Host–Pathogen Evolution, Biodiversity, and Disease Risks for Natural Populations

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Pathogens can play important roles in natural systems, from influencing host genetic diversity to altering the composition of ecological communities. Infectious diseases can also threaten natural populations (Harvell et al., 1999; Lafferty & Gerber, 2002). Virgin ground epidemics that quickly spread throughout previously unexposed plant and animal populations can cause high mortality and reductions in host abundance (see, for example, Anagnostakis, 1987; Osterhaus & Vedder, 1988; Sherald et al., 1996). Although documented cases of pathogen-driven host extinction are rare (Smith et al., 2006), several studies suggest that pathogens can cause declines in previously healthy populations and can be one of many threats to already declining species (Anderson et al., 2004; Daszak et al., 2000; Lafferty & Gerber, 2002; Pedersen et al., 2007). Recent examples include population crashes in African apes resulting from Ebola virus (Walsh et al., 2003), amphibian declines caused by chytridiomycosis (Lips et al., 2006), the near extinction of several Hawaiian forest birds as a result of avian malaria (Van Riper et al., 1986), recent declines in oaks in the western United States because of sudden oak death syndrome (Rizzo & Garbelotto, 2003), and widespread mortality among flowering dogwoods in eastern North America after the spread of anthracnose blight (Sherald et al., 1996).

The overarching theme of this chapter is that infectious diseases provide a model system to understand how evolutionary principles are relevant to biodiversity and conservation. Throughout we use the terms parasite, pathogen, and infectious disease interchangeably, and we consider both microparasites (viruses and bacteria) and macroparasites (protozoa, fungi, arthropods, and helminths) that can infect hosts and, in many cases, lower host fitness and cause outward signs of disease. Because of their potential for rapid evolution and impacts on host survival and reproduction, host–parasite interactions can generate a number of evolutionary outcomes, ranging from the maintenance of genetic variation to significant shifts in the genetic composition of both host and parasite populations. Because parasites, at times, can both contribute to and threaten biological diversity, understanding the evolutionary dynamics of host–parasite interactions is crucial for biological conservation.

In this chapter we begin by considering how host resistance and genetic diversity can help buffer wild populations against epidemics of new and existing pathogens. We discuss the genetic basis of host resistance, how parasite infection may maintain genetic diversity, and the importance of resistance variation for the conservation of threatened species. Next we demonstrate how evolutionary processes may influence pathogen emergence and host shifts. Parasites can evolve to capitalize on new transmission opportunities, alter their virulence, and adapt to novel host species or changing environments. From a conservation perspective, these issues can be important
for captive breeding programs, control strategies for existing pathogens, and landscape-level management approaches. Recent and historical examples from wild systems are provided to illustrate key points, although we caution that they are not intended to represent an exhaustive list.

As a final point, parasites can influence host diversification and, more generally, are a major component of biodiversity themselves. Parasites that live uniquely on threatened host species could go extinct long before their hosts, and more accurate knowledge of parasite biodiversity will likely compound estimates of future biodiversity loss. We conclude by echoing recent assertions that interactive networks of host and parasite populations might be necessary to protect biological diversity and evolutionary processes (Crandall et al., 2000; Thompson, 2005).

HOST GENETIC DIVERSITY AND RESISTANCE TO INFECTION

Parasites represent powerful selective agents in natural populations, in part because they can spread rapidly and cause significant negative effects on host fitness. When exposure to pathogens is high in a host population, traits conferring resistance are predicted to increase in frequency. In animals, these resistance strategies include behavioral defenses to avoid exposure or physically remove parasites, physiological and innate responses to infection, and humoral and cell-mediated immune defenses (Clayton & Moore, 1997). Resistance mechanisms in plants include biochemical defenses, receptor–protein interactions, and changes in phenology that lower contact rates with infective stages (Fritz & Simms, 1992). These defenses can be innate, or maintained in the absence of infection (and hence a “first line of defense” after infection) or adaptive, or induced during the course of infection by a pathogen (for example, antibody-mediated immunity in vertebrate animals). Moreover, defenses can be highly specific, such that they recognize or defend against a particular type of pathogen or even a single pathogen genotype, or general, in that they attack a variety of infectious organisms.

Given the strong selective pressures imposed by parasites and the benefits of host resistance traits, it is important to investigate factors that maintain intra- and interpopulation variation in resistance to pathogens. In other words, why aren’t all individuals resistant to infectious diseases? Models based on simple host–parasite interactions show that genetic variation can be maintained by at least three key mechanisms: frequency-dependent selection, balancing selection, or negative correlations between resistance and other fitness-conferring traits (Box 17.1) (Schmid-Hempel & Ebert, 2002). In addition, specific defenses against different parasites may act antagonistically, such that an immune response against one agent might suppress resistance to other infectious diseases (Yazdanbakhsh et al., 2002; but see also Pedersen & Fenton, 2007).

The Genetics and Maintenance of Host Resistance

The genetics underlying variation in host immunity in wild populations has attracted much recent interest (Frank, 2002; Schmid-Hempel, 2004), and many studies have demonstrated differential susceptibility among host genotypes in wild populations (reviewed in Altizer et al., 2003). The frequency of resistant genotypes in a population can be affected by and can feed back to local parasite dynamics. For example, long-term studies of trematode parasites infecting the freshwater snail Potamopyrgus antipodarum (Fig. 17.1) have shown that host genetic diversity can be maintained through local adaptation of parasites to their hosts and through frequency-dependent selection (Lively, 1992, 1999). Cross-infection experiments provided evidence of local adaptation by demonstrating that common host clones were significantly more susceptible to sympatric parasites than were rare host clones (Dybdahl & Lively, 1998). Further research revealed that changes in the frequencies of common and rare snail clones were driven by parasite tracking of susceptible genotypes. This evidence of frequency-dependent selection suggests that high infection rates can ultimately favor host sexual reproduction as a strategy for generating novel host genotypes that may resist infection (Dybdahl & Lively, 1998).

Plant–pathogen coevolution can similarly lead to a high diversity of host resistance and parasite virulence alleles. In fact, natural plant populations have been shown to harbor a staggering abundance of genetic polymorphisms for resistance to fungal diseases (Burdon & Thrall, 1999; Parker, 1992), and wild plant populations have been cited as a source of resistance genes for pathogens and
Multiple processes can maintain genetic polymorphisms in host resistance in natural populations. First, in the case of frequency-dependent selection, parasites can become locally adapted to common host genotypes, and thus are better able to infect them. Hence, hosts with rare genotypes may escape parasite infection, conferring a selective advantage to rare alleles and a disadvantage to common alleles. This process can cause time-lagged cycles in both host and parasite allelic frequencies, and may ultimately lead to the maintenance of genetic variation over longer timescales (Seger & Hamilton, 1988). The phenomenon of parasites tracking common host genotypes has been demonstrated in several wild systems and is important for arguments concerning the role of parasites in generating advantages to host sexual reproduction (Dybdahl & Lively, 1998).

More generally, balancing selection refers to processes that favor the persistence of multiple alleles, or genetic polymorphisms in a population, in contrast to directional selection, in which allelic frequencies tend to shift in a single direction. Balancing selection can be realized through frequency-dependent selection, as described earlier, or through heterozygote advantage, in which individuals with different alleles at any given locus tend to have greater fitness than homozygous individuals. As one example addressed in the text, individuals heterozygous for MHC alleles could experience an advantage in the face of diverse pathogen strains by virtue of recognizing a greater variety of antigens for response by the vertebrate immune system (Penn et al., 2002). Spatial and temporal changes in the risk of infection by different pathogen genotypes or species, as generated in part by environmental heterogeneity, could also favor the maintenance of multiple alleles over larger spatial and temporal scales.

Third, resistance-conferring host traits may be costly in terms of reductions in other fitness components (for example, fecundity, growth rates, resource competition) as a result of pleiotropy or resource-based trade-offs. Modeling studies have indicated that even small resistance costs (measured as differences in fitness between resistant and susceptible hosts in the absence of infection) should lead to genetic polymorphisms, such that both susceptible and resistant genotypes are maintained in the presence of parasites (Antonovics & Thrall, 1994). A growing number of field and experimental studies has identified measurable costs of resistance to pathogens infecting many host species (see, for example, Sheldon & Verhulst, 1996), although other studies emphasize that the presence and size of costs will depend on host and pathogen characteristics (see, for example, Carr et al., 2006; Mitchell-Olds & Bradley, 1996), and that the shape of the trade-off function will be important for the longer term dynamics.

In light of potential costs of host resistance, inducible defenses that are activated only after parasite infection may be beneficial when the risk of infection is rare or unpredictable (Harvell, 1990). Such defenses include antibody-mediated responses in vertebrates, antimicrobial proteins in invertebrates and plants, and behavioral avoidance in animals. As one example, recent work in sea fan corals has shown that hosts can mount inducible defenses against infection with emerging fungal pathogens, and that environmental factors that cause variation in this response may predict patterns of host susceptibility (Harvell et al., 2002; Ward et al., 2007). Understanding how inducible defenses can be mobilized rapidly against novel pathogens, their rate of evolution, and the costs that they pose on host fitness should help inform efforts to manage disease resistance for conservation.
Field and experimental studies of the freshwater snail *Potamopyrgus antipodarum* and the trematode parasite *Microphallus*, for which the snails serve as intermediate hosts, have demonstrated local adaptation and time-lagged frequency-dependent selection in a host–parasite interaction. (A) Pathology caused by infection with the *Microphallus* (top) compared with the healthy snail (pictured below). Both snails are shown without shells; parasite eggs ingested by snails develop into encysted intermediate stages and castrate the snail. (B) Experimental setup of snail clones after exposure to trematode eggs derived from specific parasite genotypes. (C) Lakes on the south island of New Zealand, such as Lake Alexandrina (pictured here), serve as key sites for field studies of snails and parasites in their native environments. (Reproduced with permission from C. Lively. Photos courtesy of G. Harp and C. Lively.)
pests for crop plants (Jones, 2001). For example, long-term field studies of wild flax and flax rust in natural populations in Australia (Fig. 17.2) indicate that a large number of resistance alleles can persist in plant metapopulations (Burdon & Jarosz, 1991). The distribution of genotypes can shift rapidly after local epidemics, and trade-offs arising from fitness costs have been linked with variation in host resistance and pathogen virulence (Burdon & Thompson, 1995; Thrall & Burdon, 2003). Studies of anther-smut infections in their wildflower hosts also demonstrated variation in resistance among plant genotypes, impacts of host resistance on pathogen prevalence, and costs of resistance in terms of delayed flowering (see, for example, Alexander et al., 1996; Carlsson-Granér, 1997).

Among vertebrate animals, a variety of genes and gene complexes are important for mediating defenses against infectious diseases (see, for example, Acevedo-Whitehouse & Cunningham, 2007). The majority of scientific interest to date has focused on MHC as playing a key role in acquired immunity. Major histocompatibility complex molecules are immune proteins that recognize and bind to pathogen proteins (antigens) inside infected host cells and transport these antigens to cell outer membranes. Here they are presented to T cells to initiate antibody production and cell-mediated immune responses. Specific MHC molecules preferentially bind to specific pathogen peptides, and hence different MHC alleles confer resistance to different pathogens. In natural populations, MHC class I and II genes show enormous variation and are important for recognizing a wide diversity of pathogens (Hedrick & Kim, 2000; Nei & Hughes, 1991). Individual hosts that are heterozygous across multiple MHC loci recognize a greater diversity of pathogens than homozygous individuals (Doherty & Zinkernagel, 1975), and at the population-level, high levels of MHC allelic variation can increase the chance that at least some hosts’ immune systems will recognize a single pathogen. Studies of humans and domesticated animals also highlight the importance of non-MHC immune genes in protecting against infectious diseases (Acevedo-Whitehouse & Cunningham, 2006), and a broader understanding of resistance evolution in wild vertebrates will ultimately require comprehensive genetic analysis of other immune regions that control aspects of pathogen defense.

**Costs, Trade-offs, and Environmental Variation**

Research in the developing field of ecological immunity (McDade, 2003; Norris & Evans, 2000) examines the ecological causes and consequences of variation in immune function. One central issue is that hosts that respond to parasite pressure through
FIGURE 17.2 Long-term studies of the dynamics of wild flax (*Linum marginale*) and its fungal rust (*Melampsora lini*) illustrate coevolutionary dynamics in a naturally occurring plant–pathogen interaction. (A) The heavily infected leaves and stem of the *L. marginale* host plant are shown covered with uredial lesions after experimental inoculation. (B) Many populations used to investigate the ecological and evolutionary dynamics of this host–pathogen interaction occur in southeastern Australia in environments such as this subalpine grassland surrounded by eucalypt forests (pictured here in the Kosciuszko National Park, N.S.W.). (Reproduced with permission from L. Barrett. Photos courtesy of C. Davies and L. Barrett.)
increased resistance could suffer lower competitive ability or reduced reproduction (and vice versa; Boxes 17.1 and 17.2) (reviewed in Lochmiller & Deerenberg, 2000). Thus, hosts might be expected to invest in greater defenses only when the risk of pathogen infection is high, leading to geographic variation in genetically based host resistance traits. Also, it is well established that environmental variation, including temperature, resource availability, and environmental stressors, can affect the expression of host resistance in plants and animals (Rolff & Siva-Jothy, 2003). These environmental processes could generate spatial and temporal variation in host defenses, and might also represent important constraints on host resistance evolution (Box 17.1).

**Implications of Host Resistance for Species Conservation**

Several studies have demonstrated that genetic variation for host resistance is common in natural populations and has significant consequences for parasite infection rates. For example, one comparative analysis showed that macroparasites were more likely to colonize fish species that had low levels of genetic variation as indicated by mean heterozygosity (Poulin et al., 2000). Field studies of intestinal nematodes affecting Soay sheep demonstrated that host allelic variation and levels of heterozygosity were associated with higher host survival and resistance to infection (Coltman et al., 1999; Paterson et al., 1998). But what are the implications of these findings for species conservation? One concern is that small or endangered host populations might suffer disproportionate impacts from infectious diseases as a result of the loss of genetic variability through population bottlenecks, genetic drift, and inbreeding (Lyles & Dobson, 1993). Hosts bred in captivity and treated to prevent and remove parasitic organisms may further experience increased susceptibility caused by relaxed selection and costs associated with resistance-conferring traits.

The relationship between the loss of genetic diversity and increased disease susceptibility has been found in many animal populations (Box 17.2) (Acevedo-Whitehouse et al., 2003). For example, recent studies of birds and amphibians have shown that loss of heterozygosity (based on selectively neutral microsatellite markers) is associated with reduced immunocompetence, greater risk of infection, and increased severity of infection (Hawley et al., 2005; MacDougall-Shackleton et al., 2005; Pearman & Garner, 2005). Some evidence from pathogen resistance and inbreeding effects in the context of wild plant populations indicates that inbreeding could increase susceptibility to fungal and viral disease (Carr et al., 2003; Ouborg et al., 2000).

Among vertebrate animals, allelic diversity at MHC loci can be lower than expected among endangered species that have undergone dramatic declines in population size (see, for example, Aldridge et al., 2006). On the other hand, a high diversity of MHC genotypes has been documented across small populations of red wolves, Arabian oryx, and some other endangered species (Hedrick et al., 2000, 2002). In one extreme example, Aguilar and colleagues (2004) demonstrated homozygosity across multiple selectively neutral loci in the San Nicholas Island fox (Urocyon littoralis dickyi). This pattern is indicative of the loss of variation resulting from genetic drift after an extreme population bottleneck approximately 10 to 20 generations before samples were collected. However, these animals showed high levels of variation across five MHC loci, leading the authors to conclude that intense balancing selection was necessary to prevent the loss of rare alleles and ultimately maintain MHC variation in the face of past bottlenecks (circa <10 individuals).

In light of these findings, one goal for conservation management is to design captive breeding, stocking regimes, and species management programs that maintain levels of immunity or resistance variation present in wild populations. One case study shows that the Hawaiian amakihi, a native bird species whose population size and geographic range were negatively affected by the introduction of avian malaria, has persisted and begun to repopulate lowland forest habitats despite high infection rates from *Plasmodium relictum* (Woodworth et al., 2005). One possible explanation for this recovery is host evolution of genetically based resistance or tolerance of infection. Findings such as these should motivate future conservation efforts to focus not just on protecting host populations in areas less affected by pathogens, but also to identify hosts inhabiting parasitized environments where significant evolutionary responses might have occurred.

A related point is that host and parasite movement among habitat patches may be crucial for both host persistence and the spread and maintenance of resistance alleles. For example, Carlsson-Graner...
Species introductions offer many opportunities to understand the strength of pathogens as agents of selection. First, most populations of introduced species are likely to originate from a few founders, thus limiting their genetic diversity and possibly increasing their susceptibility to parasites (Sakai et al., 2001). Second, invasive species that escape infection by a broad range of parasites (Mitchell & Power, 2003; Torchin et al., 2003) might reallocate resources away from enemy defense and into growth and reproduction (Wolfe et al., 2004). Indeed, greater allocation to growth and reproduction after enemy release is widely thought to underlie the increased vigor or success of introduced species in their new range (Siemann & Rogers, 2001). Together, these ideas suggest that low genetic diversity combined with evolutionary reductions in parasite defense should make introduced species vulnerable targets for future epidemics, and that detailed studies of pathogen interactions with invasive species in their native and introduced ranges are greatly needed.

Genetic variation tends to be lower among introduced populations, particularly if colonists come from a single source population or undergo an establishment phase during which population sizes remain small (Sakai et al., 2001). Founder events resulting in genetic drift and inbreeding could lower the fitness of introduced populations and limit their ability to adapt to future challenges arising from parasites and infectious diseases. For example, reduced host genetic diversity has been suggested as the reason for the unusually high susceptibility of introduced house finches in eastern North America to mycoplasmal conjunctivitis (Hawley et al., 2005, 2006). In some cases, however, repeated introductions from multiple native sites could lead to a mixing of alleles from different source populations (admixture), resulting in greater genetic variation—rather than less—in the introduced range (as has been demonstrated with brown anole lizards [Kolbe et al., 2004]). Hosts with such novel gene combinations might be highly resistant to parasite infections (Sakai et al., 2001).

Many invasive species are larger bodied, more abundant, and more vigorous in their introduced range relative to their native range (Crawley, 1987; Grosholtz & Ruiz, 2003). A specific hypothesis termed the evolution of increased competitive ability proposes that exotic species should adapt to the loss of natural enemies by allocating more energy to growth and reproduction, rather than investing in costly defenses (Blossey & Nötzold, 1995). Predictions of this hypothesis are that in the native range, growth and reproduction should be lower, natural enemies should be more common, and investment in defenses higher; whereas in the introduced range, natural enemies should be less common or absent, defenses lower, and growth and reproduction greater (Wolfe et al., 2004). Furthermore, these phenotypic differences should be genetically based and, given the choice, parasites and other natural enemies should better attack the invasive phenotypes—two predictions that can be tested using common-garden and reciprocal transplant experiments. Some recent studies provide support for genetic divergence in enemy defense and reproductive strategies between native and novel populations of introduced weeds and trees (Siemann & Rogers, 2001; Wolfe et al., 2004), and suggest that introduced species might be vulnerable to future pathogen introductions.

Another area for future research includes the role of evolutionary change in those pathogens that persist or become established in populations of exotic host species. For example, do traits such as high mutation rates or more rapid generation times favor pathogen adaptation to hosts in their new range? How might pathogen virulence change in response to shifts in host genetic diversity or abundance in their new habitats? Currently, comprehensive studies of host resistance and pathogen evolution among invasive species in both their native and introduced ranges are rare, despite the potential insights that can be gained from such comparisons. Future studies of exotic species and their parasites will likely provide new evidence regarding the role of host genetic diversity in immunity and resistance, how costs and trade-offs affect host investment in immune defenses, and how pathogens adapt to populations of exotic organisms.
and Thrall (2002) demonstrated that isolated populations of the wildflower *Lychnis alpina* were rarely infected with anther-smut disease, but when populations were infected, the prevalence was high. In comparison, highly connected populations show more widespread pathogen occurrence across sites, with low prevalence within each location. This pattern was consistent with model simulations that assumed higher rates of movement of both pathogen propagules and host resistance alleles among connected populations (Carlsson-Graner & Thrall, 2002). In bighorn sheep, larger population sizes and increased dispersal is associated with lower extinction risk and rapid population recovery after bronchopneumonial epidemics, indicating a potential role for host dispersal in genetic variation and resistance evolution (Singer et al., 2001). Together, these studies suggest that habitat size and ecological corridors can have significant effects on host dispersal and movement of resistance alleles in ways that affect host responses to future epidemics.

**ROLE OF PATHOGEN EVOLUTION IN DISEASE EMERGENCE**

The evolutionary potential of pathogens sets them apart from other major threats to biodiversity. Most pathogens have short generation times and large population sizes; hence, strong selection pressures following ecological changes can increase the probability of pathogen evolution and the likelihood of disease emergence in a novel host species. The relevance of pathogen evolution to human health is underscored by recent threats from severe acute respiratory syndrome, avian influenza, and antibiotic-resistant bacteria. However, empirical evidence of how evolutionary processes influence the likelihood of emergence and pathogen spread in natural systems is less clear and supported by only a few examples (Altizer et al., 2003; Schrag & Weiner, 1995).

Two major questions are how do parasites establish in new host populations, and does evolution affect the probability of long-term parasite success? Both epidemiology and evolutionary potential of the pathogen are important during and after pathogen entry into a novel host population. In terms of epidemiology, a newly infected individual must transmit the pathogen to more than one other host for the parasite to increase in frequency when initially rare (commonly referred to as $R_0 > 1$ [Anderson & May, 1991]). Novel infections are more likely to establish if chains of transmission allow new mutations to arise that increase $R_0$ above one, and hence evolution and mutations that influence transmission and virulence can play a crucial role in the emergence process (Antia et al., 2003).

Despite general predictions, the direct role of selection in the emergence of infectious diseases in natural systems remains relatively unknown. Recent studies of host shifts among fungal pathogens infecting plants indicate that geographic proximity and opportunities for cross-species transmission, rather than genetic changes in the parasites themselves, are primarily responsible for the origin of new host–parasite combinations (Antonovics et al., 2002; Roy, 2001). Yet, after such introductions, other studies demonstrate that genetic variants of parasites from novel hosts can rapidly diverge from ancestral genotypes (Ley & Yoder, 1997; Oldroyd, 1999), suggesting that evolution has indeed occurred. Canine parvovirus (CPV), which first appeared in wolves, coyotes, and domesticated dogs during the mid 1970s, is an example of a pathogen that likely arose as a new genetic variant of feline panleukopenia parvovirus, a closely related virus from domesticated cats (Parrish, 1990). Genetic studies following CPV emergence suggest that mutation and selection associated with a major capsid gene, rather than recombination of existing feline variants, played a key role in viral emergence (Shackelton et al., 2005).

**Evolutionary Potential, Disease Emergence, and Virulence**

Several pathogen characteristics may predispose them to high emergence potential. First, transmission strategies that increase encounters with new host species may increase the range of hosts that a pathogen can infect (Woolhouse et al., 2005). Second, greater genetic variability, high mutation rates, and more rapid generation times might allow certain pathogens to exploit new host species more readily. Specifically, parasites with high antigenic variation should have an increased ability to recognize host proteins or evade host immune defenses (Bitter et al., 1998) and infect new host species (Cleaveland et al., 2001). Viruses dominate this group because their high mutation rates, greater antigenic diversity, and short generation times allow them to adapt rapidly to a larger number of host species. In fact, emerging
infectious diseases in humans, domesticated animals, plants, and wildlife are often dominated by viruses, especially RNA viruses that are characterized by unusually high mutation rates and relatively large host ranges (Anderson et al., 2004; Holmes, 2004; Pedersen et al., 2005; Woolhouse et al., 2005).

Evolution can also cause shifts in the virulence of existing and emerging diseases. Theory on the evolution of parasite virulence suggests that parasites should evolve toward an intermediate level of virulence. This is based on an assumed trade-off between transmission and virulence, such that the production of infectious stages required for transmission to a new host is positively correlated with the damage the parasites cause to the host. Intermediate virulence is favored because highly virulent pathogens may kill hosts before successful transmission occurs, whereas parasites with very low virulence will not produce enough infective stages to be transmitted (Levin, 1996). Spatial structure changes the evolution of virulence, however, such that if most transmission occurs at a local (rather than global) scale, then less virulent pathogens are favored (Boots & Sasaki, 1999). Boots and colleagues (2004) further demonstrated that acquired immunity can lead to the coexistence of both nonvirulent and highly virulent strains. These results help explain the sudden emergence of a virulent strain of rabbit hemorrhagic disease virus that spread throughout Europe, causing high mortality in free-living rabbit populations. Molecular evidence suggests that this highly virulent strain emerged from a recombination event involving less virulent strains. The sudden emergence of the highly virulent strain and coexistence with less virulent genotypes was likely a product of the host’s social structure, as rabbits tend to have highly structured populations (Boots et al., 2004).

**Anthropogenic Effects on Pathogen Evolution and Risks for Wild Populations**

Large-scale environmental changes caused by humans could directly affect pathogen life cycles and transmission, leading to evolutionary shifts in other parasite traits. One example that highlights the role of human activity and selective pressure on sudden evolutionary changes is in the increased transmission and host range of *Toxoplasma gondii*, the protozoan parasite that causes toxoplasmosis in humans and other mammalian hosts (Su et al., 2003). *Toxoplasma gondii* is maintained by wild and domesticated cats that can shed infectious stages in their feces and transmit the parasite to humans and wildlife. Molecular genetic analyses of this parasite indicate that the ability of clonal lineages to transmit orally and without sexual recombination (as opposed to passing through an intermediate host to complete the sexual phase of the life cycle) was associated with a selective sweep that occurred around the time of human agricultural expansion several thousand years ago (Su et al., 2003). By creating high densities of multiple species of domesticated mammals, human activity may have selected for increased oral transmission. Thus, humans may be unknowingly selecting for new variants of wildlife pathogens through global commerce, changes in host density and habitat quality, and climate shifts over longer timescales (Harvell et al., 2002).

Spillover from domesticated plants and animals is a particular threat to wild species because infected reservoir hosts can facilitate epizootics in natural populations with otherwise low population density (Anderson et al., 2004; Daszak et al., 2000). As one example, African wild dogs (*Lycaon pictus*) became extinct in the Serengeti in 1991, in part as a result of spillover by canine distemper from a domestic dog outbreak (Funk et al., 2001). Other pathogens of domesticated dogs have affected wild populations—even in the ocean, where an outbreak of Morbilivirus in harbor seals was genetically similar to a strain from domestic dogs (Osterhaus & Vedder, 1988). Similarly, the anthropogenic introduction of plant pathogens from imported timber, agricultural crops, or nursery plant species has caused dramatic declines in wild plant populations (with examples reviewed in Anderson et al., 2004).

Repeated pathogen introduction events, especially from multiple sources, can influence genetic heterogeneity in the pathogen population. For example, the repeated introduction of the Dutch elm disease fungus (*Ophiostoma spp.*) via infested timber in the 20th century led to the death of billions of elm trees in North America and Europe. This was caused primarily by two different *Ophiostoma* species introduced several decades apart (Brasier, 2001). Genetic and phenotypic evidence indicates that the more aggressive causal agent (introduced later) gradually replaced the less aggressive species, and that hybridization between the two fungal
species produced novel genotypes that may have further increased pathogen virulence and environmental tolerance. This example emphasizes the need for additional studies to examine the degree to which evolutionary changes in pathogens have affected their spread and affects on novel host species.

HOST–PARASITE COEVOlUTION, GEOGRAPHIC VARIATION, AND DIVERSIFICATION

Most examples in natural systems suggest that neither host nor parasite evolution operates in isolation, but that their interaction leads to coevolutionary dynamics. Over time this could result in reciprocal adaptations of interacting lineages, possibly accompanied by co speciation events and genetic arms races (Box 17.3) (Page, 2003). Relative to other types of species interactions, the intimate associations between hosts and parasites offer many opportunities for studying coevolution on contemporary timescales. Collectively, studies of host–parasite interactions emphasize that coevolution is common, causes heterogeneity in species characteristics over space and time, and that genetic changes linked with coevolution can drive significant changes in species abundance (Thompson, 2005).

An often-cited example of coevolution of host and parasite traits involves myxomatosis in Australian and European rabbit populations (Fenner & Fantini, 1999). After intentional releases in Australia during the early 1950s, the myxoma virus rapidly shifted in virulence. Specifically, within 5 years after the introduction of a highly virulent virus, other strains with reduced severity (for example, longer times to host death and moderate mortality rates) became increasingly common (Marshall & Fenner, 1960). An evolutionary response of the host followed, characterized by greater resistance and lower viral-induced host death rates (Marshall & Fenner, 1958).

Selection operating on hosts and parasites can also lead to coevolutionary arms races (Frank, 2002; Hamilton, 1982), whereby parasites select for increased host immunity, which exerts reciprocal selection for alternative transmission strategies, manipulation of host behavior, and changes in virulence of the parasite. This cycle of parasite adaptation leads to further selection on host defenses. As one example, studies of interactions between feral pigeons and feather lice demonstrated that selection for improved defense systems (in other words, grooming for parasite removal) in the avian host is accompanied by selection for parasite mechanisms to escape these host defenses (Clayton et al., 1999, 2003). More generally, studying coevolutionary interactions in naturally occurring hosts and parasites can highlight selection pressures important in the long-term maintenance of the association, including the degree to which limited evolutionary responses might lead to higher extinction risks for either host or parasite lineages.

Phylogenetic Patterns and Cospeciation

Over longer timescales, reciprocal adaptations of hosts and parasites might lead to cospeciation and phylodiversity diversification (Clayton et al., 2003; Page, 2003) (Box 17.3). Cospeciation is defined as the parallel divergence of two or more interacting lineages (Page, 2003), and this process can generate congruent host and parasite phylogenies. Several studies have demonstrated patterns consistent with host–parasite cospeciation, yet other outcomes are possible, including host shifting, parasite extinction, and a process called missing the boat, during which the host splits into two or more lineages but the parasite remains in only one (Page, 2003). Host shifting is likely to be common among parasites that can evolve rapidly relative to host generation times, and where transmission generates frequent opportunities for cross-species transfer.

Modern molecular tools allow researchers to examine the origins and coevolution of host–parasite associations and the relative rates of host and pathogen evolution (see, for example, Holmes, 2004). Viruses and bacteria that have fast generation times and large population sizes can evolve faster than their hosts and might commonly show evidence for rapid genetic changes after shifts to new host species or transmission among host populations. Surprisingly, one study of cospeciation among strains of simian foamy viruses (SFVs; in the family Retroviridae) isolated from Old World monkeys and apes provides evidence counter to this general expectation (Switzer et al., 2005). This study showed strong evidence for congruent primate and virus molecular phylogenies (with evidence of only a few host jumps), and comparable divergence
Interspecific interactions (in other words, predator–prey, plant–herbivore, and host–parasite) have been proposed to drive major diversification between assemblages of coevolving organisms (Farrell, 1998; Percy et al., 2004) and could ultimately be responsible for the great species diversity found on earth. In terms of parasitism, one comparative study of primate–pathogen interactions demonstrated that parasite diversity (species richness) was positively correlated with rates of primate host diversification (Nunn et al., 2004). In other words, primate host species from more diverse lineages harbored a greater number of parasite species (including viruses, protozoa, and helminths). One mechanism that could give rise to this association is that parasites increase host evolutionary diversification, through, for example, their effects on sexual selection. Because sexually selected traits can also correlate with parasite resistance (Hamilton & Zuk, 1982), high parasite pressure might ultimately lead to greater potential for host speciation. A second explanation for the patterns observed by Nunn and colleagues (2004) is that parasites infecting hosts from more diverse lineages could experience greater opportunities for diversification. Specifically, related host species that overlap in geographic range might provide more opportunities for host sharing by generalist parasites, and host shifting by specialist parasites—leading to higher parasite species richness.

An arms race between hosts and parasites, involving an ongoing struggle to mount greater host resistance against infection, and higher virulence and transmissibility of the parasites, could also account for positive correlations between host diversification and parasite species richness. As a final possibility, coextinctions of hosts and parasites might also drive the associations reported by Nunn and colleagues (2004). Specifically, parasite lineages might be lost as their hosts decline in population size and ultimately go extinct. In other words, higher extinction rates in declining host lineages could generally reduce parasite diversity, especially if parasites go extinct before their hosts (Koh et al., 2004). Another study using the same host–parasite data supported this idea by demonstrating that more threatened primate hosts harbored fewer parasite species (Altizer et al., 2007). Future comparative research on host–parasite diversification will likely benefit from investigating the geographic patterning of host–parasite interactions (Thompson, 1994), incorporating information on parasite phylogeny into comparative tests (Hafner & Page, 1995), and examining the degree to which parasites themselves have gone extinct along with their hosts (Gompper & Williams, 1998).

Lastly, results of comparative studies, although provocative, do not directly examine mechanisms that underlie associations between host and parasite diversification. Theoretical studies have shown that frequency-dependent selection between prey and natural enemies can lead to evolutionary branching in both the host and enemy populations (Doebeli & Dieckmann, 2000). Small-scale experiments of coevolution between bacteria and virulent phages in spatially structured environments have also demonstrated that parasites can drive allopatric divergence among host populations, increasing host diversification by selecting for antiparasite defenses genetically linked to different host traits in different populations (Buckling & Rainey, 2002). Future studies aimed at developing and testing hypotheses for host and parasite evolutionary divergence will give insight to the degree to which hosts and parasites show evidence for coadaptation, concordant phylogenies, and mechanisms that drive patterns of diversification.
times and rates of nucleotide substitution for hosts and parasites, suggesting that primates and SFVs have evolved at similar rates. Analysis of other RNA viruses (for example, Morbilivirus, influenza A viruses, and flaviviruses), however, shows evidence for rapid substitution rates and more frequent cross-species transmission events (see, for example, Chen & Holmes, 2006; Twiddy et al., 2003). Although there is variation in a parasite’s ability to establish within a new host species, understanding how host and parasite characteristics covary with the risk of host shifts will be crucial for predicting disease emergence events in declining or endangered species, for which the impact of a novel disease could be devastating (Lafferty & Gerber, 2002; Pedersen et al., 2007).

PATHOGENS AS INDICATORS OF HOST CONTACT AND ISOLATION

Can genetic studies of infectious diseases reveal information about host biology, behavior, and disease transmission that enhance conservation efforts? In humans, it has been demonstrated that host migration events can be revealed by pathogen genetic structure, especially for rapidly evolving viruses like human immunodeficiency virus (Holmes, 2004). A handful of studies have applied this approach more recently to wildlife populations. For example, low genetic diversity and the need to examine patterns over relatively short time frames could pose difficulties in detecting patterns of host evolutionary divergence, especially for long-lived species. In such cases, evolution of some pathogens can be rapid enough to illuminate host geographic isolation and contact patterns. One analysis investigated sequence variation of two genes (pol and env) in the feline immunodeficiency virus to assess patterns of isolation and physical contact among cougars in western North America (Fig. 17.3) (Biek et al., 2006). Low cougar population densities during the past century and restricted movements were expected to result in pronounced genetic structure, but only weak isolation-by-distance was revealed using cougar microsatellite markers. By comparison, phylogenetic analysis of viral strains isolated from cougars in the northern Rocky Mountains revealed eight viral lineages and geographic population substructure, with different lineages dominating in the central versus the periphery of the cougars’ range (Biek et al., 2006). Genetic analysis further revealed that the spatial occurrence of viral lineages is expanding, most likely as a result in increases in cougar population size or movement. This work illustrates the usefulness of pathogen molecular markers for understanding contemporary population movements and geographic structuring of their hosts.

In another study, three species of whale lice (host-specific ectoparasitic crustaceans) revealed historical separation of populations of endangered right whales (Kaliszewska et al., 2005). Genetic analyses of parasite mtDNA sequences revealed that three whale populations in the North Atlantic, North Pacific, and southern oceans diverged around five to six million years ago, after the formation of the Isthmus of Panama. High genetic diversity among lice in the currently small populations of North Atlantic right whales indicates that their host population sizes probably numbered in the tens of thousands before the modern era of commercial whaling, and that these populations had not experienced prolonged historical bottlenecks prior to the past few centuries (Kaliszewska et al., 2005).

Analysis of genetic divergence among pathogen lineages can also be used to predict patterns of disease emergence and to develop control strategies for pathogens in endangered host populations. Statistical analysis of viral sequence changes over space and time has indicated dispersal patterns for the geographic expansion of fox rabies virus in North America (Real et al., 2005) and a wavelike spread of Ebola virus in Central Africa (Walsh et al., 2005). The case of Ebola in Africa is important for both human health and the future of the remaining wild ape populations, which are also susceptible to the virus. The epidemic appears to have advanced as a wavefront, and Walsh and colleagues (2005) suggest that the ladderlike phylogeny of viral isolates and concordant spatial pattern support transmission of the virus through populations of gorillas. In contrast, Leroy and associates (2005) showed that fruit bats harbor the virus, and proposed that Ebola outbreaks are driven less by direct ape-to-ape transmission. These recent analyses may help researchers pinpoint the origins of the epizootic and predict the future path of spread, with implications for concentrating control efforts in wild ape populations at the highest risk.
FIGURE 17.3 Continued
Evolutionary genetics of the feline immunodeficiency virus FIVPco have been used to elucidate the population structure of its cougar hosts (*Puma concolor*) in North America. (A) Researchers draw a blood sample from a cougar to be used for FIVPco analysis. (Photo courtesy of T. Ruth.) (B) Spatial distribution of FIVPco lineages in the natural habitat of cougars in the western United States and Canada. White circles represent negative samples (no FIVPco); filled circles represent samples from cougars that tested positive (with the several viral lineages indicated by various shadings). (C) Phylogeny of FIVPco constructed from the concatenated *pol* and *env* sequences. Eight viral lineages are designated based on more than 5% divergence, and their colors match those shown in (B). Labeled nodes represent bootstrap support based on 1,000 neighbor-joining trees generated from maximum-likelihood distances estimated from the original likelihood model and posterior proportions from the Bayesian analysis. (Figure provided by R. Biek; data are from Biek et al. [2006]. Reproduced with copyright permission from Biek, R., et al. 2006. A virus reveals population structure and recent demographic history of its carnivore host. *Science* **311**: 538–541.)
FUTURE DIRECTIONS

Parasites and Host Extinction Risk

Although managing wild host populations in light of pathogen risks may seem trivial relative to numerous other threats to biodiversity, several species have been driven to extinction or to near extinction as a result of infectious diseases (Lips et al., 2006; Smith et al., 2006; Thorne & Williams, 1988). On the one hand, models of directly transmitted infectious diseases suggest that highly virulent pathogens will disappear from small host populations before their hosts go extinct (Anderson & May, 1991). However, there are several cases in which pathogens can cause host extinction (de Castro & Bolker, 2005). First, directly transmitted parasites could drive host population sizes so low that extinction by stochastic factors becomes a concern. Second, pathogens transmitted sexually, vertically, or by biting arthropods (in other words, with frequency-dependent transmission [Getz & Pickering, 1983]) should not suffer from reduced prevalence as host populations decline, and the same is generally true for parasites that cause host sterility rather than mortality (O’Keefe & Antonovics, 2002). Third, some generalist parasites maintained in reservoir populations, particularly domesticated species living at high density, can also affect threatened species (Fenton & Pedersen, 2005). In addition, spatially explicit models show that even if parasites do not cause global host extinction, they can lead to local extinction and cause large-scale declines in host density as the infection spreads to new patches (Boots & Sasaki, 2002; Sato et al., 1994).

One of the best-known examples of host near extinction resulting from disease involves the black-footed ferret (Mustela nigripes), one of the most endangered mammals in North America. In the mid 1980s, outbreaks of canine distemper virus (affecting the ferrets) and sylvatic plague (affecting their prairie dog prey) effectively eliminated black-footed ferrets from the wild and severely threatened a captive breeding program. At one point the entire species was reduced to fewer than 20 captive animals (Dobson & Lyles, 2000). Despite current success in breeding and release of captive animals, future threats from infectious diseases will probably play a role in ferret recovery. Dramatic losses of gorilla populations in Africa as a result of Ebola virus outbreaks further underscore the ecological relevance of infectious disease for wildlife conservation. In one instance, an outbreak in the Lossi Sanctuary eliminated an entire population of 143 gorillas (Leroy et al., 2004). Disease-mediated extinction risk is not limited to wildlife species, as several plants are also suffering dramatic declines resulting from the introduction and spread of virulent pathogens (Anderson et al., 2004). In Australia, for example, the anthropogenic introduction of Jarrah dieback disease (Phytophthora cinnamomi), a globally occurring fungus with a host range of more than 900 species, has caused a national threat to endemic flora, with significant risks for the health of several ecological communities (Wills, 1993).

Host–Parasite Evolution and Conservation of Biodiversity

Many studies have highlighted the importance of genetic variation in host resistance in causing disease patterns in both field and experimental settings (reviewed in Altizer et al., 2003), but these almost always involve single-host–single-pathogen interactions. In reality, host individuals, populations, and species are affected by large numbers of parasitic organisms spanning divergent phyla from viruses to nematodes to parasitic insects, and for which different types of defenses vary in their effectiveness. Future studies of the types of pathogens that pose the greatest threats to endangered host populations, together with broader genomic surveys that examine a range of immune genes in animals and plants are needed to shed further light on the benefits and feasibility of selective maintenance of resistance traits in captive breeding programs (Acevedo-Whitehouse & Cunningham, 2006). Another important area for future research involves developing a better understanding of costs and trade-offs of resistance and how environmental variation affects host immunity. Such investigations will require measuring ecologically relevant immune defenses in the wild and understanding their correlations with other components of host survival and reproduction (Norris & Evans, 2000). In cases in which host defenses are costly, hosts that lose their parasites during population bottlenecks or while in captive breeding programs may also lose their ability to respond to future disease threats after relaxed selection for immune defenses.

As a related point, when hosts decline toward extinction, their host-specific parasites will probably also be lost (Gompper & Williams, 1998).
Figure 17.4 (A, B) Parasite diversity in free-living mammals. Each point represents parasite species richness based on counts of viruses, bacteria, fungi, protozoa, helminths, and arthropods reported from a single host species. These figures demonstrate positive correlations between study effort and the number of parasites reported from free-living host populations, suggesting that scientists have uncovered only a fraction of the total diversity of parasites and pathogens in natural populations. More generally, this association indicates that “parasites are like the stars—the more you look, the more you find” (J. Antonovics, personal communication, September 2000). Data are shown separately for nonhuman primates (n = 119) (A) and hoofed mammals (artio- and perissodactyls; n = 97) (B). In (A), the sampling effort is measured as the number of literature citations for each primate species using the online bibliographic resource PrimateLit (Wisconsin Primate Research Center and Washington National Primate Research Center). In (B), the sampling effort is based on the sum of the number of animals across all studies upon which parasite count data were derived. Lines show least-squares regression based on a linear regression model. Data are as reported based on methods described by Nunn and Altizer (2005) and are available as part of the Global Mammal Parasite Database (www.mammalparasites.org).
One question at the interface of conservation biology and disease ecology involves whether the loss of parasites is harmful or helpful to a host population. In other words, is the elimination of all naturally occurring parasites beneficial to the host? Given that most of the examples highlighted in this chapter focus on parasites as a threat to wild populations, the answer might seem to be yes. Yet, many ecologists would argue that the best approach for long-term conservation is to preserve geographically structured populations of interacting species, including parasites, in part to maintain intact evolutionary processes. Keeping host–parasite relationships intact requires landscape management strategies that might include protecting corridors and networks of multiple habitat types important to a broad range of species.

Protecting parasitic organisms has not been championed as a priority for current or future conservation efforts. However, host declines and associated coextinctions of parasites could dramatically compound estimates of future biodiversity loss (Fig. 17.4) (Koh et al., 2004). Parasites are an integral part of life on earth, with their biodiversity projected to be significantly greater than the species richness of free-living hosts (Price, 1980); yet, biologists have uncovered only a miniscule percentage of the diversity of infectious organisms from natural host communities. Many micro- and macroparasites that live uniquely on threatened host species could go extinct long before their hosts, and this poses a distinct threat for parasite extinction. As with most taxa, we do not have accurate numbers of how many species of parasitic organisms might be affected by future extinctions. From a broader perspective, interactions between hosts and parasites may be a major force promoting both genetic and species diversity in natural communities. Conservation strategies that result in loss of parasites could ultimately reduce host populations’ behavioral, physical, and immune defenses needed to respond to future ecological changes.

Given the explosive growth in scientific understanding of the ecology and evolution of infectious diseases, including noninvasive techniques for collecting information on host infection status, hormones, and host and parasite genetic identity (see, for example, Krief et al., 2003), scientists are now well positioned to address many exciting questions. How do changes in host movement patterns and population structure influence the genetic structure and evolution of their host-specific parasites? Can genetic data from contemporary host-specific parasite populations provide insights into the evolutionary histories of host populations? To what degree are multiple host resistance traits genetically correlated with each other and with fitness variables, and how does this affect host infection by a diversity of parasites? Lastly, as humans disturb natural ecosystems, break transmission barriers among species, and reduce host population sizes, outbreaks of emerging infectious diseases among rare or threatened host species may become more common. Understanding the degree to which pathogen evolution and genetic variation in host resistance traits play a role in disease emergence events in natural systems will improve efforts to manage future diseases risks for human populations and in natural systems.

SUGGESTIONS FOR FURTHER READING

Several well-known texts provide a comprehensive overview of the recent advances and status of population biology of infectious diseases in natural populations, including the edited volumes of Dobson and Grenfell (1995) and Hudson and colleagues (2002). For a summary of host–pathogen evolutionary dynamics, Frank (2002) uses a multidisciplinary approach to understand immunology within an evolutionary context, and Page (2003) provides an engaging review of phylogeny, coevolution, and cospeciation. Several reviews have been published recently that aim to understand the risks posed by infectious diseases in the context of animal and plant conservation; we specifically recommend Lafferty and Gerber (2002), de Castro and Bolker (2005), and Anderson and associates (2004). Conceptual issues and specific examples of the relevance of host–parasite evolutionary interactions for biodiversity and conservation are summarized in Altizer and colleagues (2003).