Comment

Selecting for fast and slow maturing worms

Parasites, such as viruses, bacteria, protozoa and worms, constitute a constant threat to the survival of free-living organisms. Since parasites are also one of the major limitations of modern food production and an important source of mortality in humans, a multibillion dollar industry is busy designing new drugs to control infection levels. Most drugs are designed to increase parasite mortality, some by affecting young, infective stages, while others are targeted against the reproductive stage. This massive use of drugs to control parasites can have several negative consequences, of which the development of drug resistance has received much attention. Another consequence, which has largely been ignored, is the potential of drugs to select for changes in parasite life histories. This effect of the drug industry may have alarming consequences, since epidemiological parameters like virulence, disease dynamics and host recovery rates are closely linked to parasite life histories (Anderson & May 1982; Frank 1996; Gandon *et al.* 2001). A paper in the current issue of *Proceedings B* (Paterson & Barber 2007) provides new insights into how parasite life histories may evolve under selection regimes that simulate drug treatments.

Life-history evolution is a cornerstone in modern ecology, and over the last decades we have seen significant advances in theory as well as a vast number of experimental studies of plants, invertebrates and vertebrates. However, very few of these studies deal with parasites. In 1992, two major textbooks appeared, summarizing the theoretical and empirical state of knowledge of life-history evolution (Roff 1992; Stearns 1992), and these books are still regarded as reference texts in the field. Looking at the index of these books, you will see that parasites are hardly mentioned at all. Since 1992, the situation improved somewhat, but still there are surprisingly few studies on parasite life-history evolution considering the practical importance of the subject.

So, what do we know of parasite life-history evolution? The most frequently studied taxon has been nematodes, perhaps not surprisingly, since these worms are a major cause of disease in both humans and livestock and infect most, if not all, wild vertebrate populations. Moreover, nematodes display a staggering variation in life-history traits such as body size, longevity and age at maturity (Skorping *et al.* 1991; Morand 1996). Comparative studies reveal that life-history patterns of parasitic nematodes are strikingly different from most free-living taxa. Taxa such as mammals, birds and reptiles tend to form a continuum from small, fast species with high rates of somatic growth and high fecundity to larger, slower species with the opposite suit of traits. Within nematodes, small species tend to have low somatic growth rates and low fecundity, and species that are able to postpone their age at maturity have all the advantages: they grow bigger, live longer and reproduce more. Any medical or veterinary

intervention programme that affects nematode age at maturity might therefore have far-reaching epidemiological consequences (Read & Skorping 1995; Skorping & Read 1998; Gemmill *et al.* 1999).

The majority of drugs applied against nematodes tend to have a stronger effect on adult mortality than on the juvenile, developing stage (Skorping & Read 1998). It has been suggested that such drugs could give a fitness advantage to worms spending a longer time in the juvenile phase and reducing their reproductive phase (Skorping & Read 1998). However, if worms take a longer time to mature, comparative studies suggest that they will grow larger and more fecund, and are also likely to be more virulent. On the other hand, the main purpose of the drugs is to reduce worm burden, and since fecundity in nematodes tends to be density dependent, the evolutionary effects of drug application may potentially be quite complex.

Clearly, what we need are experimental studies mimicking the effects of drugs on parasite life histories. In a field experiment, Leignel & Cabaret (2001) studied the evolutionary effect of anti-parasitic drugs on the sheep nematode *Teladorsagia circumcincta* and demonstrated that worm size (and therefore fecundity) increased after chemotherapy. These authors also found that worm isolates which were resistant to drugs were consistently larger than drug-susceptible worms, but whether this was due to differences in life-history traits in the two groups remained unclear. A complicating issue is that hosts may show a different immune response to worms with different life traits, which also could affect worm size. Disentangling the evolutionary effect of chemotherapy from the effect of host response on worm life histories is therefore not easy.

In the current issue of *Proceedings B*, Paterson & Barber (2007) publish an elegant selection experiment using the intestinal nematode *Strongyloides ratti*. The authors infected pairs of laboratory rats and collected eggs either right after the parasite had started reproducing (5 days after infection) or late in the reproductive life of the worm (34 days after infection) for each pair. These eggs were used to initiate a new infection and the procedure was repeated for 20–50 generations. Thus, two sets of replicated lines of nematodes were selected for: a ‘fast’ line where only the earliest reproducers were contributing genes to the next generation, and a ‘slow’ line consisting of genes from worms that had been able to survive until late in life. The selection for fast worms is similar to the effect of a drug with a moderate effect on the developmental stage, but which kills the adult worm population soon after maturity—yet not fast enough to prevent some worms from reproducing. Selecting for slow worms mimics a drug, or a vaccine, which kills or suppresses reproduction of a large part of the worm population, but where some

worms are able to escape the effect and manage to reproduce late in life.

Selecting only the offspring from early in an infection should remove the need for parasites to invest in future survival or reproduction. We would therefore expect that the fast line should evolve higher fecundity but poorer survival than the slow line. Another response which has been hypothesized is that during an abbreviation of the reproductive lifespan, individuals who take longer to develop and thereby grow bigger could have a selective advantage (Skorping & Read 1998). Surprisingly, the authors found no differences in survival or body size between the two lines, but the *per capita* fecundity was highest in the fast line. Moreover, although both lines showed a declining fecundity with worm density, the fecundity of fast worms declined more rapidly than that of slow worms. Density-dependent fecundity of intestinal nematodes is commonly observed and is often explained by increased host immunity with increasing number of worms (Anderson & May 1991). But, hosts infected with slow lines showed a stronger immune response than rats harbouring fast lines. This suggests that worms selected for survival, rather than short generation time, are more able to withstand, or modulate, the harmful effects of the host response. This increased capacity did not lead to better survival, but rather to the ability to keep reproducing at a high rate in a hostile environment.

Whether the effect of an anti-parasitic drug resembles the selection for fast or slow worms, it is interesting to note that both types of selection could have epidemiological consequences. Any control method that shortens the reproductive lifespan of a nematode could lead to a higher *per capita* fecundity, thereby reducing its effect on overall infection levels. On the other hand, a drug or an imperfect vaccine, leaving a few worms to survive and regain reproduction late in life, might select parasites with a higher virulence (Gandon *et al.* 2001) or an increased egg output during high worm burdens.

The results of Paterson & Barber (2007) are unexpected and novel: some assumptions of life-history theory were confirmed, but there is nothing in the theory which would predict that increased immune tolerance in nematodes selected for late reproduction should result in higher fecundity during high worm burdens, rather than in better survival. Yet, among nematodes of mammals, there is much variation in adult survival, ranging from a few days to several years (Anderson 2000). It is possible that this variation is simply a physiological correlate of body size, so that anything that affects age at maturity will also influence a range of other fitness traits. Age at maturity appears to be determined by host immune responses (Gemmill *et al.* 1999; Sorci *et al.* 2003), and a selection experiment where nematode juvenile mortality is

manipulated would be very interesting. This underlines the need for selection experiments in more host–parasite systems, before we try to use general life-history theory to predict the selective effect of drugs and vaccines.

Arne Skorping

Department of Biology, University of Bergen,
PO Box 7800, 5020 Bergen, Norway
(arne.skorping@bio.uib.no)

REFERENCES

- Anderson, R. C. 2000 *Nematode parasites of vertebrates: their development and transmission*, 2nd edn. London, UK: CAB International.
- Anderson, R. M. & May, R. M. 1982 Coevolution of hosts and parasites. *Parasitology* **85**, 411–426.
- Anderson, R. M. & May, R. M. 1991 *Infectious diseases of humans: dynamics and control*. Oxford, UK: Oxford University Press.
- Frank, S. A. 1996 Models of parasite virulence. *Quart. Rev. Biol.* **71**, 37–78. (doi:10.1086/419267)
- Gandon, S., MacKinnon, M. J., Nee, S. & Read, A. F. 2001 Imperfect vaccines and the evolution of pathogen virulence. *Nature* **414**, 751–756. (doi:10.1038/414751a)
- Gemmill, A. W., Skorping, A. & Read, A. F. 1999 Optimal timing of first reproduction in parasitic nematodes. *J. Evol. Biol.* **12**, 1148–1156. (doi:10.1046/j.1420-9101.1999.00117.x)
- Leignel, V. & Cabaret, J. 2001 Massive use of chemotherapy influences life traits of parasitic nematodes in domestic ruminants. *Funct. Ecol.* **15**, 569–574. (doi:10.1046/j.0269-8463.2001.00567.x)
- Morand, S. 1996 Life-history traits in parasitic nematodes: a comparative approach for the search of invariants. *Funct. Ecol.* **10**, 210–218. (doi:10.2307/2389845)
- Paterson, S. & Barber, R. 2007 Experimental evolution of parasite life-history traits in *Strongyloides ratti* (Nematoda). *Proc. R. Soc. B* **274**, 1467–1474. (doi:10.1098/rspb.2006.0433)
- Read, A. F. & Skorping, A. 1995 The evolution of tissue migration by parasitic nematode larvae. *Parasitology* **111**, 359–371.
- Roff, D. A. 1992 *The evolution of life histories: theory and analysis*. New York, NY: Chapman & Hall.
- Skorping, A. & Read, A. F. 1998 Drugs and parasites: global experiments in life history evolution? *Ecol. Lett.* **1**, 10–12. (doi:10.1046/j.1461-0248.1998.0007d.x)
- Skorping, A., Read, A. F. & Keymer, A. E. 1991 Life history covariation in intestinal nematodes of mammals. *Oikos* **60**, 365–372. (doi:10.2307/3545079)
- Sorci, G., Skarstein, F., Morand, S. & Hugot, J. P. 2003 Correlated evolution between host immunity and parasite life histories in primates and oxyurid parasites. *Proc. R. Soc. B* **270**, 2481–2484. (doi:10.1098/rspb.2003.2536)
- Stearns, S. C. 1992 *The evolution of life histories*. Oxford, UK: Oxford University Press.