Published in final edited form as:

Future Microbiol. 2008 October ; 3: 479–483. doi:10.2217/17460913.3.5.479.

Malaria control in Africa: a mirage à trois

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‘...we are moving forward with neither a detailed plan of attack nor the epidemiologic information necessary to establish one.’

The WHO, The Bill and Melinda Gates Foundation and the President's Malaria Initiative, among many other charitable organizations, have lately demonstrated a deep commitment to combating the rising malaria-related death toll in Africa. While one may wonder whether malaria eradication is possible, at present there is hope of providing an extended period of relief

from the disease for large regions of Africa, similar to that which occurred in India as the result of an earlier eradication program. Extended relief from the disease would not only save many lives but would also help provide a window of opportunity for economic development as it has in India. It is an issue of concern, however, that participants do not agree on either a common goal or the necessary duration of commitment. Furthermore, we are moving forward with neither a detailed plan of attack nor the epidemiologic information necessary to establish one.

The goal

The immediate goals of the three primary organizations vary considerably. The President's Malaria Initiative has set a goal of cutting the malaria death rate in half by the year 2010 when the initiative ends. Leaving the continent having reduced the death rate by half is a wonderful achievement, but one whose benefits will quickly and continually erode. Hence, preventing a million childhood deaths in 1 year does not mean that a million more children will reach adulthood. If the programs are stopped, the children again become vulnerable. The goal of the WHO is also to reduce the death rate, but the organization has not set a date of withdrawal. The Gates Foundation has announced a goal of total eradication of the disease. The need to staff each of the three organizations with experienced personnel from an already shallow pool has not served to advance any of the programs.

The plan

There is presently no agreement, or even much discussion, regarding a structured approach that would address the whole of Africa and one that would take into account the geography and demographics of the continent. Present plans often appear to focus solely on expanding the level of distribution of bed nets, insecticides and antimalarial drugs. Success against malaria will, however, also involve the initiation and implementation of regional programs whose success can be monitored and a strategy to expand these programs into all endemic regions of Africa.

George MacDonald presented a generic approach to malaria eradication that included four distinct phases (preparatory, attack, consolidation and maintenance) [1]. This approach includes all the elements that need to be addressed for there to be any hope of success. Present plans make little mention of anything but an attack phase, despite the fact that the lack of a preparatory phase invites failure and the lack of formal plans to prevent re-introduction of the disease to malaria-free regions (consolidation and maintenance phases) will almost certainly lead to disaster.

Preparatory phase

It is often said that malaria is a local disease. The various parameters that affect the degree of transmission vary from place to place and from year to year. Hence, we have neither the baseline numbers to describe the present situation(s) with regard to malaria in Africa nor the means to measure future progress in our fight against the disease. Yale University's Wilber G Downs summed up the situation over 25 years ago [2]:

'One gets a figure for how many cases were reported for the past year. This figure, to anyone who has worked seriously with malaria, can be seen to be an utter fabrication. But this figure of malaria cases rises from the clinic to the level of the statistician and gets immortalized in WHO or PAHO annual reports'.

Although of primary importance, the situation is no better today than it was 25 years ago. We do not even know the actual death rate from malaria. The estimates so often quoted in the media are based on quasi-scientific data (e.g., oral autopsies) gathered from a small area and then extrapolated to represent all of Africa. For example, while the WHO estimates that there are a

million or more malaria deaths per year, their website reports only 112 laboratory-confirmed malaria deaths in all of Africa for 2003. This is not a criticism of the WHO or those who develop approaches for the analysis of existing data; it is simply a statement about the degree of uncertainty we will face in a malaria-eradication campaign.

In addition to the above, we have no record of either the changes in disease prevalence over time, the distribution of the mosquitoes that transmit malaria or accurate regional measurement of insecticide resistance. Without this information we have no foundation on which to develop intervention strategies, and no means to judge their success.

Attack phase

Are we capable of eradicating malaria in Africa even with the increased funds at our disposal? History suggests that we are not [3].

It has been suggested that our best opportunity for achieving malaria eradication occurred during the period after World War II. We then possessed the best 'one-two punch' that has ever been available to fight malaria in the insecticide DDT, essentially a nerve gas for mosquitoes, and chloroquine, a potent antimalarial drug to treat the disease. Since these compounds were recently discovered and in use for only a brief period of time, there were no forms of insecticide-resistant mosquitoes or drug-resistance malaria parasites to confound our efforts. We do not know what would have happened had the WHO acted immediately on the advice of an expert panel in 1950 and proceeded with an eradication program, but they did not. By 1962, when the WHO's global eradication program was initiated, the use of DDT in agriculture had led to insecticide resistance in a growing number of regions and this may have factored into their decision to omit sub-Saharan Africa from the global eradication program.

The WHO did, however, conduct a number well planned and amply funded studies in each of the distinct environmental regions of Africa in the two decades following World War II to determine the feasibility of malaria eradication. These were successful in dramatically reducing the disease and interrupting the malaria transmission cycle in all the distinctive environmental regions of Africa except the lowland savannah. The pilot projects culminated in the Garki Project, whose mission was to use all available tools in a small and well-defined area to determine whether it was possible to break the malaria transmission cycle in this environment. Even with a combination of the best indoor residual sprays, the most effective antimalaria drugs and a well-staffed clinical infrastructure, they were unable to interrupt disease transmission in this hyper-endemic region. Hence, researchers were left to conclude that there would be places in Africa that would always serve as a reservoir for re-introduction of disease and that eradication was beyond their present capabilities.

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Methods used to interrupt malaria transmission have not changed dramatically over the past 70 years, raising the question as to whether we have the means to dramatically reduce malaria. Despite widespread resistance to its insecticidal properties, DDT is still one of the mainstays of our approach. The only dramatically different directions being taken today are the distribution of insecticide-impregnated bed nets and, as a result of a keener awareness about how drug resistance arises, the use of new antimalaria drugs in combination.

The insecticide-treated bed net (ITN) selectively kills the mosquitoes that are attracted to the scent of the humans sleeping inside. A single occupied net can kill a large number of malaria-carrying mosquitoes, thereby lowering the level of transmission in the local area and protecting people during the times that they are most likely to be bitten by infected mosquitoes. Perhaps the most important considerations relating to bed net use are how to prevent resistance to the

insecticide, pyrethrum, from arising and how to convince people that it is in their interest to use the nets. Keeping people under ITNs from dusk to dawn, when most transmission occurs, is difficult because the nets prevent air circulation and are claustrophobic. Furthermore, it is estimated that six lives are saved per every 1000 that are provided netting [4]. It would therefore appear that bed nets are a means of control but not eradication. However, the secondary effect of ITNs in lowering the transmission level is not well understood and may be a significant factor in reducing disease.

Consolidation & maintenance phases

Following a successful attack on mosquito and human reservoirs of malaria, a consolidation phase would require the continual presence of medical personnel to monitor for new outbreaks in the area. Malaria parasites can remain in the blood of humans for years after the transmission cycle has been broken, and therefore potentially serve as a reservoir for re-introduction of the disease [5,6]. The consolidation phase is necessary because parasites remain in the blood long after transmission has been interrupted. This phase is predicted to last about 3 years, the same period of time that immigrants from endemic areas are restricted from donating blood in the USA.

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The maintenance phase would be focused upon preventing re-introduction of the disease from an outside source such as a visitor to the area. Maintenance is especially problematic in Africa because a significant number of Africans continually migrate across great distances, creating both a moving target for treatment and a moving reservoir for re-introduction of the disease [5]. There are a number of reasons why migration is a difficult issue to address in Africa. The first has its basis in the history of Africa. Centuries ago, migrations caused by famine and war fragmented large homogeneous populations and left regions of the continent a patchwork of tribal groupings. Related villages are distributed over great distances, often across national boundaries, and these are interspersed among other village groups with different languages and social customs. Visitation between widely dispersed peoples who share language and heritage is part of the African fabric that will not change in the near future.

The migration of individuals as a result of poverty and the need to find work is a second obstacle for isolating regions for the purpose of malaria control. Mansell Prothero writes about people in West Africa who are known as ‘men who eat away the dry season’ [5]. These are men who go away from their villages in the dry season to work and by doing so help to conserve the limited food supplies of their home areas. Unfortunately they return home with diseases, including malaria [5].

A pan-African strategy

Given that we can secure local areas, there must be a plan to extend our gains throughout the continent if we want to eradicate malaria. Mansell Prothero described such a plan in 1965 in his book, *Migrants and Malaria in Africa* [5]. Recently, others have initiated debate about global strategies that are reminiscent of Prothero's approach.

In a recent issue of *Lancet*, Feachem and Sabbot proposed that countries on the margins of endemic zones should be the initial targets of malaria eradication programs [7]. The plan would gain momentum as neighboring countries were cleared in that the potential for re-introduction of the disease across their common border would be eliminated. As areas are cleared of malaria new regions would be targeted. The ratcheting effect would continue until malaria was eradicated or better approaches surfaced and were adopted. Although the process would take generations, it would continually produce sustainable gains and save more lives. The central

problem would be effectively sealing off borders between regions that have malaria and those that do not.

The danger of leaving before the job is done

In 1950, some of the most experienced and knowledgeable malaria experts in the world met in Kampala, Uganda to develop a plan to stamp out the disease with modern weapons, such as the insecticide DDT [8]. This meeting is often cited as the starting point of all such international efforts. One would think that the most pressing question addressed at the conference would have been how to do it rather than whether to do it, but it was not. The Kampala conference turned into a contentious debate that focused on the issue of ‘natural immunity’ to malaria and whether an eradication attempt would or would not ultimately reduce the malaria death rate among African people.

The loss of acquired immunity

Constant exposure to malaria elicits a protective immune response in humans. Often children become sufficiently immune to the disease by school age that they appear and feel healthy even while infected with malaria parasites. However, the number of children who die before they become immune is extremely high. Furthermore, the protection provided by naturally acquired immunity is lost if the individual is not constantly exposed to the disease. Hence, local eradication efforts would progressively result in the loss of immunity, making residents of that area susceptible to the disease should it be re-introduced.

Epidemics associated with the late stages of eradication programs

Epidemics represent a predictable element, and danger, of late-stage eradication programs. The source of malaria parasites can be a single infected individual who comes into the region or the recrudescence of the disease in a local resident. A feature of this type of epidemic is the rapidness with which it spreads. The effect is explosive. Initially, the number of cases of malaria resulting from a single infected individual can increase geometrically and cause a local calamity within a relatively short period. The rapidness of the spread relates, in part, to the waning of naturally acquired immunity (described above) in the area. Hence, the potential for malaria to spread rapidly from a few cases is much higher in such a situation than it is in an area that is endemic for malaria. Vigilant screening and rapid action to treat each case before it becomes a source for new infections is imperative long after the transmission cycle has been successfully interrupted and the program appears to be a success. Such an episode occurred during the eradication programs in India and Sri Lanka [9].

The eradication program in Sri Lanka had reduced the reported malaria to a handful of cases by 1967 [9]. Mosquitoes that commonly transmit the disease were still in the area, however, and a reservoir of malaria still existed in humans in the form of a relapsing parasite, *Plasmodium vivax*. An expansion of the mosquito population, perhaps as the result of climatic change, increased the existing potential of transmission. Popular resistance to indoor spraying programs that seemed no longer necessary, and the presence of insecticide-resistant mosquitoes were almost certainly factors as well. The available reservoir plus the expanded vector population led to a dramatic increase in the transmission of malaria and local epidemics within a short period of time. Hence, an infected individual in areas that are otherwise free of malaria presents a danger and can be the source of a large number of subsequent infections, especially if an efficient mosquito vector is in the area.

Effecting change from outside

There seems to be a common theme relating to the failure of malaria programs. They are carried out as 'blitz wars', meant to be won and withdrawn from within a fixed time. Such an approach entails gaining everyone's cooperation simultaneously.

Countries with a strong centralized government are often more successful in eradicating a disease than countries where the real power rests at the local level. The latter is often the case in Africa. National boundaries were drawn during colonial days and do not reflect the cultural diversity and tribal organization of the continent. Hence, successful cooperation in any venture, including malaria control, must be obtained at a local level, one village at a time. Administering assistance through a central government that is not representative of many sectors of society has consistently undermined our agendas.

Possible alternatives

We have a moral responsibility to help Africa with the malaria problem, but to look solely to scientific innovation for an answer may not be in their best interest. There are at least two practical areas that deserve attention and will most certainly result in long-term gains in the war against malaria.

Supporting existing programs created & run by Africans

There are a number of Africa-based organizations with the capability of addressing malaria but lacking the essential tools. Ogobara Doumbo, an outstanding physician who runs a uniquely successful protocol to reduce malaria in the African Republic of Mali remarks [Pers. Comm.]:

'Almost every day that I am in the field a child dies in my hands because of malaria. I could prevent that death. If a child has a seizure he needs gelatin. I don't have it. If he is anemic he needs blood. I don't have it. If he is in a comma he needs glucose. I don't have it. I can't do my job.'

When supplied with microscopes and the necessary medications the story is different he adds:

'Where we go there are no deaths. What I have realized is that to sustain programs we must give people at risk their own power.'

Economic development

The disappearance of malaria from the northern part of the USA and parts of western Europe are often given as examples of successful eradication programs, but few are aware that the disease was not eradicated as part of a concerted health program. Malaria had primarily disappeared from a number of formally endemic areas before the modern tools of eradication were discovered. DDT, for example, was only used in a few local areas of southern USA, where the last small pockets of the disease remained until the 1940s. The driving factors that resulted in malaria elimination in the USA and Europe are still a matter of debate, but it is generally agreed that economic development, which resulted in better housing, education and land management was a major factor. Malaria was a serious problem in the mid-1930s and was essentially gone by the mid-1940s. Africa represents a more difficult problem, yet there is no question that malaria spawns poverty and poverty spawns malaria. Breaking this cycle will create a future for many Africans.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or

materials discussed in the manuscript. This includes employment,consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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