# Hitting malaria parasites early and hard

Public health officials thought they had malaria on the run a few decades ago, but the disease has made a deadly comeback. One reason is that *Plasmodium falciparum* and other mosquito-borne parasites that cause the illness have developed resistance to the few available antimalarial drugs. Hundreds of millions of people will suffer from malaria this year, and an estimated 2.7 million, many of them children, will die.

Two recent research efforts now offer new hope in the battle against malaria. One group of scientists has discovered that a single injection of a powerful immune system protein may offer temporary protection from these parasites.

Even more promising, another research group reports tantalizing success in an initial human trial of a vaccine designed to kill malaria-causing parasites before they spread throughout a person's blood.

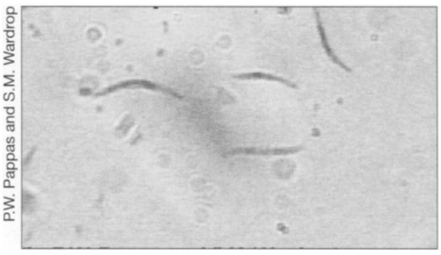
Malarial infections start with a mosquito bite. When a mosquito sucks its meal of blood, it may transmit just a dozen or so sporozoites, the first stage of the parasite's life cycle, into a person. The sporozoites travel to the person's liver, infecting cells and dividing to produce thousands of merozoites, the second stage. The merozoites ultimately leave the liver to infect and destroy red blood cells, causing the symptoms of malaria.

"If one wants to prevent malaria, the way to do that is to prevent the parasites from ever getting out of the liver," says Stephen L. Hoffman of the Naval Medical Research Institute in Bethesda, Md.

To achieve that goal, Hoffman and his colleagues have of late looked to one of the body's cytokines, the chemical messengers that stimulate immune cells. Malaria investigators have been intrigued by the cytokine interleukin-12 (IL-12) because studies have shown that injections of IL-12 temporarily protect mice against infection by sporozoites. The IL-12 appears to signal immune cells to make interferon-gamma, a chemical that instructs infected liver cells to destroy themselves and the parasites they contain.

Hoffman's group now reports in the January NATURE MEDICINE that a single injection of IL-12 given to seven monkeys 2 days before an injection of sporozoites protected all seven from malaria.

"This is a big deal. It's the first successful use of IL-12 [for any disease] in a primate," notes Alan Sher of the National Institute of Allergy and Infectious Diseases in Bethesda.



P.W. Pappas and S.M. Wardrop

*Malaria-causing parasites (wormlike shapes), about 10 micrometers long, in the sporozoite stage.*

Researchers do not yet know how long the IL-12-induced protection lasts or whether it can be achieved in humans at a safe dose. A trial of IL-12 in cancer patients produced severe side effects, including one death (SN: 6/17/95, p. 375).

Still, Hoffman argues that the research with monkeys justifies a trial with human volunteers. Though IL-12 is expensive, he suggests it might someday protect troops or travelers in malaria-infested areas. IL-12 "may not be the complete answer, but it could have a niche," he says.

Like the interleukin-12 injections, a new experimental vaccine aims to stop malaria parasites before they stream from the liver. Its main ingredient is a fragment of a surface protein from the sporozoite.

The fragment itself generates a weak immune response, so scientists fused it to another protein fragment, one taken from the virus that causes hepatitis B. They also mixed the fused particles with adjuvants, various chemicals that amplify the body's immune response.

One such vaccine formulation protected six out of seven volunteers deliberately exposed to mosquitoes infected with malaria-causing parasites, scientists from Walter Reed Army Institute of Research in Washington, D.C., and SmithKline Beecham Biologicals, a Belgian pharmaceutical firm, report in the Jan. 9 NEW ENGLAND JOURNAL OF MEDICINE.

That level of protection exceeds the immunity conferred by any other vaccine tested in people, notes malaria investigator Ruth S. Nussenzweig of New York University Medical Center.

Though they lasted less than a day, severe side effects, such as headaches and fever, did sometimes follow the vaccine injections. Experimentation with the vaccine's adjuvants may eventually reduce those unpleasant symptoms, says W. Ripley Ballou, a member of the Walter Reed group.

This spring, Ballou and his colleagues plan to test the vaccine on volunteers in sub-Saharan Africa to see whether it protects against the full range of malaria-causing parasites. The potential malaria vaccine may offer a bonus, says Ballou: It should protect people against the hepatitis B virus. — *J. Travis*

# Weight control for bacterial plastic

In their quest for better ways to synthesize biodegradable plastics, scientists are looking to polymers produced naturally by certain bacteria. So far, most research has focused on increasing the polymer yield, but a new study takes a step toward influencing the plastic's final properties.

Researchers at the Massachusetts Institute of Technology have found that they can control the size of the polymer's molecules by genetically manipulating production of a key enzyme. The larger polymers made by these modified bacteria can weigh up to four times more than those synthesized naturally.

"I think we'd be able to go higher and lower by further manipulating the genetics," says MIT chemist Kristi D. Snell.

A polymer's molecular size strongly influences the properties of the finished plastic. The MIT group's report, which appears in the January NATURE BIOTECHNOLOGY, suggests that biodegradable plastics made by bacteria could be practical for a wide range of applications.

"What exactly controls the molecular weight of biopolymers of this kind is really not well understood," says Stephen Padgette of Monsanto Co. in St. Louis. "This research is probably a first step in trying to understand that."

The MIT group studied a polymer called PHB, which the bacterium *Alcaligenes eutrophus* produces to store energy. The researchers genetically engineered *Escherichia coli* to produce PHB. Controlling enzyme activity is easier in a bacterium that doesn't normally manufacture PHB, Snell says.

The researchers inserted additional genes in *E. coli* to make them produce different amounts of PHA synthase, an enzyme that links the individual polymer units into chains. In cells with lots of PHA synthase, the enzyme joined the polymer units into a larger number of shorter chains, whereas in cells with less synthase, the enzyme made longer chains.

Altogether, bacteria make more than 100 polymers of the PHA type, many of which hold promise as components of biodegradable plastics. "We believe our method of controlling for molecular weight will apply to the whole class," Snell says.

Researchers have also turned plants into plastics factories by giving them bacterial genes (SN: 12/24&31/94, p. 420). Because bacteria must be provided with organic molecules before they will synthesize polymers, "the ultimate goal is to have the plants take carbon dioxide, sunlight, and water and produce the material," Padgette says. — *C. Wu*