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Host control of malaria infection is rarely mediated by host clearance

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Infections with the malaria parasite can lead to severe illness and mortality, with nearly half a million deaths attributed to malaria globally each year. Adults from malaria endemic regions often have immunity to malaria and are much less susceptible to disease, compared with children. Understanding how a host can control malaria infections is critical in guiding the development of a much need efficacious vaccine. Infected individuals are thought to clear infected red blood cells (RBCs) from circulation via organs such as the spleen - and this clearance is thought to play a major role in controlling malaria infections. However, no work has directly quantified clearance of infected RBCs or studied the extent to which parasite clearance is improved in, for example, immune hosts.

In this study, we developed a unique experimental approach to directly track the loss of a single cohort of infected RBCs in mice. We used this system to study the loss of infected RBCs in naïve, immune deficient, acutely infected, drug treated and immune mice. Modelling data from these experiments enabled us determine the baseline clearance half-life of infected RBCs in naïve mice (14.4 h), which suggests that about one third of infected cells are cleared every parasite replication cycle. Further, we found that this half-life was approximately doubled when phagocytes (a certain host immune cell) were depleted (33.8 h), suggesting host immune cells are important in removing infected cells. Surprisingly, with the exception of treatment with a high dose of a particular antimalarial (sodium artesunate), we did not observe an increase in the rate of clearance of infected RBCs in acutely infected mice, immune mice, or after drug treated, despite observing effective control of infection in all scenarios. Instead, of elevated host removal of infected, we observed an array of other factors that caused the control of infection, and in particular, this work revealed a novel mechanism of host control in acute infection, that is, slowing the development of parasites.

This work has revealed that the basal rate of removal of infected RBCs in murine malaria infection is very high, but this rate cannot easily be improved by host responses or drug treatment.

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