Rapid evolutionary dynamics and disease threats to biodiversity

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Existing and emerging pathogens pose unusual challenges for conservation because of their potential to drive rapid changes in the numerical abundance and genetic composition of wild host populations. An increasing number of studies indicate that host genetic diversity plays an important role in buffering populations against widespread epidemics, and that parasites represent powerful selective agents in natural populations. The observation that infectious diseases might be both mitigated by and rapidly change the genetic composition of host populations gives new significance to the role of host genetic diversity in species conservation. Less clear is the role that pathogen evolutionary change plays in the emergence and spread of new diseases, but recent examples indicate that humans might be selecting unknowingly for rapid changes in pathogen biology through habitat fragmentation, climate shifts and environmental pollution. Although the risks they pose to endangered species are apparent, pathogens and other natural enemies can be a driving force behind species and genetic diversity in natural populations, and preserving interacting networks of coevolving populations should enable hosts to respond better to future disease threats.

Infectious diseases are recognized increasingly as playing important roles in natural systems, from influencing host genetic diversity and coevolutionary processes to altering species composition in ecological communities. Because of their ability to trigger sudden epidemics and their potential for rapid evolution, parasites and infectious disease have also become a major concern in conservation biology [1–3]. Recent work has pointed to an increasing list of examples where introduced pathogens have caused stunning declines in previously thriving populations, or have been implicated as threats to already declining species [4–6]. Although infectious disease theory predicts that parasite establishment and spread should be greater in large host populations, small or endangered host populations might experience unusually large impacts from infectious diseases owing to limited genetic variability or threats from generalist parasites [7,8].

To complement recent reviews that have highlighted ecological drivers of disease emergence in human and wildlife populations [2,9–11], we focus here on the importance of evolutionary change in both generating and mitigating pathogen risks to biodiversity. Until recently, evolutionary processes had been deemed to be operating on timescales that were too slow to be of immediate concern for species facing imminent extinction risks [12,13]. However, in natural communities, genetically based phenotypic characters can evolve surprisingly fast, leading to the concept that evolution can be studied as an ecological process [13–15]. Rapid evolution (on the order of decades or shorter) has been supported by an increasing number of examples from host–pathogen systems [16–18], and it is now clear that pathogens can cause major shifts in the genetic composition of their hosts on short timescales. In spite of the fact that host–parasite interactions provide a rich showcase of coevolutionary examples, few studies have measured the strength of selection and rates of phenotypic evolution of hosts or parasites in the wild.

Here, we argue that host genetic diversity can play an important role in buffering populations against widespread epidemics. Predicting the evolutionary potential of wild host populations in response to native or novel parasites is challenging, however, because it requires at least a minimal understanding of the genetic basis for host resistance, heritability under field conditions, and the strength and mode of parasite-mediated selection [19]. Often overlooked, but of equal concern, is the potential for the extremely rapid evolution of pathogens, and the role of genetic change in host shifts and emerging diseases [20]. These issues are highly relevant to captive-breeding programs, the control of existing pathogens and predicting risk factors associated with future disease emergence. Finally, preserving networks of coevolving populations could maintain host–parasite interactions as an evolutionary process important to both biodiversity and conservation [21].

Evolutionary dynamics of host resistance

Patterns in wild populations

Parasites are likely to be powerful selective agents in natural populations, and host species exposed to a diverse array of parasites should harbor a variety of resistance alleles or a repertoire of inducible defenses. Many studies have underscored the importance of genetic variation in host resistance in causing disease patterns in both field
Box 1. Does MHC diversity predict the future response of vertebrates to epide

Genetic loci associated with the major histocompatibility complex (MHC) in vertebrates play a key role in acquired immunity, and the high variability of genes encoding the MHC is thought to be important for the recognition and response of MHC molecules to a diversity of pathogens [75,90]. Polymorphism at these loci determines the variety of foreign antigens that the host immune system can recognize and attack, and could be the ultimate response to selection in the face of unpredictable or temporarily varying disease outbreaks. Among captive experiments with mice, genes encoding MHC molecules have been shown to be important to mate selection [91], and MHC heterozygotes were demonstrated to be more resistant to multiple-strain bacterial infections than MHC homozygotes [92].

Recent studies of wild vertebrates suggest further that specific MHC haplotypes or genotypes confer resistance to a variety of pathogens [25,84], and that high allelic diversity at MHC loci combined with relatively equal allelic frequencies provides strong evidence for balancing selection [93–95]. Allelic diversity at these loci is lower than expected among endangered species, or those that have undergone genetic drift or inbreeding following dramatic declines in population size (e.g. cheetahs, Asiatic lions, southern elephant seals, Przewalski’s horses) [96]. However, recent studies of endangered salmon, red wolves, desert bighorn sheep and other threatened species indicate that strong positive and balancing selection has maintained a surprisingly high diversity of MHC genotypes [93–96], implying that a major goal of captive breeding programs should be to maintain the variation that is present in the wild.

and experimental settings (Table 1). Parasites infecting sheep, snails, fish, moths and other animals have been implicated in the maintenance of allelic diversity or sexual recombination in their hosts, and heterogeneity in host resistance has been shown to affect individual infection risk and population-wide ecological dynamics [22–25]. For example, Little and Ebert [19] showed that genetically based resistance in Daphnia affected patterns of infection by Pasteuria bacteria in the wild, and that selection on host resistance resulted from parasite-induced host sterility. Among vertebrates, the major histocompatibility complex (MHC) is one of the most important determinants of immune defence, and patterns of extreme polymorphism at MHC class I and II alleles provide strong evidence for balancing selection mediated by infectious agents (Box 1).

Plant-pathogen coevolution leads similarly to a high diversity of resistance and virulence alleles. One of the most distinctive features of natural plant populations is the staggering abundance of genetic polymorphism for resistance to fungal diseases [26–28], and wild plant populations represent a major source of resistance genes for pathogens of crop plants [29]. Long-term field studies of the interaction between wild flax and flax rust in Australia indicate that a large number of alleles can persist in the context of metapopulations, and the distribution of genotypes can shift rapidly following individual epidemics [16,30].

Factors maintaining host variation

Models of host–parasite coevolution based on simple genetic interactions show that polymorphisms in host resistance can be maintained by frequency-dependent selection, heterozygote advantage, or by correlated fitness costs of resistance traits [31]. In the case of frequency-dependent selection, advantages held by rare alleles lead to time-lagged cycles in both host and parasite allelic frequencies [32]. The phenomenon of parasites tracking common host genotypes has been demonstrated in some wild systems [17], and is crucial for arguments concerning the role of parasites in generating advantages to host sexual reproduction [33]. This process has important implications for host conservation: given that rare alleles (or high population-wide allelic diversity) might be associated with a higher probability of pathogen resistance, small or inbred host populations with reduced genetic variability should have a reduced ability to respond evolutionarily to current and future parasite threats. In support of this argument, a comparative study indicated that macroparasites were more likely to colonize fish species showing low levels of genetic variation as indicated by mean heterozygosity [34]. Empirical studies of sea lions [35] and fish [36] have also linked inbreeding with greater susceptibility to infectious diseases.

Resistance-conferring host traits might be costly in terms of reductions in other fitness components owing to pleiotropy or resource-based tradeoffs. Modeling studies indicate that small resistance costs can lead to notable genetic polymorphisms in resistance and susceptibility [37], and this has been supported by recent field and experimental studies [38,39]. Hosts bred in captivity and protected from pathogenic agents might therefore experience increased susceptibility caused by relaxed selection and costs associated with resistance-conferring traits [8]. Under this scenario, if pathogens are removed from wild or captive hosts by antiparasitic drugs, the frequency of

Box 2. Measuring the strength of parasite-induced selection

Demonstrating the evolution of host resistance in response to parasitism requires at least: (i) basic knowledge of the genetic basis for host resistance and its underlying variation or heritability in the wild, and (ii) an indication of the costs of infection with respect to host mortality or fecundity. For quantitative resistance, the selection gradient is estimated as the slope of host reproductive fitness on phenotypic resistance, and provides a measure of the direct selection on resistance to infection by removing the effects of indirect selection on correlated characters [97,98]. The rate at which evolution should proceed can be inferred from the product of the selection gradient and the heritability or additive genetic variance for resistance. Thus, phenotypic and genetic variance are of key importance to the potential evolutionary responses of hosts to current and future parasite threats.

Interestingly, most collated studies from a recent review of the strength of phenotypic selection in the wild [45] addressed morphology, or, less often, behaviour or development. No indication was given as to how pathogen-mediated selection on host resistance compares with the strength of selection on other characters, perhaps because resistance to parasitism in the wild is exceedingly difficult to quantify for most organisms. In spite of recent advances in methods for analyzing phenotypic selection in the wild, few studies have employed these approaches in studying host–parasite evolution [44]. Thus, although the genetic basis for host susceptibility in the wild has been characterized for a variety of systems, we have little information about the rate at which hosts respond to parasite-mediated selection, and how this compares with selection on other character types.
resistance should decline over time, setting the stage for potentially catastrophic outbreaks.

How potent a selective force are pathogens in wild host populations?
The evolution of host resistance traits in response to parasites has been supported by many associations between resistance frequency and levels of exposure to parasites in natural populations [40–42]. However, in spite of recent advances in methods of evaluating the strength of phenotypic selection (Box 2), only a few studies have applied this approach to demonstrate the strength of parasite-mediated selection [43,44], and recent reviews of phenotypic selection have seldom included examples

### Table 1. Characteristics of selected host–parasite systems demonstrating short-term evolutionary dynamics

<table>
<thead>
<tr>
<th>Host</th>
<th>Pathogen</th>
<th>Genetic change in hosts or parasites</th>
<th>Effects of parasite on host fitness</th>
<th>Refs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soay sheep Ovis aries</td>
<td>Intestinal nematodes</td>
<td>Allelic variation and heterozygosity associated with higher survival and resistance</td>
<td>Decreased juvenile survival</td>
<td>[24,84]</td>
</tr>
<tr>
<td>Snail Biomphalaria glabrata</td>
<td>Schistosomes Schistosoma mansoni</td>
<td>Heritable resistance associated with reproductive costs</td>
<td>Decreased survival</td>
<td>[85]</td>
</tr>
<tr>
<td>Eastern oyster Crassostrea sp.</td>
<td>Protozoan parasite Perkinsus marinus</td>
<td>Heritable resistance to protozoan, selection for resistance</td>
<td>Decreased survival and reproduction</td>
<td>[46]</td>
</tr>
<tr>
<td>Flat oyster Ostrea edulis</td>
<td>Protozoan parasite Bonamia ostreae</td>
<td>Genetic variation in resistance to parasites</td>
<td>Decreased survival</td>
<td>[86]</td>
</tr>
<tr>
<td>Bivalve mollusk Transennella tantilla</td>
<td>Trematode Parvatrema borealis</td>
<td>Heritable resistance to infection</td>
<td>None</td>
<td>[47]</td>
</tr>
<tr>
<td>Cactus Echinopsis chilensis</td>
<td>Mistletoe Tristerix sp.</td>
<td>Selection for longer spines/heritable genetic variation in resistance associated with reproductive costs</td>
<td>Decreased reproduction and reproduction</td>
<td>[44]</td>
</tr>
<tr>
<td>Stinging nettle Urtica dioica</td>
<td>Parasic dodder Cuscuta europaea</td>
<td>Selection for longer spines/heritable genetic variation in resistance associated with reproductive costs</td>
<td>Decreased growth and reproduction</td>
<td>[39]</td>
</tr>
<tr>
<td>Herbaceous plants (&gt;ten species)</td>
<td>Rust fungi Puccinia sp.</td>
<td>High polymorphism for pathogen resistance, but fixed tolerance</td>
<td>Decreased growth and survival</td>
<td>[87]</td>
</tr>
<tr>
<td>Alpine catchfly Lychnis alpina</td>
<td>Anther smut Microbotryum violaceum</td>
<td>Higher frequency of resistance in patches connected by corridors</td>
<td>Sterility</td>
<td>[52]</td>
</tr>
<tr>
<td>White campion Silene alba</td>
<td>Anther smut Microbotryum violaceum</td>
<td>Host resistance structure influences disease spread</td>
<td>Sterility</td>
<td>[27]</td>
</tr>
<tr>
<td>House finch Carpodacus mexicanus</td>
<td>Bacteria Mycoplasma gallisepticum</td>
<td>RAPD banding pattern of wild isolates distinct from poultry isolates</td>
<td>Decreased survival</td>
<td>[66]</td>
</tr>
<tr>
<td>African lion Panthera leo</td>
<td>Canine distemper (Morbillivirus)</td>
<td>Virus similar to wild-type canine distemper, but high pathogenicity towards lions</td>
<td>Decreased survival</td>
<td>[4]</td>
</tr>
<tr>
<td>Mammals (many species)</td>
<td>Protozoan parasite Toxoplasma gondii</td>
<td>Selection in favor of mutation that enabled direct transmission and increased host range</td>
<td>Variable; decreased survival</td>
<td>[71]</td>
</tr>
<tr>
<td>Water flea Daphnia magna</td>
<td>Microsporidia Pleistophora intestinalis</td>
<td>Adaptation to local hosts</td>
<td>Decreased survival</td>
<td>[60]</td>
</tr>
<tr>
<td>European rabbit Oryctolagus cuniculus</td>
<td>Myxomatosis (Pox virus)</td>
<td>Evolution towards intermediate virulence; increased resistance to common viral types</td>
<td>Decreased survival (initially high fatality rate)</td>
<td>[74]</td>
</tr>
<tr>
<td>Fruit fly Drosophila melanogaster</td>
<td>Hymenopterous parasitoids</td>
<td>Cline in virulence from north to south in Europe</td>
<td>Decreased survival</td>
<td>[88]</td>
</tr>
<tr>
<td>Freshwater snail Potamopyrgus antipodarum</td>
<td>Trematode Microphallus sp.</td>
<td>Geographical variation in host resistance; possible tradeoff</td>
<td>Sterility</td>
<td>[59]</td>
</tr>
<tr>
<td>Water flea Daphnia magna</td>
<td>Bacteria Pasteuria ramosa</td>
<td>Parasites track local host genotypes</td>
<td>Sterility and death</td>
<td>[89]</td>
</tr>
<tr>
<td>Flax Linum marginale</td>
<td>Rust fungus Melampsora lini</td>
<td>High diversity of host resistance genotypes; pathogens dominated by a few genotypes</td>
<td>Decreased growth rate</td>
<td>[30]</td>
</tr>
</tbody>
</table>

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of resistance traits [21, 45]. Moreover, in the oceans, only for heavily managed taxa such as oysters is there any understanding of the evolution of host resistance to infectious disease (Table 1) [46, 47].

Ironically, an increasing number of emerging or introduced diseases might offer new opportunities to measure short-term changes in host immunity and resistance in the wild [1, 2]. For example, a recent study by Nolan et al. [48] showed that host size and male plumage predicted house finch survival following an epidemic outbreak of a new bacterial disease, and that reduced body size and increased plumage redness occurred within just a few years. These changes might have been paralleled by underlying shifts in the genetic composition of the host population, and the strength of selection (indicated by case fatality rates of up to 50%) was probably high [6]. Multi-year studies of plant pathogens have also shown rapid changes in resistant phenotypes in populations following short-term selection by rust pathogens [16, 28], and high mortality caused by a fungal pathogen could be shaping spatial variation in anti-fungal resistance of seafan corals in the Florida Keys [49].

Habitat fragmentation and host movement
In the context of natural environments, habitat fragmentation and isolation should affect pathogen prevalence and host evolution, so that host and parasite movement among fragments could be crucial to both parasite persistence, and the spread and maintenance of resistance alleles [28]. A concern for reserve design and the movement of threatened host species is that highly connected populations might enable the global spread of new parasites and therefore could increase extinction risks [50]. However, modeling and empirical studies have shown that the benefits of corridors that allow dispersal among habitat patches probably far outweigh the risks of increased pathogen transmission [51]. Spatial structure and dispersal will not only affect host and pathogen population dynamics, but will also determine the maintenance and spread of host resistance genes. A recent study by Carlsson-Graner and Thrall [52] showed that isolated populations of the alpine campion were infected rarely with anther-smut disease, but, within infected populations, prevalence was high. In comparison, highly connected populations showed more predictable pathogen occurrence at any given site, but prevalence was low within each site. The authors concluded that this pattern was caused probably by higher rates of movement of both pathogens and host resistance alleles among connected populations. A similar study showed that larger population sizes and increased dispersal were associated with a lower extinction risk and the more rapid recovery of bighorn sheep following bronchopneumonia epidemics, indicating a potential role for host dispersal in genetic variation and resistance evolution [53]. Together, these studies suggest that higher rates of pathogen spread among large or connected patches can be outweighed by the ecological and evolutionary benefits to hosts of dispersing through the landscape.

Pathogen evolution and emerging diseases
The evolutionary potential of pathogens sets them apart from other major threats to wildlife, in part because of the unpredictable and irreversible effects of introduced diseases. Most pathogens have short generation times and large population sizes, and strong selection pressures following ecological changes might accelerate pathogen evolution. Human-imposed selection deriving from the widespread application of chemical controls is responsible largely for the emergence of drug-resistant bacteria, viruses, helminths and protozoa [54]. However, the role that evolutionary processes play in the emergence and spread of the pathogens themselves is less clear, and supported by only a few well-studied examples [10].

Selection in wild and managed systems
Throughout the past century, directional selection has increased antiparasitic drug resistance among viruses, bacteria, protozoa and helminths that infect humans and domesticated plants and animals [54–56]. In some cases, substantial resistance to anti-pest or anti-parasite treatments has appeared within just a few years of their widespread use [54]. For example, the commonly held belief that TB no longer poses a major threat to public health has been overturned by the increasing incidence of TB and emergence of multi-drug-resistant strains [57]. Human malaria is still the most prevalent and devastating infectious disease in the tropics, in part because its control has been complicated by the emergence of resistance to widely used antimalarial drugs. Most alarmingly, Levin et al. [58] showed that antibiotic-resistant bacteria evolved compensatory mutations that countered costs of resistance and make loss of resistance highly unlikely following removal of selection pressure.

How do rates of change in managed systems correspond with pathogen evolution in the wild? Commonly observed patterns point to high pathogen evolutionary potential and selection in favour of specialization on common host genotypes (Table 1). Empirical support for locally adapted parasites spans the range of trematodes infecting freshwater snails [59], microparasites infecting Daphnia [60] and bumblebees [61], and holoparasites infecting plants [62]. Although local adaptation can occur over a few generations, host and parasite migration rates should affect the rate of parasite evolution, and can even lead to local ‘maladaptation’ in extreme cases [63].

Is rapid evolution important to host shifts and disease emergence?
Several classes of pathogens pose unusually high potential for major impacts following introduction to novel host populations. These include generalist parasites capable of infecting and persisting in domesticated or reservoir host species, and pathogens in which new genetic variants are associated with shifts in host range. A recent survey of emerging diseases in humans and domesticated mammals indicates that high mutation rates, short generation times, and rapid evolution represent important factors in disease emergence [20]. Thus, emerging diseases in humans and domesticated species are dominated by viruses, particularly RNA viruses that are characterized by high mutation
rates and where the host range is relatively large. The
direct role of mutation in the emergence of wildlife
diseases remains relatively unknown, although canine
parvovirus infecting wolves, coyotes and domesticated
dogs represents one example that probably arose as a new
genetic variant of feline parvovirus from domesticated cats
[64]. These pathogens can evolve rapidly following estab-
lishment in their novel hosts, and, in some cases,
molecular or life-history variants have shown rapid
divergence from ancestral genotypes following disease
development [65,66].

In spite of circumstantial evidence, few examples point
definitively to pathogen evolution as a major factor
involved in disease emergence. Recent studies of host
shifts among fungal pathogens infecting plants indicate
that geographical proximity and opportunities for cross-
species transmission, rather than genetic changes in the
parasites themselves, are responsible for the origin of new
host–parasite combinations [67,68]. Examples of emerg-
ing infectious diseases in humans and wildlife are
dominated by zoonotic and introduced pathogens, further
pointing to ‘host jumps’ as key events driving the
emergence of pathogens on new hosts [9,11]. However,
the absence of convincing evidence that pathogen evol-
ution plays a role in host shifts might reflect simply our
limited knowledge of the evolutionary ecology of wildlife
pathogens rather than a meaningful pattern.

Human effects on the evolution of wildlife pathogens
Large-scale changes in natural habitats caused by humans
during the past century can impact pathogen life cycles
and evolution directly. For example, changes in aquatic
habitats, including irrigation or removal of wetlands,
impact clearly on the presence of aquatic invertebrates
that play a key role in the transmission of major parasite
groups [69,70]. Human activities that increase parasite
transmission or abundance might lead to evolutionary
shifts in other parasite characters through their effects on
parasite survival and reproduction. One striking example
emerged from a recent analysis of the genetics and
evolution of oral transmission in Toxoplasma gondii [71].
Molecular genetic analysis of this parasite indicated that
the ability of clonal lineages to circumvent sexual
recombination and transmit orally was associated with a
relatively recent selective sweep that coincided with the
timing of human agricultural expansion. Thus, human
activity could have selected for increased oral trans-
mission by providing new opportunities for parasite
transmission and concentrated densities of hosts [71]. At
the opposite extreme, it has even been suggested that
reducing the potential for waterborne transmission of
cholera might select for less virulent strains of this human
pathogen [72]. Thus, we could be selecting unknowingly
for rapid changes in pathogen biology by favouring the
dispersal and development of new variants of wildlife
pathogens through global commerce, climate shifts, and
changes in host density and habitat quality [73].

Full coevolutionary dynamics
Most examples from wild host–parasite systems point to
neither host nor parasite evolution operating alone, but to
joint coevolutionary dynamics (Table 1). Long-term
studies of model host–parasite systems emphasize mul-
tiple coevolutionary processes and outcomes (see example
in Box 3), including directional selection in favour of
increased host resistance and shifts in parasite virulence
[74], frequency-dependent selection leading to time-lagged
cycles in host and parasite abundance and genotype
frequencies [17], and the accumulation of a large number
of resistance and/or virulence alleles through balancing
selection or genotype-specific interactions [28,30,75].
Collectively, these studies emphasize that the high levels
of genetic diversity that underlie many host–parasite
interactions in the wild are the outcome of coevolutionary
interactions.

In developing new ideas about coevolutionary pro-
cesses, Thompson [76] highlighted the importance of the
spatial and phylogeographical structure of populations.
The ‘geographic mosaic’ theory of coevolution frames the
dynamics of species interactions in the context of spatial
and temporal scales. Of all biotic interactions, host–
parasite interactions provide some of the best examples
of a geographically structured coevolution [28,76]. From this
perspective, pathogens could be one of the major factors
promoting both genetic and species diversity in natural
communities, and it might be this coevolutionary land-
scape that is at greatest risk and most urgent need of

Box 3. Snails and their trematode parasites: coevolution
and implications for conservation
The freshwater snail–trematode system (see coevolution examples
in Table 1, main text) exemplifies time-lagged, frequency-dependent
selection that results in oscillatory dynamics of host and parasite
genotypic frequencies as predicted by the Red Queen hypothesis.
The parasites in this system are adapted locally to common host
genotypes from sympatric populations, and high levels of parasitism
might provide a selective advantage for sexually reproducing hosts
[17,23,40,58]. A five-year study followed temporal changes in the
frequencies of asexual clonal populations of freshwater snails and
co-incident changes in the parasite population. Measurement of
clonal frequencies revealed four common host clones and >100 rare
clones; common clones were found to be significantly more
susceptible to sympatric parasites than were rare (or allopatric)
clones through reciprocal cross-infections [17]. In a matching-alleles
model, Lively [59] showed that parasites track common host
genotypes and are adapted locally independent of relative gener-
ation times. This is an unexpected result because faster generation
times of parasites have been thought to be important to the
coevolutionary arms race. Instead, in situations of local adaptation
and frequency-dependent selection, the parasite and host alternate
possession of a fitness advantage [59].

Results from empirical studies were compared with simulated
results of a computer model designed to examine host frequencies
under various degrees of parasite virulence. Measured allelic
frequencies were similar to results from models that assumed
parasites responded to common clones in a time-lagged fashion.
Tracking of common host genotypes suggests that parasites play an
important role in host gene-frequency dynamics [17]. Thus, results
from this natural system indicate that long-term conservation efforts,
given an appropriate system, could benefit from maintaining native
host–parasite relationships to promote genetic variability in wild
populations.

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Consequences for biodiversity and conservation

Although habitat loss and overexploitation remain major factors in host population declines and extinctions, infectious diseases have become increasingly important factors in wildlife conservation [1,2]. ‘Virgin ground’ epidemics following novel introductions progress rapidly through previously unexposed populations, often causing high case fatality rates and stunning reductions in host abundance [5,6]. Introduced diseases have been implicated in the declines and, in some cases, extinctions of frogs in Central and North America and Australia [2], Hawaiian forest birds [77], Serengeti lions and African wild dogs [4,78], and North American chestnuts and flowering dogwoods [79,80]. These widespread epidemics can leave lasting community-wide effects, including extinctions of non-target species. That these epidemics might be both buffered by and change rapidly the genetic composition of host populations gives new significance to the role of host genetic diversity in species conservation [12,13].

Cumulative genetic changes resulting from drift and inbreeding in small or captive populations will pose challenges inevitably to conserving threatened species in the wild. When the environment changes slowly or fitness costs are relatively small, demographic processes related to stochastic and metapopulation factors might generate more immediate extinction risks than genetic factors [12]. However, parasites and pathogens pose a non-trivial extinction risk to many hosts, and feedback between evolutionary and ecological processes might have overriding effects on future persistence. Inbred host populations will probably show limited ability to respond evolutionarily to new threats imposed by parasites and infectious diseases owing to loss of allelic diversity or reduced heterozygosity. Whereas some species might have experienced severe genetic bottlenecks with little or no apparent problems from pathogens, inbreeding in other species, such as lions and cheetahs, has been linked with mortality caused by feline infectious peritonitis, *Spirometra*, and *Mycobacterium* [81,82]. Moreover, the costs of resistance traits in the wild imply a high risk that animals bred in captivity will lose resistance in the absence of parasitism and become increasingly susceptible to pathogen infections.

There are few quantitative estimates currently of selection differentials imposed by novel parasites and resulting rates of evolution of host resistance in the wild, and this area remains a priority for future research (Box 4). This information is particularly relevant to managing populations under pathogen stress, where knowing the rate of evolution of resistance to disease is important to predicting population viability. Thus, our ability to manage the spatial and genetic structure of host populations to minimize extinction risk from infectious diseases hinges upon better knowledge of host and parasite evolutionary dynamics in the wild. Further studies focusing on those classes of hosts at greatest risk of extinction and those parasites most likely to cause dramatic host declines are needed greatly, as are studies that address the effects of spatial structure and metapopulation processes on disease spread and host evolution (Box 4).

**Box 4. Outstanding questions**

<table>
<thead>
<tr>
<th>Host resistance to novel pathogens</th>
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<tbody>
<tr>
<td>• How strong is selection imposed by existing and novel pathogens in wild host populations relative to other ecological forces?</td>
</tr>
<tr>
<td>• How important are inbreeding and costs of resistance (tradeoffs) to the potential loss of genetically based resistance in captive-bred populations?</td>
</tr>
<tr>
<td>• Is it practical to identify molecular markers (e.g. major histocompatibility complex genes) that correlate with resistance to specific pathogens in threatened species?</td>
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<tr>
<td>• For what types of parasites is host genetic diversity most likely to be important in mitigating disease risk?</td>
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<tr>
<th>Pathogen evolutionary change and disease emergence</th>
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<tr>
<td>• What is the relationship between genetic diversity in parasites and their ability to colonize new host species?</td>
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<tr>
<td>• Can comparative studies of closely related parasites shed light on evolutionary factors affecting disease emergence?</td>
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<tr>
<td>• Does pathogen evolution following disease emergence reveal evidence for strong selection or adaptation to new hosts?</td>
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<tr>
<th>Conservation management and human dimensions</th>
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<tbody>
<tr>
<td>• Do empirical studies support a beneficial role of corridors and interpatch dispersal in host evolution and persistence following pathogen invasion?</td>
</tr>
<tr>
<td>• How do human activities, including effects on climate change and habitat quality, affect host–pathogen evolution in natural populations?</td>
</tr>
</tbody>
</table>

Successful conservation programs maintain populations with intact evolutionary processes [21,83]. Although the risks they pose to endangered species are apparent, diseases and other natural enemies can play an important role in maintaining both genetic diversity within species, and biodiversity at the community level. As humans disturb natural balances, break transmission barriers among species and reduce host population sizes, outbreaks of new or generalist pathogens among rare or threatened host species might become more common [2,73]. Rapid evolution of resistance traits provides a way for hosts to respond to strong selection by parasites. From a broader perspective, coevolution between hosts and parasites might be a major force determining biodiversity on Earth [55]. Conservation strategies that fail to recognize this potential and restrict disease spread might deprive ultimately host populations of the genetic diversity they need to respond to future ecological changes.

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