

Ecological immunology: costly parasite defences and trade-offs in evolutionary ecology

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Growing interest in the evolutionary ecology of host-parasite interactions^{1,2} has placed parasites firmly in the centre of many fields that are of considerable interest to ecologists and evolutionary biologists. A host of studies has sought both experimental and correlational evidence for the impact that parasites may have on host life-history evolution, sexual selection and population dynamics. Faced with a wide array of different parasite taxa, which seek to exploit hosts as a resource for their own reproduction, hosts have evolved a wide range of adaptations to prevent initial parasite infection and subsequent proliferation. These adaptations range from the extraordinary complexity of antigen-specific cell-mediated responses found in vertebrates³ and the simpler humoral and cell-mediated responses of invertebrates⁴, through (conceptually) simpler barrier mechanisms³, to behaviours that may reduce the likelihood of an individual becoming exposed to a parasite⁵ or that may act to control infections once they have developed⁶.

One common factor that links all classes of immune function is that their operation requires resources that the host might otherwise have used for some other function. The assumption that immune function is costly to the host seems reasonable and has some direct and indirect support⁷. Little is known about the direct energetic costs of mounting an immune response *per se*, as opposed to any metabolic change caused by parasites themselves: experimental infection may have dramatic effects on host metabolism⁸. However, some immune responses (fever, for example) must have substantial energetic costs. Indirect evidence that immune function is costly to hosts of particular relevance to this review is the common observation that poor nutrition is associated with disease⁷. For example, experimental reduction of nutritional status in young bobwhite quail (*Colinus virginianus*) has been shown to result in reduced development of the organs involved in immune responses (the spleen and bursa of Fabricius) and in lower levels of cell-mediated immune function⁹. Behnke *et al.*¹⁰ have discussed optimal parasite regulatory responses of hosts, and argue that one should expect the immune response of a host to be optimized to the extent that low intensity infections will be tolerated if the costs of sterilizing immunity (complete removal of a parasite) outweigh the benefits. Obviously, optimal resource allocation to immune function will depend on other demands for re-

In the face of continuous threats from parasites, hosts have evolved an elaborate series of preventative and controlling measures – the immune system – in order to reduce the fitness costs of parasitism. However, these measures do have associated costs. Viewing an individual's immune response to parasites as being subject to optimization in the face of other demands offers potential insights into mechanisms of life history trade-offs, sexual selection, parasite-mediated selection and population dynamics. We discuss some recent results that have been obtained by practitioners of this approach in natural and semi-natural populations, and suggest some ways in which this field may progress in the near future.

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sources, and their associated benefits. It is this potential trade-off that has aroused the interest of ecologists in immunology. In this review, we discuss results obtained in some recent studies that have explicitly concerned themselves with the possibility that immune responses are optimized, and hence traded off against other costly functions. The majority of our examples are drawn from birds, but future studies will no doubt show greater taxonomic breadth⁴.

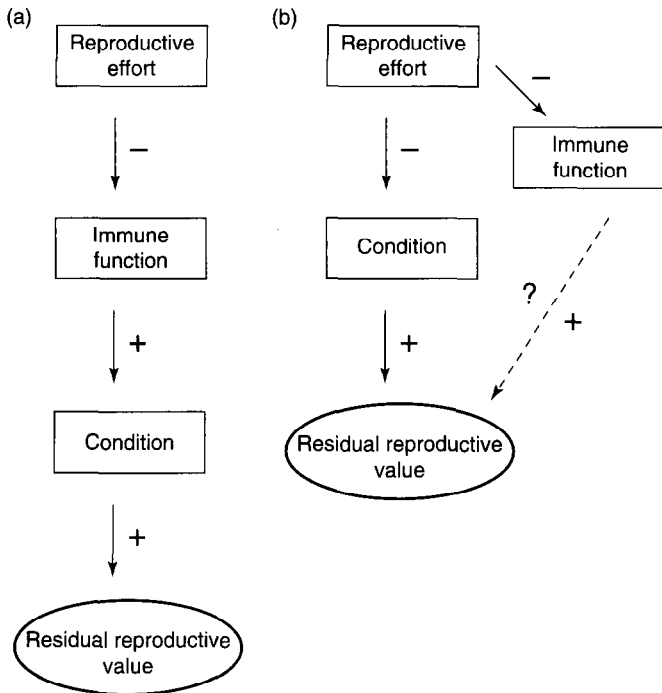
Reproductive trade-offs

Trade-offs between fitness components are a central concept in evolutionary biology. The trade-off between current and future reproduction in particular has received much attention, and the importance of the costs of reproduction (defined as a decrease in residual reproductive value as a consequence of parental effort) in the evolution of life histories is well established¹¹. However, it is not yet understood how an increase in reproductive effort leads to a reduction in reproductive suc-

cess later in life. This is a fascinating problem, because a year may elapse from the reproductive effort concerned until the costs of reproduction are paid¹². Recent developments suggest that immune suppression may form a link between reproductive effort and the costs of reproduction.

Festa-Bianchet¹³ showed that lactating bighorn ewes (*Ovis canadensis*) had greater faecal counts of lungworm larvae than non-lactating ewes, and ewes that raised sons had greater faecal counts of lungworm larvae than ewes that raised daughters (which are cheaper to produce). This suggests that bighorn ewes allocated resources to reproduction at the expense of resources available to parasite defence. Festa-Bianchet exploited natural variation in reproductive effort to investigate the effect of reproductive effort on parasite prevalence, but natural variation in reproductive effort may be confounded with variation in phenotypic quality. However, experimental studies confirm the observed pattern. Manipulations of brood size in collared flycatchers (*Ficedula albicollis*) result in negative relationships between brood size and serological parameters indicative of immune function¹⁴. Norris *et al.*¹⁵ manipulated brood size in great tits (*Parus major*), and concluded that enlarging brood size increased parasite prevalence in males, but not in females. However, reducing brood size also increased parasite prevalence in males, and interpretation of the results of Norris

Box 1. Immune suppression and the cost of reproduction: cause or correlated response?

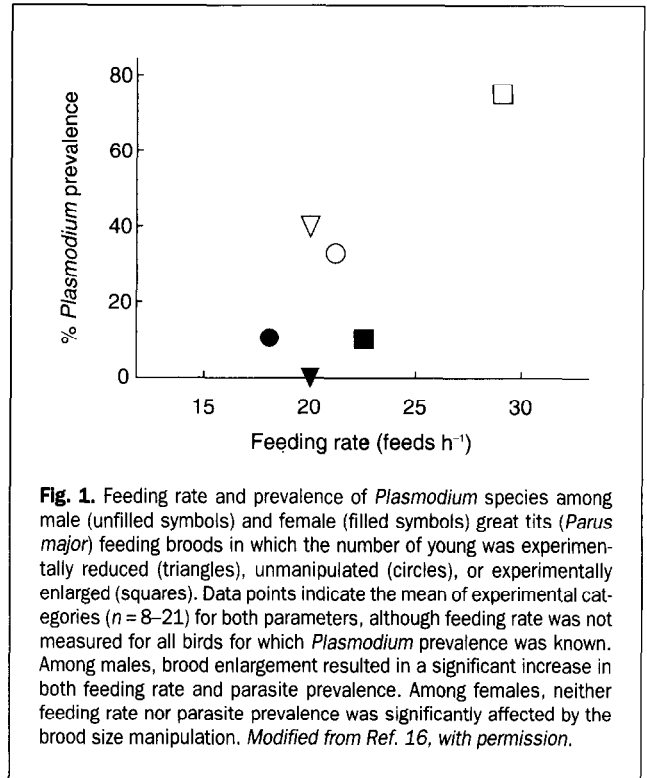


Recent studies have indicated that a relationship exists between reproductive effort and immune function (e.g. Fig. 1 and Refs 14–17), and it has been suggested that the costs of reproduction may arise through lowered condition resulting from immune suppression [see Fig. (a)]. However, the possibility cannot yet be excluded that reproductive effort affects both immune function and other aspects of condition, simultaneously [see Fig. (b)], and, that the effect of immune suppression on residual reproductive value is quantitatively unimportant. Indeed, a cynical view would be that effects of brood size manipulation on immune function are readily detected because this is not so important in determining future reproductive output. To demonstrate a role of immune function in mediating the costs of reproduction, it is required that immune function itself be somehow experimentally manipulated. This might be achieved by pharmacological treatment to control current infections, thereby reducing the extent of immune function raised by the animal. Demonstration that the expression of the costs of reproduction is dependent on (manipulated) immune function is a necessary condition needed to confirm the role of trade-offs involving parasite defence in mechanisms mediating the costs of reproduction.

et al. is hampered by the experimental design in which (on average) small clutches were enlarged, and large clutches were reduced, so that the degree of experimental manipulation was not independent of original clutch size.

Richner *et al.*¹⁶ also manipulated brood size of great tits (Fig. 1), and found an increase in the prevalence of malaria in males with enlarged broods, but no effects of brood size reduction and no effects in females. The effect of the brood size manipulation on feeding rate was also recorded. Interestingly enough the only detectable experimental effect was an increase in feeding rate of males with enlarged broods, but no effects of brood size reduction, and no effects in females. It is important that this study demonstrated an increase in reproductive effort, since an effect on immune function can only reasonably be expected when the birds adjust their effort to the new brood size.

Reproductive effort can lead to an increase in parasite prevalence through a reduction in resources allocated to parasite defence by the host, but it is also possible that reproductive effort covaries with exposure to parasite vectors. Apanius *et al.*¹⁷ presented captive zebra finches (*Taeniopygia guttata*) rearing manipulated broods with an immunological



challenge using sheep erythrocytes. They showed that immune response (antibody responsiveness) was adversely affected by brood size, thereby controlling for any difference in prior exposure with respect to treatment. Complementary results have also been obtained in bumblebees (*Bombus terrestris*), where workers that were allowed to forage showed a reduced immune response to a novel antigen compared with workers that were prevented from foraging⁴. These results indicate that resource allocation to immune function is one part of the link between reproductive effort and parasite prevalence (but do not exclude the possibility that covariation between work rate and exposure to parasites plays an additional role).

It is clear that the first steps have been taken towards an understanding of the role of parasite defence in the evolution of life histories, but it is also clear that there are some major gaps in our knowledge. Most importantly, it remains to be demonstrated that the experimental effects on parasite prevalence and immune function play a significant role in the causation of the costs of reproduction. As pointed out by Norris *et al.*¹⁵, manipulation of immune function is required to demonstrate a causal relationship between immune function and future reproductive output (Box 1). Thus, future research should focus not only on the relationship between reproductive effort and immune function, but also on the effect of variation in immune function on future reproductive output.

Sexual selection

Hamilton and Zuk's landmark paper¹⁸ alerted many biologists to the possibility that parasites were of fundamental importance in the evolution of sexually selected characters and in the maintenance of female preferences for ornamented males. Although their ideas have proven difficult to test definitively¹⁹, interest in the role that parasites play in maintaining the honesty of sexual ornaments has been further stimulated by the immunocompetence handicap hypothesis²⁰. This hypothesis, a mechanistic extension of Hamilton and Zuk's original idea²¹, proposes that androgens have a dual

role in that they simultaneously increase expression of sexual ornaments, while suppressing immune function. Recent debate in *TREE* has centred on the extent to which androgens (particularly testosterone) are actually involved in ornament expression²¹ and the possible role that other hormones (for instance, corticosteroids) may play instead of androgens^{22–24}. However, it is possible to consider a much simpler version of the immunocompetence handicap, which omits hormones entirely^{14,22}: in this case, possession or maintenance of the ornament is considered to be costly in terms of some limiting resource (energy?) with the result that less of that resource can be devoted to other important functions, of which immune function might be one. The resulting immunosuppression could have long-term fitness consequences. This particular suggestion is attractive in that it fits well with handicap theories incorporating individual variation in condition²⁵ in predicting that the cost of a given size of ornament will be lower for individuals in better physiological condition.

A further attraction of considering individual condition to be the factor that determines the immunosuppressive cost of a sexual ornament is that this model of the enforcement of ornament honesty is rather similar to immune suppression mediated models of the cost of reproduction (see previous section and Box 1). As Gustafsson *et al.*²⁶ have recently shown for male collared flycatchers, trade-offs exist between reproductive effort and ornamentation, and this raises the intriguing possibility that there may be common mechanisms involving immune function mediating physiological trade-offs between pairs of life history traits and between life history traits and sexual ornaments¹⁴.

Empirical tests of whether the costs of ornament exaggeration are due to immune suppression are more difficult

Box 2. Comparative ecological immunology

Intraspecific studies suggest that immune function may play an important role in the mechanisms behind life history trade-offs^{13–17}, and also in maintaining the honesty of secondary sexual characters^{14,27}. These findings suggest that variation in immune function might also be related to interspecific variation in life histories and sexual selection. For example, sister-taxon comparisons of North American and European birds reveal that fewer individuals of polygynous species are infected with blood parasites than is the case for monogamous species, even after controlling for numerous, potentially confounding variables⁴⁰. One possible explanation of this is that polygynous species tend to be more resistant to parasites and that polygyny results because females preferentially settle to breed with resistant males⁴⁰. This hypothesis would be supported if, under standardized conditions²⁴, individuals from polygynous species showed greater responses to immune challenge than monogamous species in the same taxon. Comparative studies of immune function might also shed light on the extent to which different life histories are associated with different degrees of threat from parasites, for example, whether coloniality is associated with a greater risk of parasitism, or whether higher reproductive rates are associated with lower levels of immune function. Indeed, comparative analyses using the size of the spleen and bursa of Fabricius as an indication of the ability to mount an immune response suggest that coloniality nesting bird species may have been selected to produce stronger immune responses than solitary nesting species⁴¹.

to perform than the corresponding tests in the case of reproductive costs, owing to the difficulty in manipulating sexual ornaments satisfactorily. However, recent work²⁷ on the barn swallow (*Hirundo rustica*), which provides a notable exception to this rule, shows that ornament exaggeration decreases immunocompetence (Fig. 2) and therefore suggests (subject to the same caveats expressed in Box 1) that immune suppression may explain why it is costly to carry exaggerated ornaments. Saino and Møller²⁷ manipulated tail length in male swallows, while simultaneously immunizing males with a suspension of sheep red blood cells (SRBCs). They then measured the change in immunoglobulin (Ig) concentrations for males in their different experimental groups. Immunization with SRBCs was performed to mimic a challenge to the birds' immune systems by a novel parasite. This controlled for any prior exposure, acquired immunity, or difference in risk of infection resulting from a behavioural change associated with the manipulation. Males that were controls, or that had had their tails shortened, showed significant increases in Ig concentrations three weeks after immunization with SRBCs, whereas males with experimentally elongated tails did not have increased Ig levels, as was the case for males that had not been subject to an immune challenge (Fig. 2). Furthermore, within the group of males with elongated tails (where the treatment had affected immune competence) males with long tails before manipulation responded more strongly to SRBCs than males with short tails: thus, large-ornamented males were apparently better able to cope with an increase in ornament size than males with small ornaments, as predicted by conditional handicap models²⁵. It is not clear from this work why males with elongated tails are immune compromised, but this might result from the direct energetic costs of carrying a longer tail, or perhaps more plausibly, through tail elongation reducing foraging efficiency.

Saino and Møller's experiment²⁷ shows a relationship between the phenotypic value of an ornament involved in female choice and immunocompetence. However, in order for this system to satisfy 'good genes' models of female choice, females must acquire the genes that affect offspring fitness via their choice of a father for their offspring. Thus, one very important future task in elucidating the role of immune function variation in female choice is to determine the extent to which genetic correlations exist between ornaments and measures of immune function. Measuring genetic correlations is not a trivial task, particularly in the field, but

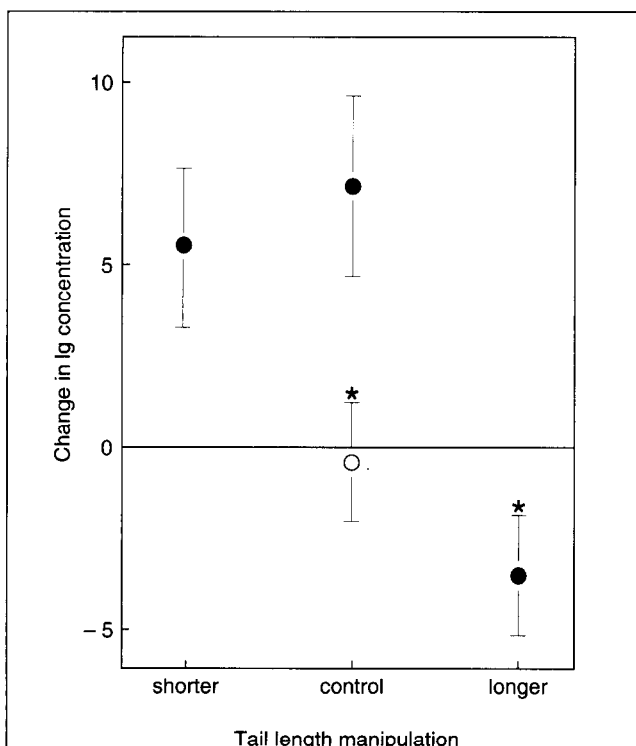


Fig. 2. Changes in relative immunoglobulin (Ig) concentrations (mean \pm SE) of male barn swallows (*Hirundo rustica*) following tail length manipulation and immunization with sheep red blood cells (filled circles). Part of the control group (unfilled circles) was not immunized and thus serves as a control for immunization. Asterisks show the means that differ significantly ($P < 0.05$) from the immunized control group. Drawn from data in Ref. 27.

Box 3. Psychoneuroimmunology: trade-offs between immune function and learning and memory?

Recent experimental work in animal learning has begun to document marked effects of parasitic infections on the ability of individuals to learn and remember certain tasks (for example, spatial learning problems)⁴². It is not clear yet whether these effects result from a detrimental effect of the parasite *per se*, or whether they are the result of the host's immune response to the parasite competing with some resource required for learning, or otherwise interfering with learning. The latter is at least a possibility: the field of psychoneuroimmunology⁴³ is concerned with the study of interactions between the brain, behaviour and the immune system, and has demonstrated remarkable links, operating in both directions, between the brain and the immune system⁴³. For example, there is considerable evidence from studies of both laboratory animals and humans, that both immune suppression and the enhancement of immune responses can be subject to classical conditioning⁴³. The possibility that learning may be traded off against immune function suggests that studies of intraspecific variation in spatial learning (e.g. food hoarding) and song learning in birds might benefit from investigation of the immune status of learning individuals. Certainly, these considerations offer a potential explanation for the puzzling observation that song repertoire size in birds appears to be a condition-dependent trait.

substantial genetic variation is known to exist in chickens for many of the measures of immune function that ecologists are starting to assess in wild organisms^{28,29}. Secondary sexual characters and signals (e.g. badges of status) involved in interactions between males do not require genetic variance in order for signalling systems to be honest, and here the question of what mechanism maintains honesty is not dissimilar to that concerning the mechanism mediating costs of reproduction. Some preliminary evidence from the collared flycatcher¹⁴ implicates immune suppression as a cost paid by males with experimentally enlarged 'badges of status', but further experiments to address this issue are needed.

Population dynamics

The role of parasites and disease in population dynamics has been much discussed, and it is now firmly established that parasites can theoretically play an important role in population regulation³⁰. For example, in a recent review in *TREE*³¹, it was argued that disease has been important in the extinction of several species, and immunosuppression,

Box 4. What to measure?

An ecologist interested in going out into the field to test whether a trade-off with immune function may limit some biological process in which he or she is interested faces the problem of deciding what to use as an assay of immune function^{24,44}. The initial studies in this field^{13,15,16} took a decidedly functional approach, since they looked for differences in parasite prevalence with respect to experimental treatment. Quite apart from the fact that these studies have been restricted to single taxa, a detectable parasitic infection occurs so far 'downstream' that many things other than immune suppression could be responsible for an increased prevalence. Encouraging results¹⁴ have been obtained using simple serological measures (haematocrit, sedimentation rate, leucocyte profiles) indicative of immune function, but the difficulty with these is one of interpretation (does a high leucocyte count represent an immune-competent individual, or a relatively immune-incompetent individual that is forced to respond to an infection?) without introducing circularity into the interpretation²⁴. More recent studies^{4,17,27} have used simple assays that might be more easily recognized by immunologists as measuring some aspect of immune competence (i.e. the ability of an individual to respond to a novel parasite), but these techniques still require the assumption, at present, that there is a positive relationship between the assay of immune competence and some component of fitness²⁴. As discussed recently⁴⁴, some evidence of this nature does exist, and toxicologists have developed a series of assays that can be successfully applied to organisms in natural or semi-natural states^{9,44}. The difficulty in doing this should not be underestimated, however⁴⁴, and some critical tests of ideas concerning immune function trade-offs in natural populations may have to be performed in populations of laboratory animals, where the potential for manipulative experiments is far greater^{39,45}.

for example, has been suggested to play a central role in population regulation in the marsupial genus *Antechinus*³².

The trade-off between reproductive effort and immune function adds a new dimension to the role of parasites in population regulation. Reproductive effort will directly affect population size, since a larger effort results in higher offspring production. At the same time, however, at the population level, an increase in the mean reproductive effort may increase parasite prevalence (the proportion of animals carrying a given parasite) and parasite intensity (mean parasites per individual). This effect arises initially because of the trade-off between reproduction and immune function in individual animals (Box 1), but will subsequently be amplified because higher parasite prevalence and intensity will result in higher transmission rates between hosts. In addition, an increase in host density generally results in higher transmission rates (e.g. Ref. 33). Thus ecological immunology bridges some traditional areas of research in ecology (life history evolution, population dynamics and host-parasite interactions).

Prospects

Promising advances have been made in our understanding of some important behavioural and ecological problems by considering the role of immune function, and considerable potential exists for comparative studies (see Box 2) and further experimental studies in those areas discussed above, and in other areas (see Box 3). For example, studies investigating the effects of reproductive effort on parasitism are producing results that are consistent with immune suppression resulting from increased effort¹⁴⁻¹⁷, and there are now some results indicating that immune function could play a role in maintaining the honesty of sexual ornaments²⁷. Unfortunately, experimental evidence showing that infection with the responding species of parasites has non-negligible fitness consequences is generally lacking, as is evidence that the measures of immune competence made in the field so far^{4,17,27} are related to fitness. The credibility of hypotheses concerning the role of immune suppression in costs of reproduction and in the limitation of ornament exaggeration depends critically on such evidence. Further studies will also need to consider carefully how to assay immune function²⁴ (see Box 4). Although some of the most recent studies of immunocompetence and its relationship to ecological questions have used general experimental assays of immune function^{4,17,27}, immune function is a multivariate response to many kinds of parasite, and one difficulty lies in measuring an adequate number of variables simultaneously.

Behnke *et al.*¹⁰ suggested that resource allocation to immune function may be subject to optimization. Studies discussed above indicate that resource allocation to immune function does seem to be a flexible process, of which the outcome appears to depend on other resource demands. The development of a more quantitative understanding of variation in resources allocated to immune function will also depend on insights into the costs and benefits associated with parasites and immune function. Such knowledge may also provide us with a functional understanding of the often described difference in disease susceptibility between the sexes^{20,34}. A related issue, but one outside the scope of this review, concerns the extent to which parasitic infection alters residual reproductive value, with the result that individuals may make adaptive changes in patterns of resource allocation to reproduction³⁵.

Immunogenetic studies of wild populations offer potentially exciting insights within the next few years. The genes of the major histocompatibility complex (MHC), which code

for proteins involved in presenting foreign peptides to T cells, are among the best known of all vertebrate gene complexes³⁶, and are present in most, if not all, vertebrate classes³⁷. Modern molecular biological techniques make it quite feasible to characterize alleles in a species where nothing was previously known about the MHC (e.g. Ref. 37). Considerable debate rages over what factors maintain the extreme diversity found at MHC loci^{38,39}, and studies of selection on MHC alleles in natural populations could provide some answers to these questions³⁶. At the same time, cooperation between ecologists with an interest in immunology and molecular geneticists has the potential to provide fascinating information into the extent to which variation in components of immune function reflect genetic differences between individuals.

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