

Title: Modeling of Malaria Parasite Populations Dynamics and Transmission

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The transmission of avian and rodent malarias are strongly affected by host factors can attack the gamete forms of the malaria parasites in the midgut of mosquito vectors. (Only the gamete forms can transmit the disease.) However, evidence that patient antibodies can directly attack the precursors of the gametes present in the patient, the gametocytes, has been nebulous until a 2008 field study in Gambia suggested that patients who have antibodies to surface antigens of the gametocytes of *Plasmodium falciparum* (the major cause of malaria in Africa) do indeed cleared gametocytes earlier. Using theory from population biology that takes into account population aging and biological processes that occur on time scales from minutes to weeks, we developed mathematical models of the interacting with host innate and antibody immune responses with the both the gametes and asexual forms of the parasite. Our models considered a wide range in host immune capacity to detect and clear parasites. We modeled infections of both *Plasmodium falciparum* and *Plasmodium vivax*, which between them cause about 90% of malaria worldwide. We show that for the same ability to detect and clear a targeted parasite stage, antibodies to the immature (not-yet-transmissible) gametocytes would be more effective in reducing the density of transmissible gametocytes than antibodies directly targeting the transmissible forms. Because of the longer time needed for its gametocytes to mature, *P. falciparum* is particularly vulnerable to transmission blocking by this method. Field studies of malaria patients indicate that gametocyte density in both types of malaria are the same, on average, the modeling results suggest that *P. falciparum* has evolved mechanisms to evade or suppress host immune responses that would otherwise eliminate its immature gametocytes.