

Coping with Infection: Resistance and Tolerance of Parasites in Soay Sheep

by

Laura A. Schoenle, Cornell University, Ithaca, NY
Cynthia J. Downs, Hamilton College, Clinton, NY

Part I – Sheep and Their Parasites

About 70 kilometers west of mainland Scotland lies the archipelago of St. Kilda, home to the Soay sheep (*Ovis aries*) (Figure 1). Soay sheep are the most primitive domesticated sheep in Europe, and they resemble the domesticated sheep farmed during the Neolithic era (circa 5000 BCE) (Boyd *et al.*, 1964).



Figure 1 (A). Adult Soay sheep. Credit: Velmc, CC BY-NC 2.0.



Figure 1 (B). Soay lamb. Credit: marcus_jb1973, CC BY-NC-ND 2.0.

An unmanaged population of Soay sheep continues to live on the island of Hirta, St. Kilda. The population size varies dramatically across years, ranging from about 600 to 1600 individuals (Clutton-Brock *et al.*, 1991; Coulson *et al.*, 2001). Over the winter, there can be high mortality of adult sheep, primarily due to starvation. Starvation is not only caused by lack of food, but is intensified by infections with multiple species of gastrointestinal nematodes (Figure 2) (Gulland, 1992).

Nematode infections increase mortality rates in Soay sheep, and the intensity of infection (the number of infecting worms, which is estimated by the number of nematode eggs in sheep feces) correlates negatively



Figure 2. A common parasitic gastrointestinal nematode of sheep, *Teladorsagia circumcincta*. Credit: Bartley *et al.* (2015), CC BY-NC-ND 4.0.

with sheep body mass (Figure 3). Because nematodes reduce survival, natural selection is expected to shape how the sheep cope with nematode infections.

There are two strategies for coping with parasite infections: resistance and tolerance (Schneider & Ayres, 2008; Råberg, Graham & Read, 2009). Resistance involves controlling the number of parasites by avoiding the infection, killing or removing parasites, or limiting the parasites' ability to reproduce in the host. Tolerance involves minimizing the costs of infection or controlling the damage caused during infection. For more background on resistance and tolerance see Schneider and Ayres (2008), and Medzhitov, Schneider and Soares (2012).

Questions

1. Imagine you are studying Soay sheep on the island of Hirta. How would you compare resistance among sheep? In other words, what would you need to know to rank sheep by their resistance to nematodes?
2. What information would you need to compare tolerance among sheep? How would you determine if one sheep was more tolerant than another? Draw a graph that illustrates the tolerance of several individual sheep. (*Hint*: Figure 3 and the background readings might provide inspiration.)
3. Do you expect sheep that invest more in resistance to nematodes or tolerance of nematodes to be more likely to survive over the winter? Why?
4. Imagine you are a nematode that infects Soay sheep. If you want to maximize the likelihood that you survive and reproduce, should you prefer a more resistant sheep host or more tolerant host? Why?

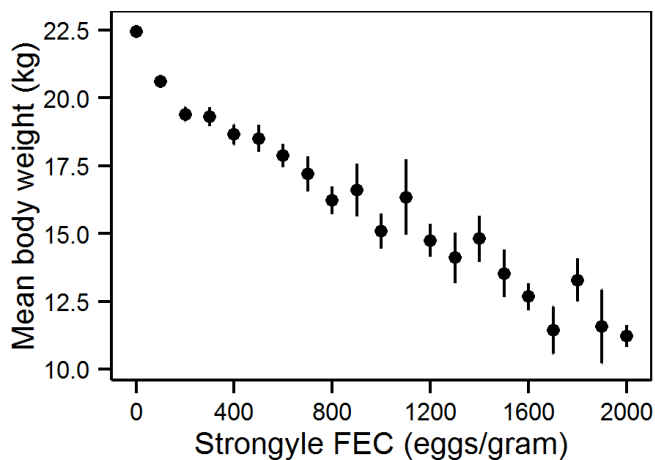


Figure 3. Sheep with higher fecal egg counts (FEC) of strongyle nematodes weigh less than sheep with lower egg counts. The negative relationship between body weight and FEC shown here is based on data of 4,934 captures of 2,438 individual sheep. Points show the mean body weight + 1 standard error. Figure reproduced from Hayward *et al.* (2014b), CC BY-NC-ND 4.0.

Part II – The Costs and Benefits of Immunity to Parasites

Soay sheep can resist gastrointestinal nematode infections by mounting an immune response. Sheep that produce more antibodies to a common nematode (shown in Figure 2) have fewer intestinal nematodes than sheep producing less antibodies (Hayward *et al.*, 2014a). These antibodies have complex relationships with two measures of fitness: survival probability and reproductive success. Among female sheep, producing more antibodies causes an increase in survival during years when there is high overwinter mortality (a population crash), but not during years with relatively low overwinter mortality (no population crash) (Graham *et al.*, 2010). In males, there is no relationship between antibodies and survival (Graham *et al.*, 2010). However, males with higher antibody levels are less likely to father offspring the following year than males with lower antibody levels (Graham *et al.*, 2010; Hayward *et al.*, 2014a). Similarly, females with higher antibody levels produce fewer lambs than females with lower antibody levels (Graham *et al.*, 2010), but the effects can vary depending on female body mass (Hayward *et al.*, 2014a).

A study by Hayward *et al.* (2014b) focused on Soay sheep tolerance of nematodes, and measured tolerance as the slope of the relationship between body weight and fecal egg count (Figure 4). They found that sheep with higher tolerance had higher lifetime breeding success (Figure 5). This means that sheep that were better able to maintain their body weight when carrying more parasites had higher reproductive success.

Questions

1. Do higher levels of antibodies indicate greater resistance to nematodes in Soay sheep? Explain your answer. Can the relationship between antibodies and resistance in the sheep be generalized to other host-parasite systems?
2. The work described here is correlational, and thus cannot determine if the relationship between two variables is causal. Design an experiment that tests whether antibodies cause greater resistance to nematodes in Soay sheep, and list specific predictions.
3. What appear to be the costs of higher antibody levels? Why might higher antibody levels have negative consequences?
4. Yikes, it's complicated! The relationship between antibody levels and fitness seems to vary by context. Why might this be the case?
5. Tolerance is also associated with reproductive success. Under what conditions might an animal benefit from investing more in tolerance? Under what conditions might an animal benefit by investing more in resistance?
6. Consider how doctors and veterinarians treat parasites (including viruses, bacteria, worms, lice, etc.). Is modern medicine more focused on resistance or tolerance? Why?

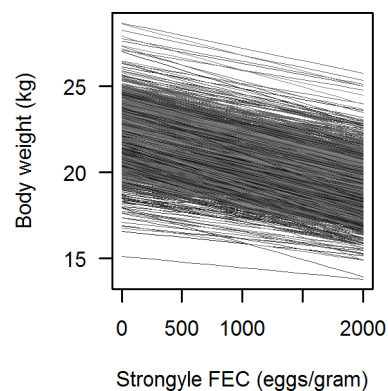


Figure 4. Tolerance can be measured as the slope of the relationship between body weight and fecal egg count. Each line represents an individual sheep sampled at multiple points during its lifetime. Figure reproduced from Hayward *et al.* (2014b), CC BY-NC-ND 4.0.

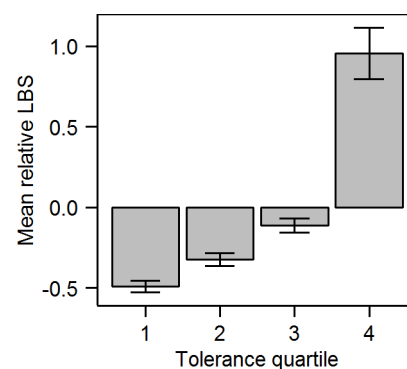


Figure 5. The relationship between tolerance and lifetime breeding success (LBS). Figure reproduced from Hayward *et al.* (2014b), CC BY-NC-ND 4.0.

Part III – Beyond the Sheep

Modern medicine tends to focus more on supporting resistance to infection rather than tolerance. However, medical treatments that promote tolerance of infection, in addition to or instead of resistance, could help those suffering from diseases. Consider the following two examples.

Example 1: Antibiotics are critical to the treatment of many bacterial infections and can be life-saving. Unfortunately, due to the evolution of antibiotic resistance and a decline in antibiotic discovery, we might reach a point where it is not possible to successfully treat many bacterial infections with antibiotics (Martens & Demain, 2017).

Example 2: About 2.4 billion people annually are at risk for malaria infection (Bousema & Drakeley, 2011). Malaria infection can result in death, and in some cases, once infected, the host can harbor the infection its entire life. Malaria infections can cause a decrease in the total number of red blood cells (anemia), reduction in iron in blood, and a decrease in the oxygen-carrying capacity of blood (Price *et al.*, 2001). Malaria-causing parasites destroy red blood cells as part of their life cycle. However, the extent of anemia can often not be explained by the number of parasites alone; in fact, the host immune system can significantly contribute to anemia by destroying healthy cells (Evans *et al.*, 2006).

Questions

1. How could addressing tolerance of infection enhance medical treatment in each example?
2. What are some potential consequences of tolerance, or treatments that increase tolerance, for disease risk in communities? From a public health perspective, when could medical treatment that increases tolerance be problematic?

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Additional Resources

The St. Kilda Soay Sheep

St. Kilda Soay Sheep Project [Internet]. Available from: <<http://soaysheep.biology.ed.ac.uk/>>.

Resistance and Tolerance

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