Variation in Parasite Virulence Is Not an Indicator for the Evolution of Benevolence

DIETER EBERT

NERC Centre for Population Biology, Imperial College at Silwood Park, Ascot SL5 7PY, U.K.

The conventional wisdom that parasites—broadly defined as any disease-producing organism—evolve to become benign over time has been strongly criticized over the last 15 years (Anderson & May 1982; May & Anderson 1983; Lenski 1988; Read 1994). The current view of the evolution and maintenance of virulence is based on the hypothesis that virulence is correlated with other fitness-related traits of the parasite and that any reduction in virulence will coincide with a decrease in another fitness-related parameter (references as above). A parasite, therefore, should maximize its fitness by optimizing the relationship between virulence and other traits, such as multiplication rate. Consequently, virulence can range from very low to very high, depending on the shape of the underlying genetic trade-off(s). This view has been supported empirically with studies on viruses (Bull et al. 1991), nematodes (Herre 1993), microsporidians (Ebert 1994), and ectoparasites (Clayton & Tompkins 1994).

In natural populations it is often found that parasite virulence varies strongly between hosts of the same species and even within populations (Fenner & Ratcliffe 1965; Burdon 1980; de Nooij & van Damme 1988; Hill et al. 1991; Ginsberg 1994). Such variation does not fit easily in the concept of an optimal level of virulence, and there is no single explanation for this finding. Recent studies have made progress, however, in identifying some important sources for such variation and their different evolutionary consequences. In a review on Lyme disease Ginsberg (1994) reports that the virulence of borreliosis can vary strongly between hosts. I use this example to discuss several possibilities that might play a role in the generation and/or maintenance of virulence in this disease of wild animals. Some of these points are of general importance for conservation biology (see Aguirre & Starkey 1994).

If *Borrelia burgdorferi* has been only recently introduced, its virulence could be far from optimum; introduced pathogens have often been observed to be virulent (although these are likely to be exceptions, see Ebert [1994] and Read [1994]). Initial reduction of virulence after introduction of a parasite has been observed in some well-investigated cases (Anderson & May 1982; Jeon 1983; May & Anderson 1983) but cannot be considered the rule. If Lyme disease is new, it is likely to undergo some evolutionary change in virulence; but whether virulence will increase or decrease cannot be predicted without detailed knowledge of the biology of both host and parasite. The simplest model predicts that the strain with the highest lifetime transmission success would outcompete other strains (Anderson & May 1982). The myxoma virus in rabbit populations is a good example of an introduced pathogen's evolution to an intermediate level of virulence.

A second possible interpretation of variability in virulence of *Borrelia* relates to host range. It is likely that a parasite will evolve to maximize its fitness in relation to the host(s) it encounters the most often. The less often a certain host is encountered, the weaker the selection pressure is on the parasite to adapt to this less familiar host (Singer et al. 1993). Parasite virulence will be maintained at a level maximizing fitness in relation to frequent hosts. In other, infrequent hosts evolutionary forces might be too weak to select for parasite adaptation. Thus, in these infrequent hosts the level of virulence would result from an interaction between two noncoadapted organisms. Therefore, any level of virulence could be the result because virulence expressed in an unusual host might not reflect the success of the parasite (Ebert 1994; Read 1994).

At present we know very little about factors determining the virulence of a parasite in a host to which it is not adapted. I suggested recently that the closer the genetic relationship between the unfamiliar host and the host to which the parasite had adapted, the more similar the virulence expressed by the same pathogen strain in both hosts (Ebert 1994). This argument may be seen as an ex-

Current address: Institut für Zoologie, Universität Basel, Rheinsprung 9, CH-4051 Basel, Switzerland, email ebeut@ubaclu.unibas.ch.

Paper submitted January 17, 1995; revised manuscript accepted May 16, 1995.

tension of host-specificity on a microevolutionary scale. Given the wide range of hosts in which *B. burgdorferi* is found it is difficult to conclude to which host the spirochete adapts.

Variation in virulence could also be the result of an ongoing host-parasite arms race. In such arms races negative frequency dependent selection is believed to be the underlying mechanism for the maintenance of genetic variance (Hamilton 1980; Ebert & Lorenzi 1994). Genetic diversity among hosts would be advantageous because parasite's adapt primarily to common host genotypes. In the case of *B. burgdorferi* those host-parasite interactions in which expressed virulence is close to the parasite's optimum would account for most parasite transmission. Hosts in contrast would be selected to resist the parasite, reducing the level of virulence. Under these conditions the observed average virulence is likely to be between the parasite's and the host's preferred level. Variation around this mean, however, could be very large (Hamilton 1993).

Finally, it has been pointed out that in long-standing host-parasite systems genetic variability for virulence can be maintained by within-host competition (Levin & Pimentel 1981; Nowak & May 1994). In cases where multiple infections are common, higher levels of virulence are expected because the more-virulent parasite is more likely to realize its transmission potential before the host dies than is the less virulent strain. Multiple infections are believed to be a major driving factor in the evolution of virulence and in the maintenance of genetic variability for host-parasite interactions (Herre 1993; Nowak & May 1994).

Every host-parasite interaction system is unique, and predictions about the outcome of coevolution are rarely possible, especially when natural populations are involved. The underlying concept that virulence is not a by-product of a maladapted parasite but rather a trait embedded in a correlation matrix of other traits appears to be general. Any change in virulence is likely to be influenced mainly by the constraints given by this correlation matrix. Within these constraints hosts can evolve toward reduced levels of virulence (or even resistance), but it appears that these adaptations are rather short-lived and of only temporary value in a rapidly evolving environment of natural enemies (Hamilton 1980; Ebert & Lorenzi 1994).

Literature Cited

Aguirre, A. A., and E. E. Starkey. 1994. Wildlife disease in U.S. national parks: historical and coevolutionary perspectives. Conversation Biology **8**:654–661.

Anderson, R. M., and R. M. May. 1982. Coevolution of hosts and parasites. Parasitology **85**:411–426.

Bull, J. J., I. J. Molineux, and W. R. Rice. 1991. Selection of benevolence in a host-parasite system. Evolution **45**:875–882.

Burdon, J. J. 1980. Variation in disease-resistance within a population *Trifolium repens*. Journal of Ecology **68**:737–744.

Clayton, D. H., and D. M. Tompkins. 1994. Ectoparasite virulence is linked to mode of transmission. Proceedings of the Royal Society, London, Series B **256**:211–217.

de Nooij, M. P., and J. M. M. van Damme. 1988. Variation in host susceptibility among and within populations of *Plantago lanceolata* L. infected by the fungus *Phomopsis subordinaria* (Desm.) Trav. Oecologia **75**:535–538.

Ebert, D. 1994. Virulence and local adaptation of a horizontally transmitted parasite. Science **265**:1084–1086.

Ebert, D., and R. Lorenzi. 1994. Parasites and polymorphism. Nature **369**:705–706.

Fenner, F., and F. N. Ratcliffe. 1965. Myxomatosis. Cambridge University Press, Cambridge, England.

Ginsberg, H. S. 1994. Lyme disease and conservation. Conservation Biology **8**:343–353.

Hamilton, W. D. 1980. Sex versus non-sex versus parasite. Oikos **35**: 282–290.

Hamilton, W. D. 1993. Haploid dynamic polymorphism in a host with matching parasites: effects of mutations/subdivision, linkage, and patterns of selection. Journal of Heredity **84**:328–338.

Herre, E. A. 1993. Population structure and the evolution of virulence in nematode parasites of fig wasps. Science **259**:1442–1445.

Hill, A. V. S., C. E. M. Allsop, D. Kwiatkowski, N. M. Anstey, P. Twumasi, P. A. Rowe, S. Bennett, D. Brewster, A. J. McMichael, and B. M. Greenwood. 1991. Common West African HLA antigens are associated with protection from severe malaria. Nature **352**:595–600.

Jeon, K. W. 1983. Integration of bacterial endosymbionts in amoebae. International Review in Cytobiology, Supplement **14**:29–47.

Lenski, R. 1988. The evolution of plague virulence. Nature **334**:473–474.

Levin, S., and D. Pimentel. 1981. Selection of intermediate rates of increase in parasite-host systems. American Naturalist **117**:308–315.

May, R. M., and R. M. Anderson. 1983. Epidemiology and genetics in the coevolution of parasites and hosts. Proceedings of the Royal Society, London, Series B **219**:281–313.

Nowak, M. A, and R. M. May. 1994. Superinfection and the evolution of parasite virulence. Proceedings of the Royal Society, London, Series B **255**:81–89.

Read, A. F. 1994. The evolution of virulence. Trends in Microbiology **2**: 73–76.

Singer, M. C., C. D. Thomas, and C. Parmesan. 1993. Rapid human-induced evolution of insect-host associations. Nature **366**:681–683.