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Clinically silent relapsing malaria may still pose a threat

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Nonhuman primates with clinically undetectable *Plasmodium* relapse infections still harbor parasitic gametocytes that may be infectious to mosquitoes, according to a study published September 19 in the open-

access journal *PLOS Pathogens* by F. Eun-Hyung Lee and Mary R. Galinski of Emory University, Tracey J. Lamb of the University of Utah, and colleagues. The study has important epidemiological implications relevant to malaria elimination strategies.

The protozoal parasite *Plasmodium vivax* is a major cause of malaria—a life-threatening mosquito-borne disease responsible for hundreds of thousands of deaths globally each year. *P. vivax* remains a major obstacle for malaria elimination due to its ability to form dormant stages in the liver. These forms can become activated to cause relapsing blood-stage infections. Relapses remain poorly understood because it is difficult to verify whether *P. vivax* blood-stage infections in patients are due to new infections or relapses. To address this gap in knowledge, researchers used a nonhuman primate model of malaria, combined with state-of-the-art immunological and molecular techniques, to assess pathogenesis, host responses, and circulating gametocyte levels during relapses.

They found that relapses were clinically silent compared to initial infections, and they were associated with a robust memory B cell response. This response resulted in the production of antibodies that were able to mediate clearance of relapsing, asexual parasites. Despite this rapid immune protection, the sexual-stage gametocytes, which may be infectious to mosquitoes, continued to circulate. According to the authors, the number of clinically silent relapse infections, and their infectiousness to mosquitoes, remains largely unknown and should be evaluated carefully in the future. As a next step on the path to eliminating *P. vivax* and other relapsing malaria parasites, studies should identify the factors that influence relapse pathogenesis, immunity, and infectiousness to mosquitoes.

"This study shows the explicit benefit of using a nonhuman primate model system to study the immune response and relate the findings to

human clinical cases and transmission," states Dr. Galinski. "It is important to know that asymptomatic individuals may carry infectious gametocytes."

Dr. Lamb adds, "This study reveals the role of B cells in the control of relapsing malaria."

Finally Dr. Lee adds, "The nonhuman primate model is ideal to study the true memory B cell responses during relapsing malaria because this question is difficult to answer in human studies."

More information: Joyner CJ, Brito CFA, Saney CL, Joice Cordy R, Smith ML, Lapp SA, et al. (2019) Humoral immunity prevents clinical malaria during Plasmodium relapses without eliminating gametocytes. *PLoS Pathog* 15(9): e1007974. doi.org/10.1371/journal.ppat.1007974

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