Eradicating Malaria in Poor Nations:
The Potential of Vector Control Measures and Vaccine Development

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Abstract

Although malaria is a growing problem affecting several hundred million people each year, many malarial countries lack successful disease control programs. Worldwide malaria incidence rates are dramatically increasing, generating fear among many people who are witnessing malaria control initiatives fail. In this paper, I explore two options for malaria control in poor countries: (1) the production and distribution of a malaria vaccine and (2) the control of mosquitoes that harbor the malaria parasite. I show that the development of a malaria vaccine is indeed likely, although it will take several years to produce because of both biological obstacles and insufficient research support. The distribution of such a vaccine, as suggested by some economists, will require that wealthy states promise a market to pharmaceutical companies who have traditionally failed to investigate diseases affecting the poorest of nations. Several scientists have recommended that prior to the development of a malaria vaccine, vector control programs, such as those using Bti toxin, should be implemented in regions with low vector capacity. This analysis indicates that both indigenous programs in malarial regions and molecular approaches to parasite control are unlikely to provide sustainable solutions to the malaria problem, although some may assist in controlling malaria burdens. The successful eradication of malaria, however, will require sustained support from wealthy nations to develop a malaria vaccine.

Obstacles to the eradication of malaria

In 1999, the World Health Organization (WHO) estimated that over 300 million clinical cases of malaria occur annually from among the 2.3 billion people (almost one-third of the world's population) who are at risk of infection with the malaria parasite. An estimated 1.1 million people annually die from the disease. While these numbers are shocking, they are probably underestimates of the world's malaria burden given that only a fraction of malaria cases are reported each year and that deaths among children with chronic malaria are often attributed to other illnesses. These statistics may vary by a factor of three, depending on the method of estimation (WHO, 1999). In Africa alone, the 28 million reported cases of malaria are believed to represent only 5-10% of the total malaria incidence on the continent (Hamoudi & Sachs, 1999).

Malaria is clearly a global challenge in need of an immediate and sustained solution. Unlike AIDS, dysentery, or other diseases affecting the tropics, malaria cannot be totally controlled by behavioral changes or education. Rather, the disease is determined by climate and ecology--malaria risk is geographically specific to tropical and subtropical zones, primarily because its pathological vector is the mosquito. And while it is true that most malarial countries are also poor countries, several wealthy nations, such as the United Arab Emirates and Oman, face serious malaria problems.

A recent study by economists John Gallup and Jeffrey Sachs reveals that although poverty does not appear to determine malaria risk, the prevalence of malaria has an enormous impact on a country's economy. Malaria dramatically inhibits economic growth (probably by restricting individual worker productivity, tourism, foreign investment, and transportation), although poverty does not appear to determine the prevalence of malaria (Gallup & Sachs, 1998). Some analysts have estimated the economic burden of malaria at 0.6-1.0% of GDP in Africa, although recent reports indicate that the economic impact of the disease on national income is likely to be much higher (Shepard, 1991; Bloom & Sachs, 1998).

The high incidence rates of malaria are, in fact, affected by the unusual nature of the parasite itself and its vector, the mosquito. Not only is the malaria parasite itself highly complex, but its vector is a sexually reproducing organism capable of mixing genes during reproduction. As a result, mosquitoes quickly evolve to acquire drug resistance. It is also believed that the malaria parasite co-evolved with the human species, so the two organisms are probably well-adapted to one another (Hamoudi, 2000).

The species-specific behavior of mosquitoes in some regions, however, has allowed for the success of malaria control programs in those areas, while mosquitoes in other regions have posed significant obstacles to those attempting to prevent malaria infection. In some temperate regions where malaria has been eradicated, mosquitoes spend their winter in hibernation or a non-reproductive state. Control programs have used this fact to their advantage by using insecticide and drug treatments during the mosquito "off-season".

In tropical zones where mosquitoes do not hibernate, individuals often receive multiple malaria infections. But populations of people in malaria endemic regions such as sub-Saharan Africa do not appear to develop protective, sterilizing immunity to the disease. Rather, they develop a non-sterilizing immunity that suppresses clinical symptoms of the conditions, allowing those infected persons to appear healthy while malaria parasites develop and circulate in their blood. These dangerously inconspicuous parasite reservoirs develop in endemic populations, inhibiting the treatment of infected individuals while providing sources for the propagation of this disease. Mosquitoes in temperate regions, on the other hand, re-infect individuals rarely. People in these regions exhibit decipherable symptoms of malaria upon infection, and can be treated promptly (Hamoudi & Sachs, 1999).

Educational prevention programs. Given our current understanding of obstacles to effective malaria control (particularly in tropical regions), we can discuss several options for both short- and long-term control programs. Malaria reduction efforts paralleling those of AIDS control initiatives--namely, programs using education and distribution of protective devices (condoms to prevent HIV infection, bednets to prevent malaria)--have supported malaria control initiatives in several regions. The use of treated bednets and curtains has substantially curtailed malaria incidence rates in China and Vietnam and has reduced child mortality rates by as much as 63% in African trials (WHO, 1999). But programs distributing bednets and other protective devices offer no panacea to the malaria problem.

In fact, the effectiveness of protective devices is often curtailed by the activities of governments privatizing their industrial sectors or agricultural markets, often under pressure from international lending institutions aiming to “develop” regions through private sector growth. As some poor countries privatize, the techniques and practices they employ for development purposes exacerbate the malaria problem. A recent report shows that large-scale irrigation programs attempting to restore fertility to Ethiopian farmlands have caused a seven-fold increase in the rate of malaria in this region because most of these irrigation systems provide breeding grounds for mosquitoes (Ghebreyesus et. al., 1999). Many other programs designed to develop agricultural industries rather than promote small-scale farming are likely to have similar repercussions. Education about safe agricultural practices and regulations on development techniques will therefore play a part in malaria reduction.

Education can also improve the quality of clinical case-management. A review of selected African health facilities has found that at least 67% of health facilities correctly manage uncomplicated cases of malaria and at least 28% correctly manage severe malaria cases (WHO, 1999). With educational programs in place, case-management of malaria cases could improve by mobilizing members of the public to identify the symptoms of malaria, facilitating early diagnosis and timely treatment. These programs could eliminate much suffering and probably prevent many deaths, although the state of many health systems in poorer countries often contributes to the malaria problem. Modern knowledge and techniques must be applied to these under-funded health care systems, although this would require a dramatic shift from current trends. International lending institutions, particularly the World Bank, have called for the redistribution of funds provided to poor countries, taking money away from the public health sector for use in industrialization programs. But even a reversal of current trends and a calling for the modernization of treatment facilities combined with the development of community education programs would fail to completely eradicate malaria, providing only an initial front to assist in the control of the disease. How, then can we initiate a plan to reduce the world's malaria burden?

The Failure of Drug Treatment Programs. Naturally, WHO and governments of malarial countries have turned toward drug treatment strategies to curtail malarial incidence rates. During the early 1900's, doctors used quinine for malaria therapy. The drug was short-lived and had no significant effect on parasites residing in the liver. It was soon replaced with chloroquine, a cheap, safe, and effective treatment for malaria that gained widespread acceptance among doctors in malarial countries during the 1950's and resulted in an enormous decline in malaria incidence rates. But after years of use, scientists began to identify chloroquine-resistant strains of the malaria parasite. As shown in Table 1, drug resistance intensified during the late 1980's, receded in the early 90's (when new treatments were being introduced), and intensified again in 1994 (WHO, 1997). Resistance to chloroquine has since spread worldwide.

Newer drug therapies, unfortunately, have not eluded drug resistant strains of the malaria parasite. The drug mefloquine was introduced in Southeast Asia in the mid-1980's, but complete drug resistance there was observed after only four years. Resistance to the newer drug atovaquone developed so quickly that doctors observed resistant strains during clinical trials (Strobel, 1999). According to scientists studying drug resistance, the malaria parasite frequently mutates and can therefore become immune to nearly any drug therapy. The basic genetics of the parasite are still being analyzed, so drugs that are not susceptible to resistance are far from production lines (NIAID, 1997). This sobering knowledge leaves us with two avenues for the eradication of malaria: either (1) we develop a vaccine to combat infection or (2) we inhibit the propagation of the disease through mosquito-control programs. In subsequent sections, we discuss each of these two possibilities.

Developing a Malaria Vaccine

The Likelihood of Developing a Vaccine. Unlike many viral diseases, malaria does not confer life-long immunity after infection. As a result, many people in malaria endemic regions must be treated for the disease several times and young children intermittently infected with the malaria parasite often live in a chronically sick condition. An ideal solution to malaria would be a safe, inexpensive, and easily administered vaccine conferring life-long immunity against the disease. In practice, few vaccines are inexpensive and easily administered, and only rarely is a vaccine potent enough to be delivered just once in a lifetime. A vaccine against malaria would need to confer resistance to several different strains of the parasite because it is unlikely that any vaccine could actually prevent infection by preventing mosquito bites altogether. Because the vaccine would be most useful in impoverished areas, including several areas without pharmaceutical manufacturing facilities, the chemical would need to have a reasonably long shelf life. In addition to these constraints, the mutability of the malaria parasite poses a significant challenge to vaccine development. Because of the parasite's mutability, a vaccine should not impose selective pressure on parasites, which would cause resistant species to rapidly become predominant.

These constraints limit the range of potential vaccine candidates against malaria. Despite these limitations, is there reason to believe that an effective vaccine can be developed?

Four biological observations suggest that a vaccine can, in fact, be developed, although its development will likely take at least a decade. Scientists have already observed that adults treated with a radiated form of the parasite can be completely protected against malaria. Patients treated in this manner are immunized against a variety of parasitic strains and their immunity lasts over long periods of time. Unfortunately, the treatment is prohibitively expensive and impractical outside of the laboratory setting (Miller & Hoffman, 1998).

A recent study on experimental animals, however, provides a second piece of evidence to suggest that immunization against malaria can be achieved. The study shows that immune globulin (a group of blood proteins) purified from the plasma of individuals living in malaria endemic regions can be used to immunize rats. The globulin samples contain antibodies that prevent malaria parasites from invading red blood cells. Because a variety of infectious diseases might be transmitted through immune globulin, this therapeutic strategy has been rejected. Its success in experimental animals nevertheless provides a strategy for the production of synthetic vaccines (Good & Doolan, 1999).

A clinical trial of one such synthetic vaccine provides a third piece of evidence supporting the conclusion that an effective malaria vaccine can be developed. The synthetic vaccine SPF-66, produced in Columbia, was recently tested on a group of one- to five-year-old Tanzanian children. The vaccine, which has been in development stages for over a decade, was the first of its kind to be tested in extensive field trials. Unfortunately, the vaccine's estimated efficacy rate was only 31% after a one-year follow-up period in Tanzania. A later administration of the vaccine in Gambia did not show any protective effect. Although SPF-66 was confirmed to be safe, the vaccine has very low immunogenicity and induces only a temporary humoral immune response of 6 months (on average). The SPF-66 test may lead to trials of more universally-effective vaccines, but African officials warn that any SPF-66-derivative will likely prove prohibitively expensive and so further research must be devoted to the production of cheaper alternatives (Acosta et. al., 1999).

Nevertheless, at least partial immunity has been shown to occur in the natural environment, providing a final piece of evidence supporting the feasibility of vaccine development. Older children and adults in endemic areas sometimes develop partial clinical immunity to malaria, which includes decreased morbidity and minimal mortality compared to young children or malaria naïve adults (although this can cause dangerously inconspicuous parasite reservoirs in the population, as discussed above). Naturally acquired partial immunity is considered highly complex, but it is mediated by antibodies and offers a guide for vaccine development (Wirth & Cattani, 1997).

Molecular models for an effective vaccine. Among the most challenging obstacles inhibiting the development of an effective malaria vaccine is the genetic complexity of the malaria parasite, which has nearly one thousand times as many genes as HIV. The malaria parasite's incredible mutability can be largely attributed to its ability to make subtle changes in its surface molecules. The parasite uses mimicry to hide within the body and simultaneously produces toxins that curb human immune responses.

As a result, an effective malaria vaccine will likely be highly complex, possibly containing five or more antigens. The complexity, however, should not be viewed as unusual or problematic. Many modern vaccines in development stages, including those used against rotavirus, streptococcus, pneumococcus , and HIV, are also highly complicated. Why should we use so many antigens? Modern malaria vaccine strategists have suggested that vaccines for malaria must attack the malaria parasite at multiple stages in its life cycle, which would require the use of several antigens. Vaccines also need to overcome allelic and antigenic variation--problems that have plagued single antigen-based vaccines. Multi-component vaccines might also induce more than one type of immune response, which could increase the probability of a more sustainable and effective host response to malaria infection (Shi, 1999).

Perhaps the most viable multi-component attack on malaria is offered by DNA vaccines, which can be genetically tailored to induce both cell-mediated and humoral immune responses. Multi-component DNA vaccines offer the best prospects for protection against malaria because they can be tailored to include a variety of numbers, types, and arrangements of epitopes (the sites within a molecule to which a specific antibody binds). DNA vaccines, unlike conventional vaccines, have high immunogenicity, unlike multi-component synthetic peptide vaccines like SPF-66. DNA vaccines are also cost-effective.

But these vaccines are far from magic bullets. Some DNA vaccines are susceptible to insertional mutagenesis processes, in which the injected DNA from the vaccine integrates into the host's chromosome. Although this event is highly unlikely, it may activate tumor-associated oncogenes. Over long periods of time, the DNA vaccines can cause a variety of immune system problems. Nevertheless, DNA vaccine technology offers the best prospect for an effective malaria vaccine.

What has delayed the production of an effective vaccine? If scientists already know about this technology and have even tested vaccines in malarial regions, why would it take an extended period of time to produce an effective vaccine? Why hasn't a vaccine been produced already?

There are two possibilities: either (1) the technical challenges to producing an effective vaccine are too difficult to overcome or (2) research into the production of a malaria vaccine has not been widely supported. There is some evidence that the first possibility plays a factor into the time-delay. Vaccine developers are faced with a parasite that has many strains, a complex life cycle, and high mutability. Although immunization is clearly possible, it will take years of genetic analysis before an effective vaccine is produced.

But the second factor--the lack of support for vaccine research--provides the greatest obstacle to effective vaccine development. The world's largest pharmaceutical companies (which are mostly American corporations) lack malaria research and development laboratories. Academic laboratories focused on malaria research are mostly foreign and usually lack funding. The Wellcome Trust recently estimated that worldwide malaria research amounted to $84 million each year, or $42 per fatality, whereas research in asthma amounts to $800 million annually, or $500 per fatality (MIM, 1999). Why? As explained by several academic economists, there is little incentive to fund research on a disease that affects people who cannot pay for medicine. There is simply no market for a malaria vaccine (Sachs, 1999).

Creating a market. Some of these economists have also suggested that a market for a malaria vaccine could be artificially created. Rich countries like the United States could pledge to purchase a malaria vaccine if such a vaccine were developed and guarantee the drug developer a minimum purchase price for each dose of the vaccine administered to an impoverished individual. While this price would cover costs of development and production, it would not be prohibitively expensive for most rich countries. If $10 were paid per dose, for example, immunization costs for Africa's 25 million children would amount to $250 million annually, only 1.5% of total aid given to Africa each year. This plan for guaranteed payment prevents public money from being spent unless a vaccine is developed. It does not require a large bureaucracy (although governmental support for basic research would continue) and it uses market forces instead of public agencies to provide incentive to pharmaceutical companies (Kremer, 1999; Sachs, 1999).

“Creating a market” is likely to make malaria research a hot topic among pharmaceutical companies because it guarantees profits. It is also economically sound over the long-term--given that malaria stunts economic growth, a vaccine for malaria would likely help countries grow enough to pay at least partly for their own medicine over an extended period of time. But there is certainly no guarantee that policymakers in rich countries would bother to adopt the plan, especially given the lack of attention malaria receives in the public sector.

The plan is also flawed for a second reason: the drug distributors involved in the plan have profit as their main motivation. American pharmaceutical companies, which are likely to be the key corporations involved in competing for the development of a vaccine, will not have suffering individuals in mind as they assist in the implementation of this plan. Long-term patents and desire for profits could cost poor countries millions of dollars that they don’t have if American foreign aid is cut as liberally as it has in the past. Patent laws in particular eliminate the possibility that poorer countries can develop vaccines themselves, making these countries dependent on rich nations. In the past, similar plans have led to controversies over AIDS drug pricing and patenting and have forced poorer countries into debt as they borrow money from international lending institutions, which often later demand further cuts in social spending to repay loans. Once again, a shift in priorities in necessary for both these lending institutions and rich nations to assist in the eradication of malaria.

If a vaccine is developed, its initial form of the chemical is also unlikely to be totally effective. A partially effective vaccine, such as one that cannot prevent transmission but does prevent an infected individual from acquiring a severe form of malaria, should still be distributed to those regions where it could help curtain the problem even as vaccine research continued.

But since a vaccine is not an immediate solution to the problem (because it will likely require several years to develop), it is essential that we look for a way to control malaria as vaccine research continues. What supplemental plan could we adopt prior to the discovery of a vaccine?

Vector Control

An alternative plan of action. While molecular approaches to malaria control are being designed and tested, they may be preceded by or supplemented with vector control measures--specifically, the control of mosquito populations in tropical and subtropical zones. Whereas DDT proved successful early in its use against mosquitoes, the insecticide has been declared by many to be an unacceptable solution to vector control problems because of its apparent ecological effects and the evolutionary development of mosquito families resistant to the chemical. Most South American countries (with the exception of Ecuador) have abandoned the use of DDT. In 1993, Ecuador increased DDT and has since seen a 60% decrease in the number of malaria cases, whereas Bolivia, Paraguay and Peru stopped DDT spraying altogether and have since observed more than a 90% increase in the incidence rate of malaria (Figure 1; Roberts et. al., 1997). As shown by the correlation between DDT use and malaria rates, the prevalence of the malaria vector in a region, not merely the efficacy of the malaria parasite, will have a significant impact on the success of malaria control programs.

Whereas use of DDT for agricultural purposes can have negative ecological effects, its use inside homes may have little negative impact on inhabitants or on the outside environment. Treatment of house walls with DDT residue has been used to interrupt malaria transmission, although the treatment does not eradicate mosquitoes. The residue on house walls has been shown to deter biting of some mosquito species. Mosquitoes avoid areas containing DDT residue, so indoor use of the chemical could help malaria control in regions where the majority of bites occur indoors (Trapido, 1952).

However, the chemical can be totally ineffective when used to combat the spread of malaria in areas affected by mosquito species that do not enter homes and rest on house walls. Whereas DDT was highly effective against the South American mosquito *Anopheles darlingi*, which bites indoors and rests on walls, vectors like *An. nuneztovari* are largely unaffected because they are "exophilic", biting outdoors (Williams, 1957). It is therefore imperative that any indoor use of DDT is preceded with a thorough analysis of the behavior of the malarial vector. Because DDT was once considered a "silver bullet" to be used on a massive scale, mosquito species in some areas have acquired resistance to the chemical. Therefore, those instituting vector control programs using DDT would also need to attain a biological profile of the vector in addition to acquiring a behavioral understanding of the local mosquito before instituting a DDT program in any region.

A novel approach to vector control? In 1988, Peruvian scientists found a way to produce a natural, ecologically-friendly alternative to DDT. Researchers at the Alexander von Humboldt Tropical Medicine Institute in Lima, Peru found that *Bacillus thuringiensis var israelensis H-14* (Bti), a bacteria producing a toxin that kills mosquito larvae, could be efficiently cultured in coconuts (which are plentiful in some malarial regions). Bti, which is harmless to humans and livestock, could be used to dramatically reduce populations of mosquitoes. If grown locally, the bacteria could be used to treat ponds where mosquitoes breed.

In 1993, the Peruvian research team began teaching local populations of three Peruvian communities how to culture Bti bacteria. The scientists made the process simple: one would need to take a supplied cotton swab doused with Bti, drop it through a hole in the coconut, plug the hole with a cotton swab and candle wax, and let the coconut sit for three days. Two or three of these coconuts could then be broken-up and distributed in local ponds, where a toxin produced by the bacteria would eradicate mosquito populations for as long as 45 days.

Mosquito resistance to the toxin was not observed because the mosquito killer prevented larvae from developing into adults capable of reproducing. Mosquito evolution was therefore inhibited by the bacteria's toxin, making it difficult for resistant strains to develop.

While this mosquito killer is normally expensive and lives too short of a time-period to be administered by governments or other large organizations, the use of coconuts to harvest and apply the bacteria to pond water provides an inexpensive and effective means for local populations to control the malarial vector (just one cotton swab of the bacteria can be used transferred from the lab to the local population, where it can be used to harvest millions of colonies). The Peruvian trial of Bti proved successful at controlling mosquito populations--in some regions, larvae mortality reached 100%. Corresponding malaria incidence rates are now being measured.

To enhance Bti distribution capability, scientists have expressed combinations of Bti genes in a variety of organisms, including a type of cyanobacteria eaten by mosquito larvae. The bacteria expresses the genes and produces the Bti toxin, making it potentially capable of eradicating whole mosquito populations (Wu, 1997). Similarly, genetic engineering methods have allowed scientists to begin constructing modified maize. The pollen and seeds from modified corn plants could blow across the landscape and make the nearby region uninhabitable to mosquitoes (Hamoudi, 2000).

Obstacles to vector control. Unfortunately, Bti toxin is no cure-all to the malaria problem. Recent studies show that Bti is highly toxic to endangered monarch butterflies and could have other effects that throw ecosystems into turmoil (Losey, 1999). There is a simple lesson from the Bti story: that attempts to kill mosquitoes are likely to affect other species and may have several unpredictable ecological effects, including the production of resistant mosquito strains. And even if a mosquito-specific version of Bti are discovered, they would not be enough to effectively control the incidence of malaria in all regions, particularly those in sub-Saharan Africa that are most desperately seeking effective malaria control measures. The toxin would likely prove ineffective in sub-Saharan African areas because mosquitoes in the region breed virtually everywhere from ponds to puddles. There is simply no insurance that all mosquito larvae will die, so using Bti or a mosquito-specific alternative as a method to control malaria may enhance conditions for surviving mosquitoes, who will in turn experience extended lifetimes with greater capacities for transmitting malaria parasites. The ultimate danger of insecticides, natural or otherwise, is the possibility that they may accelerate the selection of a stronger and healthier adult mosquito population.

A key obstacle to malaria control programs, in fact, has been the vectorial capacity of some mosquito species. Vectorial capacity refers to the ability of a mosquito species to carry the malaria parasite from one human to another. Species with high vectorial capacity, such as *Anopheles gambiae* mosquitoes in sub-Saharan Africa, can cause malaria infections in several individuals when only one infected person is part of the population.

Species with high vectorial capacity therefore provide a major obstacle to vector control programs. Historically speaking, malaria control efforts focused on reducing mosquito populations have failed to significantly reduce malaria transmission over the long term in areas outside of the United States and Europe. A case-in-point is the WHO-led "Garki Project", an intensive $6.1 million control project in Garki, Nigeria. As part of the project, WHO coordinated extensive insecticide spraying and mass drug administration in an attempt to totally eradicate malaria in 164 villages. The Garki Project had an enormous impact on the mosquito population in that area, reducing the biting rate of mosquitoes by 90%. But despite this dramatic decline, the prevalence of the malaria parasite among villagers did not significantly change. The vectorial capacity of the surviving mosquitoes was simply too high to overcome using these extensive measures that, according to the project's administrators, were too detailed and expensive to sustain over the long-term (Hamoudi & Sachs, 1999). Malaria transmission rates have escalated in sub-Saharan Africa as incidence rates for the rest of the world have dropped, largely because reductions in malaria-related mortality were thought unattainable by means of vector control in this region (Figure 2). WHO officials recently estimated that the annual number of childhood deaths from malaria in Africa now substantially exceeds the annual mortality rate reached a decade ago (WHO, 1999).

The advantages of indigenous activity and molecular approaches. Although Bti toxin and DDT may not be able to eradicate malaria in areas with high vectorial capacity, we can learn strategies for the development of other malaria control measures from the Peruvian discovery of mosquito control using Bti. It is essential that we note the origin of the Bti discovery--the means to culture and distribute the bacteria were discovered by researchers close to malaria-affected communities. Using their fundamental understanding of the lifestyle of people living in malarial areas and the resources available to them, the Peruvian researchers adapted their research process to find an inexpensive, simple, and effective means to control mosquito populations.

It is likely that indigenous discoveries like this one will provide some pragmatic means to control malaria, particularly in the years prior to the discovery of a malaria vaccine. As Tony Kiszewski of the Harvard School of Public Health states, "a program of empowerment of less wealthy nations by means of more effective application of sustainable (meaning cheap, locally available) intervention methods...reduces dependency on outside inputs from nations whose political predilections may falter or whose economic contingencies may change due to recessionary influences and the like" (Kiszewski, 2000).

But science and technology programs in countries with advanced economies (primarily the United States and European countries) acquire the vast majority of funds for research and development and patent their discoveries to enhance profit-making capabilities. Yet many of these advanced programs recruit scientists from these poorer countries. Research and development programs in malarial countries can provide concrete solutions to the malaria problem and other indigenous problems, but this would require that funds devoted to science and technology to be distributed to these groups. The success of indigenous efforts to control malaria therefore depends upon the commitment of scientists and policymakers in wealthy nations to share not only their expertise, but also their wealth.

No matter what innovative methods are produced through indigenous programs, it appears that the most effective means of malaria control will occur through research on the basic molecular biology of the parasite and vector associated with the disease. Bti toxin will likely have too many ecological ramifications and too little efficacy for widespread use in those areas most affected by malaria. Indoor use of DDT on house walls is likely to be an effective deterrent, but only in areas that are affected by indoor-biting mosquitoes. Other vector control programs are expected to have similar low efficacy. Vaccine development, on the other hand, is likely to have the most potential of any other control initiative. Vaccine development will rely on our molecular understanding of the parasite itself, which is extremely adaptable and also passes through a rapidly adapting vector, duping almost any control method that fails to combat it at a molecular level. Once again, the responsibility of sustaining research designed to counteract the effects of the malaria parasite falls on the shoulders of wealthy nations, who already have both the scientific technology and the money needed to sustain molecular research programs.

Conclusions

Controlling malaria will likely require the development and distribution of a malaria vaccine. While the development of such a vaccine is indeed feasible, it appears that the design process will take several years, both because of the biological challenge of producing such a vaccine and because of lagging support for research in this area. As some economists suggest, creating a market for a vaccine could aid its development and distribution. Before such a vaccine is produced, short-term solutions like vector control programs may assist populations in regions where mosquito vectorial capacity is not overwhelmingly high. These vector control programs, however, are unlikely to have high efficacy, particularly in regions that are most affected by malaria, although indoor DDT spraying will likely sustain the current level of control. Molecular-based research to develop a vaccine will be necessary to institute pragmatic solutions to the malaria problem in these hardest-hit areas. But tackling the malaria problem through the development of a malaria vaccine will require support from wealthy nations.

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Table 1: Number of malaria cases reported, 1985-1994

(data in thousands)

YEAR	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
Total	18 245	23 529	26 222	30 084	35 057	17 963	14 837	13 713	7 667	34 806
Total excluding Africa	5 038	5 603	5 633	5 372	5 676	5 661	5 843	5 329	5 077	7 162

Source: WHO, 1997

Figure 1

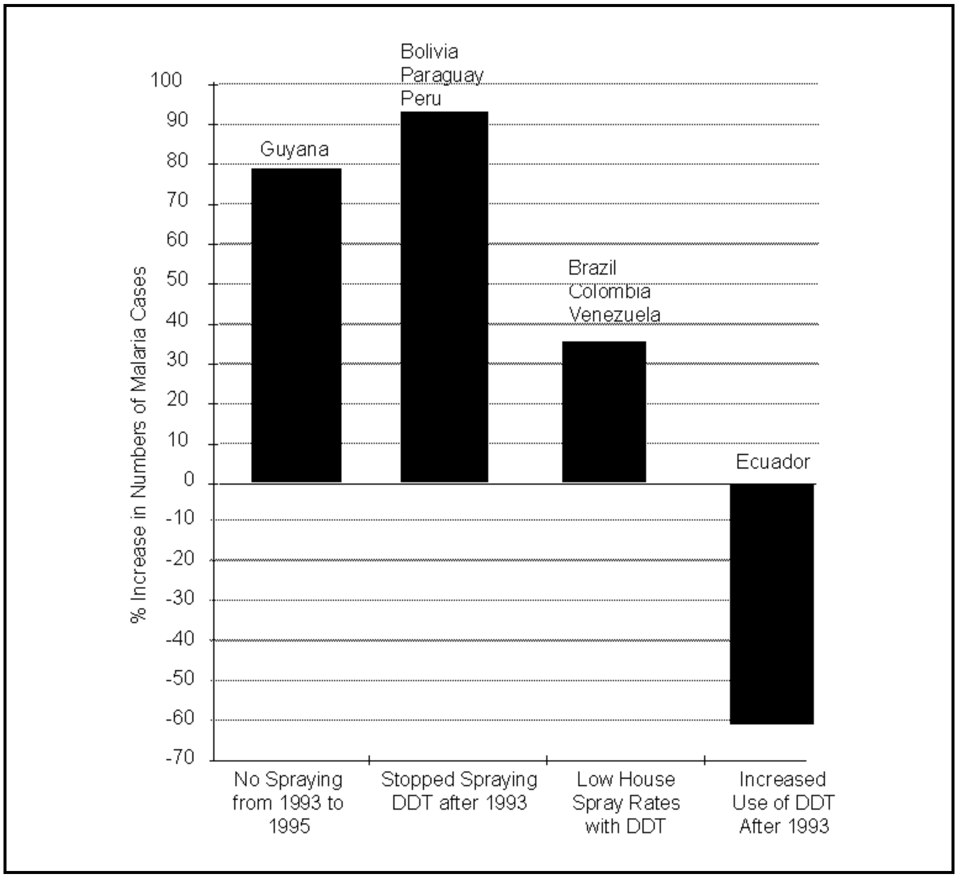

Figure 1: DDT use in Latin American countries correlated to changes in malaria incidence. Guyana stopped spraying DDT from 1993 to 1995; Bolivia, Paraguay, and Peru stopped spraying after 1993; Brazil, Colombia, and Venezuela have implemented low house spray rates since 1993; and Ecuador increased use of DDT after 1993.

Source: Basu, adapted from data presented originally in Roberts et. al., 1997

Figure 2:

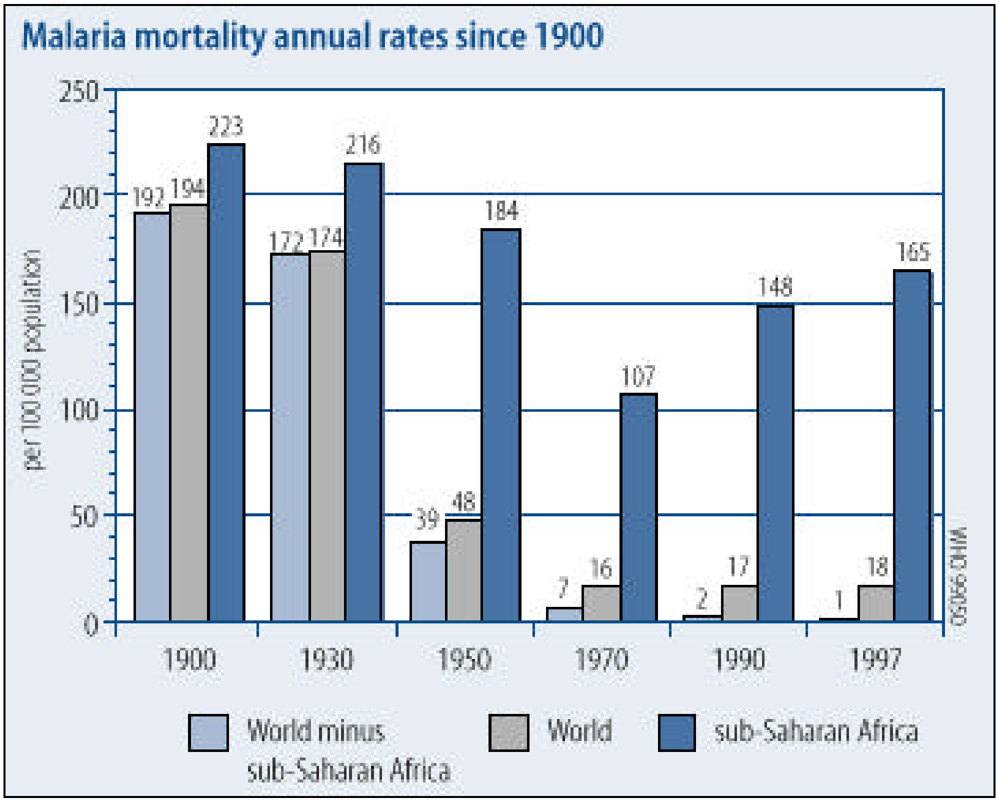

Figure 2: Although annual malaria mortality rates have sharply declined in most regions since 1900, sub-Saharan Africa continues to embrace the brunt of the world's malaria burden.

Source: WHO, 1999