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How the immune system prevents repeated malaria fever episodes in highly exposed children

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Children in Mali (and many other regions where malaria is common) are infected with malaria parasites more than 100 times a year, but they get sick with malaria fever only a few times. To understand how the immune system manages to prevent malaria fever in most cases, Peter Crompton, from the US National Institute of Allergy and Infectious Diseases, and colleagues in the US and in Mali, analyzed immune cells from healthy children before the malaria season and from the same children after their first bout of malaria fever during the ensuing malaria season.

As reported in *PLOS Pathogens*, the researchers exposed both sets of immune cells to parasite-infected red blood cells and found that their responses were different: When confronted with parasites before the malaria season, the children's immune cells produced large amounts of molecules that promote inflammation (which results in fever and other malaria symptoms). After a malaria fever episode, the immune cells responded by producing more anti-inflammatory molecules (which dampen the strength of the inflammatory response) and showed evidence of an enhanced ability to recognize and destroy parasites.

The ability of the immune cells to mount this "compromise" response (somewhat effective in controlling the parasites but avoiding systemic inflammation and fever) seems to depend on the continued exposure to parasites through bites of infected mosquitoes: When the researchers took blood again from the same children after the subsequent dry season

(when there are few or no new infections) and exposed the immune cells to parasite-infected red blood cells, they showed that the anti-inflammatory response had returned to baseline, leaving children susceptible again to malaria-induced inflammation and fever.

Discussing their findings, the researchers say they "shed light on the longstanding and enigmatic clinical notion of 'premunition'—a partially effective exposure-dependent immune response that protects against illness and high numbers of parasites in the blood without completely eliminating the infection" and suggest that it "evolved as an appropriate immune response . . . such that young children are at least partially protected from potentially life-threatening inflammation and unchecked parasite replication before they acquire . . . antibodies that reliably protect against the onset of malaria symptoms".

More information: Portugal S, Moebius J, Skinner J, Doumbo S, Doumtabe D, et al. (2014) Exposure-Dependent Control of Malaria-Induced Inflammation in Children. *PLoS Pathog* 10(4): e1004079. DOI: 10.1371/journal.ppat.1004079