

EPIDEMIC - On the Front Line

Malaria kills one child every 30 seconds worldwide, and Kyle Webster aims to stop it.
Janet Wells. *The San Francisco Chronicle*. 5 June 2005

Malaria is ancient – older than man, most likely – and has killed more of the human race than any other single entity. The deaths of Alexander the Great and Genghis Khan? Probably malaria. Oliver Cromwell and Caravaggio? Malaria. Modern luminaries who had malaria and recovered: Sir Arthur Conan Doyle, Ernest Hemingway, Ho Chi Minh and John F. Kennedy...

Only AIDS rivals malaria as a leading cause of infectious-disease fatalities each year. But much of malaria's devastation comes from its insidious persistence, rather than its deadly aim. The *P. falciparum* parasite is the cause of nearly all malaria deaths and a large proportion of the morbidity. But it, along with the other three malaria parasites that invade humans – *P. vivax*, *P. malariae* and *P. ovale* – can be readily cured. But most countries can't afford the best drugs, nor do they have the resources to keep malaria from recurring. Anopheline mosquitoes come around every evening, and malaria returns, causing widespread anemia, learning disabilities and brain damage in children...

Since 1988, an ongoing civil war and military dictatorship have driven 400,000 Burmese – many of them ethnic minorities – to flee through the malaria-ridden jungle to Thailand. Another half-million have been uprooted from their homes and pushed into makeshift villages in eastern Burma, where the conflict still simmers.

While malaria still plagues Thailand's border provinces and consumes considerable resources, it is well controlled. Next door, however, malaria is the leading cause of disease and death.

In eastern Burma, the repressive government provides little or no health care and strictly prohibits access by foreigners. Among internally displaced refugees, malaria constitutes one-

quarter of the caseload and leads to 44 percent of the deaths, according to data compiled by the Los Angeles-based Global Health Access Program (GHAP), one of the few organizations currently funding a malaria control program inside Burma's conflict zones.

With resources and training from GHAP, refugee health workers distributed insecticide-treated bed nets to 3,500 displaced villagers in eastern Burma in 2003, tested the villagers for malaria, and gave

drug therapy to those with a positive test, whether or not they were sick. The health workers returned at six-month intervals to test and treat again. The idea was for the drugs to attack malaria lurking in the human reservoir, and for the bed nets to keep the mosquitoes at bay, preventing the reservoir from filling up again. In two years, the program resulted in a 90 percent decrease in malaria in the five pilot villages.

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In one of the pilot villages in 2004, a villager broke into a betel-nut-stained grin when asked about her health by a visiting reporter. “I used to have malaria very often, three, four times a year,” said the 20-year-old woman, in Karen, a hill-tribe language translated by a medic. The woman's young children sat next to her on the bamboo slats of their rickety open-air hut. “After the net, zero malaria. The children, too. I thought I was going crazy. I didn't think a net could stop malaria.”

One of the village elders added with a laugh, “This is like malaria-free zone.”

The drug that GHAP used with such resounding success? Artemisinin. By the late 1990s, the drug was being heralded as the malaria miracle. While Western pharmaceutical companies ignored artemisinin, the Chinese quietly pioneered the development of derivatives like artesunate and artemether.

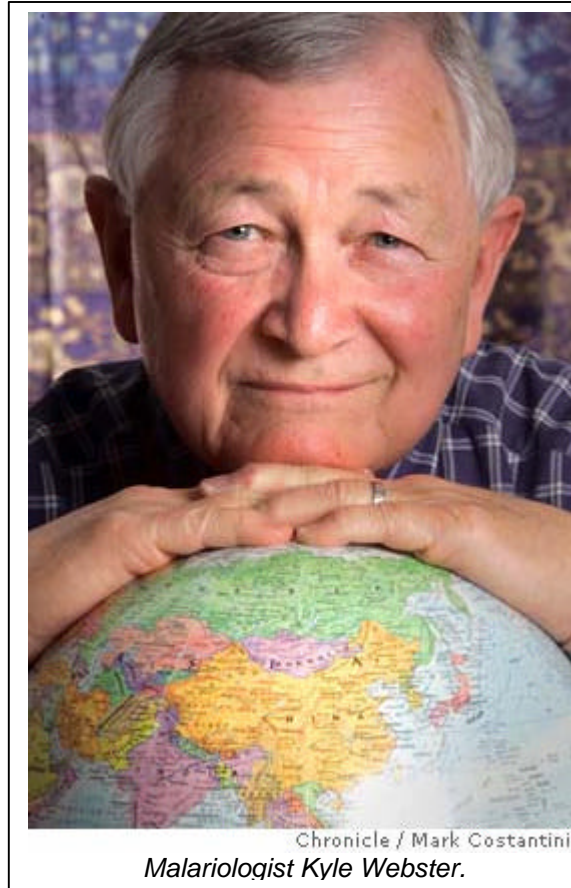
Artemisinin-class drugs have not been approved by the U.S. Food and Drug Administration, and a lack of long-term clinical safety data concerns some scientists. However, based on studies done in Asia and Africa showing minimal adverse effects, the World Health Organization adopted artemisinin therapy as its recommended malaria treatment worldwide. The derivatives have saved countless lives, and so far, the malaria parasite has exhibited negligible resistance. (To keep it that way, artemisinin derivatives are combined with older malaria drugs, giving the parasite a one-two punch.)

But artemisinin drugs have a downside: They cost as much as \$2.40 per adult dose (compared to 10 cents for chloroquine) – out of reach of most developing countries and cash-strapped humanitarian organizations. In addition, because of increased demand, the price of China's sweet wormwood tripled this year, making supplies scarcer, and rampant counterfeits have flooded the world market.

This year, GHAP expanded its malaria control program to 11 more villages, covering 10,000 refugees in eastern Burma. The group could do even more if it had cheap, ready access to drugs, test kits and nets.

“Could we expand the program to cover the majority of [internally displaced persons]? Sure, if the resources were there,” said Dr. Adam Richards, GHAP's malaria program manager. “We have the most drug-resistant malaria in the world. We need artemisinin combination therapy because nothing else works.”

That's where [Kyle] Webster and OneWorld Health come in. With a \$42.6 million grant from



Chronicle / Mark Costantini
Malariologist Kyle Webster.

the Gates Foundation, OneWorld Health, partnered with UC Berkeley and Amyris Biotechnologies, is working to perfect a microbial factory for making artemisinin and to develop the process for large-scale production. The goal: in five to seven years, a readily available, FDA-approved genetically engineered drug as potent and curative as plant artemisinin derivatives, selling for under \$1 per dose...

For Webster, the value of artemisinin isn't just academic. In Thailand, after two drugs failed him, he was on the verge of undergoing intravenous quinine therapy, which can lead to cardiac arrest.

Instead, he thought about the vial he had carried back from China years before. While the Army had none of the then-experimental drug, Webster went across the street to a Thai colleague, Sornchai Looareesuwan, whose lab was getting ready to put the drug into clinical trials. Kyle Webster was probably the first Westerner to take an artemisinin derivative for malaria. By the next day, he was back at work. Within a week, the parasites were gone from his bloodstream.

“It was,” he said simply, “dramatic.”

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Excerpts taken from “EPIDEMIC - On the Front Line - Malaria kills one child every 30 seconds worldwide, and Kyle Webster aims to stop it” by Janet Wells, which appeared in the San Francisco Chronicle on Sunday, June 5, 2005.