Pulling malaria from mosquitoes to fight disease

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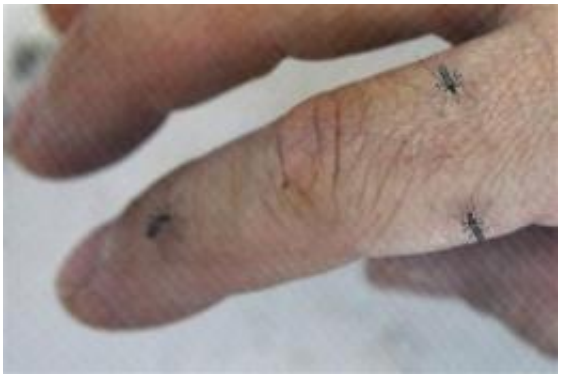

Seen through mosquito netting, mosquitos feed on Robert Harrell at the University of Maryland Biotechnology Institute's Insect Transformation Facility in Rockville, Md. on Wednesday, June 3, 2009. Think your job's tedious? Try beheading 100 mosquitoes an hour. Gently, no smushing allowed: Malaria parasites lurk in these mosquitoes' salivary glands, and a small company on the outskirts of the nation's capital needs them unharmed for a dramatic test _ attempting the first live vaccine to fight malaria. (AP Photo/Jacquelyn Martin)

(AP) -- Think your job's tedious? Try beheading 100 mosquitoes an hour. Gently, no smushing allowed. Malaria parasites lurk in these mosquitoes' salivary glands, and a small company on the outskirts of the nation's capital needs them unharmed for a dramatic test - attempting the first live vaccine to fight malaria.

Mutant mosquitoes, too, might help one day. Their eyes glow green

under a special microscope, a sign that the University of Maryland's genetic engineering has taken hold: These bugs should become super malaria incubators, a bid to eventually get more of the vaccine's key ingredient per mosquito.

If the two experiments sound far-fetched, consider: A global push is on to eradicate this ancient scourge, and increasingly scientists are exploring how to use the mosquito itself to help - not just with the vaccine research but also, conversely, by breeding insects that are less able to spread malaria.

"It's really gene therapy for insects," says Dr. David O'Brochta, who heads the Maryland university's novel laboratory and, with government funding, is creating both bug types.

It's a change in philosophy, and O'Brochta cautions that it's far from clear that any of the mosquito research will pan out.

A vaccine made of living malaria parasites "was considered laughable five to seven years ago," says Dr. Stephen Hoffman, CEO of Rockville, Md.-based Sanaria Inc.

In the Navy in the 1990s, Hoffman irradiated malaria-carrying mosquitoes to weaken the parasites inside them, and he and 13 colleagues subjected themselves to more than 1,000 bites. Usually malaria parasites race to the liver and multiply before invading the bloodstream to sicken. These weakened parasites instead sat harmlessly in the liver, unable to multiply but triggering the immune system to fend off later infections. All but one of the people in Hoffman's test, himself included, were immune when bitten by regular malaria-infected mosquitoes over the next 10 months.

The question was how to turn that protection into a long-lasting shot.

Critics said "it couldn't possibly be made," Hoffman recalls. "We were dismissed by 99 percent of the people in the malaria field."

Yet two weeks ago, with the Food and Drug Administration's OK, the first of about 100 U.S. volunteers started receiving test doses of Sanaria's vaccine, in a first-stage safety study.

Nearly a quarter-billion people get malaria each year, and it kills almost 1 million, the vast majority of them young children in Africa. Species of Anopheles mosquitoes spread the parasite. Bed netting and insecticides are the chief protection. Advanced testing of a different experimental vaccine from GlaxoSmithKline is under way in Africa, an exciting first but one expected to provide only partial protection.

Hence the push by about a dozen labs worldwide to breed malaria-resistant mosquitoes in various ways, including altering their genes.

In O'Brochta's lab, Robert Harrell peers through a microscope and jabs a mosquito egg - so small it takes a clump of them to resemble specks of dirt - with a hair-thin glass needle. He's aiming new DNA near a spot that should develop into reproductive organs, so the resulting mutant mosquito can pass its new trait to next generations.

Inheritance is a hurdle: Of the mutants that survive to adulthood, only about 2 percent of their progeny remain genetically modified.

In a humid insectary that resembles a walk-in safe, O'Brochta pulls out a bucket swarming with Anopheles gambiae, the species that drives malaria in Africa. Deprived of human blood in the lab, these mosquitoes will suck on a sedated mouse for food. (The lab mouse, which loses a little blood, then gets a two-week vacation - and no, mosquitoes don't make mice itch.)

But in the wild, this particular species hunts people like a bloodhound, so a malaria-resistance gene would have to spread a lot faster through mosquito populations to work. How to speed that spread is O'Brochta's main focus.

The flip side of his research brings us back to Sanaria.

It takes 3,000 mosquitoes - relatives of A. gambiae, dissected by hand - to make a batch of the experimental vaccine, says Sanaria entomologist Adam Richman. In an FDA-sanctioned "clean room," workers dunk frozen mosquitoes in alcohol, killing them but not the stunned parasites inside. Then, peering through a microscope, the workers carefully pull each mosquito's head from its body. Out pops an almost translucent glob, the glands, ready for purification.

The company's eventual goal: a mosquito that can harbor 200,000 sporozoites, the immature parasites, twice the typical amount. In his nearby university lab, that's what O'Brochta is trying to create by switching off a gene that protects the bug when it eats malaria-infected human blood.

"No one has ever made transgenic mosquitoes with this gene knocked out," he says. "We want to cripple its immune system so when it takes an infected meal, it gets infected at very high levels.