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Mosquitoes Can Carry, and Deliver, a Double Dose of Malaria

Insects that are already carrying one strain are more likely to pick up a second infection and harbor higher numbers of parasites



An *Anopheles* mosquito, the vector for malaria, taking a blood meal from a tasty human. (Sarah Reece & Sinclair Stammers, CC-BY)

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Mosquitoes can be infected with multiple strains of the malaria parasite, and these overburdened bugs are like supervillains for spreading disease. Lab tests show that their potent bite seems more likely to result in malaria transmission, delivering a parasite cocktail that increases the chances those mingling microbes will spread drug resistance.

Such super-charged mosquito vectors could be responsible for transmitting a disproportionate number of malaria infections, as well as for boosting the disease's deadliness, researchers say.

"I would expect that double infection has been happening as long as malaria has been a major problem," Laura Pollitt, a fellow at the Center for Immunity, Infection and Evolution at the University of Edinburgh, says in an email. "But our poor understanding of how the parasite is interacting with the mosquito has meant that it hasn't been recognized."

Pollitt and her colleagues from Pennsylvania State University and the U.S. National Institutes of Health are among the first to investigate how multiple infections with *Plasmodium*, the malaria parasite, affect mosquitoes. Previous work focused on how repeat encounters with parasites affect their vertebrate hosts—namely, humans—rather than how they impact the six-legged

vectors that often act as bridges to infection.

Pollitt and her team started with the basics: testing whether mosquitoes could indeed pick up multiple strains of *Plasmodium* through different blood meals. They loaded six cages with about 100 female *Anopholes* mosquitoes each, then provided the hungry bloodsuckers with mice. Three of the cages received mice infected with the rodent malaria parasite, while the others fed on uninfected mice. Four days later, all of the mosquitoes received a second blood meal, this time entirely consisting of infected mice carrying a different *Plasmodium* strain.

A week later, the team dissected and examined about 30 mosquitoes from each cage. They confirmed that the mosquitoes were indeed able to pick up a second infection, so that they had two strains of the parasite wriggling around inside their bodies. About 30 percent of the mosquitoes that fed on the first batch of infected mice picked up the parasite. Of those, half were re-infected upon the second feeding. As they report in the journal *PLOS Pathogens*, this means that mosquitoes infected with the first strain of *Plasmodium* were more than five times as likely to pick up the second strain than those that were not already infected.

To confirm these findings, the team performed a second set of experiments using the same design but more mosquitoes. The results mirrored those of the first test: regardless of which strain of parasite the mosquitos picked up initially, they were more likely to become infected with a second if they already had *Plasmodium* in their system.

The team also found that infected mosquitoes carried more second-strain parasites than those that were becoming infected for the first time. The more *Plasmodium* parasites a mosquito carries, the greater its chances of passing on an infection when it takes a blood meal, so the authors predict that doubly-infected mosquitoes would be better vectors of disease.

Finally, the team monitored more than 1,600 mosquitoes—some infected with single strains, some with double doses and some not at all—from birth until death. While uninfected mosquitoes lived longer than infected ones, no difference existed between those harboring a heavier, mixed parasite load and those carrying a single strain. That eliminates the possibility that higher rates of transmission might be balanced out by a more fleeting lifespan.

More detailed experiments are needed to determine why a previous *Plasmodium* infection seems to facilitate a second. And while these findings were restricted to a controlled laboratory setting, the team suspects that they will hold true in the field, and for humans as well as rodents. The implications are both good and bad. On one hand, efforts to reduce the overall prevalence of malaria would in turn cut back on the probability that a mosquito becomes infected twice and morphs into a super-vector. According to Pollitt, modest decreases could lead to a dramatic reduction in the number of malaria cases.

But on the other hand, if malaria infection increases in an area—whether due to failing control of the disease or increased incidence due to climate change—mosquitoes could begin picking up double infections and accelerate the spread of disease.

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