

Testimony for “Neglected diseases in East Asia: Are public health programs working?” .

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The manner in which an industrialized nation comes to the assistance of the tropical third world's health problems is a faithful representation of its economic and diplomatic policies. It is also a reflection of its moral and ethical values. In turn, malaria has traditionally been the “epidemiological metaphor” to analyze and assess donor health programs and strategies. But malaria, especially in its most lethal guise caused by *Plasmodium falciparum* is more than a metaphor. It is estimated to kill between 2 and 3 million each year; young children and pregnant women being its chief victims. It is a major cause in hyperendemic regions of spontaneous abortion and low birth weight babies. Billions of tropical and subtropical peoples are at risk, hundreds of millions are infected. Even in its non-lethal form, caused by *Plasmodium vivax*, it is responsible for untold sickness with the debilities of anemia and recurrent fevers. Populations burdened with malaria suffer from the lethargy and cognitive defects that inhibit economic, technological and cultural progress.

Our country has had a long, and continuing interest in malaria. First, because of our epidemiologic history in which from about 1542 to 1942 we have been a “tropical” country with entrenched “tropical diseases”. Malaria, which in my 1995 Gorgas Memorial Lecture at the National Institutes of Health I characterized as being “as American as the heart attack”, was entrenched in a vast zone between Florida and New York. Second, malaria has been a major factor in the prosecution of our tropical wars with, for example, as many troops in Vietnam being disabled from combat by malaria as by the wounds of war. The military has responded since the 1940's through their medical research establishments at home and abroad which continue to be highly productive. The Army, at Walter Reed Army Institute of Research with its satellite laboratories in endemic sites such as Thailand, Kenya, and Malaysia. The Navy at its Medical Research Center in Bethesda and satellite units in Egypt and Indonesia. I would particularly note the military's contributions to medical entomology and discoveries of new antimalarial therapies. In the civilian research arena the National Institutes of Health's Malaria and Parasitic Diseases Laboratories are internationally renowned for their basic research on the malaria parasites.

There has also been a long and large body of federally funded research coming from universities and institutions. The Centers for Diseases Control and Prevention (CDC) have continuing activities in malaria, their great strength being epidemiological and operational studies in endemic settings. There have also been American organizations to promote the public understanding of malaria and facilitate interchange of ideas and knowledge between malaria researchers throughout the world. The Malaria Foundation International, based in Atlanta with its founder Dr. Mary Galinski of Emory University at the helm is the most notable organization and has the great potential ability to be a non-biased, non-government instrument to organize working parties for strategy sessions. More recently the Bill Gates Foundation is funding malaria projects with a generosity reminiscent of the Rockefeller Sanitary Commission and Foundation of the

early 20th century.

Our government has also had a long history of contributing to international malaria endeavors. There is the \$800 million, in 1960-1970 dollars, we gave to the World Health Organization for their Global Eradication of Malaria program - that was neither global nor eradicating. The international malaria activities of our own Agency for International Development is now, quite properly, under scrutiny by this and other congressional committees. It is estimated that the USAID annual budget for malaria is \$85 million. In addition, since 1972 when USAID embarked on their malaria vaccine project I estimate a further \$250 million has been spent. The project has produced 5 convictions for criminal felonies but no vaccine.

It is the inherent nature of the scientific establishment to complain that there is never enough money to make the progress they envision to bestow the benefits of research on suffering humanity. Malariologists, basic “molecular” laboratory-based researchers and applied “field hands” alike are given to much hand wringing and in supplicating for more funding invariably citing the 2-3 million annual malaria death rate. From my now comfortable position of retirement - free at last from grant writing, I would offer the, no doubt challengeable, opinion that the total monies, from American and international sources are adequate to bring the malaria carnage to an end. That malaria is an eminently treatable disease and no child, born and unborn, no pregnant woman, no non-immune adult transmigrant need suffer or die of malaria.

1. Prevention, let alone eradication, is problematic. There are the means to reduce transmission, notably DDT and insecticide-treated bednets which I will speak to later. Priority should be to furnish and deploy appropriate, effective antimalarial chemotherapy in the endemic areas of South/SE Asia (as well as in Africa and other regions such as Melanesia).

The cheap, former sheet-anchor of antimalarial therapy and prophylaxis, chloroquine, is now virtually useless, because of parasite multi-drug-resistant strains of *Plasmodium falciparum* and to a growing extent against *Plasmodium vivax*. Furnishing of chloroquine by donor agencies is useless - and dangerous. Childhood mortality can rise as much as eleven-fold when it is not replaced. Until recently the Global Fund on the advice of the WHO representatives in Africa (and elsewhere?) were still buying chloroquine to distribute to the health services of sub-Saharan nations. The overall and nation-specific antimalarial drug policy(s), if any, of USAID must be scrutinized by unaffiliated experts as expeditiously as possible.

The antimalarial of choice is the artemisinin combined therapeutic (ACT) Coartem (artemisinin+lumefantrine) which rapidly resolves parasitemia and fever in severe, multi-drug-resistant falciparum malaria. It also has the unique property of acting against the gametocytes (the stages responsible for transmission through the Anopheles mosquitoes) and thus has a useful transmission-lowering action, especially when used in conjunction with DDT spraying. Most sub-Saharan African nations have now designated Coartem as the antimalarial of national policy and its purchase is being funded by the Global Fund and other donor agencies. Coartem is also being used, to an increasing degree, in SE Asia, especially in the hyperendemic areas of the Thai-Burma border, Cambodia, Vietnam and Laos. It is essential that USAID adhere to and support these

national policies for Coartem's use in the treatment of falciparum malaria¹. Recent work by Dr. Francois Nosten and his colleagues on treating pregnant women in the unstable situation on the Thai-Burma border indicates that Coartem is safe when used to treat malaria of pregnancy. Coartem is relatively expensive but the day of the 10 cents chloroquine treatment is over - gone! finished! - and I believe no American would deny a child his or her life for what would be the cost a bottle of aspirin.

2. DDT has once again returned to become a contentious issue as an anti-malarial strategy. A product of World War II research (in Switzerland) it remains the unique insecticide by virtue of its long residual (up to 6 months) activity, its safety for humans, and its dirt-cheapness.

There is now a coterie of American scientists and science journalists who are vigorously advocating - demanding - that DDT be returned to the antimalarial armamentarium. Indeed, countries such as Ethiopia and South Africa have effectively deployed DDT to combat recent malaria epidemics. Several months ago the National Academy of Sciences/Institute of Medicine convened a meeting to reconsider the introduction of DDT. A report of the meeting has not been forthcoming and may never be forthcoming as the NAS feels the heat from the "Silent Springers". At that meeting I voiced my belief that DDT is incomparably useful - where it is useful. And I voiced my concern that the new combative passion for DDT may unrealistically overstate the case. An axiom of malaria control is that each of the 50, or so, Anopheles species that are malaria vectors has genetically determined characteristics (biting preferences, breeding-water preferences, post-feeding behaviors, insecticide resistance) that make it a target or non-target for attack by DDT. A wry "in" joke amongst the surviving "field hands" malariologists is that the only thing the WHO global malaria eradication program eradicated was the malariologists. A real problem, as I see it, is that we do not have the contemporary epidemiological/entomological intelligence from this absent/diminished expertise to formulate region-specific logical strategies for malaria control.

3. Insecticide treated nets (ITNs) are a favorite antimalarial strategy of donors. They are easy to buy, easy to distribute (for free). Pilot studies have resulted in a 30% reduction in malaria-caused mortality. Other pilot studies have shown little or no effect and a few studies, mortality has actually risen. Going against convention I would give ITNs lower priority for funding if it competes with chemotherapeutic needs.

4. Again, contrary to fashionable molecular frontier malariology I offer my opinion that the much heralded malaria vaccine is a goal, an illusion, that has not been realized and may never be realized in combating the disease at a population level.

Research on the vaccine has been pursued for over 70 years with increasing intensification

¹Coartem is the only ACT formulation that is produced commercially. It is an approved drug in Europe but Novartis has no intention of seeking FDA approval in the United States. The Coartem treatment pack of 24 tablets sells for \$30 to \$50 in Europe; however at the 2003 consultative meeting, which I attended, called by Novartis, the company declared that as a responsible global industrial citizen they would sell it to Africa at their manufacturing cost - \$1!

of the effort during the past 30 years. Hundreds of millions of dollars, the energies and resources of some of our best scientific minds have been, and are, devoted to vaccine research. It would be appropriate to now reexamine the overall malaria vaccine programs and determine whether some of those resources, intellectual and financial, should be redirected to applied malariology.

Some recommendations for the committee's consideration:

1. We urgently need an independent American panel of experienced malaria experts who can speak with authority to authority (such as this Committee).
2. The panel should have a relatively long term working life, probably over several years and be funded for its various investigatory and administrative needs. There was such an assemblage in the early 1970s, the Effect of Herbicides in Vietnam Committee (in which I headed the epidemiological investigations) under the administration of the National Academies of Sciences and funded by Congress that worked very well. The malaria panel could similarly be organized by, and work under NAS, possibly in collaboration with the Malaria Foundation.
3. The panel should critically examine American malaria programs and American programs that interface with international programs such as the WHO Roll Back Malaria. This is especially true in respect of USAID's malaria, funding, policies and activities. The panel would therefore need authority to speak with USAID personnel within the United States and at their overseas postings, and have access to their records (much in the manner that the herbicide committee had in respect to military personnel and their spraying records).
3. The current lack of good malaria-entomological intelligence should be addressed by the panel and have the funding to act on this. The appropriate experts of the panel (and the experts they would need to coopt) should be able to obtain country-by-country inventory on vectors, their behaviors, and suitability for attack by DDT as well as the suitability of ITN distribution.
4. USAID should carefully consider, if not be obliged to follow, the expert panel's findings and decisions - especially in respect of chemotherapeutic and DDT deployments. There should be a reevaluation of United States' obligations and interactions with international bodies, notably the WHO, on the basis of the panel's findings.
5. The guiding principle of America's malaria activities should be to save lives as expeditiously as possible- to drug malaria into submission, to end the carnage of the young and pregnant in the malaria regions.