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Experimental vaccine protects healthy U.S. adults from malaria infection for more than one year

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An experimental malaria vaccine protected a small number of healthy, malaria-naïve adults in the United States from infection for more than one year after immunization, according to results from a Phase 1 trial described in the May 9th issue of Nature Medicine. The vaccine, known as the PfSPZ Vaccine, was developed and produced by Sanaria Inc., of Rockville, Maryland, with support from several Small Business Innovation Research (SBIR) awards from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. NIAID researchers and collaborators at the University of Maryland School of Medicine in Baltimore, conducted the clinical evaluation of the vaccine, which involved immunization and exposing willing healthy adults to the malaria-causing parasite *Plasmodium falciparum* (*P. falciparum*) in a controlled setting.

The parasites that cause malaria are transmitted to humans through the bite of an infected mosquito. The PfSPZ Vaccine is composed of live, but weakened *P. falciparum* sporozoites--the early developmental form of the parasite. Previous research showed the PfSPZ Vaccine to be highly protective three weeks after immunization. In this trial, researchers assessed if protection could last for five months to a year.

"Malaria remains one of the most devastating diseases in the world, especially among young children in Africa," said NIAID director Anthony S. Fauci, M.D. "A malaria vaccine that provides long-term protection is urgently needed to reduce mortality and eliminate transmission. This study is an encouraging step forward in our goal to control and ultimately eradicate malaria."

The Phase 1 trial took place at the NIH Clinical Center in Bethesda, Maryland, and at the University of Maryland Medical Center and enrolled 101 healthy adults aged 18 to 45 years who had never had malaria. Of these volunteers, 59 received the PfSPZ Vaccine; 32 participants served as controls and were not vaccinated. Vaccine recipients were divided into several groups to assess the roles of the route of administration, dose, and number of immunizations in conferring short- and long-term protection against malaria.
To determine if the number of immunizations influenced protection, vaccinated participants received either three (nine participants) or four (28 participants) intravenous (IV) immunizations of the PfSPZ Vaccine at a higher dose than tested in previous human studies. To compare the protective efficacy of different routes of administration, eight participants received four immunizations via intramuscular injection (IM) at a dose approximately 10-fold higher than the dose administered intravenously. This was done to help the research team assess if IV administration was necessary and more efficient based on the dose required.

To evaluate how well the PfSPZ Vaccine prevented malaria infection, all participants--including the control participants who were not vaccinated--were exposed at varying times to the bites of mosquitoes carrying the same *P. falciparum* strain from which the PfSPZ Vaccine was derived. The Walter Reed Army Institute of Research in Silver Spring, Maryland, carried out this controlled human malaria infection procedure--a standard process in early phase malaria vaccine trials.

To assess short-term protection, participants were exposed to the bites of parasite-infected mosquitoes three weeks after receiving their final vaccination. Scientists then took blood samples from each participant to measure parasite levels for evidence of protection. For nine participants who received three IV doses, three were protected, or had no detectable parasites in their blood. For the nine participants who received four IV doses, seven were protected. Only three of the eight participants who received four IM doses were protected, indicating that IV administration afforded higher levels of protection at a lower dose.

To assess long-term protection, an additional group of 11 participants received four IV doses of the investigational vaccine and were exposed to the bites of malaria parasite-infected mosquitoes 21 weeks after their final vaccination. Scientists found that six of 11 participants (55 percent) had no detectable parasites in their blood after this exposure. Four of these six participants, plus one of the participants who received the same four doses via IV and had no parasites in the blood after exposures at three weeks and 21 weeks, were exposed to mosquito bites again at 59 weeks after their final vaccination. All five participants exposed at 59 weeks did not develop parasites in their blood, while all six unvaccinated control participants became infected with malaria parasites.
Collectively, the data showed that the PfSPZ Vaccine provided malaria protection for more than one year in 55

percent of people without prior malaria infection. In those individuals, the PfSPZ Vaccine appeared to confer sterile protection, meaning the individuals would be protected against disease and could not further transmit malaria. The vaccinations were also well-tolerated among participants, and there were no serious adverse events attributed to vaccination.

Additional results showed that antibodies may play a role in malaria protection early after the final immunization, but inducing T cells in the liver is likely necessary for durable protection.

"It is now clear that administering the PfSPZ Vaccine intravenously confers long-term, sterile protection in a small number of participants, which has not been achieved with other current vaccine approaches," said Robert A. Seder, M.D., chief of the Cellular Immunology Section of NIAID's Vaccine Research Center and principal investigator of the trial. "Based on the favorable safety profile, we're testing higher doses in larger trials to see if even greater protection can be achieved long-term against other *P. falciparum* strains different than the vaccine strain."

Long-term, reliable protection is important for people who are vaccinated but not exposed to malaria for months, such as travelers and military personnel. Durable protection is also important for mass vaccination campaigns in malaria-endemic regions aimed at interrupting transmission, according to the authors.

Source:
NIH/National Institute of Allergy and Infectious Diseases
