques of using oils on skin to repel mosquitoes. A recent survey of forty-one essential oils found that five utterly repelled the three species of *Aedes*, *Culex*, and *Anopheles* mosquitoes submitted to trial for a period of eight hours.[41]

[40] Merlin L. Willcox and Gerard Bodeker, "Traditional Herbal Medicines for Malaria," *Clinical Research*, vol. 329, no. 7475 (2004), 1156–1159.

[41] Abdulkrim Amer and Heinz Mehlhorn, "Repellency Effect of Forty-One Essential Oils against *Aedes*, *Anopheles*, and *Culex* Mosquitoes," *Parasitology Research*, vol. 99 (2006), 478–490.

THE NEW HIGH TECHNOLOGIES: MALARIA VACCINES AND TRANSGENIC MOSQUITOES

Even during the era of chloroquine efficacy, malaria remained the primary focus of a few groups of biomedical researchers. They were keen to find a "solution" to falciparum malaria, and they sought it at the laboratory bench. Perhaps a vaccine could slay malaria. Over the course of the 1970s, 1980s, 1990s, and deep into the first decade of the twenty-first century, vaccine researchers have labored away. They have encountered enormously complex problems, sought more funds, and assured their patrons that one or more malaria vaccines would be forthcoming. The vaccine makers have made considerable progress, and yet a fully protective malaria vaccine is not thought to be a near-term prospect.[42]

Another initiative came from molecular entomologists who focused on the mosquito vectors.[43] They announced the first "transgenic" mosquito in the year 2000. Their hopes were that through the manipulation of the mosquito's genes it would be possible to control the disease by disrupting the mosquito's interaction with the malaria parasite, altering its choice of blood target from man to animal, or selectively creating sterile male mosquitoes. At present, the researchers' hopes for a sterile male mosquito are high, and plans are on hold for a massive release of sterile mosquitoes into the wild.[44] Another approach is to engineer a malaria-resistant mosquito that has a survival advantage over a malaria-tolerant mosquito. Researchers at Johns Hopkins University in 2007 published encouraging results, although they cautioned that the release of transgenic mosquitoes into the wild might not occur for ten to twenty years, and that it was extremely difficult to anticipate what would happen in the event that a release took place.[45]

[42] For a survey of these efforts over the course of the twentieth century, see R.S. Desowitz, "The Malaria Vaccine: Seventy Years of the Great Immune Hope," *Parassitologia*, vol. 42 (2000), 173–182.

[43] For an overview of the field, see A.M. Handler, "An Introduction to the History and Methodology of Insect Gene Transformation," in ed. A.M. Handler and A.A. James, *Insect Transgenesis: Methods and Applications* (Boca Raton, FL: CRC Press, 2000), 3–26.

[44] David Adam, "Scientists Create GM Mosquitoes to Fight Malaria and Save Thousands of Lives," *The Guardian*, October 10, 2005. This article is available online at http://www.guardian.co.uk/science/2005/oct/10/infectiousdiseases.medicineandhealth. On earlier sterile mosquito releases, see Mark Q. Benedict and Alan S. Robinson, "The First Releases of Transgenic Mosquitoes: An Argument for the Sterile Insect Technique," *Trends in Parasitology*, vol. 19, no. 8 (2003), 349–355.

[45] Mauro T. Marelli et al., "Transgenic Malaria-Resistant Mosquitoes Have a Fitness Advantage When Feeding on Plasmodium-Infected Blood," *Proceedings of the National Academy of Sciences*, vol. 104, no. 13 (March 27, 2007), 5580–5583.

MALARIA RESURGENT

When the global eradication campaign ended in 1969, the military metaphor of the "war against malaria" backfired. With "victory" beyond reach, public health officials were saddled with the metaphor of "defeat." The field-tested methods of environmental management, allowed to languish during the global eradication campaign, did not return to favor.[46] Anti-malarial services were either disbanded or had their funding cut. A new global public health model arose in the 1970s that stressed integrated health services and community health care rather than single-disease-control programs.[47] This model carried the day during the 1980s and into the late 1990s.

Following two decades out of the spotlight, malaria began to reemerge as a global health concern during the late 1990s (Figure 6.1; Map 6.2). Malarial infections multiplied in South America from the late 1970s to the late 1980s. Some increases were owing to the agrarian reforms of the military government of Brazil that opened the Amazon for internal colonization. Others appeared to result from a reduction in DDT use in house spraying. Ecuador increased its DDT use in 1993 and was the only South American state to report a large reduction in malaria.[48] In Southeast Asia, the countries of Vietnam, Laos, and Cambodia targeted malaria as a major public health problem and achieved progress in vector control, except in the hilly, forested regions and a few coastal areas.[49] Malaria continued to be a significant problem in the Western Pacific, South, and Southwest Asia.[50] Throughout the zone of mixed infections, where malaria control efforts improved, the mix shifted toward a higher percentage of vivax infections.[51]

[46] A recent study of the effectiveness of environmental modifications that included drainage, the filling of marshes, cleaning of anopheline breeding environments, and vegetation management reviewed forty studies, ranging from 1902 to the present, which reported clinical malaria outcomes. Most took place before the Global Eradication Campaign (1955–1969). During the era of the campaign, not a single study relied on applied environmental management as the central tool (Keiser et al., "Reducing the Burden of Malaria," 701–706).

[47] Brown, "Global Resurgence of Malaria," 122.

[48] Donald R. Roberts et al., "DDT, Global Strategies, and a Malaria Control Crisis in South America," *Emerging Infectious Diseases*, vol. 3, no. 3 (1997), 295–302.

[49] H.D. Trung et al., "Malaria Transmission and Major Malaria Vectors in Different Geographical Areas of Southeast Asia," *Tropical Medicine and International Health*, vol. 9, no. 2 (2004), 230–237.

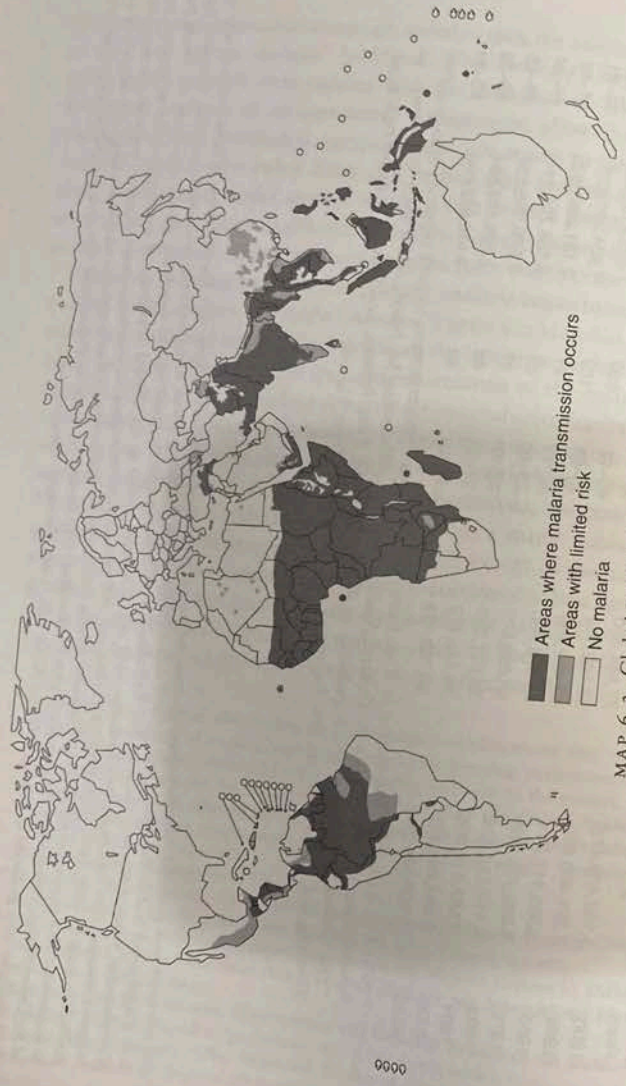
[50] R. Carter and K.N. Mendis, "Evolutionary and Historical Aspects of the Burden of Malaria," *Clinical Microbiology Reviews*, vol. 15 (2002), 579, table 3.

[51] Kamini Mendis et al., "The Neglected Burden of *Plasmodium Vivax* Malaria," *American Journal of Tropical Medicine and Hygiene*, vol. 64, nos. 1–2, suppl. (2001), 97–106.

Time *Years*	Global Population *n*	Land Area Malarious *square kilometers*	Countries at Risk *percent*	Countries at Risk *n*	Population Exposed *n*	Population Exposed *percent*
1900	1,158,409,472	77,594,480	53–16	140	892,373,056	77–03
1946	2,391,400,960	58,565,752	40–12	130	1,635,815,808	68–40
1965	3,363,417,344	53,492,988	36–65	103	1,924,360,320	57–21
1975	4,085,759,488	48,075,780	32–93	91	2,121,086,592	51–91
1992	5,419,255,808	43,650,812	29–90	88	2,565,702,144	47–34
1994	5,582,432,256	39,537,020	27–08	87	2,570,555,136	46–05
2002	6,204,095,488	39,758,172	27–24	88	2,996,419,584	48–30
2010	6,807,085,056	39,758,172	27–24	88	3,410,862,080	50–11

FIGURE 6.1. Global Population at Risk from Malaria from Preintervention to 2010 (approx. 1900–2010)[65]
Source: Simon I. Hay, Carlos A. Guerra, Andrew J. Tatem, Abdisalan M. Noor, and Robert W. Snow, "The Global Distribution and Population at Risk of Malaria: Past, Present, and Future," *Lancet Infectious Diseases*, vol. 4, no. 6 (2004), 328. Reprinted with permission from Elsevier.

[65] The area totals were generated using the maps of all-cause malaria risk distribution through time (Figure 6.1). The percentage of Earth malarious was calculated from a total global land surface area of 145,975,899 square kilometers. To estimate countries at risk territorial designations for 2002 were used throughout (Environmental Systems Research Institute, Inc., Redlands, CA). Country-specific medium "variant" population growth rates from the World Population Prospects database (http://esa.un.org/unpp) between 1950 and 2010 were applied to the Gridded Population of the World v2.025 to generate population distribution maps for 1900, 1946, 1965, 1975, 1992, 1994, and 2002 to match with the malaria risk distribution maps (Figure 1) and were also projected to 2010 to enable evaluation of potential future changes in global malaria risk. Global summary counts of these population distribution maps give accuracy to within 5% of the United Nations Development Program global population estimate (http://esa.un.org/unpp) for all calculated years. All area and population summaries from these polygons were processed in Idrisi Kilimanjaro (Clark Labs, Clark University, Worcester, MA).



MAP 6.2. Global Distribution of Malaria in 2006
Source: World Health Organization.

Within tropical Africa, the impact of malaria from the 1960s onward is difficult to assess. The African data are not robust, and thus the interpretations cannot be definitive. As mentioned in the preceding text, some researchers found that in areas of stable transmission, widespread chloroquine use had reduced malaria mortality over the period 1960 to 1989. The data gathered by the WHO indicated a dramatic increase in African malaria from an estimated 300,000 deaths in 1970, to 787,000 in 1990, and 990,000 in 1997.[52] (Much of the increase in malaria into the 1980s may have been a result of rapid population growth – i.e., the absolute numbers of Africans with malaria increased, but the rates of infection did not increase as rapidly.) In any event, the point of broad agreement was that malaria had increased sharply at least since 1990.

Faced with this resurgence, African scientists led the fight to renew the battle against malaria. The WHO launched its "Roll Back Malaria" initiative in 1998, and in 2000 at the Abuja Summit, African heads of state set goals to achieve large improvements in malaria treatment and prevention. To date, the initiative has not met its goals, and the number of malarial infections both within and outside of tropical Africa continues to rise.[53]

What caused the resurgence of malaria in tropical Africa? Climate change did not appear to be an important factor. Time-series analysis of a climate-driven model of malaria showed only limited evidence for an increase in environmental suitability during the last century across the African continent. In those areas where positive trends could be determined, the increase in infections seemed to be related to increased precipitation rather than temperature. The overall study suggested that nonclimatic factors were the drivers of increased malaria transmission across the continent.[54]

In some highland regions subject to unstable malaria, the cessation of antimalarial interventions laid the groundwork for future epidemic

[52] Carter and Mendis, "Evolutionary and Historical Aspects," 579, table 3.

[53] In 2005, a group of malaria experts estimated that in 2002 a total of 515 million clinical cases of falciparum malaria occurred worldwide. Their data suggested that one-third of the global incidence occurred outside of Africa (Robert W. Snow et al., "The Global Distribution of Clinical Episodes of Plasmodium Falciparum Malaria," *Nature*, vol. 434 [March 10, 2005], 214–217).

[54] Jennifer Small, Scott J. Goetz, and Simon I. Hay, "Climatic Suitability for Malaria Transmission in Africa, 1911–1995," *Proceedings of the National Academy of Sciences*, vol. 100, no. 26 (2003), 15341–15345.

outbreaks. The most devastating case took place in the central plateau region of the island of Madagascar. The large island is inhabited by the highly efficient tropical African vector, *Anopheles funestus*, and is very much part of the zone of falciparum malaria. There the antimalarial campaigns of the 1940s and 1950s that used DDT house spraying had succeeded in ridding the highlands of malaria. When the vector reestablished itself in the mid-1980s, malarial infections increased sharply, and most highlanders were defenseless as nonimmunes. Informed estimates of the number of people who died in the 1986 to 1988 outbreaks range from fifteen thousand to thirty thousand up to one hundred thousand.[55]

The increase in malarial infections, centered in tropical Africa, did not appear to be a result of "man-made" malaria. This term was coined in the mid-twentieth century, to refer to malaria that was intensified by development projects and the aggregation of laborers at the work sites. In tropical Africa, a recent survey found that irrigation projects played an extremely small role in malarial infections, and, in some regions, irrigation suppressed rather than intensified the problem.[56]

Recent evidence suggests that the agroeconomic changes of the "green revolution" may have had a significant effect on the transmission of malaria in highland regions. In 1998, in the Ethiopian highland district of Burie, farmers suffered an outbreak of epidemic malaria for the first time ever. It appears to be related, in part, to their adoption of hybrid maize that produces abundant pollen that in turn allows for the survival of more mosquito larvae and thus greater vector density. If this association is confirmed by ongoing research, a new field of malariological issues will open up. Hybrid maize is on the leading edge of an agrarian transformation throughout eastern and southern Africa, and public health programs will need to reintegrate environmental management techniques to control this unanticipated accelerant of malaria.[57]

The interaction of disease agents in the broader epidemiological environment is also implicated in the increase in malarial infections. This

[55] Jean Mouchet et al., "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), 124–125.

[56] Jennifer Keiser et al., "Effect of Irrigation and Large Dams on the Burden of Malaria on a Global and Regional Scale," *American Journal of Tropical Medicine*, vol. 72, no. 4 (2005), 392–406.

[57] James C. McCann, *Maize and Grace: Africa's Encounter with a New World Crop* (Cambridge, MA: Harvard University Press, 2005), 174–196.

is particularly true of the HIV pandemic. HIV-1 infection (the most common form in tropical Africa) increases the risk and severity of endemic malarial infections. In both high- and low-intensity HIV transmission zones, observers have noted the increased severity and case fatality rates from malaria, and in high-transmission zones, HIV-1 also increases the incidence of symptomatic malaria among adults.[58] The diseases have an awful synergy. Malarial infections in HIV-infected individuals boost the HIV viral load, and, in this respect, malaria seems to be an important factor in promoting the spread of HIV in tropical Africa.[59]

APPROACHES OLD AND NEW

During the first decades after World War II, indoor residual house spraying with DDT in tropical Africa had a limited trial. The early pilot projects had shown that spraying the interior house walls could not effectively stop transmission in areas of stable malaria, and thus there was little incentive to scale up. There were some exceptions: on the small islands of Réunion, Mayotte, Zanzibar, Cape Verde, and São Tomé DDT spraying effectively reduced transmission. There were some other successes in regions of unstable malaria. In South Africa and Swaziland, on the fringe of the falciparum zone, and in some highland regions, indoor house spraying achieved significant reductions in malarial infections, although after a hiatus in spraying, malaria in these regions was again on the rise by the mid-1980s.[60] In the aftermath of the 1986 to 1988 outbreaks in the highlands of Madagascar, DDT house spraying resumed there in 1993, and malaria declined by more than 90 percent after two annual spray cycles.[61]

During the 1990s, political pressure to expand the use of DDT for malaria control gained momentum, and in 2001, the DDT provision to the Stockholm Convention on Persistent Organic Pollutants preserved access

[58] E.L. Korenromp et al., "Malaria Attributable to the HIV-1 Epidemic, Sub-Saharan Africa," *Emerging Infectious Diseases*, vol. 11, no. 9 (2005), 1410–1419.

[59] Laith J. Abu-Raddad, Padmaja Patnaik, and James G. Kublin, "Dual Infection with HIV and Malaria Fuels the Spread of Both Diseases in Sub-Saharan Africa," *Science*, vol. 314 (December 8, 2006), 1603–1606.

[60] Musawenkosi L.H. Mabaso, Brian Sharp, and Christian Lengeler, "Historical Review of Malarial Control in Southern Africa with Emphasis on the Use of Indoor Residual Spraying," *Tropical Medicine and International Health*, vol. 9, no. 8 (2004), 846–856.

[61] D.R. Roberts, S. Manguin, and J. Mouchat, "DDT House Spraying and Re-Emerging Malaria," *The Lancet*, vol. 356, no. 9226 (July 22, 2000), 330–332.

to the use of DDT for WHO-approved disease-control programs.[62] By the first decade of the twenty-first century, DDT house spraying came back into favor in selected areas where DDT resistance was not a problem and where malaria transmission was unstable. The advocates of DDT use for indoor residual spraying argued that the health benefits strongly outweighed the risks. The current WHO judgment is that DDT does not pose a major risk to human health when used within approved guidelines for the sole purpose of spraying the inside walls of houses, and in 2006, the WHO began to promote the wider application of indoor residual spraying in highly endemic areas in tropical Africa.

Since the mid-1990s, insecticide-treated bed nets (ITNs) have been championed as the most powerful malaria control tool since DDT and chloroquine.[63] As of the first decade of the twenty-first century, coverage in Africa has been weak. Only 3 percent of African children sleep under ITNs, and only 20 percent sleep under any net at all. Although the ITNs are more effective than untreated nets in reducing the number of infective bites, the untreated nets are far more widely used, and thus they make a larger contribution to the reduction of malaria. A "global consensus" is emerging about the need to scale-up ITN usage in tropical Africa, although some fundamental questions about the impact of ITNs on acquired immunity have not been addressed. One of the worst case scenarios – that ITNs reduce acquired immunities and, in the case of interrupted use, result in increased vulnerability to malaria and greater morbidity and mortality – does not seem to be borne out by the few studies that have addressed these questions.[64]

In the first decade of the twenty-first century (in 2002 with the creation of the Global Fund to Fight AIDS, Tuberculosis, and Malaria and in 2007 with an additional financial commitment by the Bill & Melinda Gates Foundation), a new era in malaria research and control appeared to be dawning. The malariologists at the WHO wisely counseled against a reprise of the eradication campaigns of the 1950s and 1960s, because the tools at hand were still inadequate to the task. One or more laboratory breakthroughs were possible. But the most tangible prospects for the

[62] Walker, Ricciardone, and Jensen, "Developing an International Consensus on DDT," 423–435.

[63] Christian Lengeler, Jacqueline Cattani, and Don de Savigny, eds., *Net Gain: A New Method for Preventing Malaria Deaths* (Ottawa, ON: International Development Research Centre/World Health Organization, 1997).

[64] Jenny Hill, Jo Lines, and Mark Rowland, "Insecticide-Treated Nets," *Advances in Parasitology*, vol. 61 (2006), 77–128, esp. 90–92, 116–117.

reduction of human suffering from malaria seemed to rest upon the expansion of malaria control activities, the improvement of the standards of living of those afflicted by the disease, and the strengthening of primary health care systems in some of the poorest and most parasitized regions of the world.

* * *

In the aftermath of World War II, the miraculous insecticide DDT and wonder-drug chloroquine emboldened malariologists to advocate programs to eliminate rather than to control malaria. The WHO embarked on a global eradication campaign (1955–1969) that had mixed success. Tropical Africa was largely excluded from the "global" campaign. By the 1990s, malarial infections were rising in several parts of the world, and most malaria deaths were within tropical Africa.