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Self Experimenters: Malaria Vaccine Maven Baited Irradiated Mosquitoes with His Own Arm

Stephen Hoffman has given years of sweat—and lots of blood—on his quest to stop a global killer
By David Biello

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Stephen Hoffman allowed 3,000 mosquitoes to bite him with radiation to weaken the malaria parasites inside them to bite him and render him immune to the disease.

This is the third of eight stories in our Web feature on [self-experimenters](#).

Of the thousands of [malaria-ridden mosquitoes](#) that have bitten Stephen Hoffman over the years, he is most grateful to a batch of 3,000 that feasted on his arm in the mid-1990s. The swarming bloodsuckers had been subjected to radiation to weaken the malaria-causing parasitic *Plasmodium falciparum* sporozoites they carried. The result: he became immune to the disease that [kills at least one million people yearly](#), most of them children, in sub-Saharan Africa and elsewhere.

Unfortunately, his path to immunity will not work, at least not directly, for the estimated [500 million people worldwide infected with the disease](#). "You can't immunize people with mosquitoes. It's totally impractical," says Hoffman, chief executive and scientific officer of Sanaria, Inc., a Rockville, Md., company he founded to try to turn these irradiated sporozoites into an effective treatment.

Hoffman believed he was close to a malaria vaccine once before. In the mid-1980s, he was part of a team of military doctors at Walter Reed Army Medical Center working to attach [malaria](#) proteins to molecules the immune system recognizes. They hoped the immune system would then go after the molecule and, in the process, also attack the parasite, which normally remains hidden by burrowing into the liver or hiding inside red blood cells. The researchers were so confident their vaccine would work after initial experiments that they let infected mosquitoes bite them after injecting themselves with an early version of it.

Hoffman knew it failed, however, when he came down with a full-blown [case of malaria](#) 10 days later while traveling. Suffering through high fever, shaking and vomiting, he nonetheless had to delay treatment for several days to satisfy clinical trial guidelines. "You begin to think about what happens when people don't get diagnosed," he says.

All but one of his fellow test subjects shared his fate. "It turns out mice are very easy to protect and humans are not," says W. Ripley Ballou, another stricken former member of the Walter Reed team, who now heads malaria vaccine research for GlaxoSmithKline (GSK) Biologicals.

Reconsidering his approach, Hoffmann eventually revisited studies by David Clyde from the early 1970s that had showed that as many as 90 percent of the handful of patients tested—including Clyde himself—could be fully protected from infection if they received weakened parasites from at least 1,000 irradiated mosquitoes. (Hoffman's 3,000 bugs were overkill.) By the late 1990s, technology had advanced enough to allow the delivery of that many mosquito bites' worth of weakened parasites in one injection.

So, in 2002 Hoffman launched Sanaria ("healthy air" in Latin) in a Rockville strip mall. Delivered by mosquitoes, the so-called whole parasite vaccine protected 24 of 26 volunteers. This October the company moved to a brand new biotechnology facility nearby to begin mass production of the vaccine for larger human trials, which Hoffman says could begin by year's end.

Ballou, for his part, still believes that the original vaccine is the most promising candidate and GSK has spent years refining that approach. The company's [RTS,S malaria vaccine](#) has proved effective in adults and children—reducing the risk of infection by roughly 30 percent. If further studies go well, this treatment will also be the first available, reaching Africa and other endemic areas by as soon as 2011.

But that low percentage of protection is not good enough for Hoffman. "That's not a vaccine that could ever be considered for use in the developed world," he notes. He concedes it will take at least a decade of human testing to prove the Sanaria vaccine works in larger populations, can be produced (and kept refrigerated) on a scale of 200 million doses a year, and that it does not create any dangerous side effects. But Hoffman is optimistic. "The great thing," he says, "is we are starting with a vaccine that we know works."

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