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IN FOCUS

Parasites as weapons of mouse destruction

A white-footed mouse *Peromyscus leucopus* from Dutchess County, south-eastern New York State, USA. Population dynamics of white-footed mice and their relatives, deer mice (*P. maniculatus*), are affected by the interaction between food supply and parasite burdens. Photo credit: R. Ostfeld laboratory ©.

A. B. Pedersen & T. J. Greives (2008) The interaction of parasites and resources causes crashes in a wild mouse population. *Journal of Animal Ecology*, **77**, 370–377.

Epidemiological models illustrate that parasites can drive fluctuations in host populations, but small-mammal ecologists have tended to reject parasitism as an important factor. In one of the few experimental tests of the impact of parasites on wildlife population dynamics, Pedersen and Greives reduced prevalence of intestinal nematodes in free-ranging populations of *Peromyscus* mice with and without access to supplemental food. In isolation, parasite removal and food addition reduced rates of population decline only modestly, but the two factors acted synergistically to strongly alleviate declines. It is tempting to disregard factors that, in isolation, have weak effects, but the results from Pedersen and Greives' multifactor experiment remind ecologists that complex factor interactions pervade real ecosystems.

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In January 1937 Charles Elton and colleagues discovered that field voles (*Microtus agrestis*) throughout England, Wales and Scotland were suffering and dying from tuberculosis (causative agent *Mycobacterium microti*) (Elton 1942). These researchers were hotly pursuing the question of what causes the notorious population fluctuations in these rodents, and this discovery gave hope that the answer – disease – was imminent. Elton's student, Dennis Chitty, set out to evaluate the 'epidemic hypothesis' only to find that vole tuberculosis was absent in some declining populations and that tuberculosis was prevalent in some populations not undergoing declines (Chitty 1954). Chitty concluded that, because epidemics were not both necessary and sufficient to cause population declines, 'The disease was therefore irrelevant to this aspect of the problem [declines] ... helping to put an end to the epidemic hypothesis' (Chitty 1996: 51). Chitty's reasoning, which for decades strongly influenced other prominent researchers studying fluctuating populations of mammals and birds (Krebs & Myers 1974; Tamarin 1978; Gaines *et al*. 1991; Boonstra 1994), was that only when a putative cause of population declines was present during all declines (the 'necessary' criterion) and absent when declines were absent (the 'sufficient' criterion) could that factor be considered important (Chitty 1996). Of course, such reasoning would brand as unimportant any factor that interacts with other factors to cause an effect, such as a population decline. A paper in this issue of the *Journal of Animal Ecology* by Pedersen and Greives shows that, like reports of Mark Twain's demise, the death of the epidemic hypothesis was greatly exaggerated.

Pedersen & Greives (2008) examined experimentally the interactions between food supply and intestinal parasites in causing population declines of two ubiquitous North American small mammals – the white-footed mouse *Peromyscus leucopus* and the deer mouse *P. maniculatus*. Typically, mouse populations inhabiting deciduous forests grow rapidly to a peak following years of heavy tree seed production (i.e. in 'mast years'), particularly those of oaks (*Quercus* spp.) (Elkinton *et al*. 1996; Wolff 1996; Jones *et al*. 1998; Ostfeld *et al*. 2006), but populations often decline precipitously when food is still abundant. Pedersen and Greives noted that mice are often afflicted with various macro- and microparasites, and that parasite prevalence (proportion of hosts infected) increases with mouse density, although usually lagging a few months behind (Cavanagh *et al*. 2004; Burthe *et al*. 2006). In a field test of the effects of food and parasites on mouse population dynamics, Pedersen and Greives simulated acorn masting by adding sunflower seeds and reduced parasite loads by administering doses of Ivermectin, a potent anthelmintic drug, in a 2×2 factorial design with three replicates. Over the 2-year study, both food supplementation and parasite removal increased total and reproductive adult abundance significantly, relative to populations on control plots. However, only on plots with supplemental food and Ivermectin treatments were seasonal population declines alleviated. The impact of each factor on mouse abundance was considerably stronger in the presence of the other factor, as indicated by a significant interaction term. Neither factor by itself was necessary and sufficient for eliminating a population decline; however, food addition and parasite removal conspired together to affect population dynamics strongly.

Although food supplementation and intestinal parasite removal might have acted on the mouse populations by reducing direct mortality from starvation and disease, Pedersen and Greives quantified an additional, indirect pathway. Hypothesizing that food limitation and parasite burdens might cause physiological stress, and that stress responses might reduce immunocompetence, the researchers collected mouse faecal pellets and subjected them to an enzyme immunoassay for a group of stress hormones, the glucocorticoids. They found that mice that had been treated with Ivermectin had significantly lower faecal glucocorticoid levels, and that Ivermectin and food addition together enhanced this effect. Again, the two factors interacted to reduce stress hormone levels beyond what was predicted by their summed effect, with potentially strong indirect effects on individual fitness and population dynamics.

Experimental tests of the effects of parasites are accomplished typically by treating hosts with drugs that are more or less specific to a particular group of parasites, but hosts tend to be infected with a diverse assemblage of parasites, and the removal of one group can potentially elicit compensatory population growth in others. This is the case for *Peromyscus* mice, in which coccidial protozoans and cestodes increased in prevalence when intestinal nematodes were removed with Ivermectin (Pedersen 2005). Such compensatory increases mean that experimental parasite removals, including that by Pedersen and Greives, will generally under-estimate the impact of parasites on host dynamics. In contrast to parasite removals, predator removal studies typically include use of fences (e.g. Krebs *et al*. 1995) or removal of protective cover (e.g. Desy & Batzli 1989) that reduce or eliminate all predators. Any comparisons of the relative effects of predator- vs. parasite removal should take into account the likelihood that parasite removals tend to be partial and therefore conservative. The potentially complex consequences of removing some members of a parasite guild appear analogous to meso-predator release, whereby the extirpation of apex predators can facilitate meso-predator populations and suppress their prey strongly (e.g. Crooks & Soule 1999).

Despite the development of theory that underscored the potential for infectious diseases to regulate wildlife host populations and cause cyclic fluctuations (e.g. Anderson & May 1979), no large-scale, experimental tests of the impact of disease on free-ranging host populations were published until the seminal paper by Hudson, Dobson & Newborn (1998). These authors showed that administering anthelmintic drugs into red grouse *Lagopus lagopus scoticus*, even with as few as 15% of grouse treated, essentially eliminated cyclic population declines, and they concluded that a single factor – disease – was both necessary and sufficient to cause cycles in grouse. Controversy erupted over this conclusion (Lambin *et al*. 1999; Moss & Watson 2001). Other researchers (Moss, Watson, & Parr 1996; Mougeot *et al*. 2003) found that territorial behaviour regulates grouse density and that high aggressiveness

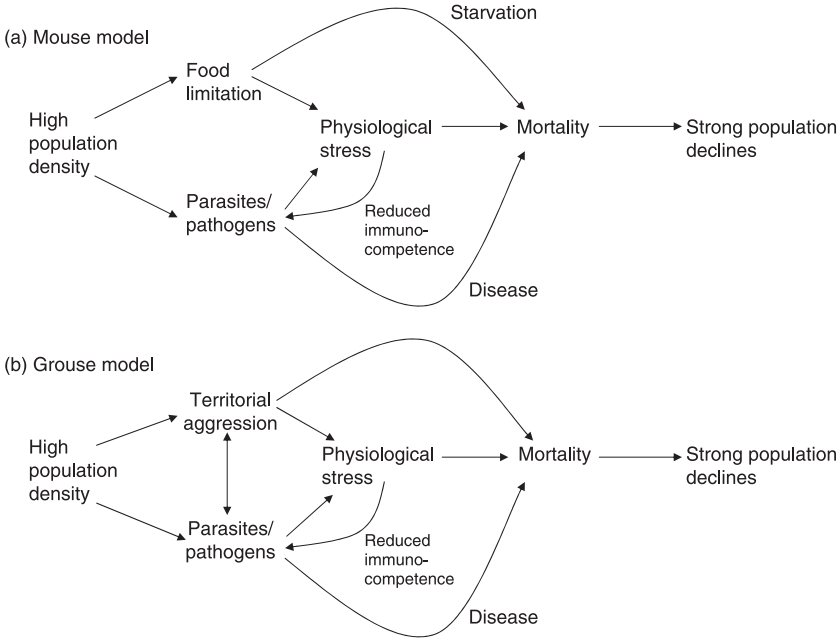

Fig. 1. Conceptual models of the major factors contributing to strong population declines in fluctuating populations of (a) *Peromyscus* mice, and (b) red grouse *Lagopus lagopus scoticus*. At high population densities of mice, density-dependent increases in parasites, with or without food limitation, can cause physiological stress. This physiological stress, in turn, can facilitate further increases in parasites owing to reduced immunocompetence. The result is either direct mortality from disease or starvation or mortality from other causes that is exacerbated by disease or poor nutrition. For grouse, food limitation appears to play a weaker role, but territorial aggression at high population densities can directly cause physiological stress while at the same time increasing susceptibility to parasites and pathogens. Territorial aggression and disease can cause mortality either directly or indirectly, leading to population declines.

mediated by circulating testosterone can cause sharp declines, concluding that changing territorial aggression was both necessary and sufficient to cause population cycles. Therefore, the controversy was largely over which single factor caused grouse cycles, not over single- vs. multiple-causation.

A series of follow-up studies has begun to reconcile these conflicting claims about which factor has primacy in causing cyclic declines in grouse populations. The emerging picture appears to be that increases in either parasite loads or territorial aggressiveness can initiate population declines and that both factors operating simultaneously can cause declines to be steep and prolonged (Redpath *et al*. 2006), a diagnostic feature of cycles. A two-way interaction between parasites and territorial aggressiveness is now indicated by the observations that high circulating levels of testosterone simultaneously increase territorial aggressiveness and parasite burdens, and that high parasite loads reduce territorial behaviour, at least in some seasons (Mougeot, Evans & Redpath 2005). By causing non-lethal illness and changing host behaviour, parasites can also engage in cryptic interactions with other factors that can cause declines, including predation. Taken together, these studies suggest that declines in mouse and grouse populations are caused by the interactions between parasites and at least one other main factor, with those interactions mediated by physiological stress and reduced immunocompetence (Fig. 1). Single-factor hypotheses appear to have been replaced by multiple-factor hypotheses regarding causes of population cycles in both small mammals and birds.

Multifactorial hypotheses regarding population cycles (e.g. Lidicker 1988) have been criticized for being vague and untestable (e.g. Gaines *et al*. 1991). Clearly, this need not be the case. It is enticing to advocate that future approaches should involve exploration of the combinations of factors that are both necessary and sufficient to cause cycles. However, dangers lurk in this approach. One key lesson we have learned from Pedersen and Greives (and others) is that the strength of any specific factor will often be contingent upon the operation of other factors. We should expect that the strength of any specific combination of factors might be subject to similar contingencies. Therefore, finding that a particular combination of factors is not both necessary and sufficient should not cause us to discard that combination as necessarily irrelevant.

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