Manipulative Malaria Parasite Makes You More Attractive (to Mosquitoes)

By CARL ZIMMER Published: August 9, 2005

Malaria is a staggeringly devastating disease, striking an estimated 300 million to 500 million people a year and killing more than a million of them. Scientists have long wondered how the parasite that causes malaria - a single-cell creature, plasmodium, carried by mosquitoes - manages to be so successful.

New research has shown an unexpected source of its success. The parasite makes infected humans smell more attractive to mosquitoes.

The research, published on Monday in the journal Public Library of Science Biology, was carried out by a team of French and Kenyan scientists led by Jacob Koella, an evolutionary biologist at Pierre and Marie Curie University in Paris. Dr. Koella is a leading expert on the ways in which parasites manipulate their hosts.

Beginning in the 1970's, scientists discovered that a number of parasites can alter the behavior and physiology of their hosts for their own advantage, sometimes drastically.

Some parasitic wasps, for example, force their caterpillar hosts to eat different foods. When one species of wasp crawls out of its host, the fatally wounded caterpillar will act as the parasite's bodyguard, defending it from predators.

Many parasites that need to live inside two different hosts during their life cycles also manipulate their hosts. A single-celled parasite called toxoplasma lives inside cats and then inside their prey, like rats. Research shows that infection with toxoplasma makes rats lose their fear of the odor of cats. Tapeworms that live in fish can turn them white and make them jump around near the surface of the water, where the fish are more likely to be eaten by birds, which the tapeworms make their new host. "It's amazing how much manipulation is going on in parasites," Dr. Koella said. "It would be hard to find a case where there wasn't some manipulation."

Scientists consider most of these examples as products of natural selection. A parasite's reproductive success depends on its ability to be transmitted toa new host. "And manipulation appears to be an obvious way to do it," Dr. Koella said.

In the late 90's, Dr. Koella documented how plasmodium, the cause of malaria, manipulated its mosquito host. When the mosquitoes first take up plasmodium in a drink of human blood, they become more cautious about finding another victim. Their reluctance makes them less likely to be killed.

Dr. Koella points out that at this stage in the life cycle the parasite needs time to develop in the mosquito before it can be transmitted. "Before the parasite is transmitted to a human, its only goal is to survive, and to help the mosquito to survive," he said.

The mosquito's behavior changes when the parasite is ready to move on to a human. Dr. Koella found that mosquitoes carrying infective plasmodium become twice as likely as other mosquitoes to bite more than one person in a night. On top of that, they spend more time on each host drinking blood.

Dr. Koella argues that this shift in behavior raises the parasite's odds of entering a human host.

Given its ability to control mosquitoes, scientists have wondered whether the plasmodium may also be able to manipulate humans. After it enters the human body, it needs time to develop in the liver. Those parasites then produce offspring that can invade blood cells, and eventually a few of these give rise to offspring, known as gametocytes, that can be taken up by a mosquito and survive.

Scientists have investigated whether infected hosts are more attractive to mosquitoes than uninfected ones. The results have been ambiguous.

"I think the main problem with the previous studies is that they couldn't really tease apart the effect of infection and the intrinsic differences in attractiveness among people," Dr. Koella said.

Mosquitoes find their victims by sniffing carbon dioxide and body odors. Some people apparently smell "better" to mosquitoes than others.

To rule out such factors, Dr. Koella and his colleagues used a new experimental plan. He and a student, Renaud Lacroix, teamed with Wolfgang Mukabana of the University of Nairobi and Louis Goagna of the International Center of Insect Physiology and Ecology in Kenya.

They set up three tents, each large enough for a person to sleep in. A fan pumped air from the tents into a central chamber swarming with about 100 mosquitoes. Mosquitoes that were attracted to one of the tents would fly toward it, only to become stuck in a trap.

The researchers asked parents in western Kenya to allow them to test their children for malaria. For each round of the experiment, they chose one uninfected child in an early stage of infection and a child who was carrying gametocytes. The children slept for a few hours in the tents, and the scientists checked the traps to measure how many mosquitoes had been attracted to each child.

After studying 12 sets of children, the scientists discovered a striking pattern. "Gametocyte-infected children attracted about twice as many mosquitoes as either uninfected ones or ones infected with nontransmissible stages," Dr. Koella said. "The results really jump out."

The infected children did not show symptoms like fever, a common situation in Africa. Nevertheless, the researchers treated them with anti-malaria drugs on the day of their study. Two weeks later, after the medicine had cleared the parasites, the scientists repeated the experiments

with the same three children. They found that the cured children were no more attractive to the mosquitoes than the others.

"It's a beautiful piece of science, and it's a tremendously exciting finding," said Andrew F. Read of the University of Edinburgh, an expert on malaria who was not involved in the research. Dr. Read cautioned that the researchers drew their conclusions from a relatively small number of trials.

"Obviously," he said, "you'd be really pleased if another group went out and found the same thing. But it's a logistical nightmare to do that stuff. So I'm very impressed with what they have managed."

At this point, Dr. Koella can only speculate about how the parasite is altering its human host. Because the children carrying gametocytes in his study did not have fevers, plasmodium probably could not attract mosquitoes by making people hotter.

He suspects that the gametocytes are releasing chemicals that somehow alter the odor of human hosts, "but which aspects of the odor are changed is difficult to say."

If future research supports his findings, that could go a long way to explain why malaria is so widespread.

"Scientists used to see the mosquito as a syringe that moves the parasite from one human to the other," Dr. Koella said. "The fact that the parasite manipulates the mosquito to this extent can help to explain the incredibly intense transmission of malaria."

"If it really is increasing attractiveness, whatever is causing that is going to be hugely interesting," Dr. Read said.

Plasmodium's manipulation may point to new strategies to fight the disease. "The obvious spin-off if you found the mechanism is that you could interfere with it," Dr. Read said. "It might suggest certain kind of repellents to deactivate things coming off of people. Or whatever these parasites are doing could be used to distract mosquitoes away from people and trap them. It would suggest a lot of possibilities."