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**Thinking Harder**

A science journalist's open notebook • By Ben Harder



Why a Man Let 2,000 Malaria-Infected Mosquitoes Bite Him

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Some people will go to extreme lengths to avoid mosquito bites. They'll wear long sleeves and pants in the heat of summer, surround themselves with citronella candles and torches, and spray foul-smelling chemicals all over their bodies—or simply not set foot outside when they know the bugs are biting.

Stephen Hoffman isn't quite like those people. In fact, he has gone out of his way to *get* bitten. Years ago, he let 2,000 mosquitoes feast on his arm and inject perhaps 200,000 parasites into his bloodstream. Why? Well, for one thing, it made him immune to malaria.

He's also the CEO of Sanaria, a Rockville, Md.-based company that aims to develop and commercialize a [malaria vaccine](#). But he doesn't plan on subjecting all of us to as many bites as he has suffered. Receiving the vaccine that Hoffman hopes to create, in fact, wouldn't involve any mosquito bites at all. "It would have to be delivered by needle and syringe," he says. *Creating* the vaccine is another matter, however, and it calls for more brave volunteers willing to serve as mosquito fodder.

Progress toward a malaria vaccine, including a major new advance that European scientists reported this week, has already demanded a blood sacrifice from hundreds of people. Some, like Hoffman, have had scientific reasons for getting involved. Others have been regular citizens with good initial health, a tolerance for inconvenience and risk, and perhaps either a deep sense of altruism or an acute need for cash. The 15 volunteers in the new European study, most of whom were students at Radboud University in the Netherlands, got paid 1,500 euros (about \$2,100) in compensation. Ten of them also gained immunity to malaria, through the infected mosquito bites they got. The other five, assigned to a control group that didn't develop immunity, came down with bad cases of the parasitic disease.

"The control group got full-blown malaria," says study leader Robert Sauerwein, a medical microbiologist at Radboud University Nijmegen Medical Center. "They got grade 3, quite severe [symptoms](#)."

While Hoffman didn't participate in that study, he too has developed malaria in the line of duty. It happened in the late 1980s when an early immunization effort he was testing on himself failed to work. Not knowing he was unprotected, he let five infected mosquitoes bite him—and came down with symptoms. In the subsequent trial, where he received bites from 2,000 mosquitoes, the bugs had first been zapped with radiation to weaken the parasites.

Hoffman's and Sauerwein's teams are now collaborating on malaria vaccine development, and they have the backing of some deep-pocketed sponsors, including two global health organizations supported by the Bill and Melinda Gates Foundation. But all the money in the world can't prove that a vaccine works unless a few folks are willing to play guinea pig. That's why volunteers are so important, the researchers say.

"Almost 1,400 volunteers have been exposed to malaria in the context of vaccine development," Sauerwein says. (He adds that tens of thousands of other people willingly got malaria—as a therapy for syphilis—from the 1920s through the 1950s. But that's another story.) Sauerwein and his colleagues recruited their group of volunteers by publishing informational leaflets and advertising the trial around campus. They gave curious respondents a short interview, then sent them more details about the study and invited them to a series of "information evenings" that featured slide shows and additional explanations of the study.

After all that, Sauerwein says, "we had about...45 people who really wanted to participate." A thorough medical checkup and psychological evaluation disqualified some of them, leaving about 25 qualified volunteers, from which they selected the 15. "You have to have an absolutely blank medical history," he says. For scientific and ethical reasons, his team turned down people with asthma, for example, and those who had abnormal psychological profiles or seemed to have a financial neediness that might make them willing to take undue risks with their health.

During the study itself, the final squad of 15 took the antimalaria drug chloroquine while being exposed on three occasions to bites from a dozen or more mosquitoes. While 10 of the volunteers fed malaria-infected mosquitoes, the chloroquine protected them from getting sick.

Meanwhile, the exposure trained their [immune systems](#) to kill the parasite. So when these volunteers were exposed to a fourth round of mosquito bites after they'd stopped taking chloroquine, they stayed [healthy](#). The mosquitoes that bit the other volunteers weren't carrying malaria, which is why those five people didn't develop immunity. Sauerwein's team reported their findings in Thursday's issue of the *New England Journal of Medicine*.

Aside from the risk of getting sick, volunteering has several drawbacks, including inconvenience and the discomfort of being subjected to numerous medical tests. "Participation is quite time-consuming," Sauerwein says. Over the course of the five-month study, each volunteer had to visit the medical research facility about 50 times. Toward the end of the study, when volunteers had to be closely monitored because they were most likely to come down with malaria, "they had to appear three times a day for two weeks or so," he says.

So why did people step forward? Sauerwein says many of the selected volunteers expressed idealism, a sense that a malaria vaccine would represent an important achievement for human health worldwide. Some had personal or academic connections to countries where the disease is endemic, he adds. [Malaria kills nearly 1 million people each year](#), most of them children in Africa.

Hoffman, the head of Sanaria, had additional reasons for stepping up to the plate. "It was most appropriate for me to volunteer," he says. "We were studying the first vaccine.... If I wasn't willing to volunteer, how could I ask someone else to volunteer?"

"I suppose," he adds, "I also wanted to be able to say I'm one of the handful of people in the entire world that is totally protected against malaria."

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