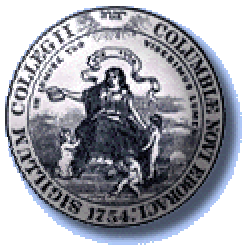

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A New Global Effort to Control Malaria

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The global campaign to eradicate malaria, launched in 1955 and phased out by the end of the 1960s, has been dubbed a misguided failure. Although the campaign did not come close to achieving its headline objective of eradicating malaria, it did lead to enormous and sustained reductions in the burden of malaria in dozens of countries around the world. Unfortunately, the world failed to heed the right lesson: global eradication is not feasible, but sustained malaria control restricting transmission to low levels is. The time has come to resurrect a worldwide effort to control malaria, albeit one not predicated on complete eradication of the disease.

There are four reasons to launch a renewed global campaign against malaria. First, the abandonment of control efforts has led to a marked resurgence in disease and deaths due to malaria in Africa and parts of Asia, partly because of the spread of drug resistance to first-line drugs and mosquitocides and partly because of the generalized collapse of public health services in Africa. The human and economic costs are horrendous, particularly in sub-Saharan Africa where malaria costs more than 1 million lives annually and 1 percentage point of economic growth per year (*1*). Second, substantial malaria control is possible by extending the coverage of existing technologies to impoverished households and communities. Third, advances in genomics including the completed genome sequences of the mosquito *Anopheles gambiae* (*2*) and the malaria parasite *Plasmodium falciparum* (*3*) offer promising new targets for drug and vaccine development (*4*). Fourth, MANY NEW PROGRAMS TO SUPPORT A GLOBAL CONTROL EFFORT HAVE BEEN ESTABLISHED IN RECENT YEARS, although lack of funds prevents THEM FROM OPERATING EFFECTIVELY AND AT THE NEEDED SCALE.

Global control efforts from the 1940s to the 1970s virtually eliminated malaria transmission in the sub-tropics (see the figure). Malaria became almost wholly a disease of the African tropics, where 90 percent of the malaria deaths now occur. The reasons for this are that the eradication campaign largely bypassed Africa and that malaria in the sub-tropics is easier to control because the intensity of transmission is much lower (*5, 6*). Still, successes in the sub-tropics and various sites in tropical regions (*7, 8*) demonstrated that intensive vector control measures combined with stepped-up coverage of medical treatment of infected individuals could bring transmission down sharply, and in some settings completely.

The eradication effort was abandoned when it became apparent that eradication was not possible. Resistance to DDT, the cornerstone of indoor residual spraying, appeared in mosquito vector species; meanwhile, the malaria parasite was becoming resistant to chloroquine and other first-line drugs. Yet, even when cases of malaria rebounded dramatically in some places (such as Sri Lanka) as a result of DDT-resistance,

malaria death rates rarely reverted to earlier levels. And even with DDT-resistance, the pesticide still proved effective in limiting transmission (9). In short, the eradication effort made real and sustained strides, and much more could have been accomplished. A deeper reason for abandoning the campaign may have been geopolitical. Malaria control had already been achieved in the Southern United States, Southern Europe, Southern regions of the Soviet Union, much of Latin America, and large parts of Asia, especially China. Moreover, by the mid-1970s, the United States had withdrawn from Vietnam, so that the U.S. military evinced a sharply reduced concern for malaria control. Impoverished Africans were not on the geopolitical radar screen.

The end of the global malaria eradication campaign coincided with a general downturn in foreign aid. Africa fell into a significant debt crisis in the early 1980s, from which it has not yet recovered. Creditor governments and international institutions such as the IMF and World Bank pushed for budget cuts in poor countries to make room for foreign debt servicing. Public health spending collapsed throughout Africa and with it the limited malaria control efforts that were in place. Spending cuts coincided with three other adverse trends in Africa, and parts of India, Southeast Asia and Latin America: (1) population growth pushed human settlements into new ecological regions supporting malaria transmission; (2) the growth of a "septic fringe" around Africa's sprawling urban settlements where urban transmission could thrive; and (3) the continuing spread of drug and pesticide resistance.

Donor fatalism also took hold in the shadow of the "failed" eradication efforts. The World Bank made only two loans in the 1990s specifically designated as malaria-control loans, to India and Laos, and not a single loan to Sub-Saharan Africa. Research programs of the U.S. military and USAID directed at a malaria vaccine or new drug development were cut back. The major pharmaceutical companies neglected malaria drug discovery or vaccine research because the travelers' market (visitors from the U.S. and Europe to malarious regions) was small and still handled by existing medicines.

By the late 1990s, much of the African political leadership had become desperate, and made a renewed malaria control campaign a pivotal demand during the election of the WHO Director-General in 1998. Roll Back Malaria (RBM) was launched by a consortium of the WHO, World Bank, United Nations Development Program, and UNICEF in November 1998. Other initiatives for drug discovery, vaccine development, and increased financing of control efforts, were launched including the research-oriented Multilateral Initiative on Malaria (MIM, in 1997), Medicines for Malaria Venture (MMV, in 1999), and the Malaria Vaccine Initiative (MVI, in 1999). The Global Fund to Fight AIDS, TB, and Malaria (GFATM, in January 2002) supports the implementation of prevention and treatment programs. All remain woefully under-funded and an effective international effort has not yet begun.

An effective campaign will need to operate on four principles. First, it should focus on the most afflicted region, Sub-Saharan Africa. Second, it should recognize that among the major epidemic diseases, malaria control is uniquely site specific, dependent on climate patterns, vector ecology and biology, and human activity. Third, the campaign should pursue two tracks: increased malaria control (both prevention and treatment) with existing technologies, as well as a major investment in R&D for new technologies. Fourth, and above all, it should be funded adequately and consistently for at least two to three decades if it is to have a chance of success. Current worldwide donor spending for

prevention and treatment programs is far below $500 million per year (and it is symptomatic of the laxity of global control efforts that up-to-date worldwide data have not been compiled). Actual needs exceed two billion dollars per year, and probably more to fund replacements for chloroquine and other drugs to which resistance has developed.

Promising new drugs already available but not yet in widespread use include the artemisinin-based compounds, developed in the 1970s by Chinese scientists from derivatives of the traditional Chinese herbal treatment *Qinghaosu*. Donors have been reluctant to support the introduction of artemisinin into Africa, both because of its high unit cost relative to chloroquine and other first-line drugs—chloroquine costs ~10 cents for a curative regimen whereas artemisinin costs $1—and out of fear that artemisinin too will rapidly generate resistance. To counteract this risk, artemisinin-based compounds should be introduced in combination with other anti-malarial drugs. Ironically, the delay in sponsoring such an approach is leading to the indiscriminate spread of artemisinin-based monotherapies through informal drug supply networks in Africa.

IN REGIONS OF INTENSIVE ECONOMIC ACTIVITY (MINES, OIL FIELDS, RUBBER PLANTATIONS, URBAN ZONES, TOURIST SITES), CORPORATE ANTI-MALARIA EFFORTS BOLSTERED BY PUBLIC SUPPORT CAN MAKE A SIGNIFICANT IMPACT (11). SUCCESSFUL CORPORATE EFFORTS GENERALLY RELY ON AN INTENSIVE MIX OF ENVIRONMENTAL VECTOR-CONTROL MEASURES, INDIVIDUAL PROTECTION FOR WORKERS THROUGH MEASURES SUCH AS HOUSEHOLD RESIDUAL SPRAYING, AND CASE MANAGEMENT. RECENT INITIATIVES BY THE WORLD ECONOMIC FORUM AND OTHER BUSINESS GROUPS AIM TO LINK THESE CORPORATE EFFORTS TO BROADER INTERNATIONAL ANTI-MALARIA CONTROL PROGRAMS, OFTEN THROUGH FORMAL PUBLIC-PRIVATE PARTNERSHIPS (12).

Longer-term solutions will come from new drug discovery and especially vaccine development efforts based on recent genomic advances. No major pharmaceutical company reports a major malaria research effort. The Gates Foundation has valiantly aimed to spearhead new research by supporting the drug-development MMV and the MVI. MMV has the declared goal of developing one new anti-malarial drug every five years at a cost of $150 million, or $30 million per year, plus significant "in-kind" industry support. These numbers are below most estimates of drug development costs, and are very unlikely to cover the high expenses of drug trials. A reasonable estimate of total worldwide public and private annual spending on malaria drug and vaccine research is less than $100 million, or less than one-seventh of one percent of the $70 billion or more of annual worldwide biomedical R&D, for a disease that accounts for an estimated three percent of the worldwide disease burden as measured by disability-adjusted life years (*13*). R&D donor needs for drugs and vaccines are around $1 billion per year on a sustained basis, compared with current annual spending of less than $150 million.

The RBM consortium, headquartered at WHO, should serve as the nerve center of a renewed global effort to fight malaria. This consortium should immediately prepare a comprehensive strategy that includes an operational multi-year plan of action together with a full assessment of donor funding needs. The proposed budget should clearly delineate the separate needs for current prevention and treatment programs, largely funded through the GFATM and the World Bank; the rapid development, clinical testing, and procurement of artemisinin-based and other drug combinations; and the outlays for

R&D for new drug discovery and vaccine development, including effective systems for high-cost clinical trials. Annual outlays by donors must reach several billion dollars per year for a generation or so to get malaria under control in endemic areas of Africa and Southeast Asia. But this will be a very small price to pay for millions of lives saved per year and hundreds of millions of people given a chance to escape from the vicious cycle of poverty and disease.

References and Notes

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5. The basic reproduction rate increases with temperature (and thus is higher in the tropics) and depends on the human biting rate of the vector, which is particularly high for the dominant African vectors Anopheles *gambiae*, *A arabiensis* and *A. funestus*.

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9. DDT still reduces the longevity of DDT-resistant mosquitoes, thereby reducing the force of transmission. DDT's use for indoor residual spraying poses no known ecological dangers, as opposed to its use in much greater volumes for agriculture.

10. Some health-sector loans included small amounts for malaria control. See the "Project Database" on the Malaria Home Page of the World Bank, http://www.worldbank.org.

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13. The WHO commission on Macroeconomics and Health (2001) estimated that the direct costs of malaria prevention and treatment would require an additional $2.5 billion per year by 2007, but that estimate does not fully account for the increased overhead costs of an expanded health system nor the costs of introducing new drugs to overcome drug resistance.

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FIGURE LEGEND

The shrinking range of malaria is depicted by overlaying WHO maps for malaria risk for the years1946 (pink), 1966 (red) and 1994 (brown). Source, (*13*).