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REVIEW

The role of infectious diseases in biological conservation

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Abstract

Recent increases in the magnitude and rate of environmental change, including habitat loss, climate change and overexploitation, have been directly linked to the global loss of biodiversity. Wildlife extinction rates are estimated to be 100–1000 times greater than the historical norm, and up to 50% of higher taxonomic groups are critically endangered. While many types of environmental changes threaten the survival of species all over the planet, infectious disease has rarely been cited as the primary cause of global species extinctions. There is substantial evidence, however, that diseases can greatly impact local species populations by causing temporary or permanent declines in abundance. More importantly, pathogens can interact with other driving factors, such as habitat loss, climate change, overexploitation, invasive species and environmental pollution to contribute to local and global extinctions. Regrettably, our current lack of knowledge about the diversity and abundance of pathogens in natural systems has made it difficult to establish the relative importance of disease as a significant driver of species extinction, and the context when this is most likely to occur. Here, we review the role of infectious diseases in biological conservation. We summarize existing knowledge of disease-induced extinction at global and local scales and review the ecological and evolutionary forces that may facilitate disease-mediated extinction risk. We suggest that while disease alone may currently threaten few species, pathogens may be a significant threat to already-endangered species, especially when disease interacts with other drivers. We identify control strategies that may help reduce the negative effects of disease on wildlife and discuss the most critical challenges and future directions for the study of infectious diseases in the conservation sciences.

Introduction

At the advent of a century characterized by dramatic environmental changes, the global community is challenged to reconcile the stresses such changes place on the planet's resources (Committee on Grand Challenges in Environmental Sciences, 2001). Of increasing importance is the need to fully understand the drivers of species extinction, as loss of biodiversity has the potential to alter the ecosystem services on which humans and wildlife depend. The current extinction rate is already estimated to be 100–1000 times greater than the historical norm (Pimm *et al.*, 1995), and 10–50% of well-studied higher taxonomic groups are at high risk of extinction [Millenium Ecosystem Assessment (MEA), 2005]. The threats to biodiversity are numerous and largely result from anthropogenic changes to the environment, including habitat loss, climate change, non-native species invasion and overexploitation (Pimm *et al.*, 1995; Wilcove *et al.*, 1998). Here, we review an additional threat to biological conservation that is critical to consider – infectious disease.

A large number of infectious diseases have recently emerged in wildlife or humans around the world (Daszak, Cunningham & Hyatt, 2000; Jones *et al.*, 2007a). In wildlife, some of the more pressing examples include marine mammal morbillivirus (Osterhaus *et al.*, 1989), increased frequency of disease outbreaks in coral reefs (Harvell *et al.*, 2002), a chytridiomycosis pandemic in amphibians (Daszak *et al.*, 1999; Schloegel *et al.*, 2006) and the rapid spread of infectious facial tumors in Tasmanian devils (Jones *et al.*, 2007b). The diversity and apparent increase in these and other diseases in wildlife have raised concerns that pathogens may pose a substantial threat to biodiversity (Wilcove *et al.*, 1998; Daszak *et al.*, 2000; Harvell *et al.*, 2002). However, infectious disease has not traditionally been regarded as a significant driver of species extinction (Smith, Sax & Lafferty, 2006). In part, this may be due to a lack of

adequate historical information on pathogens and to levels of uncertainty in existing data (see Smith *et al*., 2006) that make it difficult to gain a reliable understanding of the role infectious disease plays in species extinction.

In this review on the role of infectious diseases in biological conservation, we seek to accomplish four objectives. First, to summarize existing knowledge on the importance of disease in local and global species extinctions. Second, to review the ecological and evolutionary forces that facilitate disease-mediated extinction risk. Third, to identify science-backed control strategies that may significantly reduce the negative effects of disease on wildlife. Fourth, to consider the most critical challenges and future directions for the study of infectious diseases in the conservation sciences. We use the term 'pathogen' to include both microparasitic and macroparasitic pathogens, and 'infectious disease' to represent disease syndromes which are caused by a contagious pathogen.

Infectious disease and wildlife extinction

The International Union for the Conservation of Nature (IUCN, 2004) Red List reports that in the past 500 years, 833 animal species are known to have gone extinct. Of these known extinctions, only 3.7% have been attributed, at least partly, to infectious disease (Smith *et al*., 2006; Table 1). These include numerous Hawaiian birds, the thylacine *Thylacinus cynocephalus*, a Polynesian tree snail *Partula turgida* and the sharp-snouted day frog *Taudactylus acutirostris* (Schloegel *et al*., 2006; Smith *et al*., 2006). Whereas forces such as habitat loss or overexploitation are often listed as the single and most common causal driver of species' extinction (IUCN, 2004), infectious disease is significantly less likely than other drivers to act in isolation (Smith *et al*., 2006). These patterns also appear to hold for species on the verge of extinction. Of the 2852 plants and animals listed as critically endangered, only 8% are threatened by infectious disease (Smith *et al*., 2006). Over 24% of the world's extant mammals are currently threatened with extinction, yet infectious disease has only been listed as a major threat for a small fraction (1.1%) (IUCN, 2007). It is likely that disease is underrepresented as a contributing threat to wildlife extinction, especially given that less than half (39%) of critically endangered and endangered artiodactyls, carnivores and primates from the 2006 IUCN Red List have any published records of pathogens from wild populations (Pedersen *et al*., 2007). While the IUCN represents the best available evidence on the factors threatening species with extinction, it is not without limitations. Particularly the level of uncertainty about the actual threat of infectious disease and a temporal bias in the collection of data may affect the results (but see Smith *et al*., 2006).

Mathematical models and epidemiological theory have been increasingly used to understand the population impact of infectious diseases (Anderson & May, 1992). Within this basic epidemiological framework, pathogens are not predicted to drive their hosts to extinction when their transmission is density-dependent (i.e. likelihood of transmission increases with increasing host density). These models suggest that pathogens will be lost before the host population goes extinct, because they will drive their hosts below a density threshold that is critical for disease persistence. Under these circumstances, pathogens suffer from local extinction or 'fade-outs' (McCallum, Barlow & Hone, 2001). There are several cases, however, where pathogens are more likely to cause extinction (see de Castro & Bolker, 2005).

First, pathogens that negatively affect host fitness can decrease host population density by causing a population crash after a recent epidemic or at the trough of a pathogen-driven population cycle. Small, fragmented populations can have increased extinction risk due to decreases in genetic variability which may also increase susceptibility to infectious diseases (Lyles & Dobson, 1993), and increased likelihood of stochastic events (McCallum & Dobson, 1995).

Second, many pathogens are transmitted as a function of the frequency of infected individuals and therefore are not subject to population density thresholds. Sexually transmitted diseases and vector-borne pathogens are commonly frequency-dependent, and their prevalence can increase even when population densities are low, therefore being more likely to cause host extinction (Thrall, Antonovics & Hall, 1993; Boots & Sasaki, 2003). In addition, when host populations are spatially structured by territoriality or social interactions, or when pathogens cause sterility, as opposed to reductions in survival, transmission may approximate a frequency-dependent model (O'Keefe & Antonovics, 2002).

Third, disease-mediated extinction becomes more likely when pathogens have reservoir hosts where they can remain viable, and when the pathogen dynamics become disentangled from the specific one host–one pathogen dynamics (i.e. a reservoir host serves as the source for pathogen epidemics that would fade out in another host).

Lastly, when dispersal rates among small populations (in which a pathogen would normally fade out) are artificially high, due to anthropogenic translocation events, pathogens may also represent an important threat to species persistence. Most pathogens can infect multiple hosts and these generalist pathogens pose the greatest threat to disease-mediated extinction (Pedersen *et al*., 2007), because high prevalence in alternate hosts, coupled with cross species transmission, can increase the likelihood of disease persistence and host extinction (Fenton & Pedersen, 2005).

Drivers of disease-mediated extinction

There is concern that the extent of environmental changes in recent decades is increasing the odds of infectious disease emergence in both humans and wildlife. Today, 436 species are threatened by global environmental change (IUCN, 2007). Environmental change is likely to influence disease emergence as a result of both effects on host and pathogen physiology, and of indirect effects following changes in interactions with other species (Lips *et al*., 2008). Many

emerging infectious diseases are driven by human activities that force novel pathogens into new ecological niches or modify the environment to facilitate their establishment or transmission – an outcome termed 'pathogen pollution' (Cunningham, Daszak & Rodríguez, 2003; MEA, 2005). Examples of anthropogenic drivers that promote disease emergence are numerous and include habitat loss, climate change, non-native species introductions, overexploitation and pollution (Daszak *et al*., 2000; Lafferty, 2003; MEA, 2005). Here, we review how these human-induced drivers of disturbance can lead to specific changes in the environment that may also facilitate disease-mediated extinction via mechanisms that are directly linked to the biology of pathogens.

Habitat loss and alteration

Habitat loss and alteration is commonly cited as the primary factor driving the loss of biodiversity worldwide (Wilson, 1992). The rate at which habitats are degraded or changed into unsuitable environments accurately predicts the rate of species loss and the proportion of threatened species in that area (Pimm & Askins, 1995). At the turn of the century, 85% of endangered species in the United States were threatened by habitat loss, mostly related to agricultural, commercial, infrastructural development and outdoor activities (Wilcove *et al*., 1998).

Endangered species at greatest risk of habitat loss are those that have small geographic ranges and patchy distributions within their ranges (Gaston, 1991). The importance of infectious disease to the conservation of species threatened with habitat loss will likely increase with decreasing habitat size and quality. Infectious diseases can be important for fragmented populations because habitat loss will often restrict species movement and dispersal, likely increasing contact rates among individuals and ultimately the spread of disease (Scott, 1988). While several studies have demonstrated that density-dependent pathogens are likely to be lost in small populations, this may be limited to host-specific pathogens, while multi-host pathogens, which can be maintained by other host species, may not be affected by a reduction in the population size of one host. In addition to increasing transmission and thus prevalence, limited host movement and dispersal in fragmented habitats may be important for the maintenance of genetic diversity and the persistence of resistance alleles (Altizer & Pedersen, 2008). For example, bighorn sheep populations have suffered from highly fragmented landscapes that reduce local population sizes, and in these herds, infectious disease epidemics are most likely to cause extinction (Flather, Joyce & Bloomharde, 1994). The largest population of bighorn sheep in New Mexico (>200 individuals in 1978) was reduced to 25 individuals by 1989, and then to a single ewe by 1997 due to a severe epidemic of psoroptic scabies, drought and predation (Boyce & Weisenberger, 2005). However, species recovery efforts have demonstrated that maintaining larger population sizes and increased dispersal rates between bighorn sheep populations are associated with faster recovery rates from bronchopneumonial epidemics and lower local extinction rates (Singer, Zeigenfuss & Spicer, 2001).

Climate change

During the twentieth century, average world surface temperature increased by $\sim$0.6 °C and almost two-thirds of that warming has occurred since 1975 [Intergovernmental Panel on Climate Change (IPCC), 2007]. Climatologists forecast further warming, along with changes in precipitation and climatic variability, during the coming century and beyond (IPCC, 2007). Such effects may be a major threat to living organisms, affecting species directly or altering their habitats.

Changes in regional or local climate may directly or indirectly modify pathogen survival rates, transmission and host susceptibility (Harvell *et al*., 2002). Shifts in contemporary climatic regimes also have the potential to influence disease by shifting patterns of the abundance and distribution of pathogens and their vectors (Daszak *et al*., 2000). Dengue fever and malaria are predicted to spread dramatically in the face of global warming as high temperatures lead to higher rates of pathogen reproduction and faster time to maturity, increased geographic ranges and bite-frequency of mosquito vectors (Epstein, 2000). A well-known case of wildlife disease emergence that may be related, at least partially, to environmental change is chytridiomycosis (Box 1), a fungal infection caused by *Batrachochytrium dendrobatidis* (Bd). The role of chytridiomycosis as a driver of amphibian population declines has been linked to environmental change, a hypothesis known as the climate-linked epidemic hypothesis (Pounds *et al*., 2006; Bosch *et al*., 2007), which has found correlational evidence from empirical studies that report a significant association between local increases in temperature and rainfall, and the occurrence of chytridiomycosis (e.g. Kriger, Pereoglou & Hero, 2007). However, there is an ongoing debate about the strength of the relationship between the emergence of chytridiomycosis and climate change (Pounds *et al*., 2006, 2007; Alford, Bradfield & Richards, 2007; Lips *et al*., 2008). Both amphibians and Bd are strongly affected by temperature and moisture, and there is widespread agreement that environmental factors are indeed likely to influence their survival and growth (Pounds *et al*., 2006, 2007; Alford *et al*., 2007; Lips *et al*., 2008). To date, however, there is no direct evidence that climate change causes outbreaks of chytridiomycosis (Lips *et al*., 2008).

Domestic–wildlife–human interface

Interactions between humans, domestic animals and wildlife occur widely and can result in the spread of pathogens between species. This interaction typically involves the spread of microparasites with broad host ranges from domestic to wild animals, and in many cases, these pathogens have substantial negative effects on host fitness that lead to population declines and often dramatic consequences for wildlife (Pedersen *et al*., 2007). Over 80% of

Box 1. An infectious fungus and the global decline in amphibians

Over the last 30 years ~43% of the world's amphibian species (<1800) have undergone severe declines: 32.5% are globally threatened, >34 have gone extinct and many more are believed to be extinct (Blaustein & Wake, 1990; Stuart *et al.*, 2004). 18.8% of Australia's frog species are currently threatened with extinction (Hero & Morrison, 2003), 67% of harlequin frogs (genus *Atelopus*) endemic to tropical America have experienced extreme population declines in the past 20 years (IUCN, 2004), and rapidly declining species are commonly found throughout Neotropical riparian habitats (Lips *et al.*, 2006). It is widely believed that the recently discovered fungal pathogen, *Batrachochytrium dendrobatidis* (Bd), is directly linked to declines and extinctions of amphibians worldwide (Berger *et al.*, 1998; Daszak, Cunningham & Hyatt, 2003). Bd causes chytridiomycosis, an emerging infectious disease associated with declines in at least 43 amphibian species across Latin America and 93 species worldwide (Berger *et al.*, 1998; Daszak *et al.*, 2003; Lips *et al.*, 2006). Most recently, the fungus was directly linked to the extinction of the Australian sharp-snouted day frog *Taudactylus acutirostris* – perhaps the first case of extinction of a free-ranging wildlife species where disease acted as both the proximate and ultimate cause of extinction (Schloegel *et al.*, 2006). Arguably, Bd is the most significant infectious disease threat to species biodiversity at both local and global scales.

Researchers identified chytridiomycosis in 1998 (Berger *et al.*, 1998) and many believe the international trade in amphibians has played a key role in its now global distribution. The oldest-known hosts of Bd are African-clawed frogs (genus *Xenopus*) (Ouellet *et al.*, 2005), first recorded in South Africa in 1938. A worldwide trade of the species flourished in the 1950s following the development of pregnancy tests that used *Xenopus* tissue, and museum records suggest the fungus had achieved a global distribution by the 1960s (Ouellet *et al.*, 2005; Rachowicz *et al.*, 2005). Today, though different carrier species appear to be implicated, the spread of Bd through the global trade in wildlife continues. Several studies document the presence of Bd in frogs farmed for the trade (Mazzoni *et al.*, 2003; Hanselmann *et al.*, 2004). The American bullfrog *Rana catesbiana*, which is farmed and transported worldwide for consumption, poses a particular threat as it is resistant to chytridiomycosis and acts as a carrier host (Mazzoni *et al.*, 2003; Hanselmann *et al.*, 2004). The diversity of human activities that facilitate the spread of Bd, its extreme virulence, broad suite of potential hosts and ability to spread quickly (via direct contact between individuals as well as through the environment where zoospores remain viable for up to 3 months) make chytridiomycosis an alarming reminder of how disease-driven extinction can affect biodiversity at both local and global scales (Lips *et al.*, 2006).

domesticated animal pathogens can infect wildlife (Cleaveland, Laurenson & Taylor, 2001). Given that pathogens are more likely to be shared or jump between closely related hosts (Davies & Pedersen, 2008), it is not surprising that close relatives of domestic animals are at the greatest risk of disease-mediated extinction. For instance, 88% of mammals listed by IUCN as threatened by infectious disease belong to two orders of mammals: carnivores and artiodactyls (Pedersen *et al*., 2007), in particular, those species most closely related to domestic animals. In contrast, no bats (0.0% of 1024) and only one rodent species (<0.01% of 2041) were identified by the IUCN as threatened by pathogens. This nonrandom distribution of extinction risk across mammals suggests that relatedness to domestic animals may indeed predispose disease-mediated extinction risk. However, the pattern may also be affected by unequal sampling of pathogens across the mammalian families, with an inclination toward artiodactyls because they are hunted and often easier to sample for pathogens, or artiodactyls and carnivores based on a preference by veterinarians due to their relatedness to domestic animals.

Most of the pathogens identified as causing declines or reduced fitness in IUCN-threatened mammals are well-known diseases such as rinderpest, canine distemper, rabies, anthrax and toxoplasmosis (Pedersen *et al*., 2007); all microparasites with short generation times, high mutation rates and broad host ranges (Cleaveland *et al*., 2001; Taylor, Latham & Woolhouse, 2001). Furthermore, over 70% of the viruses identified as agents of disease-mediated extinction are ssRNA viruses (Pedersen *et al*., 2007), which have the highest mutation rates (Domingo & Holland, 1997) and possibly the greatest evolutionary potential for host switching. All threatening pathogens could infect multiple host species, with the majority (66%) able to infect mammals from several orders, and in some cases non-mammals. More importantly nearly all (96%) of the threatening pathogens were reported to infect domesticated carnivores or livestock. Contrary to theoretical expectations, 75% of all pathogens were transmitted by close contact between hosts, as opposed to being stable in the environment or being transmitted by vectors (Pedersen *et al*., 2007).

As domestic animals are globally distributed and maintained at high densities, they can easily act as reservoirs for pathogens shared with wildlife (Lafferty & Gerber, 2002; Pedersen *et al*., 2007). Spillover from domestic animals to their wildlife relatives can have dramatic negative effects. For example, spillovers of canine distemper virus have led to massive declines in many wild carnivores (i.e. African wild dog, bat-eared fox, spotted hyena and black-footed ferrets; McCarthy, Shaw & Goodman, 2007) and continue to be a conservation threat to these populations. Another example is Sarcoptic mange (caused by *Sarcoptes scabiei*), which is commonly transmitted by infected domesticated animals, infects 104 species, and can cause high-mortality epidemics in wildlife (Box 2). While more ecologically stable species may recover from sarcoptic mange outbreaks and return to pre-epidemic population sizes, hosts that are threatened by other factors, or are already limited to small population sizes can be pushed to extinction by mange outbreaks (i.e. red foxes population on Borrnholm Island in Denmark; Henriksen *et al*., 1993; Pence & Ueckermann, 2002).

Box 2. Sarcoptic mange: a global epidemic with a wide host range

Sarcoptic mange, caused by the mite *Sarcoptes scabei*, has recently been indicated as the cause of countless mange epizootics that have significantly affected wild mammals worldwide (Bornstein, Morner & Samuel, 2001; Pence & Ueckerman, 2002). *Sarcoptes scabei* is a highly contagious mite that burrows into the epidermis of the skin, causing intense irritation in the host. The life cycle lasts about 2 weeks, and while lightly infected individuals may only suffer short-term negative effects, mites on heavily infected individuals can reach densities of over 5000 mites cm^{-2} and can lead to death resulting from secondary infections, starvation and hypothermia (Bornstein *et al.*, 2001).

It is likely that *S. scabei* originated in human populations and then spread to domesticated animals, which in turn, transmitted sarcoptic mange to a diverse array of wild mammals (Fain, 1978). There is debate about the taxonomy of *S. scabei*, however, it has been suggested that infections in both domestic and wild animals is caused by one highly variable species (Pence, Casto & Samuel, 1975), and infection can be transmitted between species, even those that have limited or no direct contact (Stone *et al.*, 1974). In fact, sarcoptic mange has been found in over 104 species of domestic and wild mammals, including 10 orders and 27 families (Bornstein *et al.*, 2001; Pence & Ueckerman, 2002). Even more impressive than its wide host range, is the fact that severe sarcoptic mange epizootics have occurred in populations of wild carnivores around the world (i.e. coyotes, foxes and grey wolves in North America; artic foxes, red foxes, lynx and grey wolves in Europe, foxes and dingoes in Australia, lions and cheetahs in Africa), wild populations of artiodactyls (wild boars, chamois, ibex and Iberian ibex in Europe, impala, hartebeest, wildebeest, buffalo, eland, kudu, Grant's gazelle, Thompson's gazelle and sable antelopes in Africa), wild primates in Africa (gorillas and chimpanzees) and other mammals (wombats, koalas in Australia; reviewed in Pence & Ueckerman, 2002). Sarcoptic mange epidemics cause significant population declines in wildlife (up to 50–90%, Pence & Ueckerman, 2002), and in species that are already threatened by other factors, such as habitat loss or overexploitation, these crashes can cause local extirpation of populations. Because many of these epidemics are seeded by cross-species transmission from domestic animals, limiting direct or close environmental contact between these groups, for example by introducing barrier zones, may be a successful strategy for reducing future outbreaks and threat.

Overexploitation

Overexploitation is a significant factor affecting the conservation of species worldwide, specifically because areas with high biodiversity often co-occur with populations of poor and malnourished humans, who rely on wildlife (e.g. in the form of bushmeat) for subsistence (Mainka, 2002). Exploitation, or the use of species for food or body parts, is a common cause of extinction risk in clades of bats, primates, carnivores, ungulates and rabbits (Mace & Balmford, 2000). Particularly, large-bodied and slow reproducing species are at greatest risk of extinction from overexploitation (Purvis, 2001).

Bushmeat hunting has significantly depleted populations of several species in Africa (Bassett, 2005). While bushmeat hunting is most commonly associated with emerging infectious diseases moving to humans (i.e. SIV, Ebola and STLV-1; Nunn & Altizer, 2006), overexploitation of animals can result in small, fragmented populations with high rates of human contact and increased risk of disease-mediated declines. Recently, 50% declines in chimpanzee and gorilla populations have been documented in central Africa (Leroy *et al.*, 2004), and nearly half of a monitored population of chimpanzees in Tai National Park Ivory Coast was decimated during two Ebola epidemics in 1992 and 1994 (Formenty *et al.*, 1999). This latter population of chimpanzees also suffered sudden deaths from Anthrax infection, raising alarm over the vulnerability of even protected populations to disease-mediated extinction.

While the overexploitation of species may increase their likelihood of disease-mediated extinction in hunted species, the global scale decline in ocean fisheries (Myers & Worm, 2003), and subsequent increase in aquaculture to compensate for the demand for fish protein, may also pose a threat to wild populations. This may be primarily due to the spread of infectious diseases from farmed fish into natural populations. A recent study by Krkosek *et al.* (2007) found that salmon lice *Lepeophtheirus salmonis*, commonly found on farmed fish, are spreading to wild juvenile pink salmon as they migrate past farms. Salmon lice, which feed on tissues and impair osmotic ability, are usually found on adults during the saltwater phase of their life cycle. However, juvenile pink salmon passing fish farms were 73 times more likely to be infected than those not passing fish farms, and juvenile infections resulted in 9–95% mortality rates. At this pace, it is believed that wild pink salmon populations will plummet by 99% in British Columbia within four generations (Krkosek *et al.*, 2007).

Invasive species

The success of introduced species has been attributed, in part, to release from the pathogens that regulate their native population, as these species may escape $>75\%$ of the pathogens found in their native range (Torchin & Mitchell, 2004). The missing pathogens of introduced species can result from a number of factors including a lack of adequate host species for pathogens with complex life cycles, uninfected founder populations, or a threshold host density below which a pathogen cannot persist (Torchin & Mitchell, 2004). However, the pathogens that do become established with invasive species, while they may be few in number, have the potential to seriously threaten native wildlife (Lyles & Dobson, 1993; Smith & Carpenter, 2006). Consequently, these novel pathogens can cause dramatic declines in local populations of native species; altering community dynamics and contracting geographic ranges (McCallum & Dobson, 1995; Daszak *et al.*, 1999, 2000).

There are numerous pathways by which non-native species can introduce pathogens to new regions, but one of the largest appears to be the global trade in wildlife. The scale of the global wildlife trade is extraordinary. Estimates suggest many billions of live animals and products are

traded globally each year, generating commodities totaling in the hundred billions of dollars (Karesh *et al*., 2005). International trade has facilitated the introduction of non-native species to new regions where they compete with native species for resources, alter ecosystem services, damage infrastructure, destroy crops and introduce pathogens that threaten public health, agricultural production and biodiversity (Jenkins, Genovese & Ruffler, 2007). Box 1 illustrates how chytridiomycosis, one of the most deadly contemporary infectious diseases of wildlife, may be spreading globally through the wildlife trade, causing massive amphibian population declines and extinctions. Shipments of imported fish also pose a risk as they can carry novel infectious agents that threaten native wildlife, particularly when contaminated aquarium water, or infected animals are dumped into natural systems (Smith *et al*. 2008). In Florida alone, more than 95% of the emerging infectious agents in native fishes were reported in recently imported fish shipments (Sindermann, 1990). In the spring of 2003, monkeypox virus was introduced to the United States via a pet-trade shipment of Africa rodents, including Gambian giant rats *Cricetomys gambianus*. The rats were sold to a dealer who housed the animals with a group of prairie dogs (native to the United States) subsequently sold to private individuals. Within months the virus infected both the prairie dogs and their new owners (Centers for Disease Control, 2003).

The scope of wildlife trade is increasing and poor regulation in many countries, including the United States, suggests that future infectious diseases may be introduced through imported animals. A recent report of US live animal imports identified 302 non-native species regularly imported as posing a potential ecological or economic risk to the nation. Of these, 74 vertebrate species were determined to carry harmful infectious agents that may spread to humans, native wildlife or livestock if importation continues without informed risk assessments (Jenkins *et al*., 2007). There is growing concern that the continued shuffling of species around the global will ultimately contribute to losses in biological diversity by introducing novel infectious diseases to susceptible, naïve, potentially high-risk populations.

Environmental pollution

Environmental accumulation of anthropogenic pollutants has increased greatly in recent decades (Fairbrother, 1993; Boon *et al*., 2002), and over 1500 animal species are currently believed to be threatened by pollutants (IUCN, 2004). The majority of these are amphibians, with 696 Red Listed species, nearly 20% of which are critically endangered (IUCN, 2004). While the reliability of records on historically cited causes of declines may be questioned (see critique in Smith *et al*., 2006), there is growing evidence that pollutants may pose a risk to wildlife because they can alter the immune system. For instance, organochlorines are known to decrease the efficiency of cellular and humoral immunity in laboratory animals (Ahmed, 2000). Evidence of similar effects in wildlife has been more difficult to establish, partly because natural populations are exposed to complex mixtures of persistent organic pollutants and our understanding of differences in species sensitivity to contaminants is extremely limited (Raimondo, Mineau & Barron, 2007). However, an increasing number of studies show that common environmental pollutants may impair the immune system of a wide range of animal taxa (Selgrade, 2007). Particular attention has been focused on marine mammals that have experienced morbillivirus-related mortalities, and several studies have shown a link between contaminant concentrations and disease. Polychlorinated biphenyls and other persistent organic pollutants have been associated with immunotoxicity and disease outbreaks in marine mammals by rendering them vulnerable to infection by pathogens, particularly viruses and bacteria (e.g. Hammond, Hall & Dyrynda, 2005; Hall *et al*., 2006). Similar associations have also been reported for amphibians and birds, where exposure to metals, pesticides and herbicides was correlated with decreased immunocompetence (Snoeijs *et al*., 2005; Koprivnikar, Forbes & Baker, 2007), including resistance to iridoviruses (Forson & Storfer, 2006), a group of the pathogens implicated in amphibian mortality events (Daszak *et al*., 1999; Schloegel *et al*., 2006). Taken together, these studies highlight the role that environmental contaminants might play in rendering wildlife populations vulnerable to disease. It is possible that sustained exposure to complex contaminant mixtures may interact with other stressors (e.g. climate change, habitat loss and invasive species, all discussed previously), resulting in wildlife with a reduced ability to face infectious challenges and increasing their chances of disease-mediated extinction.

The role of host genetics

In addition to anthropogenic drivers, disease emergence and disease-induced extinction risk can be influenced by genetic factors (see Spielman, Brook & Frankham, 2004), particularly in terms of inbreeding (i.e. close-kin mating). At every generation, genomes undergo new mutations, some of which are harmful (Amos & Balmford, 2001), although generally recessive, and thus expressed only when homozygous (reviewed in Charlesworth & Charlesworth, 1999). As inbred offspring will have an increased proportion of homozygous alleles, their recessive mutations are more likely to be expressed. Furthermore, a higher proportion of homozygous alleles in immune-related regions might hamper pathogen recognition (reviewed in Potts & Wakeland, 1993).

Several studies have associated inbreeding with lower immunocompetence, higher pathogen loads, susceptibility to infections and higher disease severity in wildlife (e.g. Coltman *et al*., 1999; Reid, Arcese & Keller, 2003; Markert *et al*., 2004), suggesting that inbred populations may be more susceptible to disease. While of particular importance for small or fragmented populations, where close-kin matings are more likely to occur, inbreeding could also be relevant for large populations in which philopatry (tendency of a migrating animal to return to a specific location) and polygamous mating systems may increase the rate of inbreeding by reducing the effective population size (Briton

et al., 1994). For instance, sick California sea lions *Zalophus californianus* were found to have relatively high inbreeding levels, and were more prone to cancer and infections than outbred individuals (Acevedo-Whitehouse *et al*., 2003, 2006), although their population is large and intercolony migration ensures fairly high gene flow (Schramm Urrutia, 2002). This result is relevant for disease emergence, because inbred individuals could act as sources of entry for 'new' pathogens into the population, or act as reservoirs for immunologically naïve hosts. Some evidence for this has been found by Valsecchi *et al*. (2004) in a study of Mediterranean striped dolphins *Stenella coeruleoalba* stranded during the 1990–1992 morbillivirus outbreak, where the first dolphins affected by the disease were more inbred than those that died during later stages of the epidemic, suggesting that inbred dolphins facilitated transmission of the virus.

Genetic variation may also be relevant to disease-mediated extinction. An example of this is the facial tumor disease (DFTD) affecting Tasmanian devils *Sarcophilus harrisi* since 1996 (McCallum & Jones, 2006). DFTD is a contagious tumor spread between individuals, most likely through biting and aggressive interactions. Low genetic diversity due to an ancient genetic bottleneck of Tasmanian devils followed by intense inbreeding, is the most likely explanation of the high rate of DFTD spread (Siddle *et al*., 2007). This, combined with frequency-dependent transmission, makes the disease an immediate threat to the survival of the Tasmanian devil. DFTD has already caused population declines up to 90% and is expected to drive the species to extinction (Jones *et al*., 2007b).

As diversity at genetic regions involved with pathogen recognition is generated and maintained over generations in response to quickly evolving pathogens (Sommer, 2005; Acevedo-Whitehouse & Cunningham, 2006), long-term geographical restriction to specific pathogens may have devastating effects for wildlife. Populations challenged by novel pathogens will be immunologically naïve and thus, less likely to recognize them. For example, the Spanish invasion of the 1500s brought European diseases to the Native American inhabitants (Settipane, 1995), who were immunologically naïve and thus extremely susceptible to their effects. Severe epidemics of smallpox, measles and typhus caused drastic population declines, which together with war and forced labor, caused the death of 60–80 million people (up to 90% mortality rates for some ethnic groups; Ayala, 1995). Similar events in immunologically naïve wildlife populations could be devastating to their stability and persistence. However, the relatively few published studies on immunogenetic diversity of threatened populations, as well as the limited evidence of their associations with pathogen load and disease risk in wildlife, make it difficult to use such information as a tool to identify vulnerable populations likely to be at risk from new pathogens.

Control and when to intervene?

Efforts to provide a more comprehensive view of the role of pathogens in wildlife extinction risk will require increased collaboration among wildlife ecologists, veterinarians and conservation organizations. Characteristics of threatening pathogens highlight the possibility that future control strategies targeted at reducing cross-species transmission of high-risk pathogens, either by vaccination or by limiting contact with domesticated animals, may significantly reduce the risk of pathogen-mediated wildlife declines (Pedersen *et al*., 2007). In the case of the massive African rinderpest epidemic, once targeted vaccination of domestic cattle began, prevalence and disease-associated declines dropped dramatically in wild artiodactyl populations (Plowright, 1982). Similar vaccination campaigns are currently underway in Tanzania, using a three part vaccine to eliminate rabies, canine distemper virus and canine parvovirus from domestic dogs, in the hopes that this will reduce transmission of these deadly diseases to threatened wildlife hosts, such as African lions, African wild dogs and bat-eared foxes (Cleaveland *et al*., 2000, 2003). In addition, because many of the threatening pathogens are transmitted by close contact between individuals (Pedersen *et al*., 2007), alternative strategies could also involve minimizing contact between wildlife and domesticated animals, by creating physical barriers that reduce the potential for cross species transmission, or by setting temporal limitations on the use of shared water resources or grazing land. These strategies, specifically the construction of buffer zones between agricultural areas with domestic sheep and wild populations of bighorn sheep have been successful in reducing infectious disease outbreaks in western North America (Jessup, Boyce & Torres, 1995).

A recent study by Altizer, Nunn & Lindenfors (2007) found that threatened primates had fewer pathogens than their non-threatened counterparts. This finding may seem on the surface to be positive for threatened hosts suffering from disease mediated extinction risk. However, it also could suggest that endangered wildlife species lose pathogens due to their small, fragmented population size. This ultimately could lead to the loss of genetic variation for immunity, making threatened species more susceptible to future disease outbreaks. In terms of management and captive breeding programs, it is possible that hosts raised in captivity, who are continually treated to eliminate infections, may suffer a disadvantage when released into the wild, due to increased susceptibility to infection caused from relaxed selection for resistance, especially in traits that are costly to maintain. Given this possibility, species management programs, especially those that include captive breeding and re-introductions, may need to focus on maintaining the levels of immunity or variation in resistance that are present in natural populations (Altizer & Pedersen, 2008). While we have focused this review on cases where pathogens cause host population declines and extinction risk, in terms of management, the best strategy for the conservation of natural populations may be to conserve geographically structured species interactions (i.e. predator–prey, host–parasite) that can maintain the evolutionary history that has occurred between species. This type of strategy will need to take a landscape-scale approach to species conservation,

that accounts for the various habitats were interacting species occur, and includes corridors between fragmented populations to increase dispersal and genetic diversity between isolated populations.

Future directions and conclusions

Infectious diseases are of concern to conservation for several reasons: (1) they can deplete population sizes; (2) they can hinder the recovery of rare species; (3) they necessitate management actions that often impact the environment; (4) they can act on their own or in concert with other drivers and be the ultimate cause of species extinction (Lafferty, 2003). Future studies of the complex interactions that occur between human activities, environmental change and the emergence of infectious disease will promote healthy ecosystems and help protect biological diversity. Here, we outline what we see as the most critical challenges and future directions for the study of infectious diseases in the conservation sciences.

What do we need?

1. Quantitative understanding of habitat destruction, climate change, overexploitation, invasive species, pollution and infectious disease as threats to biodiversity, as well as how these factors are likely to interact to drive species extinction.
2. Better understanding of the circumstances when infectious diseases are most likely to cause extinction. This can occur when a pathogen is novel to a susceptible host species or utilizes a reservoir host, when the pathogen spreads via frequency-dependent transmission, when the host has small pre-epidemic population sizes or highly susceptible individuals that act as entry points for disease.
3. Enhanced methods for identifying infectious agents that cause significant pathologies, population-level effects, and increased likelihood of extinction in a threatened host.

What can we do?

1. Conduct rigorous studies to gather baseline information on pathogen prevalence and diversity for declining species; especially small, fragmented populations at risk from several other stressors.
2. Combine evidence and theory to weigh the relative effects and likelihood of threats to species. Incorporate findings into IUCN criteria used to assess threats.
3. Promote conservation medicine – interdisciplinary collaborations that link wildlife disease, human health and environmental change.
4. Advance existing surveillance programs associated with economic initiatives and incorporate these into ecological research. Current methods for tracking changes in disease ecology depend on the detection of infections in target populations. Monitoring can be improved by establishing disease registries that permit molecular identification of new diseases or new variants of existing diseases.
5. Increase efforts to determine the immunogenetic architecture of endangered and threatened populations as a means to identify those likely to be at risk from the introduction of novel pathogens.

While infectious diseases as a driver of species extinction may have been historically overlooked, contemporary extinctions – due in part to pathogens – are becoming increasingly documented and are likely to play a significant role in future species endangerment. If we are to make progress in conserving biodiversity, we need to understand the role of pathogens in natural populations, and, more importantly, how pathogens interact with other drivers of extinction to cause species loss. Currently, the majority of studies suggest that habitat fragmentation, climate change, over-exploitation and invasive species are the dominant factors causing species extinction. We suggest that while disease alone may have caused extinction in few species, pathogens may provide one of the biggest threats to already-endangered species, especially when disease interacts with other drivers. As ecologists and conservation biologists, we are just beginning to understand the role of pathogens in natural populations; however, it is imperative that we focus efforts on threatened species and their diseases, such that we can inform control and management strategies. Understanding the host species that are at highest risk of disease-mediated extinction, the pathogens likely to cause disease and their interaction with other drivers of extinction, will ultimately inform future control and prevention strategies and help preserve biological diversity.

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References

Acevedo-Whitehouse, K. & Cunningham, A. (2006). Is MHC enough for understanding wildlife immunogenetics? *Trends Ecol. Evol.* **21**, 433–438.

Acevedo-Whitehouse, K., Gulland, F.M.D., Greig, D. & Amos, W. (2003). Inbreeding: disease susceptibility in California sea lions. *Nature* **422**, 35.

Acevedo-Whitehouse, K., Spraker, T.R., Lyons, E., Melin, S.R., Gulland, F., Delong, R.L. & Amos, W. (2006). Contrasting effects of heterozygosity on survival and hookworm resistance in California sea lion pups. *Mol. Ecol.* **15**, 1973–1982.

Ahmed, S.A. (2000). The immune system as a potential target for environmental estrogens (endocrine disrupters): a new emerging field. *Toxicology* **150**, 191–206.

Alford, R.A., Bradfield, K.S. & Richards, S.J. (2007). Ecology: global warming and amphibian losses. *Nature* **447**, E3–E4.

Altizer, S., Nunn, C.L. & Lindenfors, P. (2007). Do threatened hosts have fewer parasites? A comparative study in primates. *J. Anim. Ecol.* **76**, 304–314.

Altizer, S. & Pedersen, A.B. (2008). Host–pathogen evolution, biodiversity and disease risks for natural populations. In *Conservation biology: evolution in action*: 259–278. Carroll, S. & Fox, C. (Eds). Oxford, UK: Oxford University Press.

Amos, W. & Balmford, A. (2001). When does conservation genetics matter? *Heredity* **87**, 257–265.

Anderson, R.M. & May, R.M. (1992). *Infectious diseases of humans, dynamics and control*. New York: Oxford University Press.

Ayala, F.J. (1995). The myth of Eve: molecular biology and human origins. *Science* **270**, 1930–1936.

Bassett, T.J. (2005). Card-carrying hunters, rural poverty, and wildlife decline in northern Cote d'Ivoire. *Geogr. J.* **171**, 24–35.

Berger, L., Speare, R., Daszak, P., Green, D.E., Cunningham, A.A., Goggin, C.L., Slocombe, R., Ragan, M.A., Hyatt, A.D., McDonald, K.R., Hines, H.B., Lips, K.R., Marantelli, G. & Parkes, H. (1998). Chytridiomycosis causes amphibian mortality associated with population declines in the rain forests of Australia and Central America. *Proc. Natl. Acad. Sci. USA* **95**, 9031–9036.

Blaustein, A.R. & Wake, D.B. (1990). Declining amphibian populations: a global phenomenon. *Trends Ecol. Evol.* **5**, 203–204.

Boon, J.P., Lewis, W.E., Tjoen-A-Choy, M.R., Allchin, C.R., Law, R.J., De Boer, J., Ten Hallers-Tjabbes, C.C. & Zegers, B.N. (2002). Levels of polybrominated diphenyl ether (PBDE) flame retardants in animals representing different trophic levels of the North Sea food. *Web. Environ. Sci. Technol.* **36**, 4025–4032.

Boots, M. & Sasaki, A. (2003). Parasite evolution and extinctions. *Ecol. Lett.* **6**, 176–182.

Bornstein, S., Morner, T. & Samuel, W.M. (2001). *Sarcoptes scabei* and sarcoptic mange. In *Parasitic disease of wild mammals*. 2nd edn. 107–119. Samuel, W.M., Pybus, M.J. & Kocan, A.A. (Eds). Ames: Iowa State University Press.

Bosch, J., Carrascal, L.M., Durán, L., Walker, S. & Fisher, M.C. (2007). Climate change and outbreaks of amphibian chytridiomycosis in a montane area of Central Spain; is there a link? *Proc. Biol. Sci.* **274**, 253–260.

Boyce, W.M. & Weisenberger, M.E. (2005). The rise and fall of psoroptic scabies in bighorn sheep in the San Andres Mountains, New Mexico. *J. Wildl. Dis.* **41**, 525–531.

Briton, J., Nurthen, R.K., Briscoe, D.A. & Frankham, R. (1994). Modelling problems in conservation genetics using *Drosophila*: consequences of harems. *Biol. Conserv.* **69**, 267–275.

de Castro, F. & Bolker, B. (2005). Mechanisms of disease-induced extinction. *Ecol. Lett.* **8**, 117–126.

Centers for Disease Control. (2003). *Morb. Mortal. Wkly. Rep.* **52**, 642–646. Update: Multistate Outbreak of Monkeypox – Illinois, Indiana, Kansas, Missouri, Ohio and Wisconsin. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5227a5.htm

Committee on Grand Challenges in Environmental Sciences. (2001). *National research council report: grand challenges in environmental sciences*. Washington, DC: National Academy Press. Available at http://www.nap.edu/catalog.php?record_id = 9975

Charlesworth, B. & Charlesworth, D. (1999). The genetic basis of inbreeding depression. *Genet. Res.* **74**, 329–340.

Cleaveland, S., Appel, M.G.J., Chalmers, W.S.K., Chillingworth, C., Kaare, M. & Dye, C. (2000). Serological and demographic evidence for domestic dogs as a source of canine distemper virus infection for Serengetti wildlife. *Vet. Microbiol.* **72**, 3–4.

Cleaveland, S., Kaare, M., Tiringa, P., Mlengeya, T. & Barrat, J. (2003). A dog rabies vaccination campaign in rural Africa: impact on the incidence of dog rabies and human dog-bite injuries. *Vaccine* **21**, 17–18.

Cleaveland, S., Laurenson, M.L. & Taylor, L.H. (2001). Disease of humans and their domestic mammals: pathogen characteristics, host range and the risk of emergence. *Philos. Trans. Roy. Soc. B* **356**, 991–999.

Coltman, D.W., Pilkington, J.G., Smith, J.A. & Pemberton, J.M. (1999). Parasite-mediated selection against inbred Soay sheep in a free-living, island population. *Evolution* **53**, 1259–1267.

Cunningham, A.A., Daszak, P. & Rodríguez, J.P. (2003). Pathogen pollution: defining a parasitological threat to biodiversity conservation. *J. Parasitol.* **89**, S78–S83.

Daszak, P., Berger, L., Cunningham, A.A., Hyatt, A.D., Green, D.E. & Speare, R. (1999). Emerging infectious diseases and amphibian population declines. *Emerg. Infect. Dis.* **5**, 735–748.

Daszak, P., Cunningham, A.A. & Hyatt, A.D. (2000). Emerging infectious diseases of wildlife – threats to biodiversity and human health. *Science* **287**, 443–449.

Daszak, P., Cunningham, A.A. & Hyatt, A.D. (2003). Infectious disease and amphibian population declines. *Divers. Distrib.* **9**, 141–150.

Davies, T.J. & Pedersen, A.B. (2008). Phylogeny and geography predict pathogen community similarity in wild primates and humans. *Proc. Roy. Soc. Lond. Ser. B*, **275**, 1695–1701.

Domingo, E. & Holland, J.J. (1997). RNA viruses and fitness for survival. *Annu. Rev. Microbiol.* **51**, 151–178.

Epstein, P.R. (2000). Is global warming harmful to health? *Sci. Am.* **8**, 36–43.

Fain, A. (1978). Epidemiological problems of scabies. *Int. J. Dermatol.* **17**, 20–30.

Fairbrother, A. (1993). Immunotoxicology of captive and wild birds in wildlife toxicology and population modeling.

In *Integrated studies of agro-ecosystems*: 251–262. Kendall, R. & Lacher, T.E. (Eds). Boca Raton, FL: Lewis Publishers.

Fenton, A. & Pedersen, A.B. (2005). Community epidemiology in theory and practice: a conceptual framework for classifying disease threats in human and wild populations. *Emerg. Infect. Dis.* **11**, 1815–1821.

Flather, C.H., Joyce, L.A. & Bloomharde, C.A. (1994). *Species endangerment patterns*. In United States Service General Technical Report RM-241, 1–42.

Formenty, P., Boesch, C., Wyers, M., Steiner, C., Donati, F., Dind, F., Walker, F. & Le Guennom, B. (1999). Ebola virus outbreak among wild chimpanzees living in a rainforest of Cote d'Ivoire. *J. Infect. Dis.* **179** (Suppl. 1): 120–126.

Forson, D.D. & Storfer, A. (2006). Atrazine increases ranavirus susceptibility in the tiger salamander, *Ambystoma tigrinum*. *Ecol. Appl.* **16**, 2325–2332.

Gaston, K.J. (1991). *Rarity*. Oxford, UK: Blackwell Scientific.

Hall, A.J., Hugunin, K., Deaville, R., Law, R.J., Allchin, C.R. & Jepson, P.D. (2006). The risk of infection from polychlorinated biphenyl exposure in the harbor porpoise (*Phocoena phocoena*): a case–control approach. *Environ. Health. Perspect.* **114**, 704–711.

Hammond, J.A., Hall, A.J. & Dyrynda, E.A. (2005). Comparison of polychlorinated biphenyl (PCB) induced effects on innate immune functions in harbour and grey seals. *Aquat. Toxicol.* **74**, 126–138.

Hanselmann, R., Rodriguez, A., Lampo, M., Fajardo-Ramos, L., Aguirre, A.A., Kilpatrick, A.M., Rodriguez, J.P. & Daszak, P. (2004). Presence of an emerging pathogen of amphibians in introduced bullfrogs *Rana catesbeiana* in Venezuela. *Biol. Conserv.* **120**, 115–119.

Harvell, C.D., Mitchell, C.E, Ward, J.R., Altizer, S., Dobson, A.P., Ostfield, R.S. & Samuel, M.D. (2002). Climate warming and disease risk for terrestrial and marine biota. *Science* **296**, 2158–2162.

Henriksen, P., Dietz, H.H., Henriksen, S.A. & Gjelstrup, P. (1993). Sarcoptic mange in red fox in Denmark. *Dansk Veterin.* **76**, 12–13.

Hero, J.-M. & Morrison, C. (2003). Frog declines in Australia: global implications. *Herpetol. J.* **14**, 175–186.

Intergovernmental Panel on Climate Change (IPCC). (2007). *Climate change 2007: synthesis report. Contribution of Working Groups I, II and III to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change*. Core Writing TeamPachauri, R.K. & Reisinger, A. (Eds) Geneva, Switzerland: IPCC.

International Union for the Conservation of Nature (IUCN). (2004). *IUCN red list of threatened species*. Available at http://www.redlist.org

International Union for the Conservation of Nature (IUCN). (2007). *IUCN red list of threatened species*. Available at http://www.redlist.org

Jenkins, P.T., Genovese, K. & Ruffler, H. (2007). *Defenders of wildlife: broken screens: the regulation of live animal imports in the United States*. Washington, DC.

Jessup, D.A., Boyce, W.M. & Torres, S.G. (1995). Bighorn sheep health management in California: a fifteen year retrospective. In *Proceedings of the joint conference of the American Association of Zoo Veterinarians, the Wildlife Disease Association and the American Association of Wildlife Veterinarian*: 55–67. Junge, R.E. (Ed.). Philadelphia, PA: American Association of Zoo Veterinarians Media.

Jones, K.E., Patel, N.G., Levy, M.A., Storeygard, A., Bulk, D., Gittleman, J.L. & Daszak, P. (2007*a*). Global trends in emerging infectious diseases. *Nature* **451**, 990–993.

Jones, M.E., Jarman, P.J., Lees, C.M., Estermen, H., Hamede, R.K., Mooney, N.J., Mann, D., Pukk, C.E., Bergfeld, J. & McCallum, H. (2007*b*). Conservation management of Tasmanian devils in the context of an emerging, extinction-threatening disease: devil facial tumor disease. *EcoHealth* **4**, 326–337.

Karesh, W.B., Cook, W.B., Bennet, E.L. & Newcomb, J. (2005). Wildlife trade and global disease emergence. *Emerg. Infect. Dis.* **11**, 1000–1002.

Koprivnikar, J., Forbes, M.R. & Baker, R.L. (2007). Contaminant effects on host–parasite interactions: atrazine, frogs, and trematodes. *Environ. Toxicol. Chem.* **26**, 2166–2170.

Kriger, K.M., Pereoglou, F. & Hero, J.M. (2007). Latitudinal variation in the prevalence and intensity of chytrid (*Batrachochytrium dendrobatidis*) infection in eastern Australia. *Conserv. Biol.* **21**, 1280–1290.

Krkosek, M., Ford, J.S., Morton, A., Lele, S., Myers, R.A. & Lewis, M.A. (2007). Declining wild salmon populations in relation to parasites from farm salmon. *Science* **318**, 1772–1775.

Lafferty, K.D. (2003). Is disease increasing or decreasing, and does it impact or maintain biodiversity? *J. Parasitol.* **89**, S101–S105.

Lafferty, K.D. & Gerber, L.R. (2002). Good medicine for conservation biology: the intersection of epidemiology and conservation theory. *Conserv. Biol.* **6**, 593–604.

Leroy, E.M., Rouquet, P., Formenty, P., Souquiere, S., Kilbourne, A., Froment, J.M., Bermeljo, M., Smit, S., Karesh, W., Swanepoel, R., Zaki, S.R. & Rollin, P.E. (2004). Multiple Ebola virus transmission events and rapid decline of Central African wildlife. *Science* **303**, 387–390.

Lips, K.R., Bren, F., Brenes, R., Reeve, J.D., Alford, R.A., Voyles, J., Careys, C., Livo, A., Pessier, A.P. & Collins, J.P. (2006). Emerging infectious disease and the loss of biodiversity in a Neotropical amphibian community. *Proc. Natl. Acad. Sci. USA* **103**, 3165–3170.

Lips, K.R., Diffendorfer, J., Mendelson, J.R. III & Sears, M.W. (2008). Riding the wave: reconciling the roles of disease and climate change in amphibian declines. *PLoS Biol.* **6**, 441–454.

Lyles, A.M. & Dobson, A.P. (1993). Infectious disease and intensive management: population dynamics, threatened hosts, and their parasites. *J. Zoo. Wildl. Med.* **24**, 315–326.

Mace, G.M. & Balmford, A. (2000). Patterns and processes in contemporary mammalian extinction. In *Priorities for the conservation of mammalian diversity*: 27–52. Entwistel, A. & Dunstone, N. (Eds). Cambridge, UK: Cambridge University Press.

Mainka, S.A. (2002). Biodiversity, poverty and hunger: where do they meet? In *Links between biodiversity conservation, livelihoods and food security: the sustainable use of wild species for meat*: 11–18. Gland, Switzerland: World Conservation Union.

Markert, J.A., Grant, P.R., Grant, B.R., Keller, L.F., Coombs, J.L. & Petren, K. (2004). Neutral locus heterozygosity, inbreeding and survival in Darwin's ground finches (*Geospiza fortis* and *G. scandens*). *Heredity* **92**, 306–315.

Mazzoni, R., Cunningham, A.A., Daszak, P., Apolo, A., Perdomo, E. & Speranza, G. (2003). Emerging pathogen of wild amphibians in frogs (*Rana catesbeiana*) farmed for international trade. *Emerg. Infect. Dis.* **9**, 995–998.

McCallum, H., Barlow, N. & Hone, J. (2001). How should pathogen transmission be modelled? *Trends Ecol. Evol.* **16**, 1295–1300.

McCallum, H. & Dobson, A. (1995). Detecting disease and parasite threats to endangered species and ecosystems. *Trends Ecol. Evol.* **10**, 190–194.

McCallum, H. & Jones, M. (2006). To lose both would look like carelessness: Tasmanian devil facial tumour disease. *PLoS Biol.* **4**, 1671–1674.

McCarthy, A.J., Shaw, M. & Goodman, S.J. (2007). Pathogen evolution and disease emergence in carnivores. *Proc. Roy. Soc. Lond. Ser. B* **274**, 3165–3174.

Millenium Ecosystem Assessment (MEA). (2005). *Ecosystems and human well-being: current state and trends: Findings of the Condition and Trends Working Group*. Washington D.C.: Island Press.

Myers, R.A. & Worm, B. (2003). Rapid worldwide depletion of predatory fish communities. *Nature* **423**, 280–283.

Nunn, C.L. & Altizer, S. (2006). *Infectious diseases in primates: behavior, ecology and evolution*. Oxford, UK: Oxford Series in Ecology and Evolution, Oxford University Press.

O'keefe, K.J. & Antonovics, J. (2002). Playing by different rules: the evolution of virulence in sterilizing pathogens. *Am. Nat.* **159**, 597–605.

Osterhaus, A.D.M.E., Groen, J., UytdeHaag, F.G.C.M., Visser, I.K.G., Bildt, M.W.G., van de Bergman, A. & Klingeborn, B. (1989). Distemper virus in Baikal seals. *Nature* **338**, 209–210.

Ouellet, M., Mikaelian, I., Pauli, B.D., Rodrigue, J. & Green, D.M. (2005). Historical evidence of widespread chytrid infection in North American amphibian populations. *Conserv. Biol.* **19**, 1431–1440.

Pedersen, A.B., Jones, K.E., Nunn, C.L. & Altizer, S.A. (2007). Infectious disease and mammalian extinction risk. *Conserv. Biol.* **21**, 1269–1279.

Pence, D.B., Casto, S.D. & Samuel, W.M. (1975). Variation in the chaetotaxy and denticulation of *Sarcoptes scabei* (Acarina: Sarcoptidae) from wild canids. *Acarology* **17**, 160–165.

Pence, D.B. & Ueckermann, E. (2002). Sarcoptic mange in wildlife. *Rev. Sci. Tech. Off. Int. Epiz.* **21**, 385–398.

Pimm, S.L. & Askins, A. (1995). Forest losses predict bird extinction in eastern North America. *Proc. Natl. Acad. Sci. USA* **92**, 9343–9347.

Pimm, S.L., Russell, G.J., Gittleman, J.L. & Brooks, T.M. (1995). The future of biodiversity. *Science* **269**, 347–350.

Plowright, W. (1982). The effects of rinderpest and rinderpest control on wildlife in Africa. *Symp. Zoo. Soc. Lond.* **50**, 1–28.

Potts, W.K. & Wakeland, E.K. (1993). Evolution of MHC genetic diversity: a tale of incest, pestilence and sexual preference. *Trends Genet.* **9**, 408–412.

Pounds, J.A., Bustamante, M.R., Coloma, L.A., Consuegra, J.A., Fogden, M.P., Foster, P.N., La Marca, E., Masters, K.L., Merino-Viteri, A., Puschendorf, R., Ron, S.R., Sánchez-Azofeifa, G.A., Still, C.J. & Young, B.E. (2006). Widespread amphibian extinctions from epidemic disease driven by global warming. *Nature* **439**, 161–167.

Pounds, J.A., Bustamante, M.R., Coloma, L.A., Consuegra, J.A., Fogden, M.P., Foster, P.N., La Marca, E., Masters, K.L., Merino-Viteri, A., Puschendorf, R., Ron, S.R., Sánchez-Azofeifa, G.A., Still, C.J. & Young, B.E. (2007). Global warming and amphibian losses; the proximate cause of frog declines? (Reply). *Nature* **447**, E5–E6.

Purvis, A. (2001). Mammalian life histories and responses of populations to exploitation. In *Conservation of exploited species*: 169–181. Reynolds, J., Mace, G.M., Redford, K.H. & Robinson, J.G. (Eds). Cambridge, UK: Cambridge University Press.

Rachowicz, L.J., Hero, J.M., Alford, R.A., Taylor, J.W., Morgan, J.A.T., Vredenburg, V.T., Collins, J.P. & Briggs, C.J. (2005). The novel and endemic pathogen hypotheses: competing explanations for the origin of emerging infectious diseases of wildlife. *Conserv. Biol.* **19**, 1441–1448.

Raimondo, S., Mineau, P. & Barron, M.G. (2007). Estimation of chemical toxicity to wildlife species using interspecies correlation models. *Environ. Sci. Technol.* **41**, 5888–5894.

Reid, J.M., Arcese, P. & Keller, L.F. (2003). Inbreeding depresses immune response in song sparrows (*Melospiza melodia*): direct and inter-generational effects. *Proc. Roy. Soc. Lond. Ser. B* **270**, 2151–2157.

Schloegel, L.M., Hero, J.M, Berger, L., Speare, R., McDonald, K. & Daszak, P. (2006). The decline of the sharp-snouted day frog (*Taudactylus acutirostris*): the first documented case of extinction by infection in a free-ranging wildlife species? *EcoHealth* **3**, 35–40.

Schramm Urrutia, Y. (2002). Genetic structure and phylogeography of California sea lions (*Zalophus californianus californianus*) along the Baja California Peninsula, Mexico. PhD dissertation, Universidad de Baja Califrornia, Mexico.

Scott, M.E. (1988). The impact of infection and disease on animal populations: implications for conservation biology. *Conserv. Biol.* **2**, 40–56.

Selgrade, M.K. (2007). Immunotoxicity: the risk is real. *Toxicol. Sci.* **100**, 328–332.

Settipane, G.A. (1995). *Columbus and the new world: medical implications*. Providence, RI: Ocean Side Publications.

Siddle, H.V., Kreiss, A., Eldridge, M.D.B., Noonan, E., Clarke, C.J., Pyecroft, S., Woods, G.M. & Belov, K. (2007). Transmission of a fatal clonal tumor by biting occurs due to depleted MHC diversity in a threatened carnivorous marsupial. *Proc. Natl. Acad. Sci. USA* **104**, 16221–16226.

Sindermann, C.J. (1990). *Principal diseases of marine fish and shellfish: diseases of marine fish*. San Diego, CA: Academic Press.

Singer, F.J., Zeigenfuss, L.C. & Spicer, L. (2001). Role of patch size, disease, and movement in rapid extinction of bighorn sheep. *Conserv. Biol.* **15**, 1347–1354.

Smith, K.F. & Carpenter, S.M. (2006). Spread of exotic black rat parasites to endemic deer mice on the California Channel Islands. *Divers. Distrib.* **12**, 742–748.

Smith, K.F., Sax, D.F. & Lafferty, K.D. (2006). Evidence for the role of infectious disease in species extinction. *Conserv. Biol.* **20**, 1349–1357.

Smith, K., Behrens, M.D., Max, L.M., Daszak, P. (2008). U.S. drowing in unidentified fishes: Scope, implications and regulation of live fish imports. *Conserv. Letts.* **1**, 103–109.

Snoeijs, T., Dauwe, T., Pinxten, R., Darras, V.M., Arckens, L. & Eens, M. (2005). The combined effect of lead exposure and high or low dietary calcium on health and immunocompetence in the zebra finch (*Taeniopygia guttata*). *Environ. Pollut.* **134**, 123–132.

Sommer, S. (2005). The importance of immune gene variability (MHC) in evolutionary ecology and conservation. *Front. Zool.* **2**, 16–33.

Spielman, D., Brook, B.W. & Frankham, R. (2004). Most species are not driven to extinction before genetic factors impact them. *Proc. Natl. Acad. Sci. USA* **101**, 15261–15264.

Stone, W.B., Parks, E., Weber, B.L. & Parks, F.J. (1974). Experimental transfer of sarcoptic mange from red foxes and wild canids to captive wildlife and domestic animals. *New York Fish Game J.* **19**, 1–11.

Stuart, S.N., Chanson, J.S., Cox, N.A., Young, B.E., Rodrigues, A.S.L. & Fischman, D.L. (2004). Status and trends of amphibian declines and extinctions worldwide. *Science* **306**, 1783–1786.

Taylor, L.H., Latham, S.M. & Woolhouse, M.E.J. (2001). Risk factors for human disease emergence. *Philos. Trans. Roy. Soc. B* **356**, 983–989.

Thrall, P.H., Antonovics, J. & Hall, D.W. (1993). Host and pathogen coexistence in sexually-transmitted and vector-borne diseases characterized by frequency-dependent disease transmission. *Am. Nat.* **142**, 543–552.

Torchin, M.E. & Mitchell, C.E. (2004). Parasites, pathogens, and invasions by plants and animals. *Front. Ecol. Environ.* **2**, 183–190.

Valsecchi, E., Amos, W., Raga, J.A., Podesta, M. & Sherwin, W. (2004). The effects of inbreeding on mortality during a morbillivirus outbreak in the Mediterranean striped dolphin (*Stenella coeruleoalba*). *Anim. Conserv.* **7**, 139–146.

Wilcove, D.S., Rothstein, D., Dubow, J., Phillips, A. & Losos, E. (1998). Quantifying threats to imperiled species in the United States. *Bio-Science* **48**, 607–615.

Wilson, E.O. (1992). *The diversity of life*. New York, NY: W. W. Norton & Company.