THE GLOBAL CHALLENGE OF MALARIA

Past Lessons and Future Prospects

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1 Malaria in America

Margaret Humphreys

Introduction

Malaria was once a major cause of illness and death in the United States, although it is now almost entirely limited to imported cases arriving from other countries where the disease persists.[1] By 1950, home-grown malaria had disappeared in the United States, as well as in other temperate countries such as England, Holland, Spain, and Italy. Their stories of eradication make tempting models for those seeking to control a disease that still sickens and kills millions of people in the world today, most of them living in tropical and sub-tropical environments. As major new initiatives in the twenty-first century once again take on the microscopic predator carried in the mosquito's spittle, it is worth asking whether history can offer lessons that can guide the effort.

Ten years ago I concluded that historical research on malaria in the United States bore no "relevance for the beleaguered international malarial community," as the story contained "no startling revelations about how to fight malaria," and instead described methods and processes already well known to malaria campaigners.[2] In retrospect, I have come to conclude that this assessment was too modest. George Santayana, in a now famous comment concerning history, said "Those who cannot remember the past, are condemned to repeat it."[3] While the history of malaria in the United States offers no simple solutions for today's malaria challenges, it does contain lessons that those designing modern malaria wars would do well to keep in mind. Although no one now thinks, as optimistic malariologists did in the 1950s, that the victory over malaria in the United States and Europe which

[1] This paper's title uses "America" in its common colloquial sense in the U.S., to refer to the colonies and states that ultimately formed the modern U.S.

[2] Margaret Humphreys, *Malaria: Poverty, Race and Public Health in the United States*, The Johns Hopkins University Press, 2001, 6: Baltimore, London.

[3] George Santayana, *The Life of Reason, or Phases of Human Progress*, Charles Scribner's Sons, 1905, 5 vols., 284: New York.

had been won with DDT and chloroquine could be easily duplicated elsewhere, it is important to sort out the geographical, economic, social and political differences that contributed to malaria's demise in the developed western countries in order to recognize how the possible interventions available then and now interact with these various factors.

This chapter will first briefly outline malaria's history in the United States, focusing particularly on several points along the way when malaria escalated or declined, with the goal of identifying the key causes of such expansion and contraction. It will then conclude with the policy implications that are suggested by this story.

The Parasites and Their Vectors

Although the label malaria is commonly used as if it were a single disease, there are actually four malaria parasites in humans that cause four different diseases. Only three were common in the United States, and for simplicity's sake can be divided into severe (*falciparum*) malaria and milder (*vivax* and *malariae*) malaria. *Falciparum* can be deadly, especially when newly introduced to a population. Philip Curtin found that white British troops garrisoned on the west coast of Africa had a mortality rate in one year of over 50%; while other diseases such as yellow fever contributed to this slaughter, *falciparum* was the major culprit.[4] *Vivax* is milder, and probably kills less than 5% of its victims, even without the benefit of curative drugs. *Malariae* seems to have had a minor presence in the United States, and for general purposes can be considered as similar to *vivax*.[5] The parasites destroy red blood cells, leading to anemia and weakness. The spleen grows increasingly palpable as it struggles to clean up the destroyed red blood cells of the infected host. *Falciparum* malaria is more deadly because its parasites multiply in such massive numbers that they clog the capillaries of kidney, brain and liver, leading to failure of those essential organs. The *vivax* and *falciparum* organisms tend to cycle in and out of the red cells every 48 hours, giving the disease its

[4] Philip D. Curtin, *Death by Migration: Europe's Encounter with the tropical World in the Nineteenth Century*, Cambridge University Press, 1989: Cambridge.

[5] Malarial diseases have gone under many names. *Vivax* and *falciparum* cycle through red cells every 48 hours, so earned the names benign tertian malaria and malignant tertian malaria, respectively. Tertian referred to the appearance of symptoms every third day. These diseases might also be labeled by their predominating seasonal appearance, with *vivax* more common in the spring and *falciparum* in the fall, at least in the sub-tropical climates of the United States; *malariae* had a quartan, or every fourth day cycle. Microscopes were not common in the American south during the years malaria prevailed there, and usually only researchers doing special studies had the equipment and the skills to precisely diagnose malaria based on blood smears.

common name in the nineteenth century, intermittent fever. And when the fever spikes, it causes severe chills, shaking and fever, a miserable agitation that may be related to the other common name for malaria, ague.[6]

Both diseases are particularly harsh to children and pregnant women. The malaria parasites compromise the placental blood supply, leading to miscarriage and stillbirth, while the mother's normal decrease in immune surveillance during pregnancy makes her particularly vulnerable to the disease. On the other hand, those people that grow up in an environment of endemic malaria acquire tolerance to the organisms over time. Populations that have lived for millennia with the malaria parasites (and since the higher primates all have their own malarias, it is likely that the relationship goes back to the dawn of humans in Africa) have developed various hereditary traits that all attempt to make the red blood cell less susceptible to the invading parasite. Hence the sickle cell trait, G6PD deficiency, hemoglobin C trait, and the various thallasemias all appear to protect children against *falciparum* malaria. Many Africans also lack the Duffy antigen on the wall of their red cells, a benign mutation that protects them entirely from illness by the *vivax* organism. While the humans that left Africa to migrate to other parts of Europe and Asia probably included malaria carriers, it is likely that the disease died out in the small scattered bands of migrants, only to be reintroduced by trade after population growth.[7]

The predominant "malaria mosquito" in the United States was *Anopheles quadrimaculatus* (*A. quad.*), a mosquito distributed broadly from the east coast to the middle of the country, and from Florida into lower Canada. The mosquito identified as *A. quad.* by malariologists in the mid-twentieth century has now been recognized to be a species complex, a phrase used to designate a cluster of mosquito types that may be designated sub-species by some and separate species by others. For details on these discussions, see the modern literature on genomics and

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[6]This information about malaria is widely available in textbooks and online. See, for example, Rick M. Fairhurst and Thomas E. Wellems, *Plasmodium* Species (Malaria), in Gerald Mandell, John Bennett, and Raphael Dolin, eds., *Mandell, Douglas and Bennett's Principles and Practice of Infectious Disease*, 7th ed., Elsevier/Churchill Livingstone, 2009, **2**, 275: New York, available online at http://www.mdconsult.com/book. *Plasmodium knowlesi* is another malaria parasite that can infect humans. It was thought to be primarily an infection of apes, but has recently been found widespread in humans in Southeast Asia. It can be easily confused with *Plasmodium malariae*. Whether it ever occurred indigenously in the United States is unknown but unlikely, given its limited geographic distribution today. See J. Cox-Singh *et al.*, *Plasmodium knowlesi* malaria in humans is widely distributed and potentially life threatening, *Clinical Infectious Diseases,* 2008, **46**, 165–71 for a description of *Plasmodium knowlesi* infection in Malaysia.

[7]D. J. Weatherall, Common genetic disorders of the red cell and the 'Malaria Hypothesis', *Annals of Tropical Medicine and Parasitology,* 1987, **81**, 539–48.

distribution.[8] For our purposes, the simple name will do, and the mosquito's characteristics that are relevant to malaria transmission can be briefly described. First, *A. quad.* is a "promiscuous" feeder — malariologists dissected *A. quads.* from various states in the American south and found that mosquitoes trapped in environments where farm animals and people were equally available showed no preference in their choice of blood meal.[9] Erwin Ackerknecht has argued that malaria retreated from the upper Mississippi Valley in part because as the number of farm animals increased, the mosquitoes chose them for feeding over humans.[10] This does not seem to have been the case in the south, and may explain in part the persistence of malaria in that region. *Anopheles freeborni* was the predominant vector of malaria on the west coast, especially in California.[11]

The major malaria vectors in the United States breed in still water, preferring swamps, ponds, and side pools of moving streams for laying their eggs. Once hatched, the mosquitoes rarely fly more than a mile from their breeding site, so malaria cases clustered around such wetlands. Malaria larvae float on the surface of the water, where they are susceptible to consumption by small fish, poisoning by larvicides, or smothering by a layer of oil.

Immigrants to the New World and the Arrival of Malaria

The migrants who settled in the area which would become the United States came from four major areas. First, the Native Americans arrived in prehistoric times, and

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[8]Rebecca S. Levine, A. Townsend Peterson, and Mark Q. Benedict, Distribution of members of *Anopheles quadrimaculatus* Say s.l. (Diptera: Culicidae) and implications for their roles in malaria transmission in the United States, *Journal of Medical Entomology*, 2004, **41**, 607–13; Robert F. Darsie Jr. and Ronald A. Ward, *Identification and Geographical Distribution of the Mosquitoes of North America, North of Mexico*, University Press of Florida, 2005: Gainesville. While other *Anopheles* species may have been locally important, *A. quad.* was the predominant malaria mosquito in the American South. James Stevens Simmons reviewed the research on malaria vectors in the United States in, The Transmission of Malaria by *Anopheles* Mosquitoes in North America, in Forest Ray Moultin, ed., *A Symposium on Human Malaria with Special Reference to North America and the Caribbean Region*, American Association for the Advancement of Science, 1941, 113–30: Washington.

[9]F.W. O'Connor, Biologic investigations, *Southern Medical Journal*, 1924, **17**, 599–602; S.T. Darling, Discussion on the relative importance in transmitting malaria of *Anopheles Quadrimaculatus*, *Punctipennis*, and *Crucians* and advisability of differentiating between these species in applying control measures, *Southern Medical Journal,* 1925, **18**, 452–8; and S.T. Darling, Entomological research in malaria, *Southern Medical Journal,* 1925, **18**, 446–9.

[10]Erwin H. Ackerknecht, *Malaria in the Upper Mississippi Valley, 1760–1900*, Arno Press, 1977, c1945: New York.

[11]Simmons, Transmission of Malaria, and Mark F. Boyd, *An Introduction to Malariology*, Harvard University Press, 1930: Cambridge.

appear to have been malaria-free until European settlement. The second group came from the various countries of Europe and the Mediterranean, and many of them would have brought *vivax* parasites along, as this organism is particularly adept at traveling. It can lie dormant in the liver for months, and later cause relapses which start a new cycle of infection wherever the unlucky victim may have roamed in the interim. The third population came from the west coast of Africa, when slave traders imported not only unfortunate humans but the parasites of malaria and, later, yellow fever. Africans were vehicles mainly for *falciparum*, since they were largely immune to *vivax*. Where Africans were forcibly settled and the climate was sufficiently sub-tropical, *falciparum* malaria blossomed in the settlements of the New World colonies. It is possible that immigrants from Asia contributed to the malaria prevalence on the west coasts of North, Central and South America during the last millennia.[12]

Falciparum malaria exploded most evidently in colonial South Carolina, where slave workers harvested rice from flooded fields that were ideal for breeding the *anopheles* species that carry the parasite from one person to another. The impact on mortality, particularly among whites, was so evident that we can pinpoint it fairly precisely, to the early 1680s.[13] From being a fairly healthy colony, South Carolina became deadly for white people. Not coincidentally, the slave trade from the Caribbean and Africa expanded dramatically in just the same time period.[14] One historian who studied South Carolina parish records for the eighteenth century found that 86% of white babies born in some parishes died before the age of 20, an astounding outcome likely due in large measure to *falciparum* malaria. It was no accident that well into the nineteenth century South Carolina had more black people than white, and that planter rhetoric proclaimed that only black people were physically suited to plantation work.[15] White southerners learned to take their families to the Appalachian highlands or northern retreats during the late summer months when the heat was so unpleasant and deadly malaria prevailed.

Fortunately for white settlers in the lands that were to become the United States, *falciparum* did not tolerate the temperatures much further north than Tennessee and North Carolina. *Vivax*, on the other hand, was quite adapted to temperate

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[12]Humphreys, *Malaria*, *op. cit.*, 20–6.

[13]Peter Wood, *Black Majority: Negroes in Colonial South Carolina from 1670 through the Stono Rebellion*, Alfred A. Knopf, 1974, 63–91: New York.

[14]Philip Curtin, Epidemiology and the slave trade, *Political Science Quarterly*, 1968, **83**, 191–216.

[15]Peter Coclanis, *The Shadow of a Dream: Economic Life and Death in the South Carolina Low Country, 1670–1920*, Oxford University Press, 1989: New York; H. Roy Merrens and George D. Terry, Dying in paradise: malaria, mortality, and the perceptual environment in colonial South Carolina, *The Journal of Southern History*, 1984, **50**, 533–50.

climes, and extended as far north as Ontario and New Hampshire, and as far west as Iowa, Minnesota and Nebraska. Malaria made life miserable on the American frontier, as so much travel was by river and the earliest settlements were near those transportation waterways. Frontier housing was porous, and mill ponds (created to grind the ubiquitous corn that fed the pioneers and their animals) formed ideal nurseries for *anopheles* larvae. Malaria wreaked havoc in the 18th century Chesapeake, and in the Connecticut River Valley; by the mid-nineteenth century it had traveled into the Midwest, following settlers on the Ohio, the Mississippi and the Missouri Rivers. By the time of the Civil War, both *vivax* and *falciparum* malaria were well entrenched in the United States, although by then it had become rare in New England.

Conditions during the war vastly amplified malaria's spread among Americans. Whereas pest mosquitoes and notions of ill health had kept some areas sparsely populated, soldiers had to camp and fight in places they would otherwise have avoided. The James River peninsula, the shores of the Potomac River, the swamps around Vicksburg, and the occupation of the southern low country all brought men, malaria parasites, and mosquitoes together in great numbers. And those men were living outdoors, with only the slight protection of a tent to ward off mosquitoes. At times troops were issued mosquito netting in particularly buggy locations, but for most Civil War soldiers, these were an absent luxury. Of the several million men who served as soldiers in the war, at least a third on both sides sickened with malaria and 1 to 3% of those ill died of the disease. It was a major cause of disability during the conflict, even when it was not fatal.[16]

Fighting Back

By the mid-nineteenth century, humans began to fight back against malaria with increasing success. In 1821 Parisian researchers Joseph Pelletier and Joseph Caventou isolated quinine from the bark of the cinchona tree, and by the 1840s quinine pills were widely available on the malarious American frontier.[17] As that frontier became more prosperous, settlers built houses more impervious to the

[16] *The Medical and Surgical History of the War of the Rebellion, (1861–1865)*, Prepared, in Accordance with Acts of Congress, under the Direction of Surgeon General Joseph K. Barnes, United States Army, Government Printing Office, 1870, 636–7: Washington. And see, Andrew Bell, *Mosquito Soldiers: Malaria, Yellow Fever and the Course of the American Civil War*, Louisiana State University Press, 2010: Baton Rouge.

[17] Dale C. Smith, Quinine and fever: the development of the effective dosage, *Journal of the History of Medicine and Allied Sciences*, 1976, **31**, 343–67; Thomas Findley, Sappington's anti-fever pills and the Westward migration, *Transactions of the American Clinical and Climatological Association*, 1968, **79**, 34–44.

cold, and moved to higher ground where mosquito pests were less abusive. Drainage to ready land for agriculture decreased breeding sites. With the spread of railroads from the 1830s and 1840s, settlers lost their dependence on waterways for transport. All of these actions began to cut malaria rates, especially in the more temperate northern tier of states. The Civil War temporarily reversed this trend, as veterans brought the parasite home and areas such as western New England that had not seen malaria in decades were again affected.[18] But by 1900 malaria had become largely a disease of the south, with a few outposts on the west coast and in the southernmost parts of the midwest.[19]

Whereas prior theorists had declared that malaria emerged from the stinky air of swampy lands, scientists working in the last two decades of the nineteenth century identified the *plasmodium* and demonstrated its carriage by the *anopheles* mosquito. These discoveries quickly generated new tools for fighting the disease. Mosquito larvae could be killed by oiling breeding grounds or sprinkling the water with toxic chemicals. Where possible, drainage removed the breeding sites altogether. Public health officials also recognized that giving quinine to patients or even prophylactically to a whole community would reduce the parasite burden of individuals and decrease transmission. William Crawford Gorgas was able to control both malaria and yellow fever in the Panama Canal Zone, given the power and infusion of enough money to effectively control mosquitoes and treat patients.[20]

These measures were implemented to protect American military camps during World War I, and tested in demonstration projects run by the Rockefeller Foundation in the Mississippi Delta in the post-war years. The Rockefeller Foundation recognized that malaria was most problematic in tropical and subtropical parts of the world that were marked by poverty. It sought to determine which method of malaria control was both the cheapest and most effective. Their demonstration projects targeted this objective, judging the results by cost per case of malaria reduced. They supplied free quinine at one site, organized larvicidal measures at a second, and sponsored a screening campaign at the third.

In the screening campaign, the Rockefeller men and local public health officials enlisted high school shop classes to make simple screens for doors and windows.

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[18]Francis A. Walker, *Statistical Atlas of the United States Based on the Results of the Ninth Census 1870: with Contributions from Many Eminent Men of Science and Several Departments of the Government*, Julius Bien, 1874, facs. rpt. Ross Pub, 2003: New York, plate XLII (unpaginated).

[19]Linda Nash discusses malaria in California's Central Valley in *Inescapable Ecologies: A History of Environment, Disease and Knowledge*, University of California Press, 2006: Berkeley.

[20]On the general history of this era and the development of new measures of malaria control based on parasite and mosquito vector, see Gordon Harrison, *Mosquitoes, Malaria and Man: A History of the Hostilities since 1880*, E.P. Dutton, 1978: New York, and Randall M. Packard, *The Making of a Tropical Disease: A Short History of Malaria*, The Johns Hopkins University Press, 2007: Baltimore.

They sent educators around to households to demonstrate the installation and maintenance of the screens, and advise on covering wall cracks with heavy brown paper, such as that used for grocery bags. Screens at the time were not rust free, and had to be painted frequently, as well as repaired if holes developed. The program worked well in the first year. In fact every intervention they made worked well in the first year, reducing malaria cases by 90% or more. But then the programs began to fall apart. Physicians objected to the distribution of free medication as impinging on their right to practice. And the drug method failed to prevent recurrence in the long term. The second year when surveyors came back to the screened households, they found many of the screens in disrepair. Often the household occupants had changed, as the sharecropping population was so migratory, leaving one farm at the end of a contract for another, hoping for a better deal. The new occupants knew nothing about the program, and had failed to continue maintenance. Others who had heard the first year's lessons found the screens reduced airflow into the stifling cabins, and so stopped using them.

It was the larvicidal program that seemed to work best. It did not depend on the cooperation of the larger population, but instead on the determination of the local authorities who oiled standing water, sprinkled arsenical larvicides on streams and ponds, or diverted waterways into underground culverts. Such work was popular in urban areas, where local officials reaped political acclaim by both reducing malaria and the presence of mosquito pests. Drained land had greater value in the urban setting as well. Although the disease spiked briefly in the counties affected during the 1927 Mississippi River flood, by the early 1930s, malaria was at a low ebb in the United States, and had largely been controlled in urban settings where the benefit of mosquito pest control coupled with public health efforts justify public expenditures on drainage and larvicidal treatments. The affluent had also learned the value of screening their houses, a feature that became increasingly common and expected among the middle class.[21]

The Great Depression temporarily reversed this trend of malaria decline. Many of those who had worked in town returned to the rural countryside, where malaria still thrived. This last surge of the disease in the United States peaked between 1933 and 1935; it had largely disappeared by the early 1940s.[22] The causes of its demise are hard to measure, for a variety of reasons. First, most of the statistics available concern malaria death rates, whereas the number of cases would be a

[21] Humphreys, *Malaria*, *op. cit.*, 72–87. See also Hoyt Bleakley, Malaria eradication in the Americas: a retrospective analysis of childhood exposure, *American Economic Journal: Applied,* April 2010, **2**(2), 1–45 available from: http://home.uchicago.edu/~bleakley/.

[22] Ernest Carroll Faust, Clinical and public health aspects of malaria in the United States from a historical perspective, *American Journal of Tropical Medicine*, 1945, **25**, 185–201.

much better metric for malaria prevalence (but was rarely collected). Deaths among the rural southern poor were not usually observed by a physician, so the cause of death listed officially was only a guess generated by the family report and the public official creating the death certificate. When the federal public health officials began paying for documented cases (demonstrated by a positive microscopic blood smear examination) in the late 1940s, they found that counties thought to be persistently malarious actually had no cases at all. Individual physician statements about the prevalence of malaria may be more accurate than the official statistics.[23]

It does seem clear that malaria was hard to find by 1940. At Charity Hospital in Louisiana, a malaria case was an exciting event by 1942; instructors made sure that medical students had a chance to see the rare cases. The United States Public Health Service had set up a field station to study malaria in Newton, Georgia in the 1920s, but by 1944 they converted their mission to studying mosquitoes as malaria had disappeared.[24] So what happened in the last half of the 1930s to squash the malaria parasite in the United States? It would be easy to give credit to a region-wide Works Progress Administration program that built drainage systems, including in malarious areas. But this work was poorly planned, not specifically targeted at malarious breeding sites, and offered no systematic plan for maintenance, which meant the drainage ditches quickly clogged and became ineffective (or even increased the water surface for larvae).[25] This was also an era when the Tennessee Valley Authority, Duke Power Company, and other power companies were damming rivers for hydroelectric power. They recognized the capacity of their reservoirs to increase mosquito breeding and hence malaria, and took active steps to control the disease. Their work was limited to the immediate environs of their reservoirs, however, and had little impact on malaria elsewhere, such as in the Mississippi delta region.

The most likely cause for the decline of malaria in these years was an inadvertent by-product of New Deal legislation that sought to improve southern agriculture. Government programs paid farmers to take their land out of cultivation, in order to prop up the prices of the crops that were produced. Federal loan programs supplied capital for farmers to buy machinery such as tractors and other mechanical devices. These measures in turn meant that the old system of sharecropping, in which poor blacks and whites lived in shacks on the land and cultivated it with a

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[23] Margaret Humphreys, Kicking a dying dog: DDT and the demise of malaria in the American South, 1942–1952, *Isis, 1996,* **87**, 1–17.

[24] Humphreys, Kicking a dying dog, *op. cit.*

[25] Margaret Humphreys, Water won't run uphill: the new deal and malaria control in the American South, 1933–1940. *Parassitologia,* 1998, **40**, 183–92.

hand plow and mule, became less cost effective. A massive depopulation of the southern rural landscape followed, and even where planters hired day labor, that labor lived in town (where malaria had already been controlled). As a result, large populations were removed from the one-mile flight zone around many malaria breeding sites, breaking the chain of malaria transmission.[26]

World War II and New Tools for the Malaria Wars

As the United States entered the world war late in 1941, malaria was not a major problem in the American south. Yet, military and civilian public health leaders feared an upsurge in the disease. They saw malaria as a disease of mysterious cycles, of peaks and troughs of unexplained pattern. With so many military camps in the south, troops from all over the country were at risk as the country mobilized for the war. The United States Public Health Service created a special agency to protect military sites from malaria, and dubbed it Malaria Control in War Areas (MCWA). The military authorities created malaria control programs within military camps, and MCWA's job was to create a malaria free zone around camps and other war-related sites. They used familiar tools — larvicide via oil and arsenic compounds, spraying insecticides containing pyrethrum, screens, insect repellants, and oral medication. Since Japan had occupied Java, where almost all of the world's quinine-source trees now grew, the United States authorities substituted with the drug atabrine. Atabrine was not particularly popular given its side-effect profile, but it kept men on their feet in malaria zones overseas and on American soil.

Two new weapons for the malaria wars emerged from American military research during World War II. The first was the synthesis of chloroquine, a new malaria drug that was far better tolerated than earlier malaria compounds.[27] The second was DDT (dichlorodiphenyltrichloroethane). DDT was a near magical insecticide. Pyrethrum had been used for years, but it was a "knock-down" insecticide, one that killed a mosquito if sprayed directly on it. It had no residual effect. DDT, on the other hand, could be sprayed on a wall and continue killing mosquitoes that landed there for up to three months. It was equally effective as a larvicide, and could be spread on lakes from airplanes or from boats with motorized sprayers. DDT had a major impact on the military control of malaria (and other insect-borne diseases) overseas, and in August 1945 it became available for purchase within the United States.[28]

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[26] Humphreys, *Malaria*, *op. cit.*, 108–12.

[27] Leo B. Slater, *War and Disease: Biomedical Research on Malaria in the Twentieth Century*, Rutgers University Press, 2009: New Brunswick.

[28] Edmund Russell, *War and Nature: Fighting Humans and Insects with Chemicals from World War I to Silent Spring*, Cambridge University Press, 2001: New York.

There was one attempt at a controlled study of DDT as an anti-malarial agent in the United States, which focused on an area surrounding two new reservoirs in South Carolina, components of the Santee-Cooper hydroelectric plant project. As one MCWA leader noted in 1945, "The Santee-Cooper offers what may be the last opportunity in this country to see active malaria."[29] He strongly supported a quick research program there to test the effectiveness of DDT. A combined federal and state research team sprayed one area with DDT and left another as a control, but found that malaria declined rapidly among both populations, leading to an inconclusive result.[30]

At the end of the war MCWA had more than four thousand employees, but no longer had a mandate to protect the war effort. Its leaders argued successfully to Congress that agency funding be continued, and they launched a malaria eradication campaign in the United States, using DDT as their principal weapon. Changing their name to the Communicable Disease Center (CDC), MCWA officials oversaw the DDT spraying of millions of homes in the American south from 1945 to 1950.[31] There was very little malaria to measure, so they instead counted the reduction in *Anopheles* mosquitoes, which was significant. In 1951 they declared victory; after a three century run, malaria was no longer indigenous in the United States.[32] It is likely that the CDC campaign eradicated a few remaining pockets of the disease, and deserves some credit for that result. It is also likely that malaria had largely subsided by the time the campaign began, so that their victory was not a difficult one.[33]

There are still about 1,500 cases of malaria cases in the United States each year. Over the past half century, malaria has spread from imported cases to local inhabitants at least 63 times, although the outbreaks have been quite limited.[34] Some have questioned whether with global warming and increased possibilities for the international spread of disease, the United States might be at risk for the re-emer-

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[29]L. L. Williams to Alex G. Gilliam, 13 March 1945, Louis L. Williams Papers, 1927–1970, MS C 169, box 5, Santee-Cooper Folder (no. 2), History of Medicine Division, National Library of Medicine, Bethesda, MD.

[30]Leo Slater and Margaret Humphreys, Parasites and progress: ethical decision-making and the Santee-Cooper malaria study, 1944–1949, *Perspectives in Biology and Medicine*, 2008, **51**, 103–20.

[31]On the history of the CDC, see Elizabeth W. Etheridge, *Sentinel for Health: A History of the Centers for Disease Control*, University of California Press, 1992: Berkeley.

[32]Justin M. Andrews, Nationwide malaria eradication projects in the Americas: the eradication program in the U.S.A., *Journal of the National Malaria of Society*, 1951, **10**, 99–121.

[33]Humphreys, Kicking a dying dog, *op. cit.*

[34]Data from CDC website at http://www.cdc.gov/malaria/about/facts.html. More information about individual outbreaks can be found in the *Morbidity and Mortality Weekly Report*, also available online at the CDC website.

gence of malaria.[35] Much has changed in the formerly malarious zones of the country that makes this outcome unlikely. First, most homes in the south are air conditioned, and few people are exposed to the volume of mosquito bites that characterized the malaria years. An interesting study on the border of Mexico illustrated this point.

Paul Reiter and his colleagues wondered why dengue fever, a viral disease spread by mosquitoes of the *Aedes* genus, had erupted in Nuevo Laredo, when Laredo, Texas was almost entirely spared. The two cities were only a bridge span apart, and the research team actually found a higher density of the vector in Laredo than on the Mexican side of the border. The key difference between the two communities was air conditioning. Mexicans spent the leisure hours of the early evening, when mosquitoes are most active, outside on patios or in open air bars, whereas most American housing and public places were air conditioned, limiting mosquito exposure.[36] There was no difference in climate between the two communities. The few documented instances where malaria spread locally within the United States in recent years occurred mostly in the lowest grade of housing, such as trailer parks whose residents likewise spent the early evening hours sitting outside their residences. American cities actively control pest mosquitoes, and one assumes that if an outbreak of severe mosquito borne disease did erupt, these measures would correspondingly increase. This has certainly happened in the response to West Nile Virus, an organism spread by mosquitoes, which caused significant disease in certain localities of the United States. It is hard to imagine malaria making a comeback in the modern United States, unless major changes in societal affluence and government infrastructure occur first.[37]

Lessons Learned

It is worth recognizing the factors that first amplified malaria in the United States. First, frontier populations are a prime target for the disease, especially when the mode of transport is by water. Areas of new settlement are characterized by initial poverty, porous housing, subsistence agriculture, and high cost of manufactured goods such as medicines. As humans enter a previously unsettled area, they may alter the landscape in ways that increase mosquito breeding, such as by building

[35] Margaret Humphreys, Climate change and mosquito-borne disease: a historical perspective, *MD Advisor*, 2009, **2**, 16–21.

[36] P. Reiter *et al.*, Texas lifestyle limits transmission of dengue virus, *Emerging Infectious Diseases*, 2003, **9**, 1–9.

[37] Information on West Nile Virus is available at http//:www.cdc.gov. According to one report on that site, The state of California voted an extra 12 million dollars for mosquito control in 2005 when West Nile became a major public health threat there.

dams for power. Even when modern tools are available to fight malaria, those living on the frontier fringes may be most susceptible if the malaria parasite is present.

Second, war is a grand amplifier of malaria epidemics. Humans will usually move away from mosquito hordes if they have a choice, since the insects create such misery. Wartime conditions may force the occupation of landscapes that would otherwise be lightly populated, and if the malaria parasite is introduced, it will find dense human populations ripe for mass transmission of the disease. Even with the tools of quinine and mosquito netting available, the American Civil War not only saw the rapid spread of malaria among troops on both sides, but the reintroduction of the disease to areas long free of it. War sets populations in motion, and often creates refugee camps for those fleeing the destruction generated by combat. Populations that may have once lived in villages where malaria was fairly well controlled may be forced into new locales where all of those systems fall apart and they are newly subjected to the disease.

Third, poverty is tied to malaria in multiple ways. Those weakened by malaria are unable to work at full capacity, and their infected children will suffer stunted growth and educational disabilities, perpetuating the impoverishment engendered by malaria. The poor are likely to live in substandard housing, that lacks screens or (in the modern era) the air conditioning that makes life indoors tolerable in tropical climates. This housing may, in turn, increase exposure to mosquitoes (as was the case in the Nuevo Laredo study). It may also make it difficult to institute programs designed to decrease contact between humans and mosquitoes. If shacks are so porous that the inhabitants worry about snakes entering the habitation, screens are likely to have little impact on mosquito entry. For the DDT spraying program of the 1940s to be effective, the population had to live in houses with walls. Populations that live in dwellings that lack even these simple amenities — such as people living in refugee camps, tents, or primitive shacks — may be unreachable by interventions that target mosquitoes via screening or residual spraying.

Poverty also affects access to medication. The malaria peak in the 1930s United States would have been much duller if the population had been able to afford quinine. Doctors bemoaned the fact that the sick did not visit them nor receive effective doses of quinine, and instead spent what money they had on low dose "chill tonics" that contained inadequate amounts of quinine, if any at all. Poor southerners in the Great Depression had very little cash on hand, and effective medicine was out of reach for many. If every American with malaria in the 1930s had access to a doctor and proper medication, the parasite could not have thrived. The onset of the great poverty of that decade demonstrated the impact of economic recession on health, and especially on diseases that had been fairly well controlled when economic conditions had been only slightly better.

The malaria story in the United States offers other lessons as well, lessons about human behavior and the effectiveness of public health education campaigns. The Rockefeller demonstration projects in the Mississippi Delta in the late 1910s showed that just about any viable program (drugs, screens, drainage) would be effective in its first year. But as soon as the fervor of the initial encounter had begun to wane, malaria crept back. This was particularly the case for screening, which relied on the individual to maintain vigilance against damage and persist in proper usage. Modern interventions (such as bed net programs) that require steady maintenance and strict, persistent use in the face of inconvenience or discomfort may be equally likely to succeed, at first, and then fail as the intervention's initial impact fades over time. Failure of malaria programs is particularly problematic, since when the disease returns it finds a population whose acquired immunity has waned. Any malaria control program needs to measure the effect of an intervention over more than one or two years, and be prepared for long term surveillance and continued dedication on the part of local actors.

The decline of cases during the 1930s also demonstrates the importance of location for the prevalence of malaria. Where mosquitoes have a limited flight distance from their breeding grounds, the proximity of people to those breeding sites becomes critical. One study of malaria in an eastern North Carolina village in 1940 showed that proximity to the town's major pond was a more important variable in predicting the occurrence of malaria than the quality of the housing (a marker of affluence).[38] If my research is correct, and the major decline of malaria in the United States occurred because of rural depopulation, then observers considering the American story should be careful in attributing the eradication of malaria to direct measures taken against it. In many tropical countries, it may be impossible to remove people from proximity to *Anopheles* breeding sites. But it would be incorrect to state that "DDT eradicated malaria in the United States, and it ought to be used elsewhere to similar success," an assumption that guided the tropical malaria eradication programs of the 1950s and 1960s, and has some adherents today.

Malaria seems to particularly invite facile but false assumptions about its eradication. Nathan Myhrvold, described as "Bill Gates's ideas guy" told an interviewer for Foreign Policy:

> Malaria is the only disease to ever be locally eradicated without any medicine. It turns out that if you drain the swamps, spray with DDT or other pesticides, put window screens on [the windows], and have a tremendous amount of discipline, you can defeat malaria. That's how it was defeated in the United States in the 1930s. In 1935, the peak year, there were 135,000 cases. This was a furious disease in the southern

[38] Humphreys, *Malaria*, *op. cit.*, 110.

United States. We got that fixed. The trouble is, we got that fixed because we had a combination of a high standard of living and a lot of resources and some discipline. The countries that have it worst [with malaria today] have very low standards of living and very little societal discipline. They can't put their effort into malaria right now.[39]

Myhrvold has invented a laser mosquito zapper which he thinks will stop malaria, although he concedes it is more likely to be a commercial success as a backyard insecticide in countries of affluence. His attribution of malaria's disappearance in the United States to discipline, resources, and a high standard of living contains some truth, but he misses the major explanation of its demise. Drawing conclusions based on bad history is poor public policy.

The disappearance of malaria in the United States and Europe during the 1940s led to great global optimism about the possibility of eradicating malaria worldwide. Yet in retrospect there is little evidence that DDT was key in the disappearance of American malaria, and the successful eradication of malaria in temperate climates may have little relevance to tropical areas. Public health campaigners should use care in comparing the events in one locale, with its own peculiar circumstances of climate, populations, housing, and infrastructure, with other areas where key factors may be different. Malaria is easy to control — with enough money and determination — and yet remains one of the major health hazards today, especially for children and pregnant women. The history of campaigns against this slippery antagonist over the past century provides important object lessons for those seeking once again to conquer this disease.[40]

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[39]Elizabeth Dickinson, The Ultimate Bug Zapper, [an interview with Nathan Myhrvold], *Foreign Policy*, 23 April 2010, available at http://www.foreignpolicy.com/articles/2010/04/23/interview_nathan_myhrvold (accessed on 2 May 2010).

[40]Packard, *The Making of a Tropical Disease, op. cit.*; Socrates Litsios, *The Tomorrow of Malaria*, Pacific Press, 1997: Wellington, NZ.