Malaria parasites prepare for flight

Citation for published version:
Reece, SE 2014, 'Malaria parasites prepare for flight' Trends in Parasitology, vol 30, no. 12, pp. 551-553.
DOI: 10.1016/j.pt.2014.10.004

Digital Object Identifier (DOI):
10.1016/j.pt.2014.10.004

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Publisher's PDF, also known as Version of record

Published In:
Trends in Parasitology

Publisher Rights Statement:
2014 Published by Elsevier Ltd. http://dx.doi.org/10.1016/j.pt.2014.10.004 OPEN ACCESS

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Malaria parasites prepare for flight

Sarah E. Reece¹ and Nicole Mideo²

¹Centre for Immunity, Infection & Evolution, Institutes of Evolution, Immunology and Infection Research, School of Biological Sciences, University of Edinburgh, Edinburgh EH9 3FL, Scotland, UK
²Department of Ecology & Evolutionary Biology, University of Toronto, Toronto, ON, Canada

Life in seasonal environments often means facing extreme environmental fluctuations. Many multicellular organisms have evolved strategies to cope with this lifestyle. Single-celled malaria parasites are no different. An elegant experiment reveals that they respond to the availability of mosquitoes to make the most of seasonal transmission opportunities.

Many species and populations of malaria parasite live in seasonal environments in which mosquito vectors are only available for part of the year. Given how quickly new malaria cases arise at the start of the transmission season, it has long been suspected that parasites modulate transmission effort to coincide with the reappearance of mosquitoes [1]. Previous studies have not supported this hypothesis [2], but the puzzle is now one step closer to being solved. Cornet et al. [3] reveal that parasites of the avian malaria Plasmodium relictum detect when mosquitoes blood feed on their host and respond by enhancing transmission.

These findings support the predictions of mathematical models also presented by Cornet et al. [3]: seasonality can select for the evolution of a ‘plastic strategy’ (Box 1), in which parasites invest in transmission by upregulating within-host growth only when vectors (and susceptible hosts) are available (Figure 1 in Box 1). This avoids wasting resources, or causing too much harm to the host, during periods when investing in transmission would not be rewarded. While it seems intuitive that parasites should not invest in transmission when vectors are unavailable, there are substantial evolutionary hurdles (costs) involved in plastic strategies [4]. Plasticity in a trait requires expending valuable resources on mechanisms to detect environmental change. If organisms monitor important aspects of their environment directly, then there may be a costly time lag between detecting and responding to change. Alternatively, organisms can respond to factors (cues) that correlate with relevant changes in the environment, which allows change to be anticipated and prepared for in advance, at the potential cost of responding to inaccurate information and making bad decisions. Due to these costs and risks, plasticity pays in regions where the start/end times of the transmission season are hard to predict. At the opposite extreme, when year-round transmission is possible, parasites are better off with a fixed strategy in which transmission investment is hardwired into the genome at a constant level (Box 1).

Why have previous studies failed to show that parasites monitor mosquito availability to schedule their transmission investment? The approach used by Cornet et al. [3] is superior in several respects. First, they used the natural host (canaries) and vector species (Culex pipeins) for P. relictum, which matters because parasites may not respond to non-vector mosquito species. Second, the parasites have a long evolutionary history of seasonal transmission because they were isolated from a temperate region. Third, instead of assessing only the impact of mosquito biting on blood stage infections, Cornet et al. [3] measured the intensity and prevalence of mosquito infections too. Fourth, Cornet et al. [3] investigated both the acute and chronic phases of infections because parasites appear insensitive to mosquitoes during the acute infection. Parasitaemia is highest in the acute phase, so there may be constraints limiting further growth (and thus investment in transmission) that do not apply in the chronic phase. Additionally, as investment is already high in the acute phase [3], if transmission success is a saturating function of parasite number [5] then the benefits of responding to mosquitoes may be marginal.

Exactly how transmission is enhanced following mosquito biting is unclear. The blood of a malaria-infected host contains asexual and sexual (gametocytes) stages. During every asexual replication cycle a small proportion of parasites differentiate into gametocytes, which are able to infect mosquitoes. Cornet et al. [3] propose that upon detecting mosquitoes, parasites increase their replication rate and the larger pool of asexual stages results in more gametocytes. There are several other possibilities. A larger pool of asexuals could potentially shield gametocytes from transmission blocking immune factors that are produced by the host but act in the blood meal when gametocytes differentiate into gametes [6]. Alternatively, the proportion of parasites differentiating into gametocytes is itself a plastic trait [7], so allocation towards gametocytes – as well as replication rate – could be increased in response to mosquitoes. Countering this hypothesis, there was no consistent significant difference in the number of circulating gametocytes in mosquito-exposed versus unexposed hosts, although Cornet et al. [3] point out that using microscopy to detect gametocytes may not be sufficiently sensitive to see this effect.

Teasing apart the roles of increased replication and increased gametocyte allocation is important: increasing allocation to gametocytes could mitigate the cost of increasing replication (because gametocytes contribute little to
virulence). Developing theory to explore the joint evolution of plastic virulence (replication) and plastic gametocyte allocation is now required. Rather than altering gametocyte density or allocation in response to mosquito biting, parasites may have altered the ratio of male to female gametocytes produced. Sex ratio is another highly plastic trait that can influence infectivity to mosquitoes independently of gametocyte number [8]. Finally, a parasite strategy may not be involved: blood parameters could be altered by the host reaction to mosquito biting, though whether a host immune response to biting could coincidently make gametocytes more infectious and/or increase replication rate is unknown. It is also unlikely that such a ‘host footprint’ only affects parasites in chronic infections unless hosts do not respond to the first period of mosquito biting (in the acute phase) but become primed to respond in subsequent exposure sessions.

Precisely how parasites detect the presence of mosquitoes remains an open question. Parasites could indirectly assess mosquito availability by monitoring host responses to biting or – given how quickly transmission enhancement occurred (within 3 days) – they may directly detect mosquito salivary proteins. Detecting mosquito products would also enable parasites to determine when the transmission season ends and downregulate investment at the right time. Elucidating how environmental sensing interacts with the epigenetic control of sexual differentiation (e.g., [9]) is the next step to link mechanism to evolution and reveal the sophistication of parasite strategies.

References
1 Paul, R.E.L. et al. (2004) Mosquitoes and transmission of malaria parasites – not just vectors. Malar. J. 3, 39
2 Shuter, D. et al. (2005) Rodent malaria parasites Plasmodium chabaudi and P. vincheli do not increase their rates of gametocytogenesis in response to mosquito probing. Proc. Biol. Sci. 272, 2397–2402
3 Cornet, S. et al. (2014) Evolution of plastic transmission strategies in avian malaria. PLoS Pathog. 10, e1004308
4 Figliucci, M. (2001) Phenotypic Plasticity: Beyond Nature and Nurture (Syntheses in Ecology and Evolution), The John Hopkins University Press
5 Churcher, T.S. et al. (2010) Population biology of malaria within the mosquito: density-dependent processes and potential implications for transmission-blocking interventions. *Malar. J.* 9, 311

6 Mideo, N. and Day, T. (2008) On the evolution of reproductive restraint in malaria. *Proc. Biol. Sci.* 275, 1217–1224

7 Carter, L.M. et al. (2013) Stress and sex in malaria parasites: why does commitment vary? *Evol. Med. Public Health* 2013, 135–147

8 Mideo, N. and Reece, S.E. (2012) Plasticity in parasite phenotypes: evolutionary and ecological implications for disease. *Future Microbiol.* 7, 17–24

9 Brancucci, N.M.B. et al. (2014) Heterochromatin protein 1 secures survival and transmission of malaria parasites. *Cell Host Microbe* 16, 165–176

10 Battle, K.E. et al. (2014) Geographical variation in *Plasmodium vivax* relapse. *Malar. J.* 13, 144