8-4-2022

Anticipating Infection: How Parasitism Risk Changes Animal Physiology

Patricia C. Lopes

Anticipating Infection: How Parasitism Risk Changes Animal Physiology

Received: 19 April 2022 | Accepted: 1 August 2022

DOI: 10.1111/1365-2435.14155

Functional Ecology | BRITISH ECOLOGICAL SOCIETY

PERSPECTIVE

Infection-Induced Phenotypes

Anticipating infection: How parasitism risk changes animal physiology

Patricia C. Lopes

Schmid College of Science and Technology, Chapman University, Orange, California, USA

Correspondence
Patricia C. Lopes
Email: lopes@chapman.edu

Handling Editor: Sandra Binning

Abstract

1. Uninfected animals can attempt to prevent parasitism in many ways. Behavioural avoidance of parasitized conspecifics, for instance, is documented in several species.
2. Interactions with parasitized conspecifics can also, however, lead to *physiological changes* in uninfected animals, an effect that is much less well studied, and consequently, less well understood. The way in which exposure to parasitism risk changes the physiology of uninfected animals and the impacts of those changes on animal fitness remain a significant gap in knowledge.
3. Determining how the disease environment experienced by animals impacts their physiology, survival and reproduction has major implications for our knowledge of how parasites affect populations beyond their consumptive effects. If the physiological changes triggered in uninfected animals help reduce disease burden or speed up recovery from disease, they can have cascading effects on disease dynamics; therefore, they are important to study and understand.
4. In this perspective, I highlight studies in vertebrates and invertebrates that demonstrate the existence of these responses. I also consider how these responses may be adaptive and instances when they should occur. Finally, I briefly discuss the importance of studying these responses in relation to animal welfare, human health, disease dynamics and experimental design.

KEYWORDS
anticipatory response, disease, immune defences, infection, intergenerational, parasites, pathogens, social interactions

1 | INTRODUCTION

Animals can perceive the risk of parasitism. The best line of evidence for this is the multiple studies of behavioural avoidance of parasites (Cremer et al., 2007; Lopes, 2020; Lopes et al., 2022; Meunier, 2015). Animals are able to detect parasitized conspecifics and their cues, they can detect contaminated habitats, food and water, and, in a few instances, it has even been shown that animals detect parasites

themselves (Lopes et al., 2022). Detection of these indicators of risk of parasitism elicits changes in behaviour that can help reduce parasitism. These changes in behaviour upon detection of parasitism risk are therefore considered an animal's first line of defence against parasites. The most well-studied defences against parasites are, however, the ones occurring after the onset of infection, involving a set of physiological responses that can help limit parasite growth, reduce tissue injury and support tissue repair—immune responses. Given that animals can detect parasites, why not trigger some of these immune responses pre-emptively, in a prophylactic manner, when in situations of high risk of parasitism?

In this perspective, I will highlight studies that have shown that animals produce physiological responses to parasitism risk. I then discuss our current understanding of how these responses may affect animal fitness, with implications for disease transmission. My aim is to encourage research into these mechanisms, as well as their consequences, so we can better understand the underlying causes of variation in disease susceptibility, and better predict disease spread.

Physiological responses will be considered as biophysical and biochemical responses taking place at the cellular or organ level (such as reproductive, immune or neural responses) while behavioural responses will be considered as organismal level actions (such as eating, drinking or running). Please note however that, ultimately, these responses are connected because behavioural responses can affect physiology and physiology controls behaviour. More specifically, I consider here physiological responses to parasitism risk as those physiological responses that take place in organisms that are aware of parasitism risk but are not themselves currently parasitized. I will use the terms parasite and pathogen interchangeably, as organisms that reduce the fitness of their host, and include both macro (e.g. worms and ticks) and micro-organisms (e.g. bacteria and viruses) when using these terms.

2 | PHYSIOLOGICAL RESPONSES TO PARASITISM RISK

The fact that animals can detect and behaviourally avoid parasitized animals already indicates that sensory mechanisms respond to disease cues and help activate neural circuitry that will lead to avoidance behaviours. Indeed, these sensory and neural integration mechanisms have been studied in rodents and humans (Arakawa et al., 2011; Curtis et al., 2011; Holle et al., 2012; Kavaliers et al., 2019, 2020, 2022; Regenbogen et al., 2017). While rodents may rely more heavily on olfactory cues to sense parasitism (Kavaliers et al., 2020), in humans, both visual and olfactory cues from sick donors elicit stronger neural activation in face and odour-perception neural networks than cues from healthy donors (Regenbogen et al., 2017). Observing other people scratching themselves often leads to feelings of itchiness in the observer and has been shown to activate brain regions associated with the physical perception of itch (Holle et al., 2012). Equivalent mechanisms are expected to occur in any taxa that show behavioural or physiological responses to parasitism risk. For example, in the fruit fly *Drosophila melanogaster*, the sense of sight, but not of smell, was shown to be essential for responses to the presence of a parasitic wasp (Kacsoh et al., 2013). As will be discussed later, however, it is possible that, in certain taxonomic groups, perception of parasites in the environment can directly trigger physiological responses, whereas in other groups, these responses are triggered by perception of cues produced by infected conspecifics. Here, my aim is to draw focus to physiological responses that go beyond the ones involved in sensory detection of parasitism risk.

How, after detection of parasitism risk, the brain can change other physiological systems has not been explicitly studied. One possibility would be through the activation of the stress response (including the sympathetic nervous system and adrenomedullary and adrenocortical responses), which, in turn, affects a lot of organ systems. But brain activities have also been recently shown to more directly control, for example, immunological defences. For instance, activation of certain brain neural populations (e.g. parts of the reward system or of the insular cortex) can activate both innate and adaptive immunity (Ben-Shaanan et al., 2016; Koren et al., 2021; Zhang et al., 2020). Innate immunity refers to non-specific defences (it is considered the first line of defence) while adaptive immunity refers to immune defences that are antigen specific and which can, in addition, form memory. In 2009, Oaten and colleagues suggested that disgust may be associated with immune function (Oaten et al., 2009). They proposed that cues that evoke disgust were very likely to also lead to a mobilization of the immune system, particularly the innate arm. This idea was inspired by studies that show that immune responses can be conditioned (e.g. placebo effect; Pacheco-López et al., 2006) and by the overlap between brain regions that are involved in disgust processing and those central to immune conditioning (reviewed in Oaten et al., 2009). The same way that neural disgust and immune conditioning brain regions show overlap, neurotransmitters that modulate behaviour can also have immunomodulatory roles. For example, dopamine, a neurotransmitter important for motor control, and for processes such as reward, learning and cognition, has also been shown to modulate a variety of immune cells, affecting both central and peripheral immune responses (Matt & Gaskill, 2020). It has also been hypothesized that the neurotransmitter serotonin may modulate both parasite behavioural avoidance and immune responses (Curtis, 2014). We are only now beginning to understand the full extent to which the central nervous system can affect peripheral immune responses (Veiga-Fernandes & Artis, 2018). However, the existence of this type of relationship helps explain how physiological responses to parasitism risk, as reviewed in the following paragraphs, are possible. Conversely, expanding our understanding of physiological responses to parasitism risk will lead to an increased knowledge of neuronal–immune system relationships.

In 2010, Schaller and colleagues set out to test the idea proposed by Oaten et al. (2009) that immune responses could be elicited by cues that evoke disgust. To test this, they exposed participants to either images of people with morphological (e.g. skin lesions) and

behavioural (e.g. sneezing) cues of disease or images of people carrying firearms aimed at the participants (this served as a threatening stimulus). Participants had their blood drawn before and 30 min after being shown the images, and their blood cells were tested in vitro for their ability to produce interleukin 6 (IL-6) in response to a bacterial challenge. It was found that the participant's cells produced more IL-6 when the participants were exposed to images depicting cues of disease than when exposed to images depicting a different threat (Schaller et al., 2010). Similarly, participants exposed to disgusting, but not those exposed to neutral or negative images, showed an increase in salivary tumour necrosis factor-α (TNF-α) and albumin at 10 min after being shown the images (Stevenson et al., 2011). In a separate study, researchers found that tactile sensitivity was increased following exposure to photographs or videos of disgusting images, but not following photographs or videos of threating images (Hunt et al., 2017). Since rapid changes to skin sensitivity are under physiological control (Farage, 2019), this is another indication of a physiological response to parasitism risk.

Studies in rodents corroborate the findings in humans (Table 1). Exposure of female mice to the odours of mice infected with a protozoan parasite or a nematode parasite induces an analgesic responses that can be either opioid mediated or nonopioid mediated depending on the length of exposure (Kavaliers & Colwell, 1992, 1995). Pregnant uninfected female mice housed across a perforated plastic partition from males infected with *Babesia microti* (a vector-transmitted parasite) showed blood serum levels of corticosterone higher than equivalent females housed across control males, as well as increased kidney weight (Curno et al., 2009). Interestingly, even diseases that are not contagious can elicit physiological changes in healthy animals. Female mice cohoused with a female inoculated with Ehrlich tumour cells showed a decrease in number of white blood cells (Morgulis et al., 2004). The activity of those females was also affected, with females cohoused with tumour-bearing females showing decreased exploratory behaviour, which could potentially be a compensatory mechanism for the decreased immunity. Additional studies showed that females cohoused with tumour-bearing females showed decreased levels and increased turnover of noradrenaline in the hypothalamus, altered microphage and neutrophil activity and reduced resistance to Ehrlich tumour growth (Alves et al., 2006, 2007). Later studies demonstrated that odours from tumour-bearing mice were sufficient to induce the behavioural, hypothalamic and immune changes observed (Alves et al., 2010, 2012). Changes to immune responses have also been found after cohousing of females with females inoculated with a different type of tumour (melanoma; Tomiyoshi et al., 2009), indicating that this physiological response is not exclusive to a particular tumour type. In sum, studies in mice suggest that diseases do not need to be directly contagious to elicit a physiological response in conspecifics. This may be the case because symptoms and cues expressed by non-infectious diseased conspecifics could still indicate the presence of environmental contaminants or of disease vectors. In addition, those symptoms and cues may overlap with the ones expressed by infectious animals and the precise disease may matter less for anticipatory responses. For example, itching behaviour could be used as an infection cue, but it can be elicited by both contagious (e.g. fungus or bacteria) and non-contagious sources (e.g. poison ivy or allergies). This idea could be investigated empirically by studying physiological responses upon exposure to cues from animals with contagious and non-contagious diseases.

A recent study in a bird species provided further evidence of physiological responses to parasitism risk. Uninfected domestic canaries (*Serinus canaria domestica*) with visual access to canaries infected with *Mycoplasma gallisepticum* (an infection that leads to both morphological—conjunctivitis—and behavioural symptoms of disease) showed higher complement activity and higher heterophil counts than birds housed across from control-treated birds (Love et al., 2021). Interestingly, these changes to immunity started only at the time point after inoculation when the infected birds showed the greatest degree of pathology (eye lesion score), which could suggest that visual cues are particularly important for birds.

Studies in invertebrates also seem to support the existence of physiological responses to parasitism risk (Table 1). When *Biomphalaria glabrata* snails are infected with *Schistosoma mansoni*, they increase egg laying shortly after infection. Interestingly, in laboratory experiments, exposure to this parasite in the absence of infection also led to increased egg laying shortly after exposure (Minchella & Loverde, 1981). This could suggest that parasitism risk elicits changes to reproductive physiology or other aspects of the maternal physiology that could facilitate the production of larger number of eggs. A study using beetles of the species *Tenebrio molitor* found that uninfected beetles that cohabited with beetles injected with heat-killed bacteria (*Staphylococcus aureus*) produced larger eggs than beetles that cohabited with PBS-injected or untreated controls (Gallagher et al., 2018). While egg size does not necessarily correlate with egg quality, increased egg size could suggest transfer of immune factors to the eggs, which would have a protective effect (Dhinaut et al., 2018). This study also supports the idea that parasitism risk affects maternal physiology. Another interesting host–parasite system that contributes to this idea is that of fruit flies (*Drosophila melanogaster*) and endoparasitic wasps. These wasps infect early larval stages of Drosophila by depositing their embryo and other components, which can be lethal to the Drosophila larvae. Adult Drosophila exposed to these wasps show reduced neuropeptide F production in specific brain regions, resulting in a drastic behavioural change that protects their larvae: they start exhibiting preference for laying their eggs in alcohol-laden food dishes or for food dishes with the highest alcohol content available (Kacsoh et al., 2013). Alcohol had been previously shown to reduce offspring infection by wasp larvae and to kill wasp larvae growing on offspring (Milan et al., 2012). When in the presence of the wasps, laying eggs in these alcohol dishes increased eclosion success, relative to when the alcohol dish option was not available (Kacsoh et al., 2013). An additional study using this host–parasite system identified several changes to the transcriptome of the germline of female Drosophila exposed to the wasps (Bozler et al., 2020), again showing changes to maternal physiology upon parasitism risk. Changes in gene expression

TABLE 1 Summary of some of the studies discussed in the text. Type of risk knowledge was divided into two categories: *Indirect*—Animals were never infected; *direct*—Animals were subjected to an infection or immune challenge and allowed time to recover prior to producing the physiological responses discussed in the table. In some studies, changes in reproductive output are reported because these may suggest changes in reproductive physiology, but other mechanisms may explain the changes in reproductive output (like changes in behaviour). These studies are marked with an asterisk

Species	Type of risk knowledge	Parasitism exposure	Sex tested	Physiological responses observed	Refs.
Human	Indirect	Photographs of morphological or behavioural cues of diseases	Males and females	↑ IL-6 after in vitro LPS challenge	Schaller et al. (2010)
Human	Indirect	Photographs of disgusting images	Males	↑ Salivary TNF-α and albumin	Stevenson et al. (2011)
Human	Indirect	Photographs or videos of disgusting images	Males and females	↑ Skin sensitivity	Hunt et al. (2017)
Mouse	Indirect	Odours of mice infected with a protozoan or nematode parasite	Females	Analgesic responses	Kavaliers and Colwell (1992, 1995)
Mouse	Indirect	Males infected with *Babesia microti*	Females	↑ Corticosterone ↑ Kidney weight	Curno et al. (2009)
Mouse	Indirect	Female inoculated with tumour cells	Females	↓ In number of white blood cells ↓ In noradrenaline in hypothalamus Altered microphage and neutrophil activity	Morgulis et al. (2004) Alves et al. (2006, 2007) Tomiyoshi et al. (2009)
Domestic canary, *Serinus canaria domestica*	Indirect	Females infected with *Mycoplasma gallisepticum*	Males and females	↑ Complement activity ↑ Heterophil counts	Love et al. (2021)
Fruit fly, *Drosophila melanogaster*	Indirect	Endoparasitic wasps	Females	↑ Neuropeptide F in brain Transcriptional changes to germline Transcriptional changes to head	Kacsoh et al. (2013); Bozler et al. (2020); Ebrahim et al. (2021)
Caenorhabditis elegans nematode	Indirect	Secondary metabolites or small RNAs from pathogenic bacteria	Hermaphrodites	Activation of neuromodulators ↓ In expression of *maco-1* gene in both mother and offspring	Meisel et al. (2014); Kaletsky et al. (2020)
Biomphalaria glabrata snail	Indirect	Exposure (but not infection) to *Schistosoma mansoni*	Females	↑ Egg laying*	Minchella and Loverde (1981)
Tenebrio molitor beetle	Indirect	Beetles injected with heat-killed bacteria	Females	Larger eggs*	Gallagher et al. (2018)
Blue-footed booby, *Sula nebouxii*	Indirect	Males inoculated with a diphtheria–tetanus vaccine prior to egg laying	Females	Earlier egg laying and earlier clutches with larger egg volume*	Velando et al. (2014)
Mouse	Direct	Previous infection with *B. microti*	Females	Offspring faster at clearing infection with *B. microti**	Curno et al. (2011)
House sparrow, *Passer domesticus*	Direct	Previous immune challenge (LPS)	Females	Second-brood offspring grew faster*	Bonneaud et al. (2003)

TABLE 1 (Continued)

Species	Type of risk knowledge	Parasitism exposure	Sex tested	Physiological responses observed	Refs.
House sparrow, *Passer domesticus*	Direct	Previous immune challenge (Newcastle disease vaccine)	Females	↑ Likelihood to lay replacement clutches* ↑ nbr. of eggs between 1st and 2nd clutch*	Bonneaud et al. (2004)
House wren, *Troglodytes aedon*	Direct	Previous immune challenge (LPS)	Females	↑ Body mass of sons* Stronger immune response to an antigen (daughters)*	Bowers et al. (2012)
House wren, *Troglodytes aedon*	Direct	Previous immune challenge (LPS)	Females	↑ Corticosterone Heavier offspring with enhanced immune responsiveness*	Bowers et al. (2015)
Siberian hamster, *Phodopus sungorus*	Direct	Previous immune challenge (LPS)	Males	↑ Testicular size and testicular activity	Weil et al. (2006)
Blue-footed booby, *Sula nebouxii*	Direct	Previous immune challenge (LPS)	Males	↑ Offspring produced*	Velando et al. (2006)

Abbreviations: IL-6, interleukin 6; LPS, lipopolysaccharide; TNF-α, tumour necrosis factor-α.

after exposure to parasitic wasps also occur in the heads of female Drosophila. Out of the 10 genes that showed increased expression in wasp-exposed females relative to unexposed females, nine were associated with the Gene Ontology terms 'immune response' and/or 'response to stress'. The tenth gene, and also the most strongly upregulated one, while not annotated by GO terms, also appears to be responsive to infections and stressors, and was necessary for an additional behavioural response shown by wasp-exposed females: accelerated mating behaviour (Ebrahim et al., 2021). In a different invertebrate, the nematode *Caenorhabditis elegans*, cues left behind by pathogenic bacteria (secondary metabolites and small RNAs) are sufficient to elicit changes in physiology and behaviour (Kaletsky et al., 2020; Meisel et al., 2014). These studies show that uninfected invertebrates can produce physiological responses directly to the presence parasites in the environment, which contrasts with the current knowledge in vertebrates, which show physiological responses to cues of parasitism from conspecifics.

3 | CAN EXAMPLES OF TERMINAL INVESTMENT REPRESENT PHYSIOLOGICAL RESPONSES TO PARASITISM RISK?

The terminal investment hypothesis proposes that investment in current reproduction should increase as the likelihood to survive to future reproductive events decreases (Clutton-Brock, 1984; Williams, 1966). Knowledge of high risk of parasitism (which could come from cues of parasitism or even from a previous infection) could serve a signal of reduced residual reproductive value. Physiological responses to parasitism risk could therefore also be involved in terminal investment. The snail study presented in the previous section, where snails exposed to but not infected by a parasite increased reproductive investment, would constitute such an example. In Table 1, we classified this type of parasitism risk knowledge (i.e. when an animal was never directly infected) as indirect. However, animals can also obtain parasitism risk information directly by having been recently infected and then allowed to recover, which we classified as direct risk knowledge. Four studies in female birds showed that knowledge of parasitism risk via an immune challenge (the effects of which are short lasting) led to increased reproductive investment at a later time (Bonneaud et al., 2003, 2004; Bowers et al., 2012, 2015). Similarly, female mice that had been previously infected with *Babesia microti* and allowed to recover before becoming pregnant had offspring that were better able to clear an infection against the same pathogen and that lost less weight during infection (Curno et al., 2011). These studies in vertebrates used different species and different immune/infection challenges, but the commonality is that the effect on reproductive investment was delayed relative to antigen administration. This is important as it indicates that animals had knowledge of parasitism risk but were not experiencing the acute effects of immune activation during the period of increased reproductive investment. Increasing reproductive investment during the

peak of immune activation may often be energetically incompatible (Norris, 1999; Sheldon & Verhulst, 1996). In case knowledge of parasitism risk in the absence of infection leads to activation of similar physiological pathways as the ones that trigger increased investment after infection, then physiological responses to parasitism risk could also lead to terminal investment.

These relationships between brief immune activation and terminal investment have also been found in experiments performed on males. Testicular size and activity were elevated for a long period of time (6 weeks) in male Siberian hamsters (*Phodopus sungorus*) given a single short-lasting immune challenge (lipopolysaccharide [LPS]) relative to controls, demonstrating an effect of knowledge of parasitism risk on reproductive physiology (Weil et al., 2006). After a single LPS injection prior to the onset of egg-laying, old blue-footed booby males (*Sula nebouxii*) produced more offspring than controls (Velando et al., 2006). Significantly, it is possible that some of these effects were mediated by female responses to male infection status. In a second study, blue-footed booby males received either a diphtheria–tetanus vaccine or a control injection during courtship (Velando et al., 2014). The female partners of these males laid eggs earlier and their earlier clutches had larger volume (sum volume of all eggs). This suggests that female physiology could have been responding to parasitism signals from the male. Indeed, in this same study, the authors showed that foot colour of vaccinated males was different from that of control males and that clutch volume positively correlated to foot colour. Taken as a whole, these studies show that knowledge of parasitism risk can affect both male and female physiology and that females can obtain this knowledge from their mates.

4 | ARE PHYSIOLOGICAL RESPONSES TO PARASITISM RISK ADAPTIVE?

Some interesting questions arise related to the function of these physiological responses to parasitism risk, one of the most critical being: are these responses adaptive? And, if so, under what timeframe? For example, do these responses help reduce the likelihood of the animal acquiring an infection? Do these responses help with infection resolution or with tolerance to the pathogen? Can the effect of these responses extend to additional generations, helping prepare the offspring for a high parasitism risk environment?

Not very much is known in terms of the benefit for the individual producing the responses. To answer this question, it will be interesting to know more about what aspects of the physiology are activated by parasitism risk and for how long. Let us, for example, consider the study by Schaller and colleagues in humans, where the blood cells of participants that had observed images representing disease risk had increased ability to produce IL-6 in response to LPS (Schaller et al., 2010). This physiological response would appear to be adaptative, because IL-6 can stimulate acute phase responses and immune reactions that would help resolve or reduce the burden of a bacterial infection. However, if the IL-6 response was dysregulated or too prolonged, it could lead to pathological effects and autoimmunity (Tanaka et al., 2014). The same is true for the pregnant female mice who had elevated plasma corticosterone levels when placed across from *B. microti*-infected animals (Curno et al., 2009). In the short term or at lower doses, exposure to glucocorticoids (such as corticosterone) can be immunostimulatory, but prolonged or high doses can suppress immune responses (Cain & Cidlowski, 2017). Studies focused on how knowledge of parasitism risk affects how animals respond to an infection will be needed to understand some of the benefits to hosts of these anticipatory responses.

If indeed these physiological responses to parasitism risk are linked to terminal investment, they might provide benefits to the animal producing them in terms of reproductive output, even in the absence of survival benefits. To expand on an example from the previous section, when female house sparrows (*Passer domesticus*) were given knowledge of parasitism risk through treatment with the Newcastle disease vaccine and their current clutch was removed, they were more likely to lay a replacement clutch and that clutch tended to be larger than their first clutch relative to controls (Bonneaud et al., 2004). So, even if the physiological responses to parasitism risk that led to this investment did not help with increased survival against a disease, they still helped the females produce more offspring. It will be interesting to study whether the likelihood and type of physiological response to parasitism risk produced changes depending on the life-history stage of the animal.

Where there appears to be more research is in support of an intergenerational benefit. When female mice were given knowledge of parasitism risk either prior to pregnancy (through infection) or during pregnancy (through exposure to infected animals), they produced offspring that were better able to clear an infection (Curno et al., 2009, 2011). Similarly, adult Drosophila that co-habited with a parasitic wasp had offspring with enhanced cellular immune responses following immune induction (needle piercing of the larval cuticle; Bozler et al., 2020). When adult *C. elegans* ingest a small RNA produced by *Pseudomonas aeruginosa* (a pathogenic bacterium), a gene called *maco-1* decreases in expression in both the mother and the offspring, leading to learned avoidance of this pathogen in both (Kaletsky et al., 2020). So, once again, the knowledge of parasitism risk (the adults had never been infected) led to benefits to the offspring. The benefits to offspring will most likely often depend on the degree of mismatch between the parasitism environment experienced by the offspring and the one experienced by the parent (reviewed in Bateson et al., 2014). It will be important for future studies to determine whether the reproductive period is a particularly sensitive period affecting the presence of physiological responses to parasitism risk. In the same vein, it will be relevant to understand whether these responses are sex biased and whether they depend on the mating system of the species. Given the existence of sex differences in immune responses (not all of which can be linked to reproductive hormone differences; Casimir et al., 2013; Klein & Flanagan, 2016), one would also expect sex differences in anticipatory physiological responses to disease risk, which may have implications for strategies (Figure 1) adopted by different sexes.

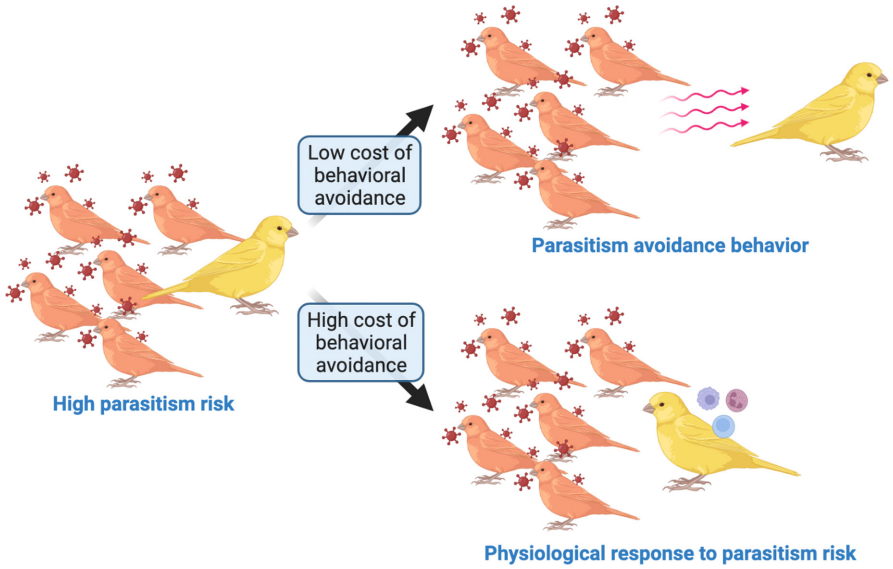

FIGURE 1 The balance between behavioural and physiological responses to parasitism risk. Animals can use behaviour to avoid parasitism, but research also shows they are able to change their physiology in response to parasitism risk. Whether animals can use both strategies at once is not clear. The image represents a high parasitism risk situation. Created with BioRender.com.

5 | WHICH TO EMPLOY: BEHAVIOURAL OR PHYSIOLOGICAL RESPONSES TO PARASITISM RISK?

The activation of a robust immune defence carries costs, including, for example, risk of tissue damage, as well as allocation of limited resources, such as energy and nutrients (Zuk & Stoehr, 2002). These defences should not therefore always be maximally activated and should be tightly regulated. Parasite avoidance behaviours are also not without costs (Buck et al., 2018). Costs can include, for example, nutritional costs of avoiding contaminated foods, reproductive costs of avoiding infected mates, energetic costs of having to spend longer periods of time searching for unparasitized nesting sites and even increased predation, when parasite avoidance behaviours are the same ones that attract predators (e.g. Raffel et al., 2010). Given the possible costs to behavioural and physiological responses to parasitism risk, I expect physiological responses to occur when the costs to parasite avoidance behaviours become too high and infection seems inevitable (Figure 1). Circumstances that increase the cost of behavioural avoidance could be used to test this idea. For example, in species where parental care is essential for offspring survival, behavioural avoidance of parasitized sexual partners may be possible, whereas avoidance of offspring may not be possible and an investment in anticipatory physiological responses to parasitism risk would be observed at this stage. Ackerman and colleagues had proposed two possible relationships between the behavioural avoidance of and physiological responses to parasitism risk (Ackerman et al., 2018): a compensatory and a complementary relationship. The compensatory relationship, which fits with the idea that animals will likely invest in one or the other strategy, would be when one form of response (e.g. physiological) can compensate for the lack of the other one (e.g. behavioural), and the complementary relationship, would come, for example, from when favourable conditions during development lead to individuals who can deploy both strategies when under high parasitism risk environments. One study in humans suggests the existence of a compensatory relationship. In that study, parasite avoidance traits were assessed using questionnaires and then tested for their relationship with markers of inflammation (Gassen et al., 2018). They found that participants that scored high in the Germ Aversion scale had peripheral blood mononuclear cells that released lower levels of IL-6 and TNF-α when unstimulated compared to levels released by blood cells of participants that scored low on that scale. In addition, participants with a high score on the Germ Aversion scale also had lower levels of plasma IL-6 and of oxidative DNA damage. These results suggest that humans that have a higher tendency to behaviourally avoid parasitism invest less in physiological preparedness to fight infections (i.e. a compensatory relationship between behavioural and physiological responses to parasitism risk). In addition to this study, given that progesterone is associated with a suppression of immune responses, researchers have tried to determine whether during periods of elevated progesterone, parasite avoidance behaviours increase (a compensatory relationship). In one study, researchers measured salivary progesterone in cycling women and found a positive relationship between progesterone and parasite avoidance behaviours (Fleischman & Fessler, 2011). In contrast, a more recent larger study found no association between salivary progesterone and parasite avoidance behaviours (Stern & Shiramizu, 2022). An experimental study using mice showed that pre-treatment with neither progesterone nor allopregnanolone (a metabolite of progesterone) altered female preference for uninfected male odours (Kavaliers et al., 2021). Interestingly,

a subsequent re-analysis of the Kavaliers et al. (2021) dataset did find that administration of either hormone reduced time spent near odours of infected males relative to the time control females spent near that stimulus (Bressan & Kramer, 2022), taken as indication that elevated progesterone raises disgust. The relationship between progesterone and parasite avoidance behaviours appears to be unresolved. Overall, little is known about the relationship between behavioural and physiological responses to parasitism risk and whether these responses can co-occur or whether they are employed separately (Figure 1).

6 | IMPLICATIONS AND CONCLUSION

Recently, it was proposed that the non-consumptive effects of parasites might overshadow their consumptive effects (Buck et al., 2018). In the context of parasitism, the consumptive effects correspond to deleterious effects inflicted by the parasites *directly* onto the infected hosts, and the non-consumptive effects correspond to responses of putative hosts to the perceived *risk* of parasitism. While non-consumptive effects are usually quantified as behavioural avoidance of parasites, this perspective highlights that the presence of parasites can also change the physiology of uninfected animals. These effects on physiology expand the scope of possible non-consumptive effects. Shining light on what type of physiological responses to parasitism risk occur and when they take place is crucial because it will expand our understanding of how variation in disease susceptibility arises (Lopes, 2017) and how anticipatory physiological responses to the risk of parasitism can influence disease and population dynamics.

It is also important to consider how the presence of parasitism risk may affect how experimental animals are housed. If the presence of diseased animals modifies the physiology of co-housed healthy animals in animal facilities, the scientific community must question what really constitutes a control treatment and how the welfare of co-housed animals and controls is impacted during experiments.

In conclusion, this perspective has combined studies from disparate fields to provide support for a phenomenon that appears taxonomically widespread but is poorly understood: physiological responses to parasitism risk. From a societal impact perspective, such responses may affect human health (Veiga-Fernandes & Artis, 2018), and an urgent understanding of how physiological responses to parasitism risk work, their costs and benefits, and when they occur is needed, given the increased likelihood of upcoming pandemic infectious disease events (Institute of Medicine, 2009) where the experience of parasitism risk is high.

ACKNOWLEDGEMENT

While this work was partly inspired by the COVID-19 pandemic, I am not thankful for the pandemic. I thank the Chapman University COVID-19 Impact Fund for summer funding and the Chapman University COVID-19 Faculty Excellence Task Force for pushing for the creation of that funding mechanism. Finally, I thank the reviewers and editorial team for the constructive comments and suggestions.

CONFLICTS OF INTEREST

I declare no conflict of interest.

ORCID

Patricia C. Lopes https://orcid.org/0000-0001-5170-3230

REFERENCES

Ackerman, J. M., Hill, S. E., & Murray, D. R. (2018). The behavioral immune system: Current concerns and future directions. *Social and Personality Psychology Compass*, *12*(2), e12371. https://doi.org/10.1111/spc3.12371

Alves, G. J., Ribeiro, A., & Palermo-Neto, J. (2012). The neuroimmune changes induced by cohabitation with an Ehrlich tumor-bearing cage mate rely on olfactory information. *Brain, Behavior, and Immunity*, *26*(1), 32–39. https://doi.org/10.1016/j.bbi.2011.07.228

Alves, G. J., Vismari, L., Florio, J. C., & Palermo-Neto, J. (2006). Cohabitation with a sick cage mate: Effects on noradrenaline turnover and neutrophil activity. *Neuroscience Research*, *56*(2), 172–179. https://doi.org/10.1016/j.neures.2006.06.012

Alves, G. J., Vismari, L., Lazzarini, R., Merusse, J. L. B., & Palermo-Neto, J. (2010). Odor cues from tumor-bearing mice induces neuroimmune changes. *Behavioural Brain Research*, *214*(2), 357–367. https://doi.org/10.1016/j.bbr.2010.06.003

Alves, G. J., Vismari, L., & Palermo-Neto, J. (2007). Cohabitation with a sick cage mate: Effects on ascitic form of Ehrlich tumor growth and macrophage activity. *Neuroimmunomodulation*, *14*(6), 297–303. https://doi.org/10.1159/000121284

Arakawa, H., Cruz, S., & Deak, T. (2011). From models to mechanisms: Odorant communication as a key determinant of social behavior in rodents during illness-associated states. *Neuroscience & Biobehavioral Reviews*, *35*(9), 1916–1928. https://doi.org/10.1016/j.neubiorev.2011.03.007

Bateson, P., Gluckman, P., & Hanson, M. (2014). The biology of developmental plasticity and the predictive adaptive response hypothesis. *The Journal of Physiology*, *592*(11), 2357–2368. https://doi.org/10.1113/jphysiol.2014.271460

Ben-Shaanan, T. L., Azulay-Debby, H., Dubovik, T., Starosvetsky, E., Korin, B., Schiller, M., Green, N. L., Admon, Y., Hakim, F., Shen-Orr, S. S., & Rolls, A. (2016). Activation of the reward system boosts innate and adaptive immunity. *Nature Medicine*, *22*(8), 940–944. https://doi.org/10.1038/nm.4133

Bonneaud, C., Mazuc, J., Chastel, O., Westerdahl, H., & Sorci, G. (2004). Terminal investment induced by immune challenge and fitness traits associated with major histocompatibility complex in the house sparrow. *Evolution*, *58*(12), 2823–2830. https://doi.org/10.1111/j.0014-3820.2004.tb01633.x

Bonneaud, C., Mazuc, J., Gonzalez, G., Haussy, C., Chastel, O., Faivre, B., & Sorci, G. (2003). Assessing the cost of mounting an immune response. *The American Naturalist*, *161*(3), 367–379. https://doi.org/10.1086/346134

Bowers, E. K., Bowden, R. M., Sakaluk, S. K., & Thompson, C. F. (2015). Immune activation generates corticosterone-mediated terminal reproductive investment in a wild bird. *The American Naturalist*, *185*(6), 769–783. https://doi.org/10.1086/681017

Bowers, E. K., Smith, R. A., Hodges, C. J., Zimmerman, L. M., Thompson, C. F., & Sakaluk, S. K. (2012). Sex-biased terminal investment in offspring induced by maternal immune challenge in the house wren (*Troglodytes aedon*). *Proceedings of the Royal Society B: Biological Sciences*, *279*(1739), 2891–2898. https://doi.org/10.1098/rspb.2012.0443

Bozler, J., Kacsoh, B. Z., & Bosco, G. (2020). Maternal priming of offspring immune system in Drosophila. *G3: Genes|Genomes|Genetics*, *10*(1), 165–175. https://doi.org/10.1534/g3.119.400852

Bressan, P., & Kramer, P. (2022). Progesterone does raise disgust. *Hormones and Behavior*, *137*, 104937. https://doi.org/10.1016/j.yhbeh.2021.104937

Buck, J. C., Weinstein, S. B., & Young, H. S. (2018). Ecological and evolutionary consequences of parasite avoidance. *Trends in Ecology & Evolution*, *33*(8), 619–632. https://doi.org/10.1016/j.tree.2018.05.001

Cain, D. W., & Cidlowski, J. A. (2017). Immune regulation by glucocorticoids. *Nature Reviews Immunology*, *17*(4), 233–247. https://doi.org/10.1038/nri.2017.1

Casimir, G. J., Lefèvre, N., Corazza, F., & Duchateau, J. (2013). Sex and inflammation in respiratory diseases: A clinical viewpoint. *Biology of Sex Differences*, *4*(1), 16. https://doi.org/10.1186/2042-6410-4-16

Clutton-Brock, T. H. (1984). Reproductive effort and terminal investment in iteroparous animals. *The American Naturalist*, *123*(2), 212–229. https://doi.org/10.1086/284198

Cremer, S., Armitage, S. A. O., & Schmid-Hempel, P. (2007). Social immunity. *Current Biology*, *17*(16), R693–R702. https://doi.org/10.1016/j.cub.2007.06.008

Curno, O., Behnke, J. M., McElligott, A. G., Reader, T., & Barnard, C. J. (2009). Mothers produce less aggressive sons with altered immunity when there is a threat of disease during pregnancy. *Proceedings of the Royal Society B: Biological Sciences*, *276*(1659), 1047–1054. https://doi.org/10.1098/rspb.2008.1612

Curno, O., Reader, T., McElligott, A. G., Behnke, J. M., & Barnard, C. J. (2011). Infection before pregnancy affects immunity and response to social challenge in the next generation. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *366*(1583), 3364–3374. https://doi.org/10.1098/rstb.2011.0110

Curtis, V. A. (2014). Infection-avoidance behaviour in humans and other animals. *Trends in Immunology*, *35*(10), 457–464. https://doi.org/10.1016/j.it.2014.08.006

Curtis, V., de Barra, M., & Aunger, R. (2011). Disgust as an adaptive system for disease avoidance behaviour. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *366*(1563), 389–401. https://doi.org/10.1098/rstb.2010.0117

Dhinaut, J., Chogne, M., & Moret, Y. (2018). Trans-generational immune priming in the mealworm beetle protects eggs through pathogen-dependent mechanisms imposing no immediate fitness cost for the offspring. *Developmental & Comparative Immunology*, *79*, 105–112. https://doi.org/10.1016/j.dci.2017.10.017

Ebrahim, S. A. M., Talross, G. J. S., & Carlson, J. R. (2021). Sight of parasitoid wasps accelerates sexual behavior and upregulates a micropeptide gene in Drosophila. *Nature Communications*, *12*(1), 2453. https://doi.org/10.1038/s41467-021-22712-0

Farage, M. A. (2019). The prevalence of sensitive skin. *Frontiers in Medicine*, *6*, 98. https://doi.org/10.3389/fmed.2019.00098

Fleischman, D. S., & Fessler, D. M. T. (2011). Progesterone's effects on the psychology of disease avoidance: Support for the compensatory behavioral prophylaxis hypothesis. *Hormones and Behavior*, *59*(2), 271–275. https://doi.org/10.1016/j.yhbeh.2010.11.014

Gallagher, J. D., Siva-Jothy, M. T., & Evison, S. E. F. (2018). Social cues trigger differential immune investment strategies in a non-social insect, Tenebrio molitor. *Biology Letters*, *14*(2), 20170709. https://doi.org/10.1098/rsbl.2017.0709

Gassen, J., Prokosch, M. L., Makhanova, A., Eimerbrink, M. J., White, J. D., Leyva, R. P. P., Peterman, J. L., Nicolas, S. C., Reynolds, T. A., Maner, J. K., McNulty, J. K., Eckel, L. A., Nikonova, L., Brinkworth, J. F., Phillips, M. D., Mitchell, J. B., Boehm, G. W., & Hill, S. E. (2018). Behavioral immune system activity predicts downregulation of chronic basal inflammation. *PLoS ONE*, *13*(9), e0203961. https://doi.org/10.1371/journal.pone.0203961

Holle, H., Warne, K., Seth, A. K., Critchley, H. D., & Ward, J. (2012). Neural basis of contagious itch and why some people are more prone to it. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(48), 19816–19821. https://doi.org/10.1073/pnas.1216160109

Hunt, D. F., Cannell, G., Davenhill, N. A., Horsford, S. A., Fleischman, D. S., & Park, J. H. (2017). Making your skin crawl: The role of tactile sensitivity in disease avoidance. *Biological Psychology*, *127*, 40–45. https://doi.org/10.1016/j.biopsycho.2017.04.017

Institute of Medicine. (2009). *Microbial evolution and co-adapttation: A tribute to the life and scientific legacies of joshua lederberg: Workshop summary* (pp. 193–272. National Academies Press. https://doi.org/10.17226/12586

Kacsoh, B. Z., Lynch, Z. R., Mortimer, N. T., & Schlenke, T. A. (2013). Fruit flies medicate offspring after seeing parasites. *Science*, *339*(6122), 947–950. https://doi.org/10.1126/science.1229625

Kaletsky, R., Moore, R. S., Vrla, G. D., Parsons, L. R., Gitai, Z., & Murphy, C. T. (2020). *C. elegans* interprets bacterial non-coding RNAs to learn pathogenic avoidance. *Nature*, *586*(7829), 445–451. https://doi.org/10.1038/s41586-020-2699-5

Kavaliers, M., Bishnoi, I. R., Ossenkopp, K.-P., & Choleris, E. (2021). Differential effects of progesterone on social recognition and the avoidance of pathogen threat by female mice. *Hormones and Behavior*, *127*, 104873. https://doi.org/10.1016/j.yhbeh.2020.104873

Kavaliers, M., & Colwell, D. D. (1992). Exposure to the scent of male mice infected with the protozoan parasite, *Eimeria vermiformis*, induces opioid- and nonopioid-mediated analgesia in female mice. *Physiology & Behavior*, *52*(2), 373–377. https://doi.org/10.1016/0031-9384(92)90286-b

Kavaliers, M., & Colwell, D. D. (1995). Odours of parasitized males induce aversive responses in female mice. *Animal Behaviour*, *50*(5), 1161–1169. https://doi.org/10.1016/0003-3472(95)80032-8

Kavaliers, M., Ossenkopp, K.-P., & Choleris, E. (2019). Social neuroscience of disgust. *Genes, Brain and Behavior*, *18*(1), e12508. https://doi.org/10.1111/gbb.12508

Kavaliers, M., Ossenkopp, K.-P., & Choleris, E. (2020). Pathogens, odors, and disgust in rodents. *Neuroscience & Biobehavioral Reviews*, *119*, 281–293. https://doi.org/10.1016/j.neubiorev.2020.09.037

Kavaliers, M., Ossenkopp, K.-P., Tyson, C.-D., Bishnoi, I. R., & Choleris, E. (2022). Social factors and the neurobiology of pathogen avoidance. *Biology Letters*, *18*(2), 20210371. https://doi.org/10.1098/rsbl.2021.0371

Klein, S. L., & Flanagan, K. L. (2016). Sex differences in immune responses. *Nature Reviews Immunology*, *16*(10), 626–638. https://doi.org/10.1038/nri.2016.90

Koren, T., Yifa, R., Amer, M., Krot, M., Boshnak, N., Ben-Shaanan, T. L., Azulay-Debby, H., Zalayat, I., Avishai, E., Hajjo, H., Schiller, M., Haykin, H., Korin, B., Farfara, D., Hakim, F., Kobiler, O., Rosenblum, K., & Rolls, A. (2021). Insular cortex neurons encode and retrieve specific immune responses. *Cell*, *184*(24), 5902-5915.e17. https://doi.org/10.1016/j.cell.2021.10.013

Lopes, P. C. (2017). Why are behavioral and immune traits linked? *Hormones and Behavior*, *88*, 52–59. https://doi.org/10.1016/j.yhbeh.2016.09.008

Lopes, P. C. (2020). We are not alone in trying to be alone. *Frontiers in Ecology and Evolution*, *8*, 172. https://doi.org/10.3389/fevo.2020.00172

Lopes, P. C., French, S. S., Woodhams, D. C., & Binning, S. A. (2022). Infection avoidance behaviors across vertebrate taxa: Patterns, processes, and future directions. In V. Ezenwa, S. Altizer, & R. Hall (Eds.), *Animal behavior and parasitism*. Oxford University Press. https://doi.org/10.1093/oso/9780192895561.003.0014

Love, A. C., Grisham, K., Krall, J. B., Goodchild, C. G., & DuRant, S. E. (2021). Perception of infection: Disease-related social cues

influence immunity in songbirds. *Biology Letters*, *17*, 20210125. https://doi.org/10.1098/rsbl.2021.0125

Matt, S. M., & Gaskill, P. J. (2020). Where is dopamine and how do immune cells see it? Dopamine-mediated immune cell function in health and disease. *Journal of Neuroimmune Pharmacology*, *15*(1), 114–164. https://doi.org/10.1007/s11481-019-09851-4

Meisel, J. D., Panda, O., Mahanti, P., Schroeder, F. C., & Kim, D. H. (2014). Chemosensation of bacterial secondary metabolites modulates neuroendocrine signaling and behavior of *C. elegans*. *Cell*, *159*(2), 267–280. https://doi.org/10.1016/j.cell.2014.09.011

Meunier, J. (2015). Social immunity and the evolution of group living in insects. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *370*(1669), 20140102. https://doi.org/10.1098/rstb.2014.0102

Milan, N. F., Kacsoh, B. Z., & Schlenke, T. A. (2012). Alcohol consumption as self-medication against blood-borne parasites in the Fruitfly. *Current Biology*, *22*(6), 488–493. https://doi.org/10.1016/j.cub.2012.01.045

Minchella, D. J., & Loverde, P. T. (1981). A cost of increased early reproductive effort in the snail *Biomphalaria glabrata*. *The American Naturalist*, *118*(6), 876–881.

Morgulis, M. S. F. A., Stankevicius, D., Sá-Rocha, L. C., & Palermo-Neto, J. (2004). Cohabitation with a sick cage mate: Consequences on behavior and on Ehrlich tumor growth. *Neuroimmunomodulation*, *11*(1), 49–57. https://doi.org/10.1159/000072969

Norris, K. (1999). A trade-off between energy intake and exposure to parasites in oystercatchers feeding on a bivalve mollusc. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *266*(1429), 1703–1709. https://doi.org/10.1098/rspb.1999.0835

Oaten, M., Stevenson, R. J., & Case, T. I. (2009). Disgust as a disease-avoidance mechanism. *Psychological Bulletin*, *135*(2), 303–321. https://doi.org/10.1037/a0014823

Pacheco-López, G., Engler, H., Niemi, M.-B., & Schedlowski, M. (2006). Expectations and associations that heal: Immunomodulatory placebo effects and its neurobiology. *Brain, Behavior, and Immunity*, *20*(5), 430–446. https://doi.org/10.1016/j.bbi.2006.05.003

Raffel, T. R., Hoverman, J. T., Halstead, N. T., Michel, P. J., & Rohr, J. R. (2010). Parasitism in a community context: Trait-mediated interactions with competition and predation. *Ecology*, *91*(7), 1900–1907. https://doi.org/10.1890/09-1697.1

Regenbogen, C., Axelsson, J., Lasselin, J., Porada, D. K., Sundelin, T., Peter, M. G., Lekander, M., Lundström, J. N., & Olsson, M. J. (2017). Behavioral and neural correlates to multisensory detection of sick humans. *Proceedings of the National Academy of Sciences of the United States America*, *114*(24), 6400–6405. https://doi.org/10.1073/pnas.1617357114

Schaller, M., Miller, G. E., Gervais, W. M., Yager, S., & Chen, E. (2010). Mere visual perception of other people's disease symptoms facilitates a more aggressive immune response. *Psychological Science*, *21*(5), 649–652. https://doi.org/10.1177/0956797610368064

Sheldon, B. C., & Verhulst, S. (1996). Ecological immunology: Costly parasite defences and trade-offs in evolutionary ecology. *Trends in Ecology & Evolution*, *11*(8), 317–321. https://doi.org/10.1016/0169-5347(96)10039-2

Stern, J., & Shiramizu, V. (2022). Hormones, ovulatory cycle phase and pathogen disgust: A longitudinal investigation of the compensatory prophylaxis hypothesis. *Hormones and Behavior*, *138*, 105103. https://doi.org/10.1016/j.yhbeh.2021.105103

Stevenson, R. J., Hodgson, D., Oaten, M. J., Barouei, J., & Case, T. I. (2011). The effect of disgust on oral immune function. *Psychophysiology*, *48*(7), 900–907. https://doi.org/10.1111/j.1469-8986.2010.01165.x

Tanaka, T., Narazaki, M., & Kishimoto, T. (2014). IL-6 in inflammation, immunity, and disease. *Cold Spring Harbor Perspectives in Biology*, *6*(10), a016295. https://doi.org/10.1101/cshperspect.a016295

Tomiyoshi, M. Y., Sakai, M., Baleeiro, R. B., Stankevicius, D., Massoco, C. O., Palermo-Neto, J., & Barbuto, J. A. M. (2009). Cohabitation with a B16F10 melanoma-bearer cage mate influences behavior and dendritic cell phenotype in mice. *Brain, Behavior, and Immunity*, *23*(4), 558–567. https://doi.org/10.1016/j.bbi.2009.02.006

Veiga-Fernandes, H., & Artis, D. (2018). Neuronal–immune system cross-talk in homeostasis. *Science*, *359*(6383), 1465–1466. https://doi.org/10.1126/science.aap9598

Velando, A., Beamonte-Barrientos, R., & Torres, R. (2014). Enhanced male coloration after immune challenge increases reproductive potential. *Journal of Evolutionary Biology*, *27*(8), 1582–1589. https://doi.org/10.1111/jeb.12416

Velando, A., Drummond, H., & Torres, R. (2006). Senescent birds redouble reproductive effort when ill: Confirmation of the terminal investment hypothesis. *Proceedings of the Royal Society B: Biological Sciences*, *273*(1593), 1443–1448. https://doi.org/10.1098/rspb.2006.3480

Weil, Z. M., Martin, L. B., Workman, J. L., & Nelson, R. J. (2006). Immune challenge retards seasonal reproductive regression in rodents: Evidence for terminal investment. *Biology Letters*, *2*(3), 393–396. https://doi.org/10.1098/rsbl.2006.0475

Williams, G. C. (1966). Natural selection, the costs of reproduction, and a refinement of Lack's principle. *The American Naturalist*, *100*(916), 687–690. https://doi.org/10.1086/282461

Zhang, X., Lei, B., Yuan, Y., Zhang, L., Hu, L., Jin, S., Kang, B., Liao, X., Sun, W., Xu, F., Zhong, Y., Hu, J., & Qi, H. (2020). Brain control of humoral immune responses amenable to behavioural modulation. *Nature*, *581*(7807), 204–208. https://doi.org/10.1038/s41586-020-2235-7

Zuk, M., & Stoehr, A. M. (2002). Immune defense and host life history. *The American Naturalist*, *160*(S4), S9–S22. https://doi.org/10.1086/342131

How to cite this article: Lopes, P. C. (2022). Anticipating infection: How parasitism risk changes animal physiology. *Functional Ecology*, *00*, 1–10. https://doi.org/10.1111/1365-2435.14155