

# Parental guidance? Trans-generational influences on offspring life history in mosquitoes

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**Parental effects are important factors that might influence evolutionary and ecological aspects of parasite vectors and the parasites they transmit. A recent study demonstrated the importance of parental rearing conditions on the malaria vector *Anopheles stephensi*. When parents are reared in a food-limited environment their offspring have increased bloodmeal sizes and larger clutches. The study highlights that ecological studies are vital for understanding vectors of disease and ultimately for developing effective control strategies.**

## Trans-generational effects

Trans-generational effects are those in which the environment of one or both parents has an impact on the phenotypes of the offspring. Studies on these effects can help improve our understanding of causes and consequences of phenotypic variation among individuals [1] because parental effects, mainly exerted by the mother, are important in forming offspring phenotypes [1–3]. Parents can adjust their parental investment into their offspring according to the environment experienced during their juvenile or adult phase [4–6], and effects (e.g. on survival, growth or fecundity) can persist into the adulthood of offspring [7] and even into future generations [8,9]. In particular, the level of environmental stress (e.g. nutrient levels) experienced by the parental generation can have lasting effects on offspring. These effects on offspring phenotypes can be seen as noise produced by the environment, having either beneficial or non-beneficial effects, or otherwise can be seen as truly adaptive [10]. Trans-generational effects might be the result of simple trade-offs in investment owing to the environment, or because of more active provisioning of the offspring to be closer to the optimum in the prevailing environment. The adaptive value of parental effects depends on the accuracy of the environmental cues taken into account by the parents and the stability of the environment [1]. The trans-generational plasticity in response to environmental change also has population dynamic consequences because it leads to a time-lag between the environmental change and the population response [11].

In a recent study, Grech *et al.* [12] examined the consequences for offspring life-history traits (i.e. survival, bloodmeal size and fecundity) of the parental rearing regime (i.e. low food and high food) in the malaria vector

*Anopheles stephensi*. Offspring survival was not influenced by the parental regime but the daughters reared in a low-food environment took larger bloodmeals when their parents had also experienced low-food conditions. This result could be because of daughters compensating for poor maternal provisioning [12]. A more surprising result is that offspring from low-food parents were more fecund than offspring from high-food parents. Although bloodmeal size and fecundity were positively correlated, the difference in fecundity between the two parental rearing environments holds even after correction for bloodmeal size. The higher fecundity in daughters from low-food parents is potentially a result of a shift to earlier reproduction in the face of reduced longevity. These daughters shift their resources to fewer, larger reproductive efforts. Although this study can not separate between investment trade-offs and adaptive parental provisioning, it shows the potential for trans-generational effects in this system.

Considering how widespread parental effects are, and their influence on several life-history traits, it seems logical that host–parasite dynamics will be affected. The exact nature of these effects will depend on the traits in question; that is whether traits have direct (e.g. on immunity) or indirect (e.g. on growth rates or feeding behaviour) influences on the probability of parasite infection and fitness.

## Trans-generational effects and host–parasite interactions

Effects of parasites on host life-histories are well documented for a variety of host species [13–15]. However, the ecological, epidemiological and evolutionary consequences of trans-generational effects that are either indirectly or directly associated with parasites remain relatively unexplored.

It is feasible that in many situations parasites themselves act as the environmental stimulus leading to trans-generational effects. Given spatial heterogeneity of parasites and some extent of stability across generations, parental provisioning of offspring, dependent on their own experiences, is likely to be adaptive. Thus, parents might provision their offspring accordingly through behavioural or physiological means to prevent or reduce the impact of infection [16]. Trans-generational provisioning to improve offspring immunity has been shown in vertebrates and insects [7,17–19]. This transfer means that otherwise immunologically naïve offspring are protected from the outset and avoid the potentially susceptible time-lag that is associated with the switching on of their own induced

responses. In the case of trans-generational resistance, the short-term outcome is relatively predictable. However, longer-term effects on subsequent evolutionary dynamics need more theoretical and empirical investigation.

Trans-generational effects that are not closely linked to parasites might have indirect consequences for host–parasite interactions. For example, in the freshwater crustacean *Daphnia magna*, poor maternal environment enhances offspring resistance to a bacterial pathogen [6]. Parasite epidemiology and the ecology of host–parasite interactions are probably influenced by any parental effects that alter offspring life-history traits. Little attention has been given to this area, but it could have significant and far-reaching consequences, particularly for vector-borne diseases. The results of Grech *et al.* [12] could impact not only on the relationship between the mosquito and a parasite, but also on future transmission to a definitive host, and consequently on the epidemiology of the disease. In the context of malaria – because blood-feeding is a central factor in the perpetuation of vectors and parasites – any change in bloodfeeding is likely to have repercussions. The greater bloodmeal size that is observed as a parental effect [12] would probably lead to an increase in the number of host contacts and increase transmission in a natural feeding environment [20,21]. Changes in the transmission probabilities would affect contemporary epidemiology for malaria, but are also likely to cause a shift in parasite virulence [22]. Concerning the second, more surprising, result of Grech *et al.* [12], it is more difficult to make predictions on the impact of a shift in the reproductive strategy of the mosquito vector (e.g. lower number of reproductive events and higher fecundity of females) [12] because this might affect the population dynamics in many ways depending on the long-term consequences of these changes. Alterations in the number of reproductive events could cause changes in the population biology of vector mosquitoes, which in turn would have an effect on parasite transmission between vectors and definitive hosts.

The parental effects observed by Grech *et al.* [12] would almost certainly impact on host–parasite dynamics. Therefore, more studies are needed that investigate not only the presence of parental effects but also the consequences in terms of ecology, epidemiology and evolution. This is particularly valid in hosts that are vectors of medically and economically important diseases for which current control strategies are unlikely to consider the impact of trans-generational effects.

### Disease control

Strategies aiming to control serious vector-borne diseases, such as malaria, often focus on the biology of the vector. The results of Grech *et al.* suggest that knowledge of trans-generational effects produced by altered parental environment will be important in the planning and ultimate implementation of control strategies. Conversely, successful control strategies could be undermined by phenotypic changes in mosquitoes that counteract the desired effect of the control strategy. A hypothetical example can be highlighted based on the tactic of targeting habitats that are ecologically favour-

able for mosquito larvae. Manipulation of mosquito larval habitats is often touted as a highly successful strategy for malaria control [12,23]. Although it has achieved success [24], the supporting models for its use ignore life-history changes in the target mosquitoes [23]. Given the results of the study by Grech *et al.* [12], we can envision a situation in which the targeting of larval habitats could lead to at least short-term detrimental effects. The origin of mosquito populations would shift to poorer larval environments, and thus would have an impact on life-history in a way that could increase malaria transmission probability.

The influence of parental environment might not only be important when considering control strategies in the natural populations. Release of mass-reared genetically transgenic mosquitoes has been suggested to enable the introgression of genes conferring refractoriness into natural populations [25]. Given phenotypic plasticity and trans-generational effects, thought must be given to the rearing conditions used in these programmes [12]. More ecological studies such as that of Grech *et al.* [12], including using naturally isolated animal stocks, will enable greater understanding of parental effects and could lead to the development of more effective and efficient control strategies. Given the potential for complex context-dependent parental effects [9] these studies should be carried out with a mature approach over several generations, considering life-history as a multivariate suite of traits.

### Conclusion

The study by Grech *et al.* [12] highlights the importance of ecological studies, particularly in important vector insects such as mosquitoes. Although genetic investigations of these organisms are vital, whole-organism ecological work uncovers potentially important phenomena that would otherwise be overlooked. This includes the effects of the parental environment on offspring phenotypes which, whether an adaptive plastic response or a mere by-product of changes in the parent, will have crucial repercussions on a variety of levels. Further studies on parental effects are important and should consider not only the short-term ecological impacts, but also the consequent evolutionary dynamics of affected traits and multi-species interactions. Furthermore, researchers should be mindful of these effects and their consequences even if they are not the main focus of their study.

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## Research Focus

# New insight into the role of dendritic cells in malaria immune pathogenesis

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**The mechanism by which the host develops protective immunity to malaria remains poorly understood. Dendritic cells (DCs) are central to the initiation and regulation of the adaptive immune response. Modulation of DC function might enable *Plasmodium* to evade the immune system. Millington *et al.* propose one mechanism by which malaria inhibits DC–T-cell interactions without interfering directly with T-cell receptor engagement. The consequence is a decrease in the co-stimulation required to develop an effective immune response.**

## Immunity to malaria infection is elusive

Malaria is a devastating disease caused by the *Plasmodium* parasite, which kills nearly 3 million people and infects more than 400 million each year. Knowledge of the mechanisms leading to protective immunity is surprisingly limited. The optimal immune response to malaria infection involves early proinflammatory, cytokine-mediated, effector mechanisms that clear parasite-infected cells, which are then suppressed equally rapidly by anti-inflammatory effectors once parasite replication has been brought under control [1]. The immune mechanisms that control and kill the parasite are also implicated in subsequent immunopathology. Thus, a potent and timely response of inflammatory cytokines

leads to an effective immune control of the parasite, but their excessive production will result in severe clinical disease or death [1].

Malaria infection can also suppress the generation of antimalarial immune responses [2–4]. The suppression is thought to be mediated through apoptosis, parasite inhibition of macrophage activation and antigen processing and, more recently, through their inhibition of dendritic cell (DC) maturation or alteration of DC function [5,6]. These inhibitory mechanisms probably include the activation of the presenting DC.

## DCs mediate the adaptive immune response

DCs initiate the immune response by providing antigenic stimulation for T and B cells. DCs provide a crucial link between the innate and adaptive immune response and are specialized in the uptake, processing and presentation of antigens to T cells. These antigens are presented in the context of major histocompatibility complex (MHC) class II to T cells along with CD80/CD86 co-stimulations. DCs are the only antigen-presenting cells (APCs) that can activate naïve T cells [7]. The activated T cells are then able to produce cytokines that promote the maturation of the cellular responses directly and help B cells produce antibody. These interactions initiate a cascade of cellular and molecular events that lead to an effective adaptive immune response. The precise nature of the DC–parasite inter-

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