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Scientists Find Young Infected but Asymptomatic ‘Super Spreaders’ Keep Malaria Viable by Regularly Infecting Local Mosquitoes

Study in Uganda reveals school-age children are reservoirs of disease – just four were linked to 60% of the malaria-infected mosquitoes

Arlington, Va. (November 18, 2020) — Malaria researchers, working in an area of Uganda where infections have been dropping dramatically, discovered a small number of infected but asymptomatic school-age children can serve as stealth “super spreaders” responsible for the vast majority of malaria parasites still circulating in local mosquitoes. The new findings, reported today at the Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH), reveal a hidden reservoir that’s a barrier to long-term efforts to eliminate malaria and an immediate threat for disease resurgence if control measures like bednets and indoor spraying falter.

“We now have the first direct evidence that even in places under very intensive malaria control, a small number of asymptomatic super spreaders can quietly sustain transmission—and finding and treating them could prove very challenging,” said lead author Chiara Andolina, MSc, a PhD student and malaria expert at Radboud University Medical Center in The Netherlands. The study was conducted as part of the Program for Resistance, Immunology, Surveillance, and Modeling of Malaria (PRISM) project in Uganda.

“The existence of asymptomatic malaria infections is well known,” she said, “but it was surprising to see just how much they can contribute to infecting mosquitoes.”

Malaria parasites are dependent on a life cycle in which they constantly move back and forth between humans and mosquitoes. Successfully interrupting transmission of the disease includes clearing parasites from human hosts, which can be accomplished with anti-malaria drugs.

Andolina and her colleagues were investigating how malaria could remain viable in mosquito populations in an area of eastern Uganda that has been targeted with intensive malaria control efforts, including regular distribution of insecticide-treated bednets, indoor residual spraying (IRS) with insecticides and access to potent malaria drugs. As a result, infections, or at least those that cause symptoms, have fallen precipitously.

Andolina said a significant challenge is that identifying potential super spreaders and treating them to clear their parasites is costly and time consuming. She and her colleagues in Uganda tested some individuals up to 19 times for their ability to transmit their infections. Densities of infections showed marked fluctuations—sometimes even the most sensitive diagnostic tests would pick up nothing while the next test would show evidence of parasites that were subsequently transmitted to mosquitoes.

On a more positive note, Andolina said the fact that school-age children are potentially the key to keeping malaria transmission viable presents new options for fighting the disease. She noted that, because most of them are in school, they represent a relatively “accessible reservoir” of infections. That means they can be more easily targeted with interventions, she said, such as malaria prophylactic medicines that can prevent them from acquiring parasites at all.

Teun Bousema, PhD, a malaria epidemiologist at Radboud and the study’s principle author, said the findings show that a hidden reservoir of asymptomatic infections, which was found mainly in children 5 to 15 years old, is sufficient to keep the disease circulating in local mosquitoes.

For example, the study, which involved two years of regularly testing more than 500 people for evidence of malaria parasites, found that just four children were linked to 60% of the infected mosquitoes studied. One child, who showed no symptoms despite harboring seven different variations of the deadly *Plasmodium falciparum* malaria parasite, was responsible for almost 25% of the infected mosquitoes. There were also two asymptomatic young people who were found to be infectious for over six months.

Bousema said that even if the parasites from the asymptomatic children are only keeping malaria circulating at relatively low levels, that could be sufficient to cause infections to quickly rebound if control efforts are not maintained. He said there is evidence that in other parts of Uganda, when funding ran out for IRS campaigns, malaria infections rebounded within weeks. Bousema said there is currently a concern that the restrictions related to curbing the spread of COVID-19 also could hinder malaria control efforts and pose a risk of causing infection rates to rise.

While malaria deaths have fallen substantially over the last decade, it still kills about 400,000 people each year, with the vast majority of deaths occurring in sub-Saharan Africa. There is currently concern that the fight is stalling and that a variety of factors—including declining budgets for malaria control and rising insecticide and drug resistance—could allow the disease to stage a come-back.

“Our study adds another challenge because it shows that making and maintaining progress against malaria cannot rely on simply treating people who are sick and thus eliminating a source of parasites that can infect local mosquitoes,” Bousema said. “Some have argued that when transmission is very low and treatment is available, you can relax somewhat—because most new infections will produce symptoms and patients will come to clinics for medicines. But what if the biggest source of parasites is a group of people who never show any signs of getting sick?”

Bousema and Andolina said that one puzzling aspect of the study is that the asymptomatic carriers clearly had developed some level of immunity, even though they grew up in an area where malaria infections had fallen significantly.

“It could be evidence that you don’t need a lot of previous exposure to acquire a level of immunity that allows you to get infected with malaria parasites without getting sick,” Andolina said. “This supports previous work showing that children can acquire immunity very efficiently and, at the same time, remain very important as a source for spreading infections.”

Also, previous malaria studies have shown that school-age children in malaria-endemic regions tend to be infected with a higher density of parasites and over a longer period of time than either younger children—who are the most likely to die from the disease—or adults.

“These new insights into the role of asymptomatic malaria super spreaders are clearly concerning,” said ASTMH President Joel Breman, MD, DTPH, FASTM. “But they are also giving us a much better understanding of the enemy, and tactics we need to develop to defeat it.”

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